A REVIEW OF DISEASES IN MALAYSIA

BY

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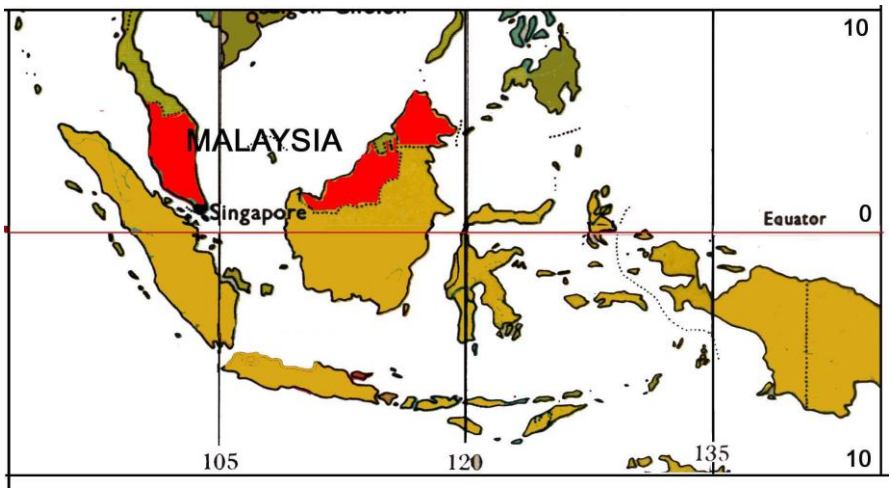
CHAPTER 1

INTRODUCTION AND DEMOGRAPHY

Malaysia is a federation of 13 states covering 32,975,000 hectares of land. It consists of two regions. 11 states are on the Malay Peninsula, between longitudes 100° to 105° E. Two other states occupy the northern part of the island of Borneo, separated from the Peninsula by 400 miles of the South China Sea. These states, Sarawak and Sabah lie between the longitudes 109° and 120° E. Malaysia has an equatorial climate, lying just 1° to 7° north of the equator.

Figure 1.1 Map of Malaysia



The climate is hot and wet all year round but modified by the prevailing monsoon winds in South East Asia. No area is more than about 100 miles from the sea and very few areas have less than 200cm. of annual rainfall. The Northeast monsoon which lasts from November to March brings rain to east coast of both regions of Malaysia. As these wind come across a wide sea they are wet and bring floods from time to time. On the whole the Indonesian islands shelter both parts of Malaysia from the Southwest monsoon from April to October. Only the west coast of the peninsula receives more rain during this period from wind that pick up rain across the Straits of Malacca. Thankfully Malaysia lies outside the path of the typhoons of Asia. Sabah lies just to the south of their path and rejoices in the name 'The land below the wind'.

THE PEOPLE

Historical Background

The ancient history of both Peninsula and East Malaysia up to the fifteenth century is sketchy. Stone implements found at Lenggong in Perak and the remarkable finds of the Niah caves in Sarawak tell us that there have been

human habitations here from the dawn of mankind. The earliest ancestors of the present day Negritos of the peninsula and the Penans of Sarawak or the Rungus of Sabah, who still pursue a nomadic way of life have probably been present here for over 5,000 years.

All through out this long period up to the fifteenth century, the population probably never exceeded more than 100,000 to 200,000. The population probably increased with the influx of the proto-Malays around 1000 B.C., who now form the other indigenous tribes of Orang Asli and bumiputera. Like them, a few centuries later, the deutero-Malays migrated south from the Asian continent into the Malay peninsula and spread out into the island of the archipelago. The Malay people came equipped with more advanced farming methods and knowledge of metallurgy. They settled down mainly in coastal estuarine communities that were small and self sufficient. The original language thus gradually evolved to the variegated dialects distributed throughout Indonesia and Malaysia today.

The earliest civilisations found by archaeologists date to this period. In the Bujang valley and Merbok estuary in Kedah there are evidences of temple sites that show Hindu-Buddhist influences. They were the result of trading contacts with India, Sumatra and Java. Evidence of such cultural contacts is also seen in a number of words adopted into the Malay language. For example, the word **Bharat**, by which Indians call their country has become the word for 'west' in Bahasa Malaysia. It referred to the greatest region known at that time that lies in that direction.

The next great influence on the history of Malaysia was Islam, which began in the Middle East, and was then carried by merchants to India. It then spread to the Malay archipelago and took root especially in the coastal Malay settlements. One of the earliest evidence of Islam in Malaysia are the inscriptions on the 'batu bersurat' from Kuala Berang in Terengganu, which has been dated to the fourteenth century. However, the more well-known influence of Islam was the rise of the kingdom of Malacca. The rise of the Malacca Sultanate marked the beginning of a new chapter in the history of Malaysia.

The state which was founded by Parameswara in the beginning of the fifteenth century in Malacca marked the start of written history in Malaysia. Unlike other estuarine settlements, Malacca grew from a trading post for Indian and Chinese traders to become a kingdom with great influence over the whole region. The language of Malacca spread over the Indonesian islands such that it became the lingua franca for the Javanese and the Bugis and other peoples and has remained so even till today. Malacca however, was not the only kingdom in those days. The Brunei Sultanate in north Borneo probably dates back to this period. We know also that the Sultanates of Johore and Perak which started after the fall of Malacca to the Portugese, are directs heirs of the Malacca Sultanate.

During this time the population grew slowly to probably a few hundred thousand in number. Diseases such as malaria, were largely responsible for keeping the population from growing faster. Over the next two hundred years despite the change of dominant foreign power, from the Portugese to Dutch, the fabric of local society remained much the same under Islamic Sultans. Besides controlling trade, these colonist left the economy much alone. Things however changed from the latter part of the eighteenth century and the nineteenth century with the arrival of the British Empire.

The British signed agreements with the local sultans to settle in Penang in 1786 and Singapore in 1819 to rival the Dutch in Malacca. No longer was there just one port of foreign power in Malacca. Later as Britain overtook Holland as the great sea power it eventually took charge of Malacca in 1824. Penang, Malacca and Singapore were then united administratively as

the Stratits Settlements. In 1841 James Brooke, a British adventurer, founded Sarawak in Borneo and in 1846 the island of Labuan became a British colony by cession from the Sultan of Brunei. It became part of the Straits Settlements in 1866. British companies also obtained various concessions from the ruler of Sabah which were then transferred to the British North Borneo Company in 1882.

Britain was however not the only colonial power at work in the South East Asian archipelago. The Dutch ruled Java and the islands around it. The Spanish colonised Philippines. Although the South East Asian island kingdoms had earlier trade, cultural and language links, Malaysia, Indonesia and the Philippines developed into separate political entities as a result of these political influences.

With British administration in Malaysia, the economy and society changed tremendously. The concurrent British influence in China facilitated the immigration of Chinese, especially from the southern provinces of China, to work the tin mines in Malaysia. Many new settlements grew around these tin mining areas. Kuala Lumpur which is now Malaysia's modern capital is the prime example. By 1850 the population in the peninsula was estimated to be 500,000.

The British also introduced rubber trees from South America to be planted in Malaysia for rubber export. At first the diseases which had curbed population growth in the past nearly crippled these economic programmes. The high attendant death rates due to malaria caused a few plantation ventures to fail, but the advent of malaria control came at just the right time. From about 1890 rubber estates began to be successful and to work the plantations the British imported labourers from southern India. The later part of the nineteenth century thus saw a tremendous rise in the population of Peninsula Malaysia.

The Twentieth Century

The population growth of the nineteenth century, though great in comparison to the past was only a trickle in comparison to the growth to be seen in the twentieth century, as shown in Table 1.1. A 1911 census recorded a population of just over a million (1,036,999) for the first time. But this included only the four Federated States of Perak, Selangor, Negeri Sembilan and Pahang. The influx of immigrants from China and India continued up to the Second World War with the rapid economic expansion under way. In addition to that, Malays migrated in from Java, Sumatra and other islands in the archipelago. At the same time, disease control brought down both the total mortality rate as well as the infant mortality rate, enabling the population to grow more healthily.

Malaya was overrun by the Japanese army in late 1941 in the Second World War. All medical and health services were severely affected until 1945. Expatriate doctors were interned and the Japanese occupation forces neglected the health of the population. The Annual Report if the Medical Department of 1946 and following years show epidemics of several infectious diseases. Smallpox which had nearly been eradicated claimed over 7,800 victims and 1,000 deaths over two years. Over 100,000 cases of yaws were treated. There were 240 cases of diphtheria, 7669 cases of pulmonary tuberculosis and 624 cases of typhoid in 1946 with mortality rates of 30.8%, 27.4% and 23% respectively.

However these epidemics were contained within five years and the pre-war health services were re-established and slowly developed and improved upon.

The most significant change in the life of the country came in the middle of the century. Nationalism which had grown over the first half of the century gave birth to independence from Britain in 1957. Under the leadership of Tunku Abdul Rahman, the first prime minister, the 11

states on Peninsula Malaysia formed the Federation of Malaya. In 1963, Sarawak and Sabah joined the federation to form Malaysia. Singapore which historically has many links with the rest of the nation joined too, but left to be an independent state in 1965.

The most noticeable socio-economic changes that the country has experienced since independence is embodied in the New Economic Policy set out in 1970. In it the government set out to alter the association of race with economic activity, and to eradicate poverty in the rural areas. Implementation of these goals was done through several 5 year plans.

Over the next 20 years, the country grew less dependent on the primary industries of tin and rubber. Tin resources became depleted but manufacturing industries grew. Oil palm proved to be a better plantation crop and replaced rubber in many estates. Petroleum discoveries off the coasts of Malaysia further boosted the economy and tourism also became an important source of income. The population became more integrated. Chinese and Indians were less confined to the mining and plantations sectors. Malays were no longer left out of the economic mainstream as village fishermen and padi planters. Urban centres grew drawing population in from the rural areas.

The health programmes have been successful in reaching right down to even the most remote areas with immunisation, sanitation, child and maternal care, making it among the best in the region. The medical care which to a large extent was provided by the government at minimal cost to the patients however suffers from lack of funds and manpower. Demand for medical care has increased substantially through the years. Admissions to government hospitals has grown from 40 per 1,000 in 1955 to 62 per 1,000 in 1975 and has reached 70 per 1,000 in 1990. It remains steady at 70 per 1,000 population in 1998. Acceptance for medical care has increased especially among Malays. Traditionally they had the lowest hospital utilisation rates as seen in 1960 where only 25% of admissions were Malays, while 46% were Chinese and 27% Indians. However, by 1975 Malays accounted for 41% of admissions.

Because of the advances in medicine that require more doctor care per patient, government hospitals have not been able to meet the demand for medical care for the whole population. As a result, with the rise of affluence, private medical care has grown tremendously since the 1970s, unfortunately draining manpower, from the government hospitals even further.

As of 1998 there were 15,016 medical practitioners issued with practising certificates in Malaysia giving a doctor:population ratio of 1:1,477. 43% of doctors work in the private sector and the private sector accounts for 21% of the hospital beds in the country. The Ministry of Health received 6.6% of the Government Budget in 1998 which totalled nearly RM 4 billion and amounted to an allocation of RM191 per person. This amount forms about 1.5% of the country's gross national product. On top of this the Malaysian public spend about another 1.6% of the gross national product on health out of their own pockets.

The Population Today

Today more than 40 years after independence we have passed the dateline set for the New Economic Policy. The population enjoys the fruits of being a fairly successful developing nation with a per capita annual income of RM12,000 (US$3,200). In terms of purchasing power parity this translates to about US$9,000. The economy is diversified and natural resources are plentiful. The prime minister, Dato Seri Dr Mahathir has set a vision for the country to join the ranks of the developed nations by the year 2020.

New population characteristics alter the profile of diseases in the country. The

percentage of the population employed in the agricultural sector has decreased from 52% in 1970 to 26% in 1990. Female participation in the workforce has increase from 36% in 1957 to 47% in 1991. Increased affluence has reduced the morbidity and mortality caused by infectious disease and poor nutrition. Cardiovascular diseases and cancers have become the main causes of ill health instead of infectious diseases.

In the 2000 census the population of Malaysia was recorded at 22,202,614. 35% of the population were under the age of 15 years. The elderly, over 65 years, constitute 4% of the population. From being principally a rural population, 57% of Malaysian now live in cities. Natural population growth has declined. The average Malay family had 6 children in 1957 but has dropped to 3.7 children in 1999. The average Indian family has 2.6 children in 1999 compared to 7.9 in 1957. The largest drop however is among Chinese families who now average 2.5 children in 1999 compared to 7.3 in 1957.

Table 1.1 Population of Malaysia

	Peninsula	Sarawak	Sabah	Total
1920	3,328,000			
1930	3,788,000			
1950	4,908,000	565,000	334,000	5,807,000
1960	6,279,000	780,000	454,000	7,513,000
1970	8,801,000	977,000	656,000	10,434,000
1980	11,427,000	1,308,000	1,011,000	13,746,000
1991	14,182,000	1,649,000	1,737,000	17,567,000
2000	17,671,000	2,013,000	2,519,000	22,203,000

Source: Department of Statistics, Malaysia

Nevertheless pockets of people remain in poverty and have been bypassed in the country's development. The Orang Asli in Semenanjung who number slightly over 100,000 have fallen behind the main 3 ethnic groups in many health indices. They have higher prevalences of tuberculosis, leprosy and malaria, poorer nutrition and higher mortality rates. However, because they amount to less than 0.5% of the total population they are grouped together with other races or sometimes with Malays in mortality and specific diseases indices and it is not always clear how they are faring in comparison with the general population.

As a region Sabah records much poorer scores of many diseases. Much of it is due to migrants of many diseases. Much of it is due to migrants along its coasts who have come in recently from the Philippines and Indonesia.

Rapid economic growth in the 1980s created a labour shortage which resulted in a new flux of immigrant labourers from Indonesia and the Philippines even in the peninsula. During a peak before the economic recession in 1997 there were an estimate of 2,000,000 foreign workers. The number of legal immigrants in Malaysia was first documented in 1994 and they numbered 363,519. They reached a peak in 1996 at 861,565. However many more come illegally and probably more than double that figure. With them has come new disease trends such as a resurgence of some infectious diseases. Between 1993 and 1995 they accounted for about 11% of reported cases of tuberculosis, 32% of leprosy, 14% of malaria, 2% of dengue fever and 5% of filiariasis.

THE ETHNIC COMPOSITION

Malaysia has one of the greatest diversity of ethnic groups among the nations of the world today. Besides the many tribes of Orang Asli and Malay stock in both East and West Malaysia, there four or five major Chinese dialect groups made up of immigrants from South China. As mentioned most came starting from the latter half of the last century, when tin mines were opened up till the Second World War. Indians although consisting of mainly Tamils are actually quite a diverse group and include Punjabis, Sri Lankans and Indians from all over the sub-continent. The Tamils came mainly to work in the estates from the turn of the century and other groups came also roughly along certain

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Table 1.2 Population of ethnic groups in Malaysia

Peninsula Malaysia				
	Bumiputera(%)	Chinese(%)	Indians(%)	Others
1920	1,630,000(50)	1,180,000(35)	472,000(14)	46,000
1980	6,324,000(55)	3,894,000(34)	1,179,000(10)	75,400
1990*	8,493,000(58)	4,579,000(31)	1,441,000(10)	91,900
2000**	10,459,100(58)	4,773,700(26)	1,583,800 (9)	770,500

Sarawak				
	Bumiputera(%)	Chinese(%)	Others(%)	Non-citizens
1980	939,800(70)	394,700(29)	16,600(1)	
1990*	1,242,000(71)	490,400(28)	22,000(1)	
2000**	1,430,500(71)	551,500(28)	18,900(1)	64,000(3)

Sabah				
	Bumiputera(%)	Chinese(%)	Others(%)	Non-citizens(%)
1980	874,600(83)	171,100(16)	9,400(1)	
1990*	1,294,000(85)	209,700(14)	13,700(1)	
2000**	1,626,100(52)	327,900(10)	275,800(9)	906,800(29)

projections based on 1980* and 1991** census

NB. Bumiputera includes Malays and other indigenous groups.

Source: Department of Statistics, Malaysia

occupational lines; for example the Punjabis for the police and armed forces.

This peculiar ethnic mix has a bearing on disease patterns. The incidence of a disease is often different in different populations. Although there may be differences within these ethnic groups, what is usually more striking is the differences between the three major groups of Malays, Chinese and Indians. These differences make Malaysia a unique place to observe some diseases.

Although the bumiputera in Peninsula Malaysia are almost all Malay, the bumiputera in Sawarak and Sabah are a diverse group. In Sarawak in 1998, the bumiputera consists of 44.4% Iban, 32.5% Malay, 12.5% Bidayuh, 1.4% Melanau and 9.2% other groups. In Sabah, the. Kadazandusun (34.5%), Bajau (21.7%), Malay (12.6%), Murut (5.7%) and other groups (25.5%) form the bumiputera population

POPULATION GROWTH AND DEATHS

Today many have forgotten how common infant mortality was in the past. Of a total in 36,566 births registered in the Federated Malay States in 1920, 6,920 (19%) infants died. (see Table 1.3) The principal diseases that killed children were malaria, dysentery, tuberculosis and beri-beri. Although the infant mortality rate (I.M.R.) had halved by 1946 it was still tragically high with 16,877 infants dying out of 183,960. The war years actually did not badly disrupt the declined of the I.M.R. although we do not have records for these years. Better nutrition is most likely the chief reason for the further decline, such that the I.M.R. was further halved by about 1967 and yet again halved by 1980.

Among the ethnic groups, Chinese have had the lowest I.M.R. from the earliest records. At independence in 1957, The I.M.R. for Chinese was 47 per 1,000 compared with 96 for Malays and 70 for Indians. But the gap has narrowed with the overall decrease. In 1989 the rates were 14.5 for Malays, 8.8 for Chinese and 13.16 for Indians in Peninsula Malaysia. The Orang Asli, Dobbins estimated had an infant mortality 1.4 times greater than the Malays but a comparable life expectancy.

Table 1.3 The Infant Mortality Rate in Malaysia

Year	I.M.R.
1927	203
1937	130
1947	102
1957	75.6
1967	45.0
1977	31.8
1987	14.3
1997	9.5

Source: Information and Documentation System Unit, Ministry of Health, Malaysia

In population growth, the Chinese are increasing at a slower rate than the Malays and Indians. One reason is because of a lower birth rate. The national birth rate has declined from about 45 per 1,000 in the 1950s to about 26 per 1,000 in 1998, but the Chinese have a birth rate of about 5 per 1,000 lower than the other races.

In 1990 the I.M.R. in Sarawak was 10.5. The ethnic breakdown was 10.5 for Malays, 15.3 for Melanaus, 9.0 for Ibans, 8.2 for Bidayuhs, 12.0 for other bumiputeras and 8.7 for Chinese. In 1998 Sarawak recorded an I.M.R. of 6.2 which was lower than all the other states except Selangor and has had among the lowest rates the last few years. The birth rate in Sarawak is comparable to that of Peninsula Malaysia. The incidence of low birth weight babies (less than 2.5kg), from a study between 1986 and 1988 in Lundu Hospital, reflects the I.M.R. being 6.7% in Chinese, 13.6% among Ibans, 13.0% among Bidayuhs and 12.5% among Malays.

In Sabah the I.M.R. was 18.1 for bumiputeras and others and 12.5 for Chinese in 1990. In 1998 the I.M.R. in Sabah was 11.5 and it is among the states with higher rates though not the highest. Sabah has attracted a large migrant population from the neighbouring areas of the Philippines and Indonesia who are economically more disadvantaged and they have a higher infant mortality rate compared to local citizens.

Besides infant deaths, what was maybe even more staggering in the past was the gross death rate. At the turn of the century more than 100 people per 1,000 were dying annually. This was chiefly among immigrants in the tin mines and rubber estates and with nearly half dying from malaria. The economic development we enjoy today was gained at a very costly price which many are not aware of. But by 1911 the mortality rate had dropped to 37 per 1,000 and by 1947 it was 17 per 1,000. In 1976 the crude death rate had dropped even further to 6 per 1,000 and in 1999 stands at 4.6 per 1,000.

Table 1.4 Percentage of medically certified and inspected deaths among ethnic groups, Peninsula Malaysia, 1970-1990.

Race	1970	1975	1980	1985	1990
Malay	15.3	20.8	24.0	26.6	29.1
Chinese	52.8	54.1	51.8	50.4	50.9
Indian	55.8	57.0	57.1	56.1	56.3
Others	45.3	39.9	37.9	38.1	39.5
Overall	32.3	36.4	37.9	38.1	39.5

Another indicator of this decrease in mortality is the life expectancy at birth, which for Malaysia, increased from 57 years at independence to 65 year in 1976 and has further increased to 70 years for men and 75 years for women in 1999. Bumiputeras have a life

expectancy of 69 years and 73 years for males and females respectively, Chinese 72 years and 78 years respectively and Indians 66 years and 74 years respectively.

It is most regrettable that in Malaysia medical certification of deaths has not progressed. The rate of medically inspected deaths has risen from 32.% in 1970 to only 39.5% in 1990 (Table 1.4) The infrastructure and manpower is not lacking. It is that it has just not been given priority.

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NORMAL PHYSICAL GROWTH

At a glance one can see that Malaysians are not as big as Europeans and Americans. Therefore what is normal for Caucasians cannot be applied here. So not only for the sake of records but in order to detect malnutrition that produces underweight and stunted children, it is important to establish local normal values for heights and weights.

Pre-school Children

The first large scale survey to produce local growth charts was reported by Thomson in 1961. Her data covered children seen at the Maternal and Child Health Clinic in Perak over the years 1949-1954. In all 14,604 weights were taken, the majority of whom (79%) were from Chinese boys and girls. The Chinese were slightly heavier than the Malays and Indians. Dugdale in a series in 1969 and another with other co-workers in 1972 sampling children in a welfare clinic and children of soldiers respectively recorded values similar to Thomson's.

Chen produced growth charts based on 227 children born between 1968 and 1974. The mean growth rate had increased when compared with the data taken 20 years before. In weight, the mean in Chen's series was higher, but fairly close to that in Thomson's series, up till one year, after which the disparity increased. The mean weight in the pre-school children above one year in Thomsom's series stood only at about the 25th percentile in Chen's series. The reason for this must be partly due to improvement in nutrition throughout the country. Another factor accounting for the higher mean anthropometric measurements was probably the sample selection. In Chen's series 38% of the fathers of the children were professional or administrative workers.

School Children

Figures of weight and height curves of school children have been measured in a few studies. Chen produced charts in 1977 based on 686 children from the Petaling Jaya area. Her findings are similar to others where healthy children are measured; and in healthy children the heights and weights of the three different races do not differ. In a report 16 years later in 1993, Osman et.al. surveyed 871 Malay children from a middle class area in KL (Figure 1.2-5). The percentile lines for weight and height were a little above Chen's series all round, but

especially higher for girls from 10 to 12 years. When these children were compared with Americans from the National Centre of Health Statistics figures, however, they were about 3-5cm shorter and 2-4kg lighter.

Biological maturity

Age at biological maturity in girls has been noted by Noorlaily in a 1983 report. The mean age was 15.3 years in Malay girls, 15.4 years for Chinese and 14.7 years in Indians. The maximum age of attaining biological maturity was 20 years in Malays and Chinese but 19 years for Indians.

Figure 1.2 Percentile Chart of height for Malay boys in KL 1993

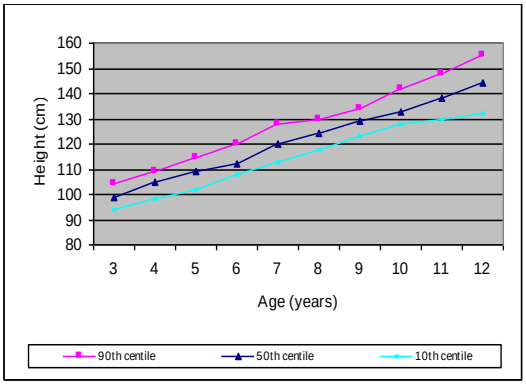


Figure 1.3 Percentile Chart of height for Malay girls in KL 1993

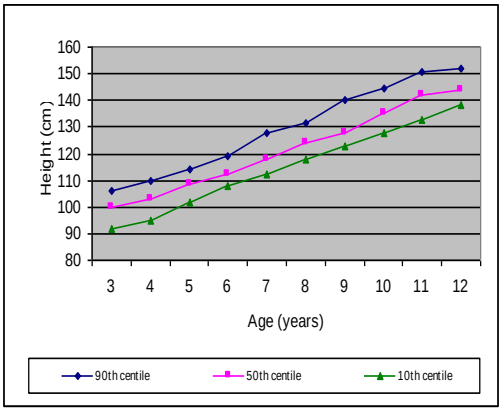


Figure 1.4 Percentile Chart of weight for Malay boys in KL 1993

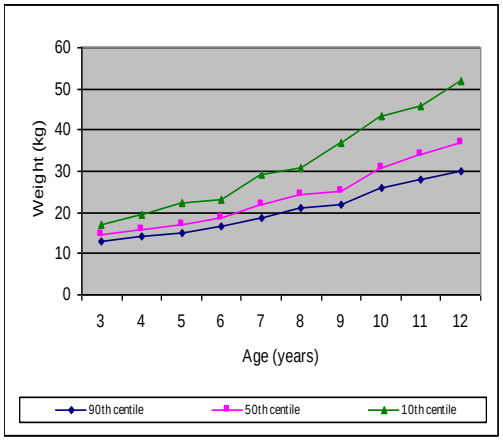
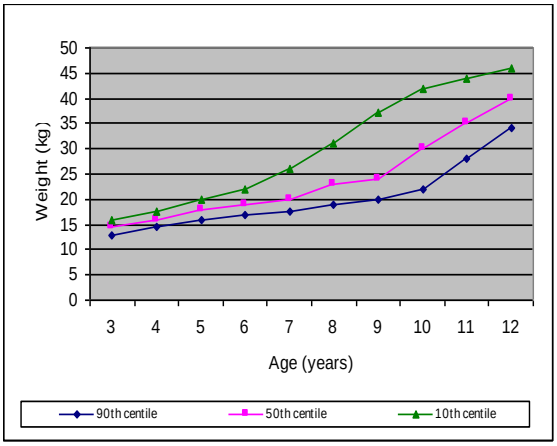


Figure 1.5 Percentile Chart of weight for Malay girls in KL 1993



Adult heights and weights

Young Malaysian adults now are taller on average than those two or three decades older. Figure 1.6 and 7 shows the median heights of men and women of the different ethnic groups in different age groups from a sample of 28,737 individuals from the National Health and Morbidity Survey in 1996. Allowing for the fact we can lose a few cm. in height, better nutrition

and health has made younger Malaysians taller over the last 4 decades, as has been seen in other countries that have undergone rapid socio-economic development. The 1996 survey also found that the mean body mass index prevailing in all ethnic groups was low (between 20-25kg/m^2 in almost all age groups) in sharp contrast to Western populations. However obesity does affect a segment of the population and is a growing problem. (see Obesity).

Figure 1.6 Median height of males in Malaysia 1996

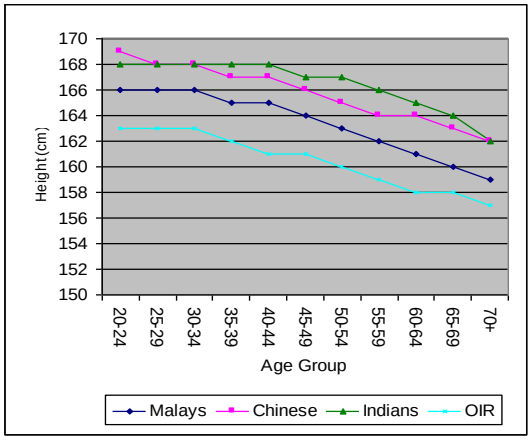
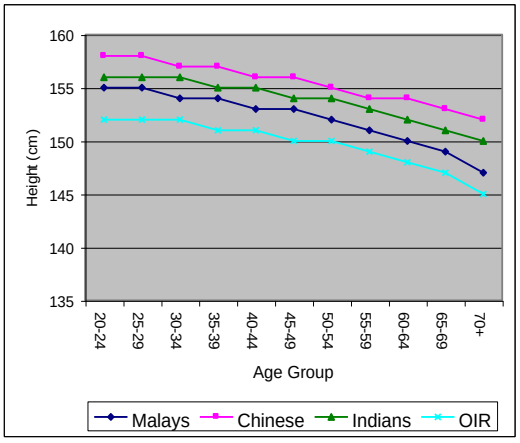


Figure 1.7 Median height of females in Malaysian 1996



(OIR=other indigenous races)

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THE ELDERLY

Malaysia has a broad base population pyramid. The majority of the people are under 25 years old as the life expectancy in the past was not high. But with life-expectancy rising as it has to above 70 years now, the elderly population is growing. In 2000 there are an estimated nearly 1,400,000 Malaysians above 60 years old forming 6% of the total population. The projected growth is that in the year 2020 they will form 9.8% of the population and number 3,261,000.

Chen looked into a sample of the demographic characteristics and health of 1,000 of the elderly in 1987. Among physical disabilities the leading problems were sight problem (67%), 57% had evidence of cataract. 48% had chewing problems, 15% had walking difficulty and 13% had hearing problems. In mental health, 58% were forgetful, 34% had sleep difficulties and 31% had loss of interest in life. However, 65% of the elderly helped make family decisions, almost 90% left home at least once a week and 95% lived with at least one

other person. Zaitun and Terry performed a small survey of 317 elderly Malay women in Negeri Sembilan and found most were satisfied and free of worry about their health. Arthritis (64%) was the commonest complain.

Table 1.5 Population by age groups in Malaysia 1998

Years	
0- 4	2,576,300
5- 9	2,523,900
10-14	2,447,100
15-19	2,243,100
20-24	2,087,000
25-29	1,904,300
30-34	1,737,500
35-39	1,572,200
40-44	1,325,100
45-49	1,054,700
50-54	785,600
55-59	610,400
60-64	482,900
65-69	347,900
70-74	229,400
75+	252,100

In a study of medical admissions among the elderly above 65yrs, in the UH, it found that , strokes (20.3%), heart failure (17.6%) and ischaemic heart disease (13.5%) were the commonest cause for their admission. The elderly accounted for 19% of all medical admissions. 12 (16%) patients died during their stay in hospital the commonest causes being pneumonia (3) and heart failure (2).

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THE DISABLED

Any form of chronic ill health constitutes a disability. It is therefore hard to define who a disabled person is. The UN gives a general definition for the term 'disabled person' as "any person unable to ensure by himself or herself, wholly or partly, the necessities of a normal individual and social life as the result of a deficiency, either congenital or not, in his or her physical or mental capabilities". In developed countries it is estimated that about 8% of the population suffer from some disability while 4% are sufficiently disabled to be considered handicapped. However, in Malaysia we have insufficient data to categorise and determine the true number of our disabled population.

Table 1.6 Estimated number of disabled persons in Malaysia 1980

Type of Disability	Number
Physical handicap	58,380
Blindness	44,480
Deafness	25,020
Mental retardation	11,120
	139,000

The Ministry of Welfare Services however has a register. In 1980 it was estimated that in the four main categories of disability, as given in Table 1.6 there were a total of 139,000 disabled persons. Of these actually only 19,478 are registered with the Ministry to avail themselves of the services offered including special education, vocational training, medical treatment, special appliances and financial aid. It has been estimated that about 20% of the blind are enrolled and about 10% of the deaf known. But, less than 1% of the physically handicap and

mentally subnormal are registered.

Chen, Arokiasamy and Gan from the UH conducted a screening survey of 2,518 persons for disability, in the rural district of Kuala Langat in 1981. 9.5% of the sample had some disability. 0.2% had a disabling condition severe enough to be considered handicapping. The commonest disability was hearing impairment (4%), followed by visual impediment (2%), and musculoskeletal problems (1.8%). Mental handicap was present in 0.6%.

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CHAPTER 2

PROBLEMS IN PREGNANCY

Maternal and Child Health services were launched in Malaysia in 1923 with the introduction of legislation (Midwife Act) to control the practice and training of midwives in the Straits Settlements. Prior to that antenatal care was non-existent and deliveries were conducted by traditional birth attendants who continue to practice even today in rural Malay kampongs. The 1923 Act provided for the commencement of midwifery training and the setting up of antenatal welfare clinics. These clinics continued to function in some way even through the Japanese Occupation in 1941-1945. Services were strengthened after the war and through the 1948 Emergency with the establishment of Maternal and Infant Welfare Clinics in resettlement villages and rural areas. These facilities were instrumental in changing the proportion of "safe deliveries" in the last few decades and is shown in Table 2.1. Today the Maternal and Child Health Centres (MCHC), and Midwife clinic cum quarters, each serving a population of about 4,000, are run by trained midwives and supervised by visiting doctors, form the backbone of antenatal and obstetric care in the country.

Table 2.1 Proportion of "Safe" and "Unsafe" deliveries in Peninsula Malaysia.

Year	Safe	Unsafe
1966	58%	42%
1976	89%	11%
1984	93%	7.1%
1992	97%	2.9%
2000	99%	<1%

In 1998 in Peninsula Malaysia, 96% of deliveries were institutional deliveries as opposed to 4% being domiciliary deliveries. The rate is even higher in Sarawak, with more than 97% being institutional deliveries. In Sabah however 46% of deliveries occur at home and only 77% are attended to be trained personnel in 1998.

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NORMAL PREGNANCY

Human gestation in Malaysia lasts 280 days as it does the world over. Thambu noted that 63% of women were delivered at between 39-42 weeks of pregnancy and that there was a rather low percentage of post-maturity pregnancies (4.3%) in 2,989 women.

Hassan, Kulenthran and Thum have shown that there was no significant delay in return to fertility in Malaysian women following cessation of oral contraception.

Sinnathuray and Wong found that the average weight gain of a Malaysian woman in pregnancy from the pre-pregnancy to the 40th week was 11.3 kg. Primigravids gained about 0.65kg more than multiparae. This figure is about 1 kg less the American and European women but more than women in Africa and India who gain as little as 6 kg. in some places. The period of greatest weight gain is between to 21-24th. week with a gain of 0.45kg. per week. Women do not return to their pre-pregnancy weight after birth. At the end of puerperium, the average Malaysian woman had gained 4.9kg.

Figure 2.1 Mean rate of cervical dilatation for multiparous Malaysian women

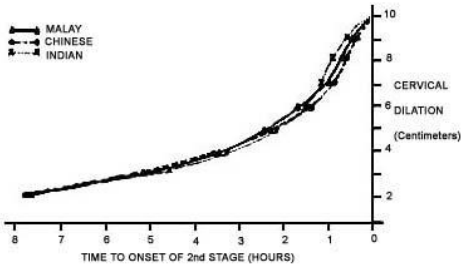
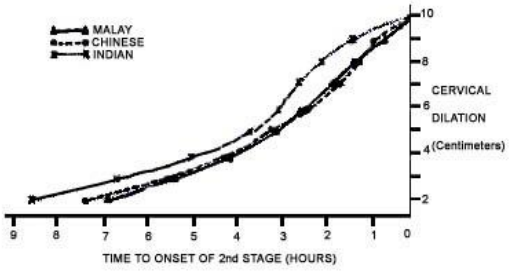


Figure 2.2 Mean rate of cervical dilation for primiparous Malaysian women.



The duration of labour in Malaysia is also no different from women elsewhere. Wong and colleagues at the UH have devised some graphs for the normal progress in cervical dilatation in Malaysian women. From a study of obstetric records of 977 women with 'normal labour' in 1975 they reported that the mean duration of the first stage of labour was 3-4 hours in primiparae and 2-7 hours in multiparae. The mean duration of the second stage of labour was 23-7 minutes and 13 minutes respectively. Indian primiparae had a slower rate of cervical dilatation and seemed to reach the accelerated phase of dilatation later. This is seen more clearly in the cervicogram constructed at probit 80% (Figure 2.3). Among these 977 normal births, they foumd that Indian babies were significantly

Figure 2.3 Cervicogram of Malaysian primiparae drawn at probit 80%

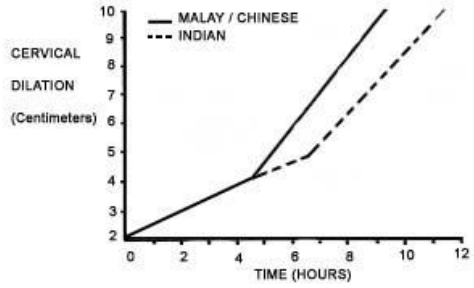


Figure 2.4 Percentile chart of birthweights of Malaysian male infants between 28 and 42 weeks gestation

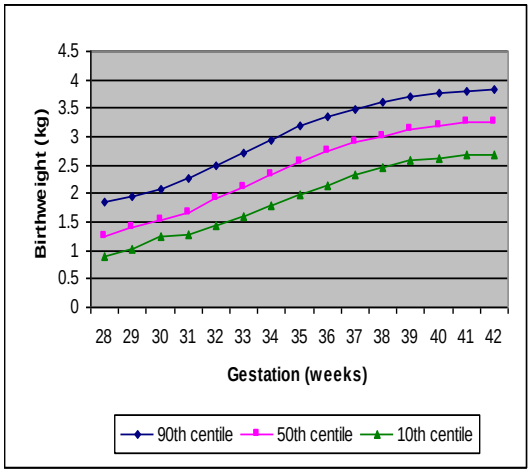
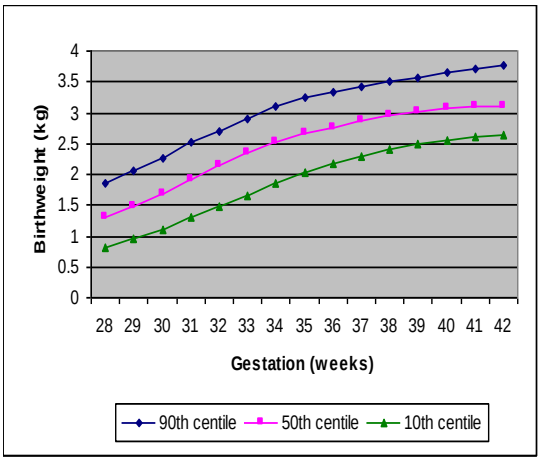


Figure 2.5 Percentile chart of birthweights of Malaysian female infants between 28 and 42 weeks gestation.



smaller than Malay babies who were significantly smaller than Chinese babies.

Boo, Lye and Ong carried out a cross-sectional study of birthweights, crown-heel lengths and head circumference of 8,478 normal singleton neonates born at the KL GH at gestational ages between 28-42 weeks. They could not detect any significant difference in these parameters by ethnicity, or gravidity for babies born at 34 weeks of gestation or below. Above the gestational age of 34 weeks birthweights were significantly influenced by materanal gravidity, ethnic origin and the sex of the neonate. Babies of multigravida mothers were heavier than primigravida mothers. Indians were significantly lighter than Malays and Chinese. Males were heavier than females. Head circumference and body lengths of neonates were also significantly influenced by these factors. The birthweights of Malaysian male and female infants between 28 and 42 weeks gestation are given in Figure 2.4 and 2.5 and the full charts in Table 2.2 and 2.3

Postnatal Practices

Lee et.al. noted in 1995 that 86% of women in Malaysia took a special diet, and 64% still observed traditional beliefs such as avoiding washing the hair, eating cold food, going outside, being blown by wind and having sexual intercourse. 79% had some to look after them.

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Table 2.2 Intrauterine growth of Malaysian male neonates

Gestation weeks		Birthweight in grams						Crown-Heel Lengths in centimetres						Head Circumference in centimeters					
	n	Smoothed Percentiles						Smoothed Percentiles						Smoothed Percentiles					
		10th	25th	50th	75th	90th		10th	25th	50th	75th	90th		10th	25th	50th	75th	90th
28	6	877	1040	1253	1543	1838		34.1	35.6	37.5	38.9	40.0		23.8	25.0	26.5	27.2	28.7
29	8	1005	1161	1391	1680	1943		35.7	37.0	38.7	40.0	41.2		24.8	26.1	27.4	28..3	29.7
30	10	1125	1278	1528	1796	2064		37.3	38.5	39.9	41.2	42.3		25.8	27.3	28.3	29.6	30.7
31	12	1289	1434	1670	2012	2270		38.7	40.0	41.5	42.8	44.1		26.8	28.2	29.2	30.6	31.7
32	21	1435	1623	1910	1221	2495		40.2	41.7	43.2	44.6	45.9		27.6	29.0	30.2	31.5	32.5
33	46	1602	1837	2115	2448	2724		41.2	43.1	44.8	46.2	47.4		28.5	29.8	30.9	32.3	33.2
34	49	1780	2043	2336	2690	2946		42.4	44.4	46.1	47.8	49.0		29.4	30.5	31.7	32.9	33.8
35	109	1976	2270	2542	2905	3191		43.6	45.6	47.3	49.0	50.2		30.0	31.0	32.3	33.3	34.3
36	179	2148	2461	2734	3059	3339		44,8	46.6	48.0	49.6	50.6		30.4	31.4	32.6	33.6	34.6
37	437	2328	2621	2890	3201	3477		45.6	47.2	48.6	50.0	51.0		31.0	32.0	33.0	34.0	34.9
38	850	2464	2737	3013	3303	3597		46.6	47.8	49.0	50.4	51.4		31.4	32.4	33.4	34.4	35.3
39	1046	2584	2841	3126	3414	3701		47.2	48.2	49.4	50.6	51.7		31.6	32.6	33.6	34.6	35.5
40	871	2628	2891	3193	3473	3756		47.6	48.6	49.8	50.8	51.9		31.8	32.8	33.8	34.8	35.6
41	614	2667	2930	3238	3525	3807		48.0	49.0	50.0	51.0	52.2		32.0	33.0	34.0	35.0	35.8
42	166	2671	2946	3267	355 t	3838		48.3	49.3	50.1	51.1	52.3		32.1	33.1	34.1	35.1	35.9

Table 2.3 - Intrauterine growth of Malaysian female neonates

Gestation weeks		Birthweight in grams						Crown-Heel Lengths in centimetres						Head Circumference in centimetres					
	n	Smoothed Percentiles						Smoothed Percentiles						Smoothed Percentiles					
		10th	25th	50th	75th	90th		10th	25th	50th	75th	90th		10th	25th	50th	75th	90th
28	6	809	997	1288	1586	1855		34.0	35.8	37.5	39.4	41.3		24.5	25.4	26.7	27.7	28.7
29	7	977	1169	1491	1793	2067		35.6	37.4	39.1	41.2	43.0		25.5	26.4	27.8	28.7	29.7
30	16	1108	1337	1691	1981	2266		37.0	38.9	40.7	42.7	44.6		26.2	27.4	28.7	29.6	30.7
31	14	1309	1553	1924	2231	2506		38.5	40.5	42.2	44.3	46.2		27.4	28.6	29.8	30.7	31.7
32	20	1475	1736	2139	2446	2706		40.0	42.1	43.3	45.9	47.6		28. 1	29.4	30.6	31.5	32.5
33	43	1656	1944	2348	2660	2914		41.1	43.3	45.2	47.2	49.0		28.9	30.3	31.4	32.3	33.2
34	66	1850	2118	2518	2858	3093		42.3	44.5	46.4	48.4	50.3		29.5	30.9	32.0	33-3	33.8
35	98	2028	2297	2666	2997	3235		43.1	45.3	47.2	49.2	51.1		30.2	31.4	32.4	33.4	34.2
36	154	2162	2416	2764	3077	3334		43.7	45.8	47.8	49.9	51.8		30.4	31.6	32.6	33.6	34.4
37	331	2288	2548	2859	3166	3425		44.2	46.2	48.2	50.3	52.4		30.7	31.8	32.8	33.8	34.6
38	693	2402	2654	2948	3234	3514		44.7	46.4	48.4	50.5	52.6		30.8	31.9	32.9	33.9	34.8
39	951	2488	2746	3024	3298	3585		44.9	46.6	48.6	50.7	52.7		31.1	32.1	33.1	34.1	35.1
40	905	2554	2789	3066	3354	3655		45.0	46.8	48.8	50.9	52.9		31.2	32.2	33.2	34.2	35.2
41	595	2610	2830	3105	3407	3718		45.2	47.0	49.0	51.0	53.0		31.3	32.3	33.3	34.3	35.3
42	147	2654	2841	3106	3440	3768		45.2	47.1	49.1	51.1	53.1		31.5	32.5	33.5	34.5	35.5

JUVENILE PREGNANCY

A piece of research in 1966 put the mean age at first marriage in Malaysia at 17.6 years and mean age at first birth at 19.8 years. This is seen in Table 2.6 where quite a number were having upwards of their third pregnancy while still teenagers. Over the years the number of teenage marriages have declined and as a result

teenage pregnancies have also decreased. As shown in Figure 2.6 teenage age births were and and still are, but to a lesser degree, more common among Indians and Malays. In 1964 there were 33,348 teenage mothers and constituted over 10% of total births. In comparison, there were only 18,172 teenage mother comprising 4.7% of total births in 1984.

Nevertheless, in 1984 there were still 164 mothers below 15 years of age.

Figure 2.6 Teenage births as a percentage of all births in Peninsula Malaysia.

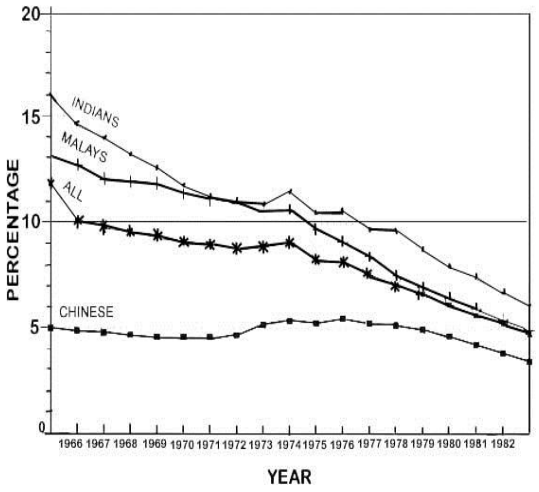

Table 2.4 Percentage of births occurring to women below 20 years of age by birth order.

	Year			
Birth order	1966	1970	1975	1984
1st	61%	67%	73%	72%
2nd.	29%	26%	22%	23%
3rd.	8%	6%	4%	4%
4th. & over	2.1%	1.4%	1.1%	0.7%

Reference

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ELDERLY PRIMIGRAVIDITY

This term was defined at the 1958 Council of International Federation of Obstetrics to mean mothers aged 35 years or more at first delivery and recognised as a risk factor in pregnancy. Over a period of 3 years from 1983, Sivalingam and Avalani observed 90 (0.6%) elderly primigravids among 13,858 pregnancies prospectively at the Muar District Hospital. Malays formed a higher proportion of elderly primigravids (66%) in comparison to the overall proportion of pregnancies they comprised (51%). The biggest reason for late first pregnancy was late marraige. 83% married after age 35 years. Involuntary infertility of more than 5 years was reason in 9%. 61% of the elderly primigravids conceived within 2 years of marraige.

The only antenatal complication Sivalingam and Avalani observed that was more common among elderly primigravids (31%) in comparison to other primigravids (11%) was pregnancy induced hypertension (PIH). Caesarian section was performed in 55% of the elderly primigravids mainly for prolonged labour or severe PIH but perinatal mortality was much lower in this group being only half that of the whole population. Siva Achana and Monga also recorded more PIH in elderly primigravidae in Kelantan (23.7% vs 13.3%), and breech presentation (6.8% vs 3.3%) and Caesarian section was performed in 75% of their patients compared to a rate of 10% in young primigravidae.

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MULTIPLE PREGNANCIES

Twins are generally found to be adorable in society but multiple pregnancies carry a slightly higher perinatal risk and are more taxing on parents to raise. The local incidence as among Asian countries is lower than in Africans and Caucasians. Of 193 twin pregnancies in the UH Teoh and Wong reported the incidence to be 1:92 in Malays, 1:117 in Chinese and 1:109 in Indians. The rate of twin rose from 1:263 for mother under 20 years old to 1:36 for those above 40 years. The monozygous:dizygous ratio was 1.6:1. The rate of antenatal complications was 29% anaemia, 30% toxemia, 17% hydramnios and 16% post-partum haemorrhare. But there were no maternal deaths. The perinatal mortality was 88 per 1,000, explained mainly by abnormal presentation (32%), operative deliveries (50%) and low birth weights (59%).

In a study of triplets at the UH, Kulenthran, Raman and Sinnathuray found 9 over 15 years, with an incidence of 1:6,349. This slightly high ratio may be due to the fact they were in a referral hospital. Like twins there was an association with a higher parity and higher maternal age. The perinatal mortality was 74 per 1,000. Pregnancy complications included, polyhydramnios (22%), anaemia (33%), toxemia (44%) and pre-term labour (56%).

Baskaran reported a rare case of a pair of conjoint twins in a triple pregnancy. Conjoint twins occur from time to time and on occasion have been successfully separated locally.

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ABORTIONS

Miscarriage is the term normally used for spontaneous abortions, as opposed to 'induced' abortions. Together with stillbirths these add up to the term 'foetal loss'. Thambu noted that the number of spontaneous abortions met with in all government hospitals in Peninsula Malaysia rose from 8,118 a year in 1960 gradually to 13,665 in 1972. In a study in 1974 by interview, of 6,368 women who among them had 29,030 pregnancies, Takeshita, Tan and Hamid recorded a total foetal loss rate of 6.5% in Malaysia. This consisted of 15.5 per 1,000 stillbirths, 42 per 1,000 miscarriages and 7.7 per 1,000 induced abortions. The breakdown of foetal loss by pregnancy order is given in table 2.5. It shows that the risk of foetal loss rises with parity, but remarkably a woman in a 15th pregnancy still has more than a 70% chance of producing a live baby.

Table 2.5 Number of pregnancies and rate of stillbirths, miscarriage and abortions by pregnancy order

Pregnancy order	Number of Pregnancies	Stillbirth (	Miscarriage per thousand	Abortion)
1	6,037	16.2	34.5	2.8
2	5,286	10.6	35.0	3.6
3	4,422	12.0	32.3	6.3
4	3,560	16.0	50.0	9.0
5	2,849	15.4	43.5	8.1
6	2,153	20.0	47.8	11.6
7	1,618	22.2	55.0	6.2
8	1,161	18.9	48.2	12.1
9	786	14.0	59.8	8.9
10	507	17.8	61.1	23.7
11	297	33.7	87.5	33.7
12	171	17.5	81.9	52.6
13	83	36.1	60.2	72.3
14	50	60	80	100
15-18	50	40	120	120
All orders	29,030	15.5	42.0	7.7

Besides a higher foetal loss rate with grandmultiparity, Tan, Yahya and Adeeb noted

that age increased the chance of having a spontaneous abortion. Compared with those under 30 years, those in the 30-39 years groups had a relative risk of 1.6 of a spontaneous abortion, and those above 40 an even higher relative risk of 3.68. Housewives had a lower risk of abortions (0.45) compared to career women. Other factors, like previous ectopic pregnancy, parity, ethnic group, subfertility and even previous induced abortions did not increase the risk of spontaneous abortions.

Induced Abortions

As regards induced abortions Sinnathuray *et.al.* found that in a purposive sample, 10.7%of married women under 50 years reported having had one. The rate was higher among urban (16%) women compared to rural (6%) women and much higher among Chinese (19%) than Indians (5%) and Malays (3.5%). Whether such estimates are reliable is questionable. In contrast to obtaining a history of induced abortion, attitudes towards induced abortion have been measured reliably for many populations. Takeshita, Tan and Hamid reported such a survey in 1986 finding Malay-Muslims most conservative but Chinese and Indians of various religions almost equally permissive.

The laws on abortion in Malaysia set out in sections 312-316 and 512 of the Penal Code permit only abortion when the woman's life is endangered by the pregnancy. Nevertheless requests for illegal terminations of pregnancy are common demands general practitioners face. They usually present in the form of a woman complaining that her period is late, in 60% the period is just 4 to 14 days late, and she wishes to have an injection to bring on the period. This is principally an urban problem that Ooi found in 98% involved Chinese. He describes a survey of 214 personal cases seen just within 6 months in 1970. In similar series Chia found 148 cases also in 6 months in 1981. In a UH series of 42 women, Vachher and Yusof found in contrast that all the races were almost evenly represented.

The typical woman is married, between 21-35 years old and already has a child. She comes from the middle income group and the previous child is usually either under 1 year or already over 5 years old. Most often (over 60%) the couple have been careless about contraception. Sinnathuray *et.al.* have reported that induced abortions was a significant risk factor for women with acute pelvic inflammatory disease.

Septic Abortion

Serious complications of criminally induced abortions usually present in the form of sepsis. In GH KL, Hooi found that in 1962 septic abortions formed 239 of 1,000 admissions for abortion problems. Marzuki and Thambu noted 6 years later in 1968 and 1969 that these septic abortions had decreased to only 36 out of 1,000 cases. The number of septic abortions seen in all government hospitals in the Peninsula ranged from 606 to 1,100 a year between 1960 and 1972. There were a total of 152 deaths, or an average of 11 annually over this period. In England and Wales such abortions have become the leading cause of maternal deaths. Ng and Sinnathuray reported 4 such maternal deaths in the UH over 6 years.

In Sarawak, Teo, Tiong and Teo described a series of 100 cases of septic abortion in a 28 month period. There were 2 maternal deaths. The women were seen from all the races in the Kuching area in equal representation. The 15-24 year age group accounted for 70 of the women. 58 were unmarried. The unemployed and bargirls formed 40% while housewives made up 31%. In the majority where bacteria were grown Gram negatives were the organism cultured as objects had been commonly inserted per vaginum.

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CERVICAL INCOMPETENCE

Cervical incompetence is recognised as a cause of mid-trimester abortions. Being a referal centre UH had a comparatively high rate of 16 patients (1:451) in 4 years. The women had on average 2.5 previous abortions between them. Cerclage ligature produced successful pregnancies in just above half the pregnancies.

Reference

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ECTOPIC PREGNANCIES

The rate of ectopic pregnancies has been reported as 1:212 deliveries by Sambhi in KL GH, 1:358 deliveries by Sivalingam in Johore Baru, and ranging between 1:59 to125 in UH between 1969 and 1987. However, these figures do not reflect the true incidence as many deliveries occur in other hospitals and at home, whereas hospitals should catch all ectopic pregnancies, hence the true rate must be lower than the numbers given above. Usually just above 50% of women affected are in their third decade. All orders of parity are almost equally affected locally but a history of relative infertility was common. 5-10% have had a previous ectopic pregnancy. The commonest length of amenorrhoea is 6-8 weeks (38%) and range from 4 to about 16 weeks.

Probably 90% and more of ectopic pregnancies are tubal pregnancies. One series had an ovarian and an abdominal pregnancy. In a rare case one woman had a simultaneous intra-uterine and a left tubal combined (heterotopic) pregnancy. Most patients present with a short acute history but unusual cases can run a slow course of days.

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HYDATIDIFORM MOLES

Ong *et.al.* reported in 1978 that the rate of molar pregnancies was 1:669 based on 102 cases seen in the Maternity Hospital. However as this is not population based it is biased by the way patients choose which hospital they go to as well as the pattern of referral of patients to the hospital. Malays and the lower social class seemed to be affected more often. No specific age group or parity was exempted. Pre-eclampsia complicated 23.5% and spontaneous abortion occurred in 58% at a mean gestational age of 19 weeks.

Sivanesaratnam and Ng reported that between 1968 and 1973 the rate of gestational trophoblastic disease was 1:330 pregnancies and 1:35 abortions in the UH from a collections of 41 patients with molar pregnancies. Tharmaseelan estimated that the rate at the Seremban GH was 1:420 deliveries and the incidence of invasive mole and choriocarcinoma was 10% of these. In a study 20 years later at the UH, Cheah, Looi and Sivanesaratnam found that over 2 years, 1989 and 1990, they had an incidence of hydatidiform moles in 1:384 pregnancies. The rates among the races was 2.43 per 1,000 for Malays, 2.66 per 1,000 for Chinese and 3.29 per 1,000 among Indians. Partial moles comprised 30% of all moles and choriocarcinomas and invasive moles accounted for 7.9% of the total.

Tharmaseelan had a case report of a molar pregnancy in an unusually elderly woman of 54 years. Thavarasah and Kanagalingam reported an unusual case of a Chinese woman with 7 consecutive molar pregnancies between 1979 to 1986.

Kamariah, at the IMR, studied the regression of ßhCG in a series of 47 patients in GH KL in between 1988 and 1991. The study used an RIA assay and found the time taken for the serum level of ßhCG to regress to normal ranged from 39 to 135 days, with a mean of 83 days.

References

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ECLAMPSIA

Eclampsia is the occurrence of convulsions or coma in pregnancy in a woman with pre-eclampsia. It has been known to produce maternal deaths as high as 20-50% and foetal loss of 60-70% in the last century. Its rate seems to be related to poverty. In Malaysia, Llewellyn-Jones noted a rate of 1:220 deliveries in GH KL in 1961. Ong et.al. in the UH found a rate of 1:476 between 1968 and 1976. They found the rate highest in Indians (1:250) followed by Malays (1:453) and Chinese (1:1615). Most (63%) were primigravids and from the lower socio-economic group (75%).

In the UH series of 48, 56% were

antepartum, 29% were intrapartum and 15% were postpartum eclamptics. There were 3 (6%) maternal deaths and 15 foetal deaths, with a corrected perinatal mortality of 15%. There was no recurrence of eclampsia in the known 16 subsequent pregnancies.

Sivalingam and Abdul Rahman reported that in Kelantan from 1983-1988 there were 146 documented cases of eclampsia giving a rate of 1:1,515 deliveries. 46% of women were primigravids. The distribution of ante-,intra and post-partum eclamptics was similar to the UH series. There were 8 maternal deaths, 3 due to cerebral haemorrhage, 3 to pulmonary oedema and 2 to coagulopathy. The perinatal mortality was 19%.

Hypertension in Pregnancy

UH workers have noted a decline in their rates of hypertension in pregnancy over 20 years from the opening of the hospital. From rates of about 14% in 1969 it decreased steadily and quite significantly to between 2-4% of livebirths in the early 1980s. Hypertension was not classified in all years but in 1987, from when there was a change in classification, 94% were classed mild pre-eclampsia without pre-existing hypertension, 4.5% severe pre-eclampsia and 0.6% eclampsia.

References

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Sivalingam N and Abdul Rahman A. Eclampsia in Kelantan. Med.J.Mal. 45:49-55 1990.

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ANTE-PARTUM PSYCHOSES

Loke reported on 33 cases of antepartum psychoses at the UH seen in one year, which he said had an unusually large number of cases. 27 were classed schizophrenia and 6 bipolar mania. Coexisting temporal lobe epilepsy, thyrotoxicosis and bronchial asthma were seen in one or two cases. Chinese (64%) were most often affected, especially those of the lower social group (61%). The peak period of occurrence was between the 28-32 week of gestation. Marital and family relationship problems were usually present. Most cases recovered but there was one suicide.

Reference

Loke KH. Epidemiological aspects of antepartum psychoses seen at the University Hospital, Kuala Lumpur. Family Practitioner 11:40-44 1988.

POST-NATAL DEPRESSION

From a survey sample of 154 women interviewed in the post-natal clinic in Seremban Hospital in 1995, Lee et.al. found that 4% suffered from post-natal depression according to the Edinburgh Postnatal Depression Scale. The rate was highest among Indians (8.5%), compared with 3% among Malays and none among Chinese.

Reference

Lee KK, Grace J and Ravindran J. Incidence of postnatal depression in Malaysian women. J Obstet Gynaecol Res. 23:85-89 1997.

MALPRESENTATION

Malpresentation is the term used whenever any part of the baby other than the vertex presents at labour. Breech is the commonest situation.

Face presentation was reported on by Ong and Teo in 1976. There were 16 cases between 1968 and 1975 at the UH, occuring in 1:1306 pregnancies. The majority (88%) were multiparous, but contracted pelvis was not a prominent feature. 9 patients delivered

spontaneously, 2 by forceps and 5 by Caesarian section. There was no foetal loss directly related to face presentation, but one died of anencephaly and another because of gross prematurity.

Brow presentaion is the most unfavourable of all cranial presentations. Ong and Chelvam reviewed 6 cases over 7 years from 1968 noting an incidence of 1:2665 deliveries. Prematurity and foeto-pelvic disproportions were important factors. All were delivered by Caesarian section.

References

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Ong HC and Teo SP. Face presentation. Med.J.Mal. 31:42-45 1976.

RUPTURE OF THE PREGNANT UTERUS

Between the time UH began its obstetric service in Aug 1968 and December 1989, 21 years, a total of 34 cases of uterine rupture were managed there. The rate was 1 in 2,966 pregnancies but as the hospital is a referral centre this may not reflect a true incidence for the population. 53% were scar ruptures, 38% were spontaneous ruptures and 9% were traumatic ruptures. Grand multiparity and oxytocin stimulation were the most important causes of a spontaneous rupture. There was no maternal mortality in the series, and no fetal deaths among those with scar ruptue but spontaneous and traumatic ruptures of the pregnant uterus carried a fetal mortality of 69% and 67% respectively.

Reference

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ACUTE PEURPERAL INVERSION OF UTERUS

Inversion of the uterus at the time of delivery occurs as a result of injudicious traction on the placenta. Rachagan *et.al*. reported that it occurred in 15 cases (1 in 4,836 deliveries) over 17 years at the UH. They found that blood loss was greater if the placenta was removed before it was replaced.

Reference

Rachagan SP, Sivanesaratnam V, Kok KP and Raman S. Acute puerperal inversion of the uterus – an obstetric emergency. Aust NZ J Ostet Gynaecol 28:29-33 1988.

MATERNAL MORTALITY

Records of maternal mortality going back to the years after the Second World War show that the rate then was around 7 per 1,000. However, as medical services did not cover much of the remote rural areas under-reporting probably occurred. At independence, in 1957, the rate was 2.8 per 1,000. In 1960, it was reported that 685 women died in pregnancy giving a rate of 2.4 per 1,000. In 1980 by the notification means of reporting there were 60 maternal deaths and in 1990 there were only 41. The corresponding rates are given below in table 2.6.

Reporting on the years 1967-1969, Ariffin and Thambu noted that the chief cause of death of women in pregnancy in hospitals in Malaysia was haemorrhage (43%), followed by toxemia (13%) and infection (5-10%). They amounted to 211-253 deaths a year in government hospitals giving a maternal mortality rate of 2.9 per 1,000 in 1967, 2.3 in 1968 and 2.2 in 1969.

Table 2.6 Maternal mortality (per 1,000) by ethnic groups in Malaysia

Year	Malays	Chinese	Indian	Total
1957	3.99	1.40	2.05	2.82
1970	2.15	0.48	1.16	1.48
1976	1.19	0.18	0.43	0.78
1982	0.69	0.10	0.35	0.50
1989	0.24	0.05	0.22	0.20
1995				0.20

Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Table 2.7 Maternal mortality in Sabah and Sarawak (per 1,000)

Year	Sabah	Sarawak
1976	0.72	0.30
1981	0.22	0.30
1985	0.21	0.10
1989	0.25	0.12
1995	0.20	0.10

Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Nafisah reported that from 1978 to 1981 there were 39 maternal deaths in the largest maternity unit in the country at GH KL, giving a rate of 0.7 per 1,000 which was slightly better than the overall national figure. 31% of deaths were associated with abortions. 26% were due to toxemia, 23% to bleeding, 15% to embolism, 15% to medical diseases and the remainder to other causes. In the next 10 years, from 1981 Abdullah *et.al*. found that the maternal mortality rate in GH KL was still the same at 0.74 per 1,000 and was highest (1.22 per 1,000) among Indians. This probably reflected socio-economic status. Of the 61 deaths, 12 (20%) were indirect causes, 10 (16%) fortuitous deaths and the remaining 39 direct cause maternal deaths. The 4 main causes of direct maternal deaths were hypertensive disease (28%), haemorrhage (23%), embolism (23%) and sepsis (18%).

By ethnic group, as Khairuddin highlighted in 1974, Malays had, up till then, always recorded the highest maternal mortality rates. This was true in every state in Peninsula Malaysia.

By 1989, the maternal death rate had dropped in all races. It dropped by about ten fold compared with the 1960s. Malays (0.24 per 1,000) still had the highest figures, but were closely followed by Indians (0.22 per 1,000) (Table 2.2). The Chinese had a much lower rate, of 0.05 per 1,000, which in actual figures was only 4 deaths in 1989 in Peninsula Malaysia.

Studying one district, Yadav reported that for Kerian in Perak a worse than average district the maternal death rate was 1.5 per 1,000 between 1976 and 1980. Grandmultigravids were the largest identifiable risk group accounting for 57% of deaths. Primigravids too, (23%) were a risk group. The main cause of death was post-partum haemorrhage and retained placentas which alone or in combination made up 60% of deaths. Traditional midwives who handled 41% of the deliveries accounted for 58% of the deaths. Studying another rural district, Hulu Terengganu from 1981 to 1985, Lim found that the same groups were affected and the causes of deaths were the same.

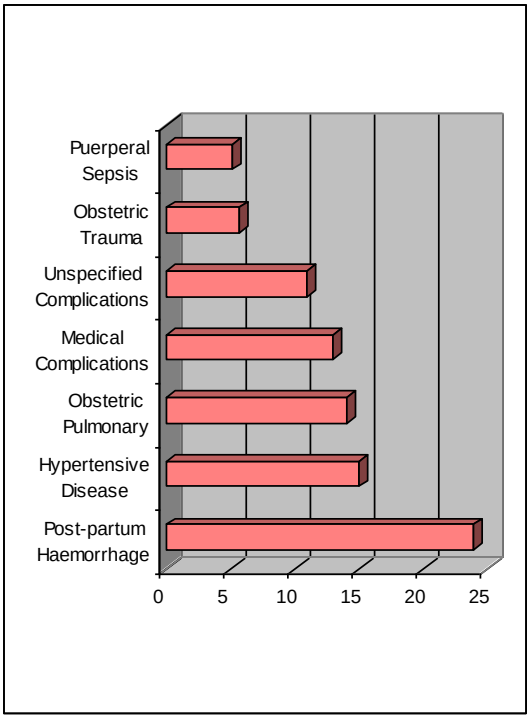
Kelantan was one state that lagged behind in the decline in maternal mortality. Achanna noted 169 maternal deaths over 8 years from 1985, with a rate of 0.61 and 0.51 per 1,000 at the beginning and end of the period respectively. Haemorrhage, sepsis and pregnancy hypertension accounted for 62% of the deaths. Grandmultigravids constituted 47% of the deaths and 56% of the deaths occurred in the home setting or in transit to a hospital.

Sabah and Sarawak did not appear to fare badly with regards to maternal deaths, according to the notification system as shown in Table 2.7. The figures are comparable, if not better than the peninsula. This was however, according to the notification system in use in the MOH. With the new system of maternal death enquiry a different picture has come to light.

Confidential Enquiry into Maternal Deaths

Since 1991 Malaysia has had a confidential enquiry system under a national technical committee to review all maternal deaths. With this improved enquiry in place the number of maternal deaths discovered has increased. Over 5 years from 1991 there were 1066 maternal deaths discovered, but only 929 directly or indirect due to pregnancy. The remainder were due to fortuitous deaths. From these enquiries a higher maternal mortality rate has come to light instead of the one derived from the traditional disease reporting means, given in the tables above. There were 251 maternal deaths discovered in Malaysia in 1995 giving a rate of 47 per 100,000 and 220 deaths and a rate of 41 per 100,000 in 1996.

Figure 2.7 The percentage of cumulative maternal deaths from the 7 leading causes between 1991 and 1996 in Malaysia (n=1400).



These data however show that the 4 main causes of maternal deaths remain as post-partum haemorrhage, hypertensive disease of pregnancy, obstetric pulmonary embolism and associated medical conditions. The relative proportions of these causes over 6 years from 1991 to 1996 are given in figure 2.7.

Sabah has recorded the highest maternal death rate over the last few years in review with rates between 70-90 per 100,000. Kelantan falls within the average and Sarawak fares as one of the better states. Kuala Lumpur has the lowest maternal death rate.

By ethnic breakdown, Chinese have the lowest maternal death rates, followed by Malays and Indians (Table 2.8). However, as a group the other indigenous races (OIR) have a noticeably higher maternal mortality rate. Within that group the Orang Asli in Semenanjung, the Bajau and the smaller and more remote tribes of Sabah and Sarawak are the ones who account for the higher rates. The Orang Asli who form only about 0.6% of the national population account for 2-5% of the maternal deaths, and therefore have a rate 4-8 times the national average. Immigrants also form another high risk group. In 1995 and 1996 they accounted for 17% of maternal deaths. 70% of maternal deaths among immigrants occur in Sabah and they account for more than half the maternal deaths there.

Table 2.8 Maternal mortality (per 1,000) by ethnic groups in Malaysia

Year	Malays	Chinese	Indians	OIR	Total
1995	0.43	0.18	0.49	0.93	0.47
1996	0.36	0.24	0.39	0.46	0.40

(OIR=other indegenous races)

In a review of maternal deaths over 5 years from 1991, Ravindran *et.al*. found that 2.2% (23 cases) of maternal deaths were due to liver disease. Hepatitis (26%), acute fatty liver of pregnancy (26%) and septicaemia (17%) were

the main liver diseases. These diseases tended to affect women of low parity and presented between the 28th-37th weeks of gestation.

Reference

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Suleiman AB, Matthews A, Ravindran J et.al. A strategy for reducing maternal mortality. Bull of the WHO. 77:190-193 1999.

Ravindran J, Jayadev R, Lachmanan SR and Merican I. Maternal deaths due to liver disease in Malaysia. Med J Mal. 55:209-219 2000.

OBSTETRIC PULMONARY EMBOLISM

Ravindran reported that obstetric pulmonary embolism accounted for 37(18%) of maternal deaths throughout Malaysia in 1991. The majority of patients died withing an hour of developing symptoms. Obstetric pulmonary embolism consists of amniotic fluid embolism and blood clot embolism. The former acounted for 15 deaths and the latter 22 deaths, however these were clinical diagnoses as post-mortem examinations were not done in most cases. The typical profile of such a patient was a Malay mother in the "non-risk" parities aged between 31-35years.

Reference

Ravindran J. Sudden Maternal Deaths probably due to obstetrical pulmonary embolism in Malaysia for 1991. Med.J.Mal 49: 53-61 1994.

NEONATAL PAEDIATRICS

PERINATAL MORTALITY

Stillbirths and early neonatal deaths (before 7 days of life), that constitute perinatal mortality, is accepted as an indicator of the efficiency of obstetric services in a population, though it is also used as an indicator of nutrition. Looking at the services in the largest centre, the KL Maternity Hospital in 1970 Ariffin and Thambu observed an overall rate of 42 per 1,000. It was most significantly different between 'booked', that is, ante-natally seen cases, (24 per 1,000) and 'unbooked' (102 per 1,000) cases. Prematurity (35%), bronchopneumonia (21%) and hyaline membrane disease (17%) were the leading causes of neonatal deaths. Toxemia, abnormal presentation and abruption were the commonest causes of stillbirths.

Table 2.9 Perinatal mortality rate by ethnic groups

Year	Malays	Chinese	Indians	All races
1970	41.6	26.4	55.5	37.8
1975	36.0	23.7	42.3	32.2
1980	30.7	19.3	34.9	27.9
1985	21.3	12.4	24.4	19.3
1989	16.6	10.3	18.3	15.5
1995				9.8

Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Table 2.9 gives the perinatal mortality rate in Malaysia over the last 20 years. The rate has consistently been higher among Indians than either Malays or Chinese. Arumugam, however,

noted that in the UH, perinatal mortality was lowest among Malays, noting that these Malays had a significantly better social class distribution. This indicates that perinatal mortality was a function of socio-economic circumstance and not intrinsic to a race. Ong studied the obstetric outcome of Orang Asli women at the Gombak Hospital in 1974 and found a comparable perinatal mortality rate and other problems. The perinatal death rates in Sabah and Sarawak also fell within the range of those of the other states.

The Malaysian Paediatric Association collected data on very low birth weight infants in first 6 months of 1993. 868 babies weighing less than 1500gm at birth were admitted to 23 paediatric centres which was estimated to be more than 90% of all such admissions in the country. The death rate in hospital was 35% among those born in centres with 'level 3' intensive care nurseries compared to 45% for those born outside such centres. 73% were born in 'level 3' centres. Hyaline membrane disease accounted for 48% of these deaths. Other major causes of death were post-partum infection (18%), pulmonary immaturity (14%) and congenital malformations (6%).

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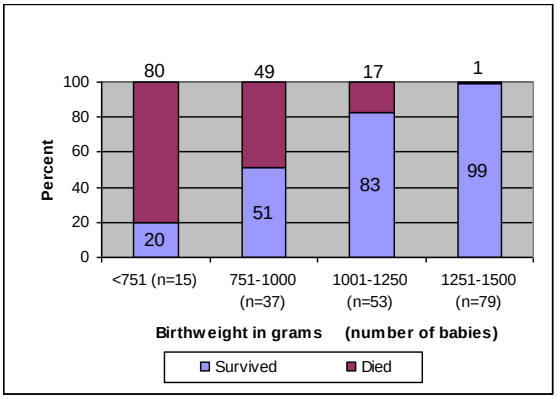
PREMATURITY AND LOW BIRTH WEIGHT

In the KL GH, Boo reported that out of 52,877 livebirths in 2 years, 1987 and 1988, there were 102-113 low birth weight babies (LBW ≤2.5kg) per 1,000 livebirths, and 9-11 very low birth weight babies (VLBW≤1.5kg) per 1,000 livebirths. The risk of neonatal mortality (death before 30 days) was 1.15 times normal for LBW babies and was 1.27 time normal for VLBW babies. Neonatal mortality was highest among Indians and lowest among Chinese. More than 75% of neonatal deaths were perinatal deaths (before 7 days of life). In a further series of 329 consecutive VLBW neonates over 16 months from 1989, Boo noted that 60% died and they accounted for 60% of all neonatal deaths. The 3 most common clinical problems were respiratory distress syndrome (73%), septicaemia (28%) and intraventricular haemorrhage (22%). The prime causes of neonatal septicaemia were multiresistant *Klebsiella* (52%), and *Acinetobacter* (15%). Septicaemia was fatal in 71%. The leading causes of death was respiratory distress syndrome (33%), septicaemia (30%) and intraventricular haemorrhage (18%).

Figure 2.8 Survival rates by birthweight in the UH 1994 to 1996.



Over 2 years from 1994, Chye and Lim reported that for 184 VLBW infants without congenital malformations, 78% survived to be discharged from special care nursery in UH. Of the 40 who died, respiratory distress (63%), infections (30%), gastrointestinal pathology (5%) and intracerebral haemorrhage (2%) were the

causes of death. Mortality was higher for babies ≤1kg (odds ratio [OR]3.9), gestational age ≤28 weeks (OR1.8) babies who needed ventilatory support (OR 2.7) and for boys (OR 1.8). The rates of survival for babies of 4 different birthweight categories is given in Figure 2.8.

In Kelantan, Halder *et.al*. observed that there were 7.5 VLBW babies per 1,000 livebirths in HUSM in 1992. They numbered 60 in total. In addition there were 32 outborn VLBW babies admitted to the neonatal care unit. 33% of these 92 babies had neonatal sepsis and the mortality rate was 43%. 80% of the babies had blood cultures positive for gram negative bacteria, sensitive only to imipenem.

In a prospective study of 88 VLBW babies seen over 5 months, Boo *et.al*. reported that periventricular haemorrhage was detectable on ultrasound in 98%, all occurring by the 5th day of life. This appears to be much higher than developed countries where figures of less than 50% are reported. 20% had grade I, 61% grade II, 8% grade III and 12% grade IV lesions. 64% were symptomatic. Symptoms included shock, pallor, a low haematocrit, convulsions and a bulging anterior fontanelle. 43 of the 86 (50%) of those affected died. 67% of the survivors had residual enlarged ventricles.

Folllowing up 103 VLBW babies at 6 months Teoh *et.al*. noted that 32% developed retinopathy of prematurity. 61% had stage 1 and 2 disease, the rest fared worse. Duration of oxygen therapy and exchange blood transfusion were the only two significantly associated risk factors. Among 100 surviving VLBW infants at the UH over 2 years from 1994, 15 had retinopathy of prematurity, 5 of which were severe.

Among 127 VLBW babies who survived the neonatal period over 3 years from 1989, Boo *et.al*. found that, compared to normal weight babies, they had an 8 times risk of failure to thrive, 8.6 time risk of cerebral palsy, 12 times risk of hearing loss and 8 times risk of visual loss. They also had a 3.7 times risk of wheezing and were 2.3 times more likely to be hospitalised again.

The Malaysian Paediatric Association carried out a 6 months study of VLBW babies (≤1.5kg) at 23 centre in Malaysia with Level 3 nurseries in 1993. 77% were born in government hospitals with paediatricians, 8% were born in government hospitals without paediatricians, 4% were born in private hospitals and maternity homes, 7% were born at home and 4% were born in other places, mainly on the way to hospital. There was a total of 868 babies. All the races were almost equally represented, boys slightly outnumbering girls (54:46).The survival rate was 71% for babies weighing 1251-1500gm, 61% for those 1001-1250gm, 30% for those 751-1000gm. There were 38 very small babies weighing 501-750gm of whom 3(8%) survived. 9 obstetric factors did not have a significant influence on the survival of these neonates, namely, maternal age, parity, maternal diabetes melitus, maternal anemia, placenta praevia, abruptio placenta, premature rupture of membranes, prolonged rupture of membranes and maternal infection. 3 factors improved the survival rates of these infants. These were the use of antenatal steroids in mothers, the presence of hypertension in pregnancy and delivery by Caesarian section. Hypertension is noted to be a favourable factor because these babies were generally more mature, as more of them were of greater than 32 weeks gestation. They were small for their age.

In a 7 month study from 1995 at the KL GH, Boo and Goh reported that 73% survived to go home, meaning a decrease in neonatal mortality in this group to 27%. Of the surviving children the breastfeeding rate at discharge was 40%. The significant predictors of breastfeeding were, Malay mothers, mothers with 7-9 years of education and earlier commencement of enteral feeds in the VLBW infants.

Among 152 Extremely Low Birthweight (ELBW≤1000gm) babies seen over a 21 month period at the KL GH, Boo reported that 32% survived. Besides a better birthweight and being

given nasal continuous positive airway pressure for the treatment of respiratory distress syndrome, the only other factor correlating to a better survival was when the babies received expressed breastmilk. Lim *et.al*. however found that expressed breastmilk-fed LWB babies (1.8-2.5kg) in the neonatal intensive care did not gain weight as much as formula fed ones.

(see protein energy malnutrition)

References

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Boo NY, Ong LC, Lye MS et.al. Periventricular haemorrhage in very low birth weight Malaysian neonates. J Trop Pediatr. 39:224-229 1993.

Teoh SL, Boo NY, Ong LC et.al. Duration of oxygen therapy and exchange transfusion as rick factors associated with retinopathy of prematurity in very low birthweight infants. Eye 9:73-737 1995.

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Suleiman AB, Matthews A, Ravindran J et.al. A strategy for reducing maternal mortality. Bull of the WHO. 77:190-193 1999.

Boo NY, Puah CH and Lye MS. The role of expressed breastmilk and continuous positive airway pressure as predictors of survival in extremely low birthweight infants. J Trop Peadiatr 46:1-20 2000.

Lim NL, Cheah I and Soosai. Breastmilk feeding status and weight gain of low birthweight infants in a neonatal intensive care unit. Med J Mal. 56:65-70 2001.

MECONIUM ASPIRATION SYNDROME

Malik and Hillman noted that meconium staining of neonates occurred in 5.6% of 2677 deliveries over 5 months in HUSM in 1991.The meconium aspiration syndrome occurred in 2.0% or 53 neonates. Neonates with meconium in the trachea were more often ventilated mechanically and stayed in hospital longer than those without. There was one death and one case of cerebral palsy among the those with the meconium aspiration syndrome.

Reference

Malik AS and Hillman D. Meconium aspiration syndrome and neonatal outcome in a developing country. Ann Trop Paediatr 14:47-51 1994.

NEONATAL SEPTICAEMIA

Boo and Chor showed that over 6 years from 1986 to 1991, neonatal septicaemia occurred in 5.2-10.2 per 100 admissions in GH KL. Septicaemia accounted for between 11 to 30% of all neonatal deaths. Case fatality ratios ranged from 23% to 52%. The most common pathogens isolated were *Staph. aureus* and *Klebsiella sp*.

Choo, Wan Ariffin and Chuah estimated that the incidence of neonatal septicaemia was 2.13 per 1,000 live births in Kelantan in 1985 with a case fatality rate o 42%.Of the 84 cases 52% had early onset (before 1 week of life) septicaemia. The main organism in this group were *Klebsiella*, *Pseudomonas sp*, *E. coli* and *Streptococcus*. The mortality was higher in this group especially among the premature. The remainder 48% had late onset (after 1 week of life) septicaemia, with a mean age of 13.6 days at presentation. In this group *Staphylococcus* was the main pathogen.

Reference

Choo KE, Wan Ariffin WA and Chua SP. Neonatal septicaemia in Kelantan Malaysia. Ann Aca Med Sing. 17:438-442 1988.

Boo NY and Chor CY. Six year trend of neonatal septicaemia in a large Malaysian maternity hospital. J Paediatr Child Hlth. 30:23-27 1994.

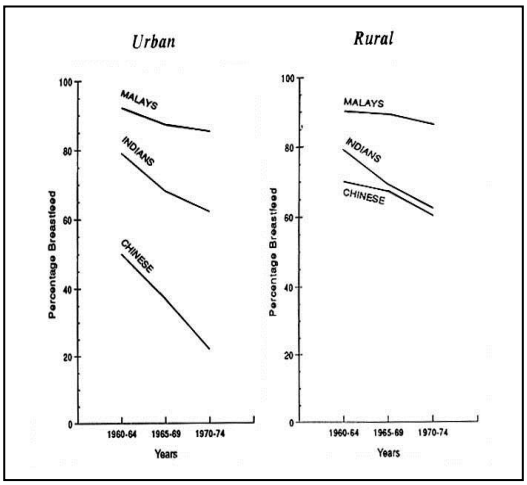
BREAST FEEDING

It is generally believed that Malays breast feed their babies more than Chinese. Pathmanathan showed this to be in fact true in a wide survey of 8,750 infants. In urban areas 47% of infants were breastfed compared to 78% in rural areas. Overall 64% of infants were breastfed but only 40% continued to for a period of six months. Figure 2.9 shows the prevalence of breastfeeding in the three main races in Malaysia over the period 1960-1974. Malays consistently show a prevalence of greater than 80% and the prevalence in Indians decreased from 80% to less then 70% in that period. In contrast, Chinese, especially urban Chinese, recorded rates dropping from about 50% to less than 30%. Ironically, among urban Chinese those with a higher income and education tended to practice breastfeeding less. Chen who looked at a smaller sample of 100 mothers in an urban setting at about the same time, observed a breastfeeding rate of 49%, which was 78% among Malays, 55% among Indians and 35% among Chinese.
mothers. It revealed that only 48% of mothers breastfed and only 3.6% continued for 6 months, an undesirable trend. The Malaysian Code of Ethics for Infant Formula Products was introduced in 1979 and revised in 1983. Since then the Ministry of Health has tried hard to promote breastfeeding.

In 1990 Chia observed, in a general practice in Batu Pahat, that 61% of mother breastfed with similar racial and economic status trends. Only 14% were breastfeeding at 6 months.

In 1993 Yusof *et.al* surveyed 96 mothers in Kelantan about their knowledge about breastfeeding. 98% of mothers knew at least some of the benefits of breastfeeding. However 66% thought that colostrum was bad or dirty and discarded it. 78% believed breast milk was best while 22% believed that infant formula was best. In practice 95% of the mothers (91% of whom were Malays) breastfed, but 72% gave infant formulas in addition to breast milk. 64% continued to breastfeed for up to 6 months.

Figure 2.9 Trends in breast feeding in urban and rural areas in Malaysia 1960-1974



A decade later a large Ministry of Health Survey was done in 1983 among 91,73. The Ministry of Health launched a large campaign to encourage breast feeding throughout all its hospitals and agencies beginning 1993 following the UNICEF Global Criteria of 1991. Hospital were required to meet set criteria and in 1998 the WHO recognised Malaysia for having attained 'baby-friendly' status in all its government hospital.

The National Health and Morbidity Survey of 1996 found that 97% of Malays, 83% of Indians but only 61% of Chinese mothers breastfed their

babies. This extensive study showed a reassuring reversal of the declining prevalence of breast feeding that was observed in 1983. The Chinese however continue to lag behind. Ho found in 1994 that although 82% of Chinese mothers in Ipoh initiated breastfeeding only 10% were still doing it after 8 weeks. Teh *et.al*. determined to study whether this was intentional in a survey of 30 Chinese primiparae. 19 actually intended to breatfeed for 6 weeks or more but 73% did not achieve their aim and their experience discouraged them from exclusive breastfeeding in future pregnancies.

References

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Chen ST. Infant feeding practices in Malaysia. Med.J.Mal. 33: 120-124 1978.

Chia SE. A survey of breastfeeding practices in infants seen in a general practice. Med.J.Mal. 47:134-138 1992.

Yusof YAM, Mazlan M, Ibrahim N and Jusoh NM. Infant feeding practices and attitudes of mothers in Kelantan towards breastfeeding. Med.J.Mal. 50:150-155 1995.

Yasmin AM. Infant feeding practices and attitudes of mothers in Kelantan towards breastfeeding. Med J Mal. 50:150-155 1998.

eh SC, Chong SI, Tan HH and Ho J. Chinese mothers intention to breastfeed, actual achievement and early postnatal experience. Med J Mal. 55:347-351 2000.

Chan SK and Asirvanthan CV. Feeding practices of infants delivered in district hospitals during the implementation of baby friendly hospital initiative. Med J Mal. 56:71-76 2001.

CHAPTER 3

CHROMOSOMAL AND GENETIC DISEASES AFFECTING MULTIPLE ORGAN SYSTEMS

There are now over 1,000 human chromosomal abnormalities, and over 5,000 human single gene traits known. There are over 2,000 autosomal dominant diseases, over 600 autosomal recessive and nearly 200 X-linked conditions known. Year by year these numbers keep increasing. The entire human genome of about 3,000,000 bases was completely sequenced in the year 2000 and it is estimated that there are between 30,000 to 100,000 human genes. However only a fraction of the genes have been mapped and their function determined. But with the complete sequence of the genome available human knowledge about the genetic basis of diseases is set to expand greatly in the next few decades.

Many rare genetic diseases occur sporadically in Malaysia as in other parts of the world but there are some local peculiarities. Therefore, where there have been local reports mention is made when possible. However, many genetically determined diseases affect mainly one system and they are discussed in the section on that system. Only the chromosomal defects and those gene defects that affects more than one organ system or fits no system are listed here. Congenital syndromes that appear to be genetic in origin in which the mode of inheritance is uncertain are also listed here.

CHROMOSOME DISORDERS

In 1990, 24,295 babies were delivered alive in the Maternity Hospital Kuala Lumpur. A study detected chromosomal abnormalities in 29 neonates giving a rate of 1.2 per 1,000. The classic trisomy syndromes were observed in 26. 2 had translocations and one had an abnormal chromosome. The frequency per 1,000 was 1.4 among Malays, 1.2 among Chinese and 0.6 among Indians.

Reference

Norlasiah IS, Clyde MM and Boo NY. Cytogenetic study of Malaysian neonates with congenital abnormalities in Maternity Hospital Kuala Lumpur. Med.J.Mal. 50:52-58 1995.

DOWN'S SYNDROME

Down's syndrome is certainly the most common of the well known chromosomal disorder. It is usually associated with trisomy 21, although it can be caused by other conditions such as translocations. In 1966 Stevenson *et.al.* mentioned that out of 10,000 births at the KL GH there were 3 cases of Down's. That is really a very low rate if it is accurate. In a 3 year survey, from 1984 at the Alor Star GH, Goh and Yeo found a rate of 1:791 livebirths or 1.26 per 1,000. The incidence in Malaysia was again explored in 1987 by Hoe, Boo and Clyde at the UKM. Looking at 34,522 births at the KL GH over 18 months they noted similar rates in all the major races. In Malays the rate was 1:981, Chinese 1:940 and Indians 1:860. The overall rate was 1:959 or 1.04 per 1,000 livebirths. In the karyotype study in 1990 mentioned above, the rate of Down's syndrome was 1:1012 births, 85% of those having clinical features of the syndrome. As elsewhere mothers above the age of 35 years showed a higher incidence of Down's syndrome babies. The rate rises from 1:1,670 for women 35 years and below to 1:96 at the age of 40 years and 1:29 at 45 years.

Our incidence appears to be in the lower range. Other countries mainly report rates between 1:550-850. Unlike other studies this

latter study noted a female preponderance which was accounted for mainly by the Indians among whom there were 6 girls and no boys.

Hoe *et.al*. remarked that in a series of 34 neonate's with Down's syndrome, they found that 50% had congenital heart defects. The commonest lesions were ventricular septal defects (VSD)(7), patent ductus arteriosus (PDA)(3), atrio-ventircular canal defects (2), VSD with PDA (2), and a case each of hypertrophic cardiomyopathy, hypertrophic obstructive cardiomyopathy and complex cyanotic heart disease. Only 47% of these babies with congenital heart defects had symptoms.

References

Goh PP and Yeo TC. Major congenital anomalies in livebirths in Alor Star General Hospital during a three-year period. Med.J.Mal. 43:138-149 1988.

Hoe TS, Boo NY and Clyde MM. Incidence of Down's syndrome in a large Malaysian maternity hospital over an 18 month period. Sing.Med.J. 30:246- 248 1989.

Boo NY, Hoe TS, Lye MS et.al. Maternal age-specific incidence of Down's syndrome in Malaysian neonates. J Sing Paediatr Soc. 31:138-142 1989.

Hoe TS, Chan KC and Boo NY. Cardiovascular malformations in Malaysian neonates with Down's syndrome. Sing Med J 31:474-476 1990.

PATAU'S SYNDROME

This is due to trisomy 13. In a series of chromosome studies between 1973 and 1975, from cases all over KL, Yip, Yong and Dhaliwal detected 3 cases of Patau's in comparison to 51 Down's cases. Goh and Yeo however, found 4 in 19,769 livebirths in Alor Star giving an incidence of 1:4,942 or 0.2 per 1,000. 2 cases were detected among 24,295 livebirths in KL in 1990 giving a rate of 1:12,148.

References

Yip MY, Yong HS and Dhaliwal SS. Human chromosomal studies in Kuala Lumpur. Med.J.Mal. 32:316-320 1978.

Goh PP and Yeo TC. Major congenital anomalies in livebirths in Alor Star General Hospital during a three-year period. Med.J.Mal. 43:138-149 1988.

EDWARD'S SYNDROME

Trisomy 18 causes Edward's syndrome. In the series by Yip, Yong and Dhaliwal 4 cases of Edward's syndrome, all females, were noted. Goh and Yeo recorded 3 cases in Alor Star in 3 years estimating the incidence at 1:6,590 livebirths, or 0.15 per 1,000 and the karyotype study in 1990 in KL detected 2 cases giving a rate of 1:12,148.

TRISOMY 9

Features of complete or partial trisomy 9q consists of psychomotor retardation, dolichocephaly, beaked nose, deep set eyes and long fingers and toes. Three siblings with a partial trisomy 9 due to a translocation involving chromosome 6, 8 and 9 inherited from their mother has been reported. They had features compatible with that described in the literature.

Reference

Ten SK, Chin YM, Tan SK and Hassan K. Three cases of partial trisomy 9q in one generation due to maternal reciprocal t(6;8;9) translocation. Clin Genet 31: 359-365 1987.

TURNER'S SYNDROME

Turner described the syndrome that bears his name in 1938. They were short females with amenorrhoea, webbed necks and cubitus valgus. Other hallmark features have since then been added on. At first they were found to have the chromosome constitution, 45 XO, but various other karyotypes have been described that give the same phenotype, with the common factor

being one defective X chromosome. HB Wong in Singapore has documented some cases.

In Malaysia, Yip, Yong and Dhaliwal noted 4 cases in comparison to 51 Down's. This is probably a low detection rate as Turner's is thought to be only about 4 times less common than Down's. But Goh and Yeo found an even lower rate of 1:19,769 livebirths in Alor Star.

FRAGILE X SYNDROME

This is a fairly newly described entity whose faetures are mental retardation and a cytogenetically detectable marker X chromosome. With the exception of Down's syndrome, this is the most common chromosome abnormality associated with mental retardation in males. Affected males have a moderate to severe mental handicap. Female heterozogotes have a wider range of intellectual capacity. In Malaysia the prevalence has not been studied either in mental institutions or in the community but Ten, Chin, Jamilatul Noor and Hassan have demonstrated an Indian family with 3 sons who are all affected.

Reference

Ten SK, Chin YM, Jamilatul Noor MBP and Hassan K. The fragile X syndrome: first family reported in Malaysia. Sing.Med.J. 26:372-378 1985.

KLINEFELTER'S SYNDROME

Klinefelter, Reifenstein and Albright first describe this syndrome in 1942. Persons affected are phenotypically males with small testes, gynaecomastia and a feminine voice. Karyptypically they have one or more extra X chromosomes. Kannan Kutty *et.al.* reported the first example in Malaysia in 1968. It is rare and its incidence here is probably not any different from elsewhere.

XX MALE SYNDROME: It has been estimated that 1:20,000 to 25,000 phenotypical males have a 46XX karyotype. Affected individuals resemble Klinefelter's syndrome but tend to be shorter, have a higher incidence of hypospadias and no increased incidence of mental deficiency. One patient has been described in Malaysia.

References

Kannan Kutty M, Dutt AK, Lopez G, Ramanathan K, Pillay RP and Omar A. Klinefelter's syndrome, a case report. Med.J.Mal. 23:51-53 1968.

Tan TT and Khalid BA. Primary infertility in a phenotypic male with 46XX chromosomal constitution. Postgrad Med J 69:315-317 1993.

HERMAPHRODITE

A true hermaphrodite is a person with a chromosome mosaic of 46XX/46/XY. A case, male in phenotype has been reported, diagnosed at age nine. He grew up and married.

Reference

Yip CH and Pathmanathan R. True hermaphrodite - a case report. Sing Med J 37:117-118 1996.

SINGLE GENE DISORDERS AFFECTING MULTIPLE ORGAN SYSTEMS

LEOPARD SYNDROME

Pedigree studies indicate that this is an autosomal dominantly inherited condition with high penetrance and variable expressivity. Its features include lentigines (brown macules) cardiac abnormalities and sexual infantilism. It is a rare condition and only one case has been reported by Ting and Ng at the UH. He had no other affected family member.

Reference

Ting HC and Ng SC. The Leopard (multiple lentigines) syndrome: a

case report. Med.J.Mal. 38:98-101 1983.

OTHER CONGENITAL SYNDROMES OF UNKNOWN INHERITANCE AFFECTING MULTIPLE ORGAN SYSTEMS

CEREBRO-COSTO-MANDIBULAR SYNDROME (CCM)

The CCM is a very rare dysmorphic syndrome closely resembling Pierre-Robin syndrome with the added characteristic multiple posterior rib-gap defects seen on radiograph. These consist of fibroconnective tissue, striated muscle and small foci of cartilage undergoing calcification. Inheritance appears to be autosomal recessive but also been documented to occur autosomal dominantly. The karyotype appears normal. Lim and Koh have reported one case in the UH.

Reference

Lim CT and Koh MT. Cerebro-costo-mandibular syndrome. Australas Radiol 36:158-159 1992.

CHONDRODYSPLASIA PUNCTATA SYNDROME (CD)

The CD syndrome is characterised by punctate calcifications in the epiphyseal regions of the long bones. Wong and Lin described an Indian child of a consanguinous marriage with the severe rhizomelic type of the disease. The child was first seen at 14 days of life, was below the 3rd percentile in head circumference and weight, had bilateral cataracts, contractures of the knees, elbows and interphalangeal joints of the hands. The child died at 9 months.

Reference

Wong CS and Lin HP. The chondrodysplasia punctata syndrome – the rhizomelic type. J Sing Paedtr Soc. 21:160-162 1979.

ECTRODACTYLY ECTODERMAL DYSPLASIA CLEFTING (EEC) SYNDROME

The collection of congenital malformations the form the EEC syndrome was first described by Cockayne in 1936 but gained its name later following more case reports. As its name describes those affect with this condition have lobster claw deformities of the extremities, clefting of primary and secondary palate, and abnormalities of the teeth, hair and atresia of the lacrimal apparatus. Omar and Jidon reported one case of a girl born in 1983 and Ram *et.al*. have reported a neonate who died with a perimembranous type of ventricular septal defect who died of sepsis at 27 days of life. Choong and Norazlina described another case in 2001, a Chinese man 36 years old. It is a very rare syndrome estimated to have an incidence as low as 1.5 per 100 milion. It shows both an autosomal dominant inheritance with variable penetrance as well as sporadic occurrence.

References

Omar I and Jidon AJ. EEC syndrome with urogenital anomalies and compound naevus. Med.J.Mal. 48:364-368 1993.

Ram SP, Noor AR and Ariffin WA. A neonate with ectrodactyly ectodermal dysplasia clefting syndrome and ventricular septal defect. Sing.Med.J. 35:205-207 1994.

Choong YY and Norazlina B. Ectrodactyly, ectodermal dysplasia and cleft lip-palate syndrome. Med J Mal. 56:88-91 2001.

GOLDENHAR'S SYNDROME

Described by Goldenhar in 1952, this condition is characterised by oculo-auriculo-vertebral dysplasia. Besides these constant features, other associated anomalies may be present. Fong *et.al.* described two cases at the UH in 1976 and Mohandas and Selvarajah reported another case at GH KL in 1988, of these cases two were Chinese one was an Indian. Goh and Yeo noted one case out of 19,769 livebirths in Alor Star GH.

References

Fong ACH, Vijendran M, Chandran S and Ng KK. Goldenhar's syndrome. Med.J.Mal. 30:299-303 1976.

Mohandas K and Selvarajah S. Failed intubation in a case of oculoauriculovertibral dysplasia (Goldenhar's syndrome). Med.J.Mal. 43:255-258 1988.

GORLIN'S SYNDROME

Gorlin's syndrome, also known as multiple basal cell naevi syndrome, classically consists of a triad of basal naevi, jaw cysts and rib anomalies. There can be a wide associated array of signs and symptoms involving nearly every system of the body. Ling, Couper and Hu noted one case, an Indian boy, at the UH.

Reference

Ling KC, Couper NTA and Hu WS. The Gorlin's syndrome: a case report. Med.J.Mal. 39:173-176 1984.

HOLOPROSENCEPHALY

Holoprosencephaly results from a failure of the embryonic prosencephalon, the anterior segment of the brain, to undergo segmentation and cleavage. Concurrent facial anomalies can include cyclopia (one eye), cleft lip, cleft palate and hypotelorism. Ram *et.al* have described 2 cases of female babies affected in Kelantan. One had a single nostril and asphyxiated at birth. Karyotyping on this child and her family members was normal.

Reference

Ram SP. Noor AR, Mahbar Z and Krishna TN. Holoprosencephaly in neonates. Int J Pediatr Otorhinolaryngol 29:65-71 1994.

NOONAN SYNDROME

Described by Noonan in 1963, this collection of congenital malformations include facial anomalies, short stature, congenital heart disease, delayed puberty, skeletal, genital abnormalities and mental retardation. Cases are seen in Malaysia and case reports of 3 Malay children in Kelantan have been recorded.

Reference

Ram SP and Krishna TN. Cardiopathy and ocular abnormalities in Noonan syndrome. Sing Med J 35:397-399 1994.

SITUS INVERSUS

Some rare individuals who are perfectly normal have all their organs right to left internally. Zohra Banu described one case and Goh and Yeo reported one case in a study of 19,769 livebirths over 3 years in Alor Star. Wong and Chong have noted a case with severe coronary artery disease who underwent successful coronary bypass grafting like any ordinary person.

References

Zohra Banu S. A case of situs inversus. Med.J.Mal. 31:236-240 1977.

Wong PS, Chong CL. Multiple coronary artery bypass grafting in dextrocardia: case report. Med J Mal. 54:514-516 1999.

PROGERIA

Ageing is still a mystery to science and these incredible rare cases where little children turn into old people are often reported in the mass media. In Malaysia one case has been reported in the medical literature and two cases, special in that they are twins, were reported in the newspaper.

Reference

Omar A. A case of the Hutchinson-Gilford progeria syndrome. Med.J.Mal. 37:362-364 1982.

The New Strait Times, Lifestyle p1 31 December 1991.

CHAPTER 4

NUTRITIONAL DISORDERS

INTRODUCTION

It is well established that the overall nutritional status of the population of a country is closely linked to its economic wealth. Like most countries in the world Malaysia has a history in which hunger and malnutrition were prevalent. In this respect Malaysia has done well this century, achieving an average annual economic per capita rate of growth of about 7 to 8% in the past few decades since independence, ensuring enough resources for food supply.

Table 4.1 Calories and protein availability in Peninsula Malaysia per person per day

	Calories		Protein (gm.)	
	1961-70	1971-78	1961-70	1971-78
Cereals				
Rice	1023	1095	18	19
Wheat	221	250	6	6
Others	89	48	2	2
Roots and Tubers	31	32		
Sugar	306	324		
Pulses	31	24	2	1.5
Tree nuts	48	44	2	2
Vegetables	26	25	1	1
Fruits	87	81	1	1
Meat	89	86	5	5
Poultry	16	21	2	2
Fish	41	43	7	7
Eggs	21	30	2	3
Milk	70	83	2	3
Oils and Fats				
Vegetable	161	186		
Animal	58	50		
Stimulants/Spices	22	20		
Alcohol beverage	113	108		
Total	2453	2550	50	53

National food supply analysis and its presentation as a food balance sheet was developed by the FAO for disclosing trends in the availability of food which can be translated into calories and protein per head of population. The analysis done for Malaysia for the 1960s and 1970s is shown in Table 4.1.

Expressed as a percentage of requirement, calorie availability stood at 123% in 1984, while protein availability was at 108%. This indicates that at a national level, if food was equitably distributed without wastage, every person in Malaysia would have sufficient nutrition. However, in the present world that would not be possible and the problems of health due to inadequate nutrition are still prevalent.

Between 1961 and 1984 the total available calorie intake per person in Malaysia increased by 8.4%, although the amount of calories available from animal sources increased by 35%. The proportion of calories accounted for by cereals decreased by 10% in that period. The increase in the fat supply per person was 38% with animal fat consisting 36% of total fat supply. In 1961 the per capita consumption of fats (and oils) in Malaysia was 49g a day, with vegetable oils forming 20%. By 1984 the per capita consumption of fats had increased to 84g a day and in 1994 to 88g a day. Vegatable oils now form 43-50% of fats consumed.

Muslims in Malaysia observe a fast during the month of Ramadan. In a small study of 21 subjects Husain et.al. noted the subjects experienced a decrease in body mass, females losing more weight and subcutaneous fat than males while males experienced a greater reduction in resting heart rate than females.

Table 4.2 Incidence of poverty in Peninsula Malaysia 1970-1984.

	Total households ('000)		Incidence of poverty (%)	
	1970	**1984**	**1970**	**1984**
Rural	1,203	1,629	59	24
Rubber smallholders	350	155	65	43
Padi farmers	140	116	88	58
Estate workers	148	81	40	20
Fishermen	38	34	73	28
Coconut smallholders	32	14	53	47
Other argiculture	144	462	89	34
Other industries	351	764	35	10
Urban	403	992	21	8
Trade and services	251	473	18	5
Manufacturing	84	132	24	9
Transport and utilities	42	74	31	4
Construction	20	87	30	6
Mining	5	8	33	3
Agriculture	-	38	-	24
Others	-	181	-	17
TOTAL	1,606	2,621	49	18

Reference

Husain R, Duncan MT, Cheah SH and Ch'ng SL. Effects of fasting in Ramadan on tropical Asiatic Moslems. Br J nutr. 58:41-48 1987.

Malaysia has a longstanding history of nutrition research. In fact many of the descriptions of nutritional defienciency and pioneering work in vitamin research originated in Malaysia under people such as Fraser and Staton who were directors at the IMR. Because of the great amount that has been written, it would be difficult to review all the work especially from the historical point of view. Tee, at the IMR has compiled an annotated bibliography of over 800 papers on nutrition research in Malaysia. This chapter is a modest attempt to summarise some of the relevant work.

PROTEIN ENERGY MALNUTRITION

It is very obvious that it is possible for total national figures of food supply to conceal poverty and malnutrition in segments of the population bypassed by the economic growth around them. In this respect the prevalence of poverty and several other indicators gives a picture of the general nutritional status of the populace. Direct studies on selected populations also add to the picture.

Population indicators:

Poverty.

Not going too far back in history, the prevalence of poverty by the criteria set by the government was 49% in 1970. But it had dropped to 18% by 1984. The distribution of poverty in the various sectors of the population is given in Table 4.2.

Due to the process of industrialisation and subsequent urbanisation in the early 1970s, there was a large migration into the Kuala Lumpur area. Urban squatters mushroomed and was estimated to be between 25-30% of the population of Kuala Lumpur at its peak. Resettlement of squatters into low-cost flats and wooden long-houses have resulted in a decline in the number of the urban poor in squatter areas to 16% in 1987 and 12% in 1990

Toddler Mortality.

The death rate of children 1 to 4 years has for many years been accepted as a rough indicator of protein-calorie malnutrition. In countries where toddler mortality is high, malnutrition and infective diseases are known to be widespread.

In 1957 the toddler mortality rate in Malaya was 14.1 per 1,000 among Malays, 6.6 among Chinese, 9.0 among Indians and 10.7 per 1,000 overall. Along ethnic lines it was observed that in the first decade after independence, the average annual percentage decline in toddler mortality was highest among the predominantly urban Chinese (8.7%), while the Malays (6.0%) and Indians (4.9%) lagged behind. In the next ten years from 1967 to 1977, the decline in toddler mortality changed in favour of the predominantly rural Malays (7.7%); the Chinese (6.7%) following and Indians (6.3%) again lagging behind. This indicates a quickened pace of improvement in the health and socio-economic conditions of the rural Malays, which was a consequence of government policies to improve the standard of living of the rural people. Twenty years after independence, in 1978, the toddler mortality stood at 2.91 per 1,000 for Malays, 2.38 for Indians and 1.18 for Chinese. In the next decade toddler mortality fell a further 50% and stood at 0.91per 1,000 in 1990. Malays still had the highest rate at 1.04, followed by Indians at 0.77 then Chinese at 0.56. Sabah had a rate of 1.4 while the rate in Sarawak was 0.7. With the toddler mortality rate low the decline in the 1990s has been less noticeable falling to just 0.7 per 1,000 nationally in 1998.

There wass also considerable variation of toddler mortality from state to state and was higher in rural areas. The districts with the highest rates in 1978 were Marang (8.98), Dungun (5.35) and Hulu Terengganu (5.09) in Terengganu, Baling (6.24) in Kedah and Pasir Mas (5.22) in Kelantan. However by 1990 these districts were no longer out-liers. Instead two other remote districts, Ulu Kelantan and Ulu Perak recorded the highest rates.

Low Birth Weight

Maternal nutrition is a major factor influencing birth weight although many other problems of pregnancy can also be responsible. In the early part of this century studies on the maternal health of Indian women in the estates revealed a grim picture of maternal nutritional anemia and high maternal and neonatal mortality, and no doubt low birth weight babies that must have ranked them as one of the most badly off populations in the world. But over the years the nutrition among estate workers has improved. Nevertheless, taking 2.5kg. as the cut-off, in 1978 nationally the rate of low birth weight was highest among Indians (17.5%) followed by Malays (10.8%) and Chinese (7.9%). In the city of Kuala Lumpur, the figure were lower being 14.5% for Indians, 7.6% for Malays and 5.6% for Chinese. Measuring thyroid hormone parameters in mothers in the third trimester in KL in 1993, Sakinah found evidence that Indian women had significantly more protein malnutrition.

Analysing the trend in the birth weight of babies in the different ethnic groups in Malaysia between 1953 and 1959, Thomson noted that Chinese babies were on average heavier than Malays followed by Indians. There seemed to be a trend of the average birth weights increaseing over the years but the Indians lagged behind. In a review of birthweight trends for the years 1973-1977, Chong and Hanis found that the mean weight

of newborn Chinese males (3.16 kg.) was significantly heavier than Malay (3.12 kg.) and Indian (2.97 kg.) babies. Chinese (3.04 kg.) and Malay (3.05 kg.) baby girls were significantly heavier than Indians (2.97 kg.) Malay and Indian babies were significantly heavier than their counterparts a decade earlier but this increase was not seen in the Chinese. The mean gestational period (39.9 weeks) and proportion of full-term births (78%) was similar in all races. Mean maternal age at first birth, 22.9 years, was close in all races.

(see Prematurity)

Direct Assessment:

In contrast to indirect population indicators, cross-sectional nutrition surveys give a comprehensive picture but is limited in scope. Anthropometry is the most widely used index. One common method to categorise malnutrition is to use Waterlow's classification. Deficit in weight for age form a group called `underweight'. Deficit in height for age is termed `stunting' and thought to indicate a previous history of malnutrition. Deficit in weight for height is termed `wasting' considered a sign of current undernourishment. Below in Table 4.3 is a summary of a number of reported studies.

What perhaps needs to be highlighted from the table are the findings among the Orang Asli in remote villages. Studies even in the 1980s, by Khor and Kasim revealed a high rate of moderate and severe stunting and underweight children exceeding 50% among these children.

For Sarawak, papers by Anderson from 1976 to 1978 cover a wide scattering of the population, including Ibans along the Mukah, Lemanak, Sut and Mujong rivers, Bidayuhs at Tebakang, Melanaus along the Tullian, Malays in the Sarawak river delta and Penans in the Mulu area. They report high rates of malnutrition in remote areas. Similar findings are noted in remote areas of Sabah as well.

Ng has expressed doubts about the measurement of mid-arm circumference as a method for detecting malnutrition in our population. Nevertheless data on the normal range of mid-arm circumference and triceps skin-fold thickness have been recorded in several anthropometric studies in children.

Figure 4.1 Percentage of children below 5 years moderately malnourished

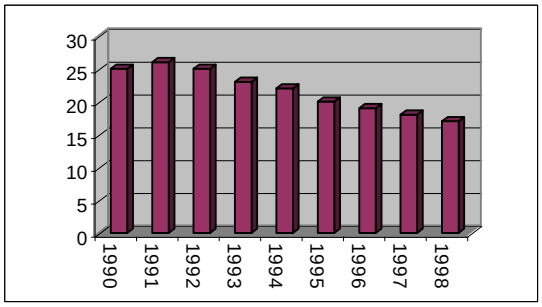
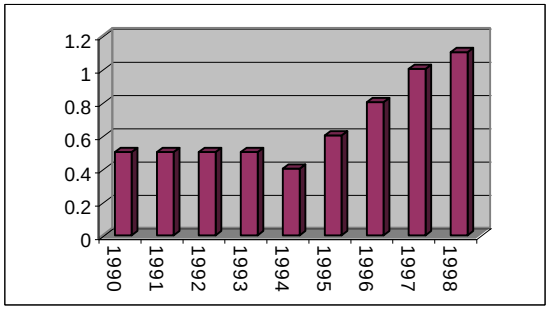


Figure 4.2 Percentage of children below 5 years severely malnourished.



NB: Harvard Standard reference used from 1990-1994 and National Centre for Health Standard used from 1995-1998 for both charts.

Besides antrhopometry, biochemical markers are used in some studies to measure malnutrition. The haematocrit, serum haemoglobin, serum viatmin A, vitamin B1, albumin, and the urine hydroxyproline index have been used. These findings are difficult to tabulate for comparison.

Table 4.3 Prevalence of Protein-Calorie Malnutrition

Area	Population	Race (no.)	Age (yr)	Study	Underweight	Stunting	Wasting
Kuala Langat		Malays (474)	0-5	IMR (1969)		29%	7%
Hulu Terengganu		Malays (207)	0-5	IMR (1969)		58%	14%
Kuala Terengganu		Malays (271)	0-5	IMR (1972		31%	15%
KL& PJ	School Children	(2,340)	6-10	Chen (1977)	27%	25%	9%
		Malays (761)	6-10	Chen (1977)	35%	38%	7%
KL	Urban School Children	Malays (915)	7-12	Rampal (1977)	49%	2%	2%
		Chinese (882)	7-12			2%	2%
		Indians (456)	7-12			6%	5%
Klang	Rural School Children	Malays (836)	7-12		74%	11%**	6%
		Chinese (1531)	7-12			5%**	6%
		Indians (740)	7-12			13%**	9%
KL	Urban Squatters		0-6	IMR (1979)	12%	5%	1%
KL	Urban Squatters	Malays (220)	0-12	Yap (1989)		18.2%	5.4%
		Indians (89)	0-12			14.6%	11.2%
PJ	Urban Squatters	Malays (88)	0-9	Chee (1992)	29%	26%	16%
		Chinese (34)	0-9		4%	5%	3%
		Indians (46)	0-9		11%	3%	9%
Kelantan	Fishing Village	Malays	0-6	IMR (1979)	18%	24%	3%
		Malays (241)	0-12	IMR (1979)		47%	2%
Johore	Padi Farms		0-6	IMR (1981)	37%	36%	3%
Pahang Kelantan Perak	Remote Villages	Orang Asli (566)	0-10	Kasim (1987)	56%	66%	
Batang Padang	Orang Asli Villages	Semai (40g49b)	0-1	Khor (1988)	23%g 24%b	44% 42%	
		(201g) (234b)	1-6		49%g 53%b	63% 73%	8.5% 8.0%
		(252g) (226b)	6-12		46%g 51%b	65% 71%	4.5% 5.5%
		(91g) (87b)	12-18		20%g 65%b	71% 78%	
Sarawak	6th Div	Ibans (140)	0-6	Yap (1985)		25%*	68%*
	Sampled Rural Villages	(641)	0-4	Kiyu (1991)		23.9%	7.8%
Sabah			0-4	(1981)	22%	9%	8%
			5-12		10%	45%	10%
	Tambunan	Kadazan(896)	0-6	Gan (1993)		67%**g** 68%**b**	8% **g** 12% **b**

Note: Underweight, Stunting and Wasting are Waterlow's moderate and severe unless otherwise stated.

- ***** *includes Waterlow's mild, moderate and severe classes*
- ****** *Waterlow's severe class only* ***g****=girls* ***b****=boys*

UKM workers have investigated the thyroid function of 10 undernourished children aged between 7-17 years in Kuala Pangsoon near KL and found that children with a body mass index of <15, (moderately malnourished) had a higher TSH levels compared to 16 better fed children. There was no difference in thyroxine (T3 and T4) levels indicating that these children required a higher TSH drive to maintain a euthyroid state. There was no difference in cortisol, fasting growth hormone and calcium levels with children of different nutritional status.

Nutrition surveillance of children below 5 years in MOH clinics throughout the country show that although moderate malnutrition (between 2-3 standard deviations below normal) has been decreasing, severe malnutrition (less than 3 standard deviations below normal) has not. Figures 4.1 and 4.2 show the rates based on several hundred thousand new cases attending clinics each year.

Very severe protein-calorie malnutrition presents clinically in two classical forms, marasmus and kwashiokor. These have been described as entities in their own right and have been described locally in several papers.

MARUSMUS

Will described 5 cases of marasmus in the Kinta district in 1949. In a nutritional survey of 5,360 primary school children in 1976 in KL and Klang, Rampal reported that marasmus (<60% weight for age, was present in 5-37% of Indian children, 1-11% of Malay children and 1-12% of Chinese children in rural areas. Girls were more often affected than boys. In the urban area, no Chinese boy was affected, as were less than 5% of Malays boys. 10% of 12yr old Indian girls were affected compared to 37% in rural areas.

KWASHIOKOR

The nutritional status of the Malaysian population as a whole experience quite a setback during the Second World War. It was in the post-war period that reports describing kwashiokor in Malaysia appeared. Thomson described 100 cases of it in children in Perak in 1954 and Mohamed described 9 cases of kwashiokor among Malays and Indians in Negeri Sembilan in 1955 highlighting the prevalence of poverty and ignorance. Dean reported the findings of a large scale survey in 1961 covering many states in Peninsula Malaysia where 192 children up to 7 years old, all Malays, were found to have kwashiokor.

Even in 1975 in KL, George, Foo, Chong and Abraham reported they observed 25 severe cases of malnutrition in GH KL. 13 were cases of marasmus, 7 marasmus-kwashiokor and 5 kwashiokor. They ranged in age from 6 months to 7 years. 20 were Indians, 4 Malays and 1 Chinese. They identified large families, unemployment and neglect owing to parental separation as common causes.

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OBESITY

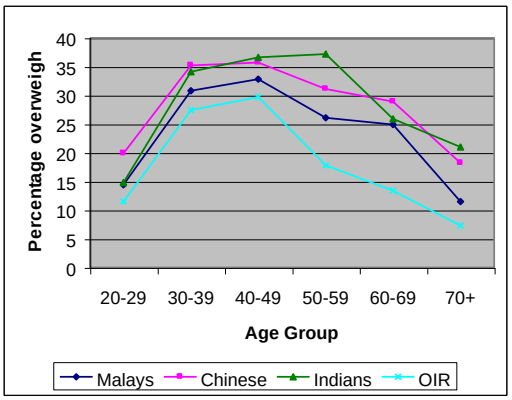
In a study of obesity among adults in KL in 1976, Jones reported that obesity was uncommon before the age of 30 years, and in Chinese men uncommon throughout life. After the age of 30 years, 28% of Malay and 23% of Indian men were more than 20% overweight. Among women 21% of Malays, 28% of Chinese and 40% of Indians were more than 20% overweight. Obesity was particularly prevalent in Indian women aged 31-40 years and Chinese women over 50 years old.

In a study of 406 executive and professional males in KL between 1982-1985, Teo, Chong and Zaini found that overall 29% had a (body mass index) BMI between 25-30kg/m^2 and another 3% had a BMI above 30kg/m^2. Malays had the highest rates with 41% having a BMI above 25kg/m^2. 35% of the Indian subjects had a BMI above 25kg/m^2 while only 22.5% of Chinese were in that class. The percentage of those overweight (BMI $\geq$ 25kg/m^2) rose with age from 29% in those between 25-34yrs to 37% in the 45-54yrs age group. A similar study of 733 senior civil servants in 1993 found that 36% had a BMI between 25-30kg/m^2 and 6.5% had a BMI above 30kg/m^2. Men had a slightly higher rate of obesity than women. Malays had the highest prevalence of obesity followed by Indians (4.6%) and Chinese (1.2%). Indians had more central obesity, measured by the waist hip ratio. 44% had a ratio greater than 0.9 for males and 0.8 for females, compared to 31% for Malays and 29% for Chinese.

In a community study of 2,284 subjects above 20years old chosen by cluster sampling in 9 districts reported in 1996 in Kelantan, Wan Mohamed *et.al*. noted that 21.3% were overweight (BMI 25-30kg/m^2), and 4.5% were obese (BMI $\geq$30kg/m^2). The overweight and obese were significantly younger than the lean suggesting a generational change. Although these rates are lower than in KL they are likely to increase over the coming years.

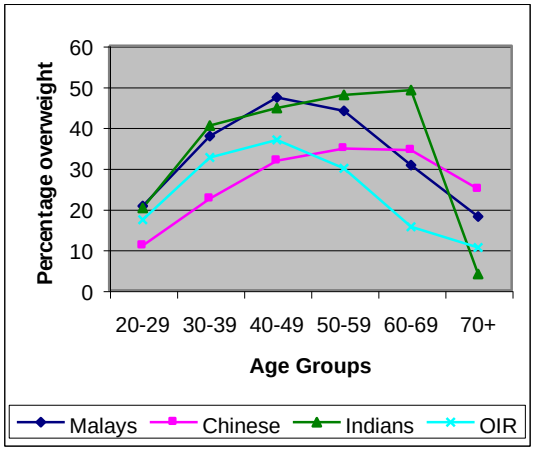
A community survey of 187 Chinese women in 1997, aged between 25-62 years (mean 40years) found a similar rate of 29% of women who were overweight (BMI 25-30kg/m^2) and 7.8% obese (BMI $\geq$30kg/m^2). 47% of those above 40years were overweight or obese compared to 27% of those 40 years or under.

Fig 4.3 Percentage of males in Malaysia overweight in 1996(BMI ≥25kg/m^2)



The most complete description of the prevalence of obesity in Malaysia however is data from the National Health and Morbidity Survey of 1996. 28,737 adults were purposely sampled throughout the country and a representative distribution of BMI obtained. The published report produced centile charts of BMI that can be referred to. The percentage of men and women overweight and obese, by age groups is given in Figure 4.1-2. Overall 26.5% of the adult population had a BMI above 25kg/m^2 , but only 6% were obese (BMI ≥30kg/m^2). On the other end 13% of the adult population had a BMI of <18.5kg/m^2. These results show that Indians were most likely to be overweight and the prevalence increases with age. The prevalence drops sharply in Indian women above 70 years indicating possibly an alarming mortality rate among the obese in this age group. More Malay and other indigenous women were overweight compared to Chinese women in the younger age groups, but the prevalence of overweight declines above 40 years, so that curves cross and more Chinese women above 60 years are overweight compared to Malays and other indigenous races. This might be explained by increasing affluence and the availability of more calories in the diet together with a change in lifestyle among younger Malays and other indigenous groups. But the pattern among men is different. In men the decline in prevalence in overweight is also seen at the age of 40 years in all races except Indians. Young Chinese men have the highest rates of being overweight among the different ethnic groups but the rate also declines from the age of 40 year. Perhaps the reason younger Chinese women defy the trend is a more widespread consciousness among them of body image and the desire to stay slim.

Fig 4.4 Percentage of females in Malaysia overweight in 1996(BMI ≥25kg/m^2)



(OIR=other indigenous races)

Volunteers at National Heart Week surveys appear to be more likely to be overweight than a randomly selected population as they are to have high cholesterol. Among 6,858 participants in screening in 10 urban areas between 1995-1997 Khoo *et.al*. reported that 40% were overweight and 7.6% obese. Indians (52%) again were most likely to be overweight but it seems urban Ibans (48%) and Kadazans (44%) may indicate a changing pattern among them, as they are not the group least likely to be overweight.

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VITAMIN A DEFICIENCY

Viswalingam in 1928 and Field surveying 1,585 Indian and 1,259 Malay children in Perak and Negeri Sembilan in 1931, the early investigators, pointed out that Indians in particular were more affected by vitamin A deficiency.

In 1955, McPherson observed that Vitamin A deficiency was the commonest cause of blindness in Kelantan in his survey of 140 blind people. They formed 42% of the blind and had an onset of blindness tragically between the age of 2-3 years. In a survey of rural Malay school children Bitot spots were present in 2 to 4% of the children. Amar Singh also mentioned that 60 cases of Vitamin A deficiency were reported yearly between 1969 and 1972.

Chandrasekharan reported that in 1976 , 18 cases of xerophthalmia and keratomalacia were found among primary school children in Hulu Terengganu. These findings suggest that Malays were probably was badly affected as the Indians.

Chong and Soh have tabulated the carotene content of common Malaysian vegetables and fruits in 1969 and it should not be beyond the means of nearly all Malaysians to obtain an adequate nutritional supply of Vitamin A. However, Teoh found in a survey of four rural villages in Negeri Sembilan in 1973 that the median value of the percentage requirement met by households was only 47%. 70% of households hadintakes lower than the suggested dietary needs. Even in 1981 a nutritional survey by the IMR in Endau, Johore detected biochemical Vitamin A deficiency in 10% of children and adolescents.

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BERI-BERI – VITAMIN B1 DEFICIENCY

Beri-beri must be considered the most significant nutrition deficiency disease in Malaysian history. It was also in Malaysia that the correct understanding of its nature emerged. It was formerly considered a tropical disease that was a scourge of the mines and plantations of the Far East. From Japan to the Malay Archipelago it had occured for centuries endemically sometimes assuming epidemic proportions. It also affected the workers building the Panama Canal and Congo Railway but was also found among the inmates in mental institutions in the West and onboard some ship crews.

In 1911 the medical records in Malaya attributed 1,469 deaths to beri-beri, and there were over 6,000 patients diagnosed with the

disease, and that does not include the many not brought to medical attention. The death rate then was between 10 to 18%. It was the fourth most important disease after malaria, acute diarrhoea and tuberculosis. Conditions here improved somewhat over the next decade probably due, in part, to the improved economy. In 1922 there were only 1,122 cases and 443 deaths known. The full impact of the discovery of the cause and cure for beri-beri which began at the turn of the century were being felt. Eijkman in Java is cited to have first observed that fowls fed on polished rice developed a polyneuritis akin to beri-beri in 1897. For this he shared the Nobel Prize for Physiology and Medicine in 1929.

Branddon who was State Surgeon in Negeri Sembilan also deserves part of the honour for discovering beri-beri's cure. Like many with a strong conviction he may have been over zealous for his theory. In 1907 he published a treatise on "The cause and prevention of beri-beri" in which he formulated his 'grain intoxication' theory. He had been studying the disease from 1889 and pointed rightly to polished rice as the cause. He made two categorical statements. "Every beri-beric in the East is a rice eater" and "persons who do not eat rice do not get beri-beri".

Where Branddon was wrong, Stanton, once a director of the IMR, put his finger on correctly, that beri-beri was not due to an intoxication but a deficiency. He showed in classical experiments in 1911, that the crucial nutritive element that prevents beri-beri, was located in the pericarp of the rice grain. In experiments on 24 life prisoners he proved that beri-beri was not a communicable disease and that it was caused solely by diet. Acting on these findings the Singapore and Malayan governments banned the use of polished rice in jails, hospitals, schools and mental institutions. The result was that beri-beri almost vanished as a disease.

Today beri-beri has taken a low place in the differential diagnoses doctors entertain such that many doctors do not think about and may not know how to recognise either the 'dry' neuritic type nor the 'wet' generalised oedema type due to cardiac muscle atrophy. Nevertheless it is not completely eradicated and surprises us every now and then. Jayakumar reported three cases among East Timorese immigrant workers seen in 1992 and a further 27 the next year among inmates in a detention centre.

'Polyneuropathy gravidarum'.

Such an entity was described with various names in a number of papers published internationally by investigators such as McGoogan in the United States in the 1930s. It seems though, that since then it has nearly vanished. In Malaysia however, Chan studied a series of 10 such cases in Taiping in 1962. Very probably, this syndrome which occurs usually within a month of delivery, is a form of vitamin B1 deficiency. It occurs mainly among Malays who adhere to a very restricted diet in pueperium. It is still seen occasionally in the rural areas.

It would follow also that B1 deficiency should be suspected in multiparous women from a rural background presenting with cardiomyopathy in pregnancy.

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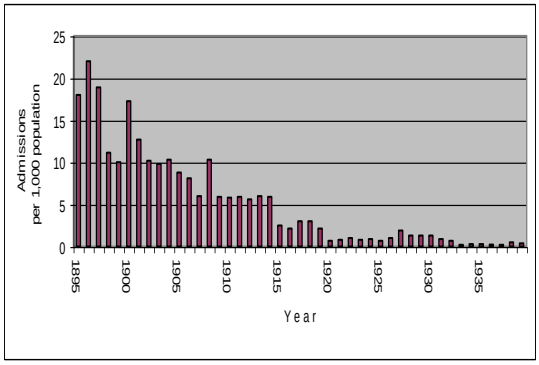
Figure 4.5 Beri-beri in the Federated Malay States, 1895-1949



VITAMIN B2 DEFICIENCY

Riboflavin was recognised as vitamin B2 in 1933. It is abundant in local food. A report by Caldwell and Enoch for example shows its presence in many vegetables. Deficiency is rare but if not borne in mind, it might be overlooked in the malnourished. It has nevertheless been noted by Landor and Pallister in 1935 among prisoners. Clinical features include eczema of the scrotum, cheilitis and glossitis. Marmite proved to be an effective treatment.

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PELLAGRA – VITAMIN B3 DEFICIENCY

Pellagra is a clinical picture of dermatitis, stomatitis, proctitis and diarrhoea, and mental depression due to niacin deficiency. Niacin is an essential part the pyridine nucleotides NAD and NADP which are co-enzymes in the oxidation-reduction reactions at the heart of metabolism. Niacin is the generic name for nicotinic acid and nicotinamide, the form it is usually given in vitamin supplements.

It is principally a disease where maize is the staple food because it is low in both niacin and tryptophan from which nicotinamide can be derived. It was apparently unknown to classical and mediaval physicians and was first encountered as tropical disease. The breakthrough in understanding pellagra came in 1937 when the effects of niacin on dogs was first realised.

In Malaysia, the first case of pellagra dates to the period before the discovery of its cause. Viswalingam described one adult Chinese man in 1917 and noted four more within a year. Pallister recorded more cases in Penang in 1940; including 15 cases among Chinese, one a 15 month old child who died of the disease.

Leong has highlighted which local foods have the highest sources of niacin. Although niacin deficiency is rarely seen today clinically, in some rural nutrition surveys, based on recall food eaten, like one by Noorhayati *et.al.* niacin has been found to be one of the vitamins most lacking, alongside, iron and calcium.

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VITAMIN B12 DEFICIENCY

Vitamin B12 deficiency is uncommon in Malaysia because of the variety of food most people consume. One group however, that is an exception are the vegetarians who eat a South Indian diet. It has been noted that they are prone

to megaloblastic anaemia. B12 deficiency may also present solely as a neuropathy. Chiew, Goh and Loh have reported a case of a 70 year Chinese man with defective vitamin B12 absorption due to a lack of intrinsic factor, who did not have anaemia. (also see Megaloblastic anemia)

Reference

Chiew IS, Goh KL and Loh TG. Vitamin B12 neuropathy in the absence of anaemia - case report. Sing Med J. 30:221-222 1989.

FOLATE (see Megaloblastic anaemia)

SCURVY

Vitamin C deficiency has probably never been a serious problem in Malaysia due to its plentiful supply in cheap local food. However, scurvy has been noted in children due to ignorance. Hughes described a Chinese girl in Penang with scurvy in 1936 and MacLean and Kamath reported 4 Orang Asli children in Gombak with scurvy due to a diet mainly of sweetened condensed milk in 1970.

References

Hughes W. Infantile scurvy. Mal.Med.J. 11:55-57 1936.

MacLean JD and Kamath KR. Infantile scurvy in Malaysia. Med.J.Mal. 24:200-207 1970.

VITAMIN D DEFICIENCY

In contrast to beri-beri, concerning rickets and osteomalacia, another well known deficiency disease there is a paucity of literature written in Malaysia. It would appear that rickets is practically unknown in Malaysia.

VITAMIN E

Vitamins were initially discovered as minor nutrients which caused disease when a person was deficient in the vitamin. For a long time no particular disease was known to be due to a deficiency of tocopherol or vitamin E so its place among the vitamins was unusual. But recent discoveries of the anti-oxidant effects of vitamin E and clinical trials of vitamin E supplements show that it is effective in the prophylaxis of cardiovascular disease and cancers.

In 1975 Ng and Chong reported that normal healthy Malaysians have a mean serum tocopherol of 0.92±0.36 mg/dl. Indians had the highest mean levels followed by Chinese and then Malays but the difference was not statistically significant. Hyperlipoproteinaemic individuals, however, were noted to have higher levels of vitamin E. This difference disappears when serum tocopherol is expressed per g of total serum lipid (Horwitt's ratio). The mean Horwitt's ratio for Malaysians was 1.32±0.34.

Reference

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BURNING FEET SYNDROME

No known vitamin deficiency has been linked to this syndrome. But outbreaks have been documented in Europe and tropical America, Africa and Asia. It was often seen locally during the Second World War among European prisoners but was recorded here from before the war mainly among Tamil estate workers. It was thought to be linked to the B group of vitamins but further study does not seem to be forthcoming as the disease has nearly vanished.

References

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CHAPTER 5

PHYSICAL INJURIES

ACCIDENTS

In the last two decades, injuries due to accidents constituted the cause for 10-11% of admissions in government hospitals. They account for nearly 7% and formed the third largest cause of medically certified deaths, after cardiovascular diseases and malignancies. Injuries were also listed as the cause of death in 3% of non-medically certified deaths in 1998.

ROAD ACCIDENTS

Everyday nearly 17 people are killed and over 120 others are injured as a result of motor vehicular accidents in Malaysia and the number still rises every year. We have one of the highest rates of road accidents in the world. Most who die are young and who would normally have had many productive years before them. Three quarters (75%) of road fatalities occur in those below 45 years of age and children under 15 years constitute 16% of these deaths. Those who sustain injuries often lose months from their usual pursuits, and many are maimed permanently.

Over the last three decades road accidents have risen to become the second commonest cause for hospital admission, next only to childbirth. The admission rate to government hospitals due to road accidents increased six fold from 53 per 100,000 population in 1960 to 324 per 100,000 in 1988. It further doubled the next decade reaching 673 admissions per 100,000 in 1998. It needs to be constantly highlighted as a disease of epidemic proportions that is in fact amenable to control by preventive measures.

In 1952 the Annual Report of the Federation of Malaya showed there were 82,591 registered vehicles and 6,062 miles of road surface. In 1960 the number of vehicles had risen to 190,103 for 6,868 miles of surfaced road. In 1970 the number of vehicles had risen 3.5 times to 669,294 and road milage by 56% to 10,715. It is against this background of development that accidents have risen as a consequence.

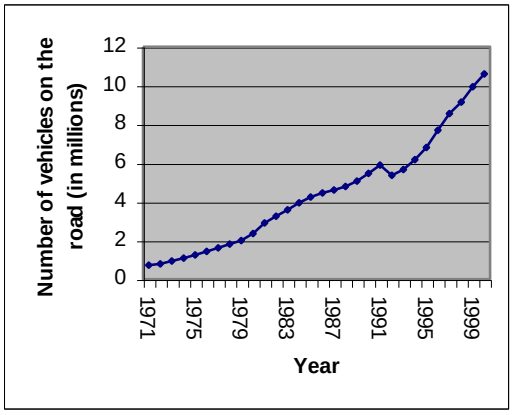
In 1971 there were 16,847 road accidents reported. There were 1,548 deaths of which 697 occurred on the spot. 1,392 sustained serious injuries and another 6,392 minor injuries giving a total of 8,481 casualties of all sorts. Over the decade the number of accidents increased at an average of 15% annually to 59,084 in 1980. The number of deaths rose on average 6% a year to a total of 2,568 in 1980 of which 2,001 were on the spot deaths. The total number of casualties rose by 1.4% annually to 22,404. By 1980, Peninsula Malaysia had 2,357,386 vehicles on the road, a rise of 3.5 times as in the previous decade. Motorcyclists formed 60% of road users. The mileage of road surface however, went up only 35% to 14,454. The obvious result is that road congestion has increased.

In 1980, the largest number of casualties and deaths from road accidents were motorcyclists and pedestrians who accounted for 35.5% and 18.6% of all the casualties respectively. Cyclists, another vunerable group, accounted for 12.9% of all casualties, including deaths. Together these road users accounted for 67% of all casualties. The fault in traffic accidents lay with drivers in 88% of cases. Intoxication does not feature (0.2%) as it does in western countries but driving without due care, dangerous driving including speeding and inconsiderate driving were common sins of Malaysian drivers.

In 1990 the number of vehicles rose to

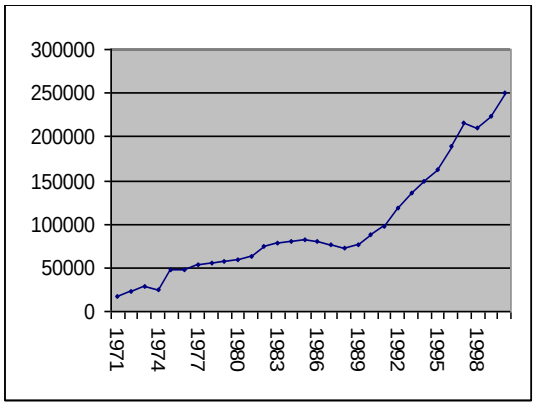
5,462,792, a doubling of the number from 1980. The figures include vehicles in Sabah and Sarawak from 1981. From 1980 the number of accidents increased at a much lower rate of 4% annually, or 49% over the decade. The number of death and casualties both increased by about 2.7% annually or 30% over the decade.

Figure 5.1 Number of Registered Vehicles in Malaysia 1971-2000



Source: Traffic Division, Royal Malaysian Police

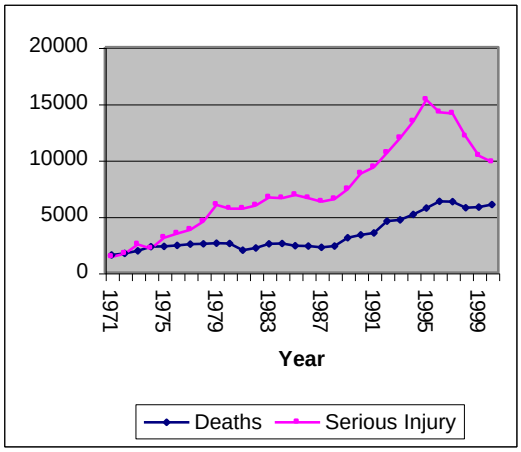
Figure 5.2 Number of Road Accidents in Malaysia 1971-2000



Source: Traffic Division, Royal Malaysian Police

In 1997 Kulanthayan noted that motorcycles represented 51% of registered vehicles and motorcyclists accounted for 49% of all reported accidents, 60% of all deaths in accidents and 68% of all road casualties. Pedestrians who rank second accounted for only 12% of road deaths and 9% of road casualties.

Figure 5.3 Number of deaths and serious casualties from Road Accidents in Malaysia 1971-2000



Source: Traffic Division, Royal Malaysian Police

Since 1971 Malaysia has enforced a law compelling the use of safety helmets for motorcyclists. However, Kulanthayan *et.al*. surveyed 500 motorcyclists in Kajang in 1997 and found that overall 46% did not use their helmets properly. Those who were more likely not to use helmets properly were males (50%), riders under 20 years old (63%), Indians (60%), those with only primary school education (71%), and riders with no licence (70%). Pang *et.al*. studied 412 seriously injured or fatal motorcycle accident victims admitted to the Kajang and KL Hospitals in 1998. 92% of the injured or dead were riders while the remainder were pillion passengers. 95% were males, 72% were under 30 years old. More than 40% of riders had a valid licence for less than 3 years. Large engine motorcycles, collision with commercial vehicles, collision at non-junction sites (ie straight or curved roads) and head-on collisions were more likely to be fatal.

The seriousness of the continued increase of casualties from road accidents cannot be over emphasized. Strategies to combat road

accidents take the form of a three pronged attack. 'Engineering', first to provide safe roads, 'Education' of the public and finally 'Enforcement' of legislation for road safety. Following the upsurge in road accidents in the late1980s, a Cabinet committee was formed at the highest level in 1991 to stem this modern disease. A target of a 30% reduction in 10 years was set as the target.

However, by the year 2000, the number of vehicles had again doubled to 10,598,804 and the number of accidents increased to 250,429 showing no sign of decline. The number of accidents increased by 2.8 times from 1990, an annual increase of 11% which is higher than the previous decade. The number of death from road accidents however increased also at an annual rate of 11% but peaked in 1996 and has plateaud over the last 5 years. The number of serious casualties also increased at a similar rate to a peak in 1995 but has since declined quite dramatically from 15,313 to 9,790 in 2000, a drop of 36% to almost its level in 1990. Traffic safety campaigns by the police over all the festive seasons might be having a positive effect but the war is far from over.

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OCCUPATIONAL INJURIES

The total number of occupational injuries had been on the rise the previous decade (1980-1990) principally because of the increase in number of the workforce. In the last few year however, not only the rate but even the total number has shown a slight decline. The occupational injury rate reported to the Social Security Organisation (SOCSO) was 25 per 1,000 registered employees in 1988. The permanent disability rate was 0.8 per 1,000 while the fatal injury rate was 0.1 per 1,000 registered employees. However, among a workerforce of 8.1 million people in Malaysia in 1996, there were 106,508 occupational injuries reported to SOCSO, a decline in the rate to 13 per 1,000 registered workers. 10% of these cases resulted in permanent disability. 14,771 (14%) of these accidents occurred while commuting to or from the workplace.

The manufacturing and agricultural sectors, not surprisingly, recorded the highest number of accidents accounting for 52% and 13% respectively, of all occupational accidents in 1996. These figures however, may be off the target because some workers were not registered with SOCSO. Data from available sources indicated that in Sarawak alone in 1988, there were 71 deaths in the logging industry. In comparison the total number of occupational fatalities reported was 356 nationwide in 1988 according to SOCSO.

Three quarters (75%) of occupational fatalities in 1988 occurred among those below 45 years and those below 25 years constitute 23%. Injuries causing permanent disablement show the same pattern. Falls and being hit by objects are the most common injuries. In 1988 SOCSO paid out a total of RM 42,800,000 in compensation to victims of injuries or their dependants.

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OIL PALM THORN INJURIES

Because of Malaysia's large oil palm plantation industry, oil palm thorn injuries are fairly common. The local tissue reaction seen is out of proportion to the size of the foreign body, suggesting that a toxic substance is released by

the thorn. Balasubramaniam and Prathap reported 3 cases where a pseudotumour developed in the hand following injury by oil palm thorns.

Reference

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HOME ACCIDENTS

There were 319 deaths in children under 14 years recorded in 1975 from home accidents compared to 52 deaths in road accidents. This fact alone shows the importance of a vigilant attitude towards preventing such accidents. In 1986, of the 54,000 injuries seen in the Accident and Emergency Department, GH KL, about 10% occurred at home. Of these patients 80% were children below 12 years and women.

In a study carried out in all general hospitals in Peninsula Malaysia over 6 months from 1976, a total of 1,542 home injuries with 15 deaths were noted in children. If the death rate of 1% is a good reflection it means there would have been over 30,000 home accidents victims treated at government hospitals in 1976, not counting those treated elsewhere. Injuries from falls (39%), cuts and bruises (29%) and burns and scalds (19%) were the most common injuries. These were followed by lodged foreign bodies and accidental poisoning. About 57% of the injuries occurred in children below 4 years of age. 20% of the children had a history of a previous home injury while in 24% there was a history of injury in other family members.

Ariff and Schattner reviewed home accidents seen in a rural general practice in Perlis over 17 months from May 1995. Out of 171 children under 12 years involved, injuries from falls accounted for 28%, trauma not from falls another 26%, scalds and burns 22%, animal bites 9%, poisoning 7% and foreign bodies stuck in orifices 6%. Boys were 1.7 times more likely than girls to be injured.

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FIRES AND BURNS

There were 7,358 fires reported in the country in 1988. There were 46 deaths and 43 injuries in these fires. About RM206 million worth of property was estimated lost in these fires. About one billion ringgit of property was estimated to be saved by the Fire Department in 1988. A significant proportion of fires were attributed to carelessness and ignorance. Cigarette butts alone contributed to 16% of fires in 1988. Another 25% of fires were due to electrical faults, sparks, fireworks, mosquito coils, candles, cooking apparatus, chemical reaction and matches.

Between 1991 and 2000, the Fire and Rescue Department recorded an average of 15,478 fires a year. There were on average 70 deaths and 95 injuries annually. Losses incurred amounted to RM451 million, on average, a year.

From the doctor's point of view, fires are only a small proportion of causes of burns. Clinically burns are heat injury to the skin. No accurate figures exist for the incidence of such burns in the Malaysian population but it is certainly one of the common reasons for acute admission to hospital, and probably the leading cause of admission to peadiatric surgical wards.

The pattern seen in a study at the General Hospital KL probably reflects closely the pattern for other parts of the country. 50% of the patients, seen there as reported by Ali in 1987 were below the age of eight years. Only 38% of burns were seen in adults above 20 years. 83%

of the injuries were sustained at home and of these 61% were caused by hot liquids. The next most common cause of burns at home were explosion of kerosene lamps and stoves. About 50% of patients thankfully had burns of 10% or less of the body surface area. About 5% had burns involving greater than half the surface area of the whole body. The rest fell in between. The upper and lower limbs (57% and 59% respectively) were most commonly involved followed by the trunk (53%) then the face (29%) and hands (23%).

In a prospective study of children under 12yrs at the UKM paediatric unit over 22 months from 1993, Ibrahim *et.al* accumulated 94 cases. Infants (aged <1yr) and toddlers (aged 1-3yrs) accounted for most cases (27% and 53% of cases respectively). 64% sustained burns in less than 10% of body surface area. Only one child, who sustained 80% burns from generator explosion, died. 96% of burns occurred at home. 81% of burns were scalds. 66% of children affected came from homes with a low monthly income of less than RM1,000. In a series of burns cases seen at UH in the same period, Sendut, Tan and Rivara noted that 4 out of 10 infants were scalded in association with their use of a baby walker.

The incidence of bacteriologically proven infection associated with burns was (57%) in the 2 year study in KL GH by Ali and Sharif, the which is not surprising as most patients are nursed in open wards. The common organisms isolated were *Staphylococcus* (37%) and *Pseudomonas* (30%). Septicaemia was noted in 22% of which a third of these succumbed to the infection. Renal failure was seen in 3.4% and Curling's ulcer in also 3.4%. In the paediatric study, 31% of wound cultures were positive. 86% were due to *Staphylococcus aureus* of which 36% were methicillin resistant.

Mortality was 75% in those whose burns were more than 50% the body surface area(BSA). It was 41% in those who had 31%-50% BSA burns, and 8% in those with 16%-30% involved. None of those with less than 15% BSA burns died. Considering the high number of burns cases seen and the high morbidity and mortality it is hoped that proper burns units will soon be available in all general hospitals to better deal with the problem.

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IATROGENIC INJURY

It is difficult to discuss the role of traditional healers in our local cultures, but 'bomohs' and 'bidan kampongs' produce some "iatrogenic" illnesses that one needs to be aware of.

CHARM NEEDLES

Insertion of needles for 'charm', 'beautification' or 'medicinal' purposes is not an uncommon practice in Malaysia. Unlike acupuncture these needles are left inside the soft tissue in various parts of the body. In the 1970s, Soo and Singh reported seeing 14 cases over 18 months at the UH and 2 more from Alor Star. Oon observed 42 cases in just one year at the Singapore GH. Males were more usually involved and all the races are represented. In 1991, Shanmuhasuntharam and Ghani reported another 9 cases in UH. These were incidental findings on radiography but it is possible complications can arise.

Insertion of another foreign object, namely ball bearings to the foreskin of the penis for

increasing sexual enjoyment, may be something peculiar to this region. Occasionally they may result in complications that need medical attention. Wallace, in 1952, noted that in Sarawak such insertion of iron rods called "palang" was a common practice among the Dyaks. Other forms of genital self-mutilation in mentally disturbed men have also been reported.

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MASSAGE

One of the most popular forms of treatment by 'bomohs' and 'bidan kampongs' is the use of massage or 'urut' in quite a vigorous manner. Bowel perforation, usually of the sigmoid colon can occur and speaks of the vigour with which the 'urut' is applied. Uterine rupture in labour for 'urut' has also been reported. A case of 'urut' resulting in haematoma of the testes in a neonate has also been documented.

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OTHER INJURIES

DROWNING

According to the Life Saving Society of Malaysia, 108 persons drowned in 1988. Of these, 94(87%) were 30 years of age or below.

DIVING

5 cases of decompression illness, two of them fatal, were reported by Loke *et.al*. among untrained foreign workers doing underwater logging in the Kenyir lake between 1994 to 1996. Decompression chambers are available only in Kuantan and Lumut.

HEAT STROKE

With a warm humid climate all year round, Malaysian generally avoid the heat and heat stroke in not common. A fatal case, however, was reported in a young woman who went jungle trekking after she had joined a weight reduction programme.

RAILWAY ACCIDENTS

In 1988 a total of 67 persons died and 86 others were injured in railway accidents. Of those killed, 63 were trespassers who were hit by trains.

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Nadesan K, Chan SP and Wong CM. Sudden death during jungle trekking: a case of heat stroke. Mal J Pathol 20:49-54 1998.

NON-ACCIDENTAL INJURY

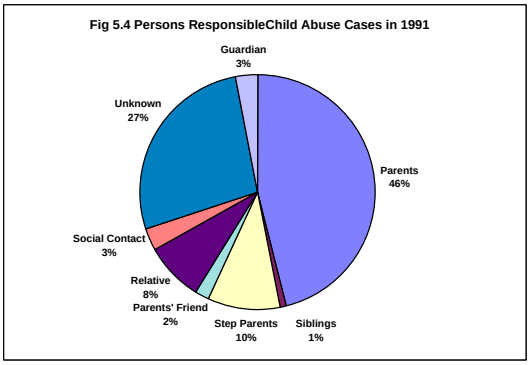
THE BATTERED CHILD

Medical interest in the physically abused child suffering as a result of displaced anger of adults arose in the West in about the 1940s. It would be presumptious to say if the incidence here is as high or as low as much of it is swept under the carpet and only realised on careful medical probing. In order to stimulate interest in the diagnosis Woon, Lam and Chin reviewed all the cases known at the University Hospital KL from its establishment in 1967 till 1973. They had 7 cases from a total of 10,224 paediatric admissions. In 4 a complaint of suspected abuse was obtained. In 3, medical suspicion of abuse was confirmed when family members were interviewed. 4 of the children were under 3 years, all were under 6 years. The abuser was the mother in 3 instances. Others involved were a grandmother, a father, a step-brother and a baby-sitter. 6 of the families involved were from the lower socio-economic group.

In 1985 a group in the GH in KL formed a Suspected Child Abuse and Neglect (SCAN) team to document such cases in the hospital. They reported in 1989 that in one year from 1985 they diagnosed 86 such children. 62 were physically abused, 6 sexually abused, one both physically and sexually abused and 17 neglected. There were 61 girls compared to 25 boys. 34 of the children were Malays, 16 Chinese, 26 Indians, 3 of mixed races and 7 illegal immigrants. No age group of children were exempt. The abusers were mainly close family members. There were 5 deaths. 35 children were sent back to their parents or relatives, 27 were taken into institutional care, 11 were abducted from hospital by their families and the 7 children of illegal immigrants were repatriated along with their parents. The report highlights the need for such teams in all hospitals.

One particular case caught the nation's attention in the mass media in May 1990. A baby named Balasundram was found abandoned with severe trauma near the KL General Hospital. The poor child died two days later. Following this 14 cases of child abuse were reported to the police in one week. That year has also seen the setting up of more agencies to check on the matter.

Figure 5.4 Persons Responsible For Child Abuse Cases in 1991



In subsequent studies the SCAN team in GH KL collected about 100 cases of child abuse a year. Of 119 cases seen in 1991 they reported that 82 cases were categorized as mild where 37 were severe. Those with mild abuse were on average older (8 years). On the other hand the average age of those severely abused was only 4.2years. Parents tended to be mild rather than severe abusers. 77% of cases were from Social classes IV and V. Among the severely abused, there were 14 cases (38%) of divorced or separated parents, 7 cases of personality disorders, 6 cases of the abusers using drugs and 9 alcoholics.

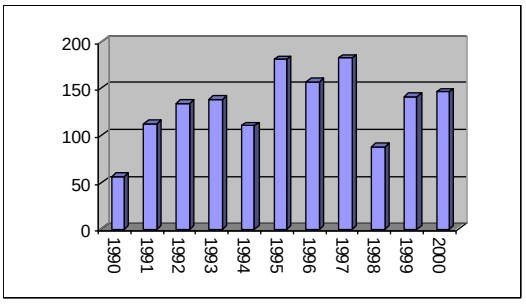
Intracranial haemorrhage is a major cause of mortality and severe morbidity in child abuse cases. The SCAN team found evidence of intracranial haemorrhage in 11.4% (41/369) of cases over 4 years. 90% of the children affected were under 2 years old. Most of these (80%) did not report a history of trauma and of those that did, only 1in 4 was the trauma described compatible with the injuries seen. 54% (20/37) of

the children under 2 years old had no external signs of trauma, but 11 of these had retinal haemorrhages. Subdural haemorrhages accounted for 80% of the intracranial haemorrhages. Skull fractures were present in only 9 cases. The overall prognosis was very distressing, with an early mortality rate of 32% (13/41) and at least another 17% (7/41) with severe neurological sequelae.

In another report in 1995, Kassim and Kasim from the SCAN team noted that 18.2% of child abuse cases were sexually abused. Bad psycho-social factors were evident. The age of the children most often affected was 6-8 years. Indians were over-represented.

The SCAN team also review 30 cases of deaths caused by physical child abuse in 1995. There were 12 Malay children, 6 Chinese, 9 Indians, 1 Indonesian and 3 cases in which the ethnic origin could not be ascertained. There were 13 boys and 17 girls whose average age was 29 months. Intracranial and intrabdominal haemorrhage were the commonest causes of death. Of the abusers that could be identified, fathers formed the largest group, followed by mothers and childminders.

Figure 5.5 Number cases of child abuse reported to the Royal Malaysian Police



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THE BATTERED WOMAN

Because of the traditional subservient status of women they are more likely to suffer from the social disease of repeated physical abuse in the home environment than men. Most cases of woman battering almost certainly remain unreported. Medical interest in most cases goes beyond just the physical injury and involves related psychiatric problems such as marital disharmony, suicide attempts, depression and even psychotic illness. The Utusan Consumer of December 1989 said that from 1984 to 1988, 2,182 Malaysian women reported being beaten by their husbands.

In Kuala Lumpur alone there were 249 reported cases of wife battering in 1989 and 148 in 1990. 49% were Chinese, 22% Malays and 26% Indians. The largest age group are women between 20 to 30 years old. They form 52% of the total.

The Domestic Violence Act has been enforced since 1996 and annual statistics have shown an increasing trend in reported cases with 532 cases in 1994 and 1,409 in 1995. The Women's Aid Organisation estimated in1995 that 39% of women may have been physically abused by their male partners and disturbingly,

15% of people interviewed felt it was acceptable for women to be beaten.

References

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RAPE

Rape is a medical problem for two reasons. First, the doctor has to deal with both the physical as well as the psychological injury the victim sustains.. Second, the doctor may be called upon to examine the victim in order to be an expert witness in a court of law.

Reported Cases

There were about 200 cases of alleged rape reported to the police in the late 1960s. In the decade to 1979 the number rose by about 6.4% annually to 388 cases. In the 1980s the number of cases rose at a slightly faster at about 6.6% and in the 1990s the annual increase has been even more at about 8%.

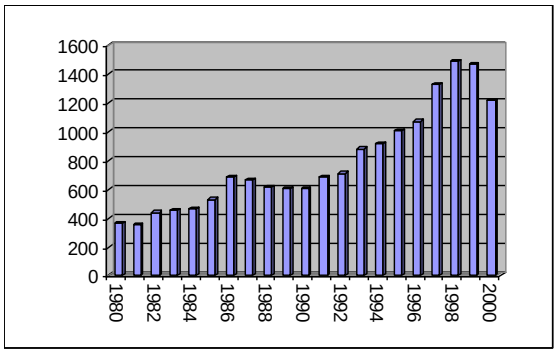
The highest for one year has been 1489 in 1998. The number of rape cases that go unreported is of course unknown. Kuala Lumpur, Perak and Sabah have the highest number of cases. Malacca and the East coast states had the fewest cases.

By ethnic group, those who were other than the three main ethnic groups were more often victims. In a report in 1988 they accounted for 18% of the total, while Malays (53%), Chinese (20%) and Indians (9%) were represented in proportions not far different from that of the general population. The ethnic group of suspected rapists also showed the same pattern (Malays 56%, Chinese 19%, Indians 9% and Others 16%). This may indicate that migrants and temporary residents are more often involved.

Unemployed women (39%) were the largest group of victims, followed by students (28%). The incident occurred most often in a house or building (54%), then in a public place (32%) or hotel (11%). The assailant was known to the victim in just over half (53%) the instances. Relatives accounted for about 7% of cases.

In 24% of cases the report was lodged only when the victim was found to be pregnant or when a settlement could not be reached. A further 18% were on account of a false promise to marry although there had been "consent" during the event. 30% of cases were statutory rape and 17% were labelled "genuine" rape.

Figure 5.6 Number of reported rape cases in Malaysia



Source: The Criminal Investigation Department. Royal Malaysian Police)

Unreported Cases

Underneath what comes to criminal and medical attention the incidence of rape and sexual abuse in children can only be guessed. Sexually transmitted disease (STD) is an indicator of rape in children below 12years. Cheah and Kasim diagnosed STD in 32 out of 55 girls with a vaginal discharge. In addition 7 more of the 55 girls not proven to have STD were also sexually abused.

References

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Cheah GS and Kasim MS. Vaginal discharge is prepubertal girls - a strong indicator of sexual abuse. Med.J.Mal. 51:199-204 1996.

CHAPTER 6

CHEMICAL INJURY

This chapter covers acute poisonings, chronic substance abuses and poisons from animal stings.

ACUTE POISONING

The most comprehensive records of poisoning in Malaysia are available in the decade from 1963 to 1972. Amarasingham with other colleagues, published two reports, covering five year periods were able to document all poisoning cases in Malaysia as all specimen of human poisoning were sent to the Chemistry Department. There were 1,396 cases between 1963 to 1967 and 1,749 from 1968 to 1972. Unfortunately, since then data at the Chemistry department has not been analysed for publication.

Over 140 types of poisons were catalogued in the second reported period, compared to 90 in the first. 33 (23%) of the 142 poisons consisted of pesticides. 51 (36%) were medicinal drugs. Most poisoning cases were self inflicted. Indians formed the largest group accounting for 50% of the cases. There were very few Malays (6%) especially in view of fact they form about 50% of the population. Calculation shows that Indians were 46 times more likely than Malays to ingest a poison. Chinese had a relative risk of poisoning 11 times higher than Malays. Youth between the ages of 11 to 30 years accounted for 62% of the cases and male slightly outnumbered females in a ratio of 1.1:1. Children affected were usually cases of accidental poisoning. Victims of poisoning under 10 years in age accounted for 2% of the total.

Another angle on acute poisoning is seen from a review of admissions to the KL GH government medical unit in a more recent survey in 1987 by Syed, Nik, Tariq and Sarvanathan. Of 582 cases in the year 43% involved pharmaceuticals, 30% involved household items like kerosene and 13% involved insecticides and herbicides.

Children

In a review of 70 children involved in accidental poisoning with household items, Azizi, Zulkifli and Kassim found 36 ingested kerosene, 19 medications, 8 insecticides and 7 other household items. None were fatal. Kerosene was often kept in soft drink bottles on the kitchen floor, household safety measures were generally poor. In a case control study in KL GH, Azizi *et.al*. found that being Indian, having parents under 21 year old and being resident less than one year at the current address were risk factors for children to be hospitalised for ingestion of a poison. Boys were more often affected than girls and children under 3 years were at higher risk.

The following are a summary of the common poisons:

ACIDS

Formic acid which is used as a coagulant of rubber latex was the second most commonly used poison for suicide throughout 1963 to 1972. There were 527 instances in that decade, 74% of which were fatal. 50% were Indians while 41% were Chinese. For some unclear reason it was the commonest poison used by the elderly. 32% of those above 60 years old used formic acid when they took poison. Those who survive the poisoning often had oesophageal strictures.

Sulphuric acid was used in 88 instances of self-poisoning with a fatality rate of 56%.

ALCOHOLS

Less than 10 cases of methanol poisoning were recorded between 1963-1968 and there were 24 cases in the next five years. Ng reported what he observed as the third epidemic of methanol poisoning in Negeri Sembilan which occured in January 1977. He was puzzled as to why it appears as if this occured only in Negeri Sembilan whereas moonshine liquor, usually known as `samsu' can be found anywhere in the country. 20 adults were involved, all Indians including one Indian Muslim. 5 were women the rest men. There were 15 deaths in that episode which all occured within 24 hours.

Ng knows of only one other outbreak since that occurred in the state of Kedah.

Reference

Ng TS. Methyl alcohol poisoning - a report of 20 cases. Med.J.Mal. 33:13-16 1978

ALKALIS

During 1954 and 1955 Hardy recorded 146 persons with caustic soda poisoning in the KL General Hospital. Of these 33 (23%) died. In the ten years from 1963 to 1972 reported by Amarasingham there was a total of 376 cases. It decreased from joint second to fourth place over the ten years from 1963 to 1972. Women using it outnumbered men in a ratio of 1.35:1. The outcome of poisoning was fatal in 44%.

Caustic soda is usually taken by the lower income group of Chinese, 69% of the total, who live in urban areas. Survivors usually suffered from oesophageal stricture. They constitute the largest group of patients with oesophageal strictures in Malaysia.

Reference

Hardy EA. Some medical observations on caustic soda poisoning, its treatment by passage of a Ryle's tube and its prevention. Med.J.Mal. 11:201-207 1957.

ANALGESICS

Paracetamol and the salicylates are an increasingly popular group of drugs used in self poisoning among the urban population. It was the second commonest agent and accounted for 32% of the pharmaceuticals that were used by poisoning cases in 1987 at the GH KL. They are potentially lethal.

Doctors ought to take note seriously of the danger of prescribing too high a dose of paracetamol. Kuan has described 3 children in Malacca in 1998 who developed hepatic encephalopathy, one of whom died, for whom general practitioners prescribed excessive doses of paracetamol. Parents sometimes expect a fever to be instantly cured and doctors can foolishly yield to such expectations and overdose their patients. Unfortunately the warning sounded by this report was not noticed. The next year another 6 year old girl in KL died of paracetamol overdosage according to a reports in the newspapers. Two doctors from one clinic who prescribed the medication faced a legal suit.

Reference

Kuan GL. Repeated paracetamol overdosage in children. Med.J.Mal. 53:188-191 1998.

Matthews E. Parents of dead girl ponder legal suit. The Star 1999: September 7:3(col1)

ANTIASTHMATICS

Because bronchial asthma is common, drugs such as terbutaline and theophylline are widely

prescribed in Malaysia. As such they are one of the commoner drugs found in poisoning cases. They made up 6% of the pharmaceuticals used in self poisoning cases in GH KL admissions in 1987.

ANTIPSYCHOTICS

It should be borne in mind that drugs like the tricyclic antidepressants prescribed for depressed patients may consumed by them in a suicide attempt. They accounted for 8% of the drugs used in acute poisoning cases admitted to GH KL in 1987. In this respect the newer tetracyclics are probably safer.

ARSENIC

In the 1963-1968 period this was the most commonly consumed poison in West Malaysia. There was a total of 308 cases of which 60% were fatal. The poison, found in the form of sodium arsenite, was readily available in rubber estates where it was extensively used as a weedkiller. Not surprisingly Indians accounted for 71% of those who took it. Between 1969 and 1972 the number of arsenic cases dropped to 271 and it was the third commonest poison. The decrease no doubt was due to many estates switching to other weedicides. The use of arsenic in poisoning has decreased even more since.

BLOWPIPE DART POISON

Not many Orang Asli still hunt with the blowpipe but some still do. The poison used on the dart can be made from the latex of the Ipoh tree (*Antiaris toxocaria*) and the root bark of akar ipoh (*Strychnos sp*.) Ho reported one fatal case from accidental ingestion of blowpipe dart poison. The patient had rhabdomyolysis and actue oliguric renal failure.

Reference

Ho LM, Cheong I and Jalil HA. Rhabdomyolysis and acute renal failure following blowpipe dart poisoning. Nephron 72:676-678 1996.

CARBON MONOXIDE

Two victims died of carbon monoxide poisoning in the bathroom from faulty gas water heaters in Cameron Highlands in 1995. In another tragic accident, a cobbler in Johor Baru left his family in a car with its engine and air-conditioner running for nearly 3 hours in 2001 while he went to work. His 23 year old wife and 3 children fell unconscious and died of carbon monoxide poisoning.

Reference

Chong CK, Senan P and Kumar GV. Carbon monoxide poisoning from gas water heater installed and operated in the bathroom. Med J Mal. 52:169-171 1997.

Children left in car die three hours later. The Star. 2001. September 8:3 col 6.

HYPNOTICS

Barbiturates

Barbiturates were the commonest drug used in self-poisoning in decade Amarasingham studied. It remained constantly the sixth most frequently used poison. Of a total of 223 cases in ten years 79 (35%) were fatal. 72% of those using barbiturates were Chinese who tend to be from the middle and upper income groups.

Non-barbiturates

Like barbiturates users tended to be Chinese (79%). There were 95 cases between 1963 to 1972 and only 13% were fatal. Drugs like diazepam are of late usually the most favoured in urban centres as it is readily available. It was the commonest pharmaceutical among acute poisoning patients admitted to the KL GH in

1987. Fortunately for such victims they are not very lethal.

INSECTICIDES

Organochlorines

Dieldrin, BHC, Thiodan, DDT and Endrin were the common organochlorines found in victims of poisoning. The number of cases rose quite rapidly in the decade from 1963, from 115 in the first five years to 206 in the next five. This is another chemical found in the estates and used mainly by Indians (65%). 46% of poison cases died.

Organophosphates

Like organochlorines, from 1962 onwards the use of organophasphates rose rapidly. From fourth position organophosphates rose to become the commonest poison in the period studied by Amarasingham. Since then it has been overtaken by paraquat. Indians accounted for 71% of the 523 cases. It had a high fatality rate of 68%. The University Hospital however reported a fatality rate of 36% prior to 1975; after which the fatality rate fell to only 3.4% with management in the Intensive Care Unit with ventilatory support when necessary.

Those who survive poisoning with organophosphates may suffer from delayed chronic polyneuropathy. This neuropathy could cause laryngeal paralysis making extubation following endotracheal tube ventilation difficult as reported in one case.

Reference

Delilkan AE, Namazie M and Ong G. Organophosphate poisoning: a Malaysian intensive care experience of one hundred cases. Med.J.Mal. 39:229-233 1984.

Low ET and Loh TG. Delayed chronic polyneuropathy following organophosphate poisoning: a case report. Med.J.Mal. 42:113-114 1987

Indudharan R, Win MN and Noor AR. Larnygeal paralysis in organophosphorous poisoning. J Laryngol Otol 112:81-82 1998.

KEROSENE

This was recognised as the commonest household item in acute poisoning cases admitted to GH KL in 1987. Children were the usual victims and it has been pointed out that adding colour to kerosene may help prevent accidental poisoning with kerosene.

WEEDICIDES

Paraquat

Paraquat was introduced into Malaysia in 1961. Only a few cases of poisoning occurred up to 1967. But between 1968 and 1973 there were 56 cases noted. Its usage in attempted suicide has steadily increased since, until it is now the leading poison being use. Although comprehensive statistics are not available there have been a few reports highlighting the issue and calling for review of legislation.

Reporting 30 cases over 2 years from 1978 from GH Kuala Lumpur, Chan and Cheong noted that 67% were Indians. The age distribution corresponds to that of poisonings in general. Females slightly outnumbered males. It is very significant that 9 cases were accidental poisoning. Hopefully steps taken like giving commercial paraquat a bad odour and colour will help eliminate this problem. In these 30 cases the outcome was fatal in 90%. This high fatality rate is the cause for concern of many physicians. It can result in death even when as little as 5ml. is consumed.

In an effort to find all paraquat cases admitted to hospitals in Perak over 18 months from January 1981, Wong and Ng found 94 patients using a questionnaire survey, giving an incidence of about 3.3 per 100,000. 73% were suicidal attempts. Indians accounted for 82% of

all cases. A positive chemistry identification of paraquat was available in only 40%. In 54%, data was not available in the study questionnaire and the remaining 6% were tested but were negative. Of the 94, 12% survived. 65% were known to have died and in 23% the outcome was not known.

Howard, Sabapathy and Whitehead have studied the lung, renal and liver function in Malaysian plantation workers who regular spray paraquat and found no significant difference with 2 control groups.

Ong and Glew described an unusual case where a 28 year old prostitute inserted a tampon soaked with paraquat into her vagina but removed it 10 minutes later after a severe burning sensation. She died of liver and lung failure two weeks after admission.

Reference

Ng TS and Thong KW. Paraquat poisoning. Med.J.Mal. 32:278-281 1978.

Chan KW and Cheong IKS. Paraquat poisoning: a clinical and epidemiological review of 30 cases. Med.J.Mal. 37:227-230 1982.

Wong KT and Ng TS. Alleged paraquat poisoning in Perak. Med.J.Mal. 39:52-55 1984.

Howard JK, Sabapathy NN and Whitehead PA. A study of the health of Malaysian plantation workers with particular reference to paraquat spraymen. Br J Ind Med 38:110-116 1981.

Ong ML and Glew S. Paraquat poisoning: per vagina. Postgrad Med J. 65:835-836 1989.

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Syed Zahir I, Nik Aziz S, Tariq AR and Sarvanathan K. The pattern of acute poisoning in the government medical unit, general hospital Kuala Lumpur, 1987 J.Per.UKM 12:147-156 1990

Azizi BH, Zulkifli HI and Kasim MS. Risk factors for accidental poisoning in urban Malaysian children. Ann. Trop. Pediatr 13:183-188 1993.

Azizi BHO, Zulkifli HI and Kassim MS. Circumstances surrounding accidental poisoning in children.Med.J.Mal. 49:132-137 1994.

POISON FOODS

Unlike acute poisoning where a person consumes a chemical that is known to be toxic, poisoning from foods are cases where the substance ingested was thought to be food and the presence of the poison not suspected.

Aflatoxin

Aflatoxin is a secondary metabolite of some specific strains of the fungus *Aspergillus flavus* and *Aspergillus parasiticus*. Chong and Beng in perhaps the first report of the presence of aflatoxin in unrefined groundnut oil in 1965 remarked on the possible human hazard of consuming some contaminated oils. Moir reviewed research on aflatoxins in Malaysia and pointed out the need for legislation to control the import and sale of such foodstuffs in 1968.

In October 1988 an outbreak of food poisoning occurred in six towns, first in Hilir Perak on the 14th and 15th of the months and on the 19th in the Kinta district. The epidemic was traced to a common source which was a of batch of 'loh see fun', a Chinese noodle originating from one factory in Kampar. 17 people were admitted to various hospitals, 16 were under 12 years old. Children were most severely affected in the outbreak, 12 of whom died. Besides children, the only other fatality, the thirteenth was an elderly man. From the onset of illness, death occurred between 1 to 7 days. Post mortem findings included centrilobular liver necrosis, haemorrhagic pancreatitis and acute renal tubular necrosis. Initially the toxin was elusive. The necropsy finding however, were consistent with aflatoxin which was detected in specimens sent to a U.S. laboratory. Investigators could not determine when the aflatoxin got in to

the food process. The time interval from production of the 'loh see fun' to its consumption appeared rather short for the mould to have produced the toxin and investigations into the raw ingredients did not yield any results.

References

Chong YH and Beng CG. Aflatoxins in unrefined groundnut oil. Med.J.Mal. 20:49-50 1965.

Moir GFJ. Aflatoxins Scientific Malaysian 1:24-25 1968.

Lye MS, Azizan AG, Mohan J et.al. An outbreak of acute hepatic encephalopathy due to severe aflatoxicosis in Malaysia. Am.J.Trop.Med.Hyg. 53:68-72 1995.

Bacterial Toxins

It was estimated that 9.6 per 100,000 cases of food poisoning occurred in Malaysia in 1981. The Information and Documentation System Unit of the MOH publishes data on the number of food poisoning recorded in Malaysia annually together with other notifiable diseases. Although these cases of vomiting, abdominal pain and perhaps diarrhoea are not entirely poisoning from bacterial toxins alone, they are the large majority. There were 1,255 cases notified in 1990, giving us a rate of 7.1 per 100,000 in 1990. There was only one death. In 1998 there were 6,976 cases and 3 deaths.

The mass media also report many outbreaks of food poisoning from time to time but not all are medically investigated to identify the cause. *Staphylococcus aureus* is however no doubt a common cause. There is an example in one report by Rampal of school children who fell ill after eating fried meehoon in Kapar, Selangor. It has been found in a study of *S. aureus* isolated from food samples that 23% of strains are enterotoxic. Rampal, Jegathesan and Lim reported another incident due to *Bacillus cereus* in fried noodles in a school hostel in Klang in 1984.

References

Lim YS, Jegathesan M and Kang SH. The occurrence of enterotoxigenic strains of Staphylococcus aureus in foods. Med.J.Mal.38:27-30 1983

Rampal L. A food poisoning outbreak due to Staphlococcus aureus, Kapar, Malaysia 1983 Med.J.Mal. 38:294-298 1983

Rampal L, Jegathesan M and Lim YS. An outbreak of Bacillus cereus food poisoning in a school hostel, Klang. Med.J.Mal. 39:116-122 1984

Crabs

It is generally not well known that crabs can be poisonous. But of the 10,000 species only a handful are poisonous. Most of these poisons are neurotoxins. There has been a death in Singapore in a Thai from eating the Mosaic crab (*Lophozozymus pictor*) and a death from another genus *Demania* has been described in the Philippines. However, in general such events are rare and so far unknown in Malaysia.

References

Ng PKL, Chia DGB, Koh GL and Tan LWH. Poisonous Malaysian crabs. Nature Malaysiana 17:4-9 1992.

Dhatura

The `thorn apple', dhatura is a commonly seen wild fruit in the Malaysian jungle. A few cases of poisoning have been known to occur. Dhaturine, the poison, contains laevoscyamine, hyoscine and other alkoloids and causes both central and peripheral anticholinergic manifestations.

Reference

Gimlette JD. Datura poisoning in the Federated Malay States. Br.Med.J. 1:1137-1139 1903.

Gururaj AK and Khare CB. Dhatura poisoning: a case report. Med.J.Mal. 42:68-69 1987.

Jering

Jering is the fruit of the *Pithecellobium jiringa*, (or *Pithecellobium lobatum*). It is a traditional Malay food, usually eaten as 'ulam', a form of salad. In 1991, UKM physicians reported 2 cases of acute renal failure that followed ingestion of jering. The clinical presentation included loin pain, fever, nausea, vomiting, oligouria, haematuria and sandy particles in the urine. The renal failure resolved with conservative therapy and alkalinisation of the urine. Another case from the same unit was reported in 1995 under the name 'djenkol bean' (it may also be known as 'jengkol').

Reference

H'ng PK, Nayar SK, Lau WM and Segasothy M. Acute renal failure following jering ingestion. Sing Med J. 32:148-149 1991.

Segasothy M, Swaminathan M, Kong NC and Bennett WM. Djenkol bean poisoning (djenkolism): an unusual cause of acute renal failure. Am J Kidney Dis 25:63-66 1995.

Yong M and Cheong I. Jering induced acute renal failure with blue urine. Trop Doctor. 25:31 1995.

Margosa Oil

Margosa oil is an extract from the seed of the Indian neem tree *Azadirachta indica*. It is yellow and has a bitter taste. It is occassionally used by Indians as a general household remedy. In large doses it can cause nausea and diarrhoea. Simpson and Lim described a suspected case with a fatal outcome in 1935. In 1978 there was a report of 4 cases of infants who consumed between a teaspoon to two tablespoons of the oil and developed severe tonic-clonic convulsions. The causative toxin was unknown and was thought may have been a contaminant.

Over 3 years from 1977, Sinniah and Baskaran described 13 cases of Indian children, aged between 21 days to 4 years, who presented to the UH with margosa oil poisoning. None were malnourished. They had been given 5-30ml of the oil. Symptoms of drowsiness, tachypnoea, and seizures began 30 mins to 4½ hours after ingestion of the oil. 8 patients required assisted ventilation. 2 of the children, including the neonate, died. Necropsy of one patient showed, liver and proximal renal tubule damage, cerebral edema together with mitochondrial damage resembling Reye's syndrome. The oil, imported from India in 44 gallon metal drums were traced and samples obtained from several retailers were found to be toxic to mice.

Although contamination cannot be ruled out it is obvious that the oil itself is toxic and the concentration of toxin varies from batch to batch. Repeated cases and experimentation in rats indicate that margosa oil itself can cause Reye's syndrome. Margosa oil acts an a mitochondrial uncoupler disrupting the respiratory chain. Animal experiment suggests also that L-carnitine and glucose infusion may be useful in management of margosa oil induced Reye's syndrome. Chronic ingestion of margosa oil could possibly be causally related to Indian childhood cirrhosis.

References

Simpson IA and Lim EC. Margosa fruit suspected to be cause of a case of fatal poisoning. Mal.Med.J. 10:138-139 1935.

Paranjothy M. Suspected contaminated margosa oil poisoning. Med.J.Mal. 33:17-19 1978.

Sinniah D and Baskaran G. Margosa oil poisoning as a cause of Reye's syndrome. Lancet i:487-498 1981

Koga Y, Yoshida I, Kimura A et.al. Inhibition of mitochondrial functions by margosa oil: possible implications in the pathogenesis of Reye's syndrome. Pediatr Res 22:184-187 1987.

Mushrooms

It is a common general belief that some mushrooms are poisonous in Malaysia. Actually fewer than 10% of all known mushrooms are poisonous and instances of poisoning are rare. Reported cases are few.

12 soldiers were involved in an incident in Perak, with one death in 1980. Although the species of mushroom could not be identified in this instance, the clinical features were of muscarine toxicity.

Reference

Supramaniam V and Mohandas R. Outbreak of mushroom poisoning among Malaysia soldiers in Perak. Med.J.Mal. 35:28-30 1980

Puffer Fish

The 'ikan buntal' which belongs to the family Tetraodontidae is a common fish in estuarine and inshore areas of our Malaysian waters. Most fishermen are aware of its poisonous nature although allegedly some Sabah fishermen consume the meat without much morbidity. There have two reports of poisoning have come from Sabah in the 1980s. Lyn, reported one episode where 4 were poisoned and 1 died in Sandakan in 1985. Kan, Chan and David reported an incident on Pulau Tambisan, off Sandakan in 1987 where 18 people were involved with 9 deaths. In 1997, a 69 year old woman of Cambodian descent was successfully resuscitated in the Casualty Department and ventilated in Intensive Care in Kuala Terengganu without a diagnosis. 24 hours after cardiac arrest her prognosis was thought hopeless, her pupils fixed and dilated and her medullary reflexes absent. The next day, she opened her eyes and coincidentally the history was obtained that she consumed the roe of the 'ikan buntal'. She eventually recovered completely.

The poison called tetraodontoxin, is found in the viscera (ovaries, testes and liver) of the fish. It is a very potent neurotoxin that can cause acute respiratory cessation probably both from depression of the medullary centres and muscular paralysis. A report from Singapore points out that anti-cholinesterase drugs is able to produce rapid muscle power recovery.

References

Berry PY. Puffer fish poisoning. Malayan Scientist. 5:42-46 1970.

Chew SK, Goh CH, Wang KW, Mah PK and Tan BY. Puffer fish (tetrodotoxin) poisoning: clinical report and role of anti-cholinesterase drugs in therapy. Sing.Med.J. 24:168-171 1983.

Lyn PCW. Puffer fish poisoning: Four case reports.. Med.J.Mal. 40:31-34 1985.

Kan SKP, Chan MKC and David P. Nine fatal cases of puffer fish poisoning in Sabah, Malaysia. Med.J.Mal. 42:199-200 1987.

Loke YK and Tan MH. A unique case of tetrodotoxin poisoning. Med.J.Mal. 52:172-174 1997.

Shellfish

Many shellfish or molluscs like the 'kerang' are common local foods and harmless. Some species however are poisonous. There has been one report of 5 fatal cases from neurotoxic illness in Sabah, involving the species *Oliva vidua fulminans*. The olives, well known to shell collectors, are generally not known to be poisonous.

The Red Tide

Usually bacterial gastroenteritis is the most serious ill effect that results from the clams and mussels that are widely consumed all over Malaysia when they have been improperly cooked and stored. However, the West Coast of Sabah has been assailed several times by a much more deadly form of shellfish poisoning known as the 'red tide'. Roy reports that its first ever known occurrence in Sabah was between January and April 1976. It is caused by planktonic dinoflagellates which bloom in the sea at certain times. As a result of as yet unknown triggers, it blooms in quantities sufficient to produce brick red patches in the coastal waters. The species of dinoflagellete implicated in Sabah has been identified as *Pyrodinium bahamense*. The dinoflagellate, besides being poisonous to man, is also poisonous to fish and molluscs, which may die or get washed up in large numbers on the

beaches.

The disease has been known to occur along the West coast of the USA and Canada, Japan, the Philippines and also along the Atlantic coast of Canada, Britain and Portugal.

The first human poisoning epidemic in Sabah occured in January 1976 when children in the village of Kampong Maruntum became ill hours after a meal of shellfish. 2 died and 7 others were admitted for food poisoning. In March another outbreak occurred in Sipitang involving a total of 186 people. 2 children died. The third incident happened within three weeks on the island of Mantanni in the district of Kota Belud. Of 7 cases, a 6 year old boy died.

The poison is a neurotoxin which causes death by respiratory paralysis. Patients who survive recover within 24 hours enough to be discharged although weakness may remain for a longer period. Prevention of such outbreaks depends on the Fisheries and Medical departments organising a monitoring system to check for the toxin level in shellfish and the appearance of the "red tide".

Reference

Roy RN. Red tide and outbreak of paralytic shellfish poisoning in Sabah. Med.J.Mal. 31:247-251 1977.

Kan SK, Singh N and Chan MK. Oliva vidua fulminans, a marine mollusc, responsible for five fatal cases of neurotoxic food poisoning in Sabah, Malaysia. Trans.R.Soc.Trop.Med.Hyg. 80:64-65 1986.

Star anise

The fruit of the Chinese star anise, *Illicium verum* is widely used as a flavouring in curries in Malaysia. However, a poisonous variety *Illicium religiosum*, the Japanese star anise, which resembles the former and has been reported to have caused poisoning in an adult Tamil male.

Reference

Simpson IA. A poisonous variety of star anise. Mal.Med.J. 10:140-141 1935.

Tapioca

Tapioca, or cassava, is widely consumed in Malaysia and in some areas of Sarawak it is the staple food for some tribes. It contains cyanide in either free form or combined as a glycoside called limarin. An enzyme linase releases cyanide from limarin once tubers are dug out of the ground. Tapioca leaves also contain high amounts of cyanide. The cyanide content of tubers depends on the variety, and varies with the soil it is cultivated in. A higher concentration is also found in the deeper and smaller tubers and increase with duration of storage.

In Sarawak, 2 cases of poisoning were reported in 1978 in Malay children. It occurred after they had consumed some tapioca cake. Both children recovered. Chemical analysis of the cooked tapioca revealed a level of 3 mg/kg of cyanide.

In Kelantan , HUSM paediatricians reported an incident involving a family in which a 1½ year old girl died. Her 6 year old sister was admitted seriously ill, while an 8 year old sister and mother who also ate the tapioca had no significant illness. The uncooked tapioca which had been dug out 8 days ago contained 181mg/kg of cyanide. The 6 year old girl who survived had a blood cyanide level of 4mg/l on admission.

UKM workers have studied the effect of consuming large amounts of tapioca leaves on thyroid function. Volunteers fed 200gm of tapioca leaves over 12 consecutive days had their triiodothyroxine (T3) and thyroxine (T4) levels significantly lowered. Urinary iodine excretion was also significantly decreased. Tapioca contains thiocyanate which interferes with iodine uptake and inhibits iodine concentration in the thyroid gland.

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CHRONIC DRUG ABUSE AND POISONING

ALCOHOL

There is little data available on the extent of alcoholism or alcohol abuse in Malaysia. However it was in the past mostly a problem faced by families of plantation workers. The root cause of this alcohol problem in the estates is to be found with the colonial plantation owners, who introduced 'toddy' to keep the Indian labourers under control and dependent.

While Indians tended to drink toddy, Chinese in the past consumed alcohol in the form of 'samsu' made from distilling rice wine or 'tuak'. The British also introduced drinking beer, stout and spirits like whisky, brandy and vodka through imports. The local brewery industries in Malaysia started after 1930.

Today the alcohol problem is probably still greatest in the Indian community because of this history but it is now growing mainly in the culture of social life in urban areas across racial barriers. The growth of this habit is largely due to Western commercial advertisement. A study, by Maniam, of patients visiting general practitioners in the business district of Kuala Lumpur, found that 70% of Chinese, 42% of Indians and 11% of Malays had consumed alcohol in the past or present. The vast majority of these however only consumed alcohol on social or special occasions. But of those currently consuming alcohol 81% of Malays compared to 14% of Indians and 10% of Chinese imbibed more than 5 units a session. Islam keeps more Malays away from alcohol but those who do drink, drink more.

In a survey of patients in the orthopaedic, surgical and medical wards in KL GH, Saroja and Kyaw noted that 10% were alcohol dependent or abusers and another 36% alcohol 'drinkers'. Indians formed the majority (53%) of alcohol abusers, but among their sample of 198 'drinkers', Chinese were most numerous (40%).

In a 3 year series from 1993 in Seremban Hospital, George and Chin observed 34 subjects with alcohol induced psychotic disorders admitted to the psychiatric ward. 30 (88%) were Indians, 3 were Chinese and only 1 was Malay. 32 were men. These patients had a mean weekly consumption of 70 units of alcohol and a mean duration of drinking for 14 years. They were predominantly from the low social class. The majority consumed samsu, beer was the second commonest choice. 44% had abnormal liver function. 2 developed delirium tremens and one died from it.

Shahrom *et.al.* have noted in a series of forensic post-mortems in KL that of 59 road accident victims, 11 (19%) had blood alcohol levels greater than 100mg/dl. The largest group (6) consisted of Indian males between the ages of 20-40 years.

In the 1990s Malaysians have spent around RM 2 billion on alcohol annually. This amounts to 6.3 litres of spirits per capita a year which is many times higher than our neighbouring countries.

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ANALGESICS

Segasothy, in 1982, studied three selected sections of the population for analgesic abuse. These were the Kuala Lumpur GH inpatients, a Malay kampong and two rubber estates with a predominantly Indian population. The findings were fairly similar in all groups. Together just over 1,000 individuals were surveyed. 0.5% to 2.0% of the people had consumed more than 2 kg. and 5% to 10% had consumed more than 250gm. of analgesic. For about half these people the reason for using the analgesic was headache.

The commonest analgesic consumed was paracetamol followed by two proprietary drugs namely *Cap Kaki Tiga* and *Cap Harimau* which used to contain phenacetin together with aspirin and caffeine. The phenacetin has now been substituted with acetaminophen and salicylamide respectively. Mostly adults between 20 to 60 years were involved. Neither a sex nor racial predilection could be determined. Chang and Lim analysed many illicit analgesic preparations seized from Chinese medical halls in Johore in 1989 and reported finding phenylbutazone in 25 out of 30 such medicines.

In related studies, Segasothy and others have looked at renal papillary necrosis and found that they were almost exclusively caused by analgesic abuse. The rate of renal papillary necrosis in intravenous urograms was 20(2.0%) out of 1011 in KL GH from 1968 to 1981, 11(1.8%) out of 594 in GH Ipoh from 1981 to 1985 and 8(1.3%) out of 601 in GH Terengganu from 1981 to 1985. Males were predominant, and were mainly in the 30-60 age group. In a prospective study, 12 cases of analgesic nephropathy were seen in GH KL in just over a year. Headache and arthritis were commonly cited as reasons for analgesic abuse. One particular group of patient prone to excessive analgesic use are leprosy patients who have neuritis pain. 46 (20%) of 235 leprosy patients admitted to having consumed more than 2kg of analgesics. Intravenous urograms done on 28 of these subjects however did not show evidence of renal papillary necrosis in any of them.

In a study of 180 patients with end-stage renal disease at GH KL it was found that 6.7% admitted to consuming excessive quantities of analgesics. These analgesics were thought to be the primary cause of the renal failure in 3.9% and a contributing factor in 2.8%. Besides salicylates, paracetamol is a major causes of end-stage renal disease from renal papillary necrosis. Segasothy has noted at least 15 cases that could be attributed to paracetamol.

See and Venketesh, from Kapit Hospital, Sarawak, reported that over two years from 1991, 68 patients were admitted with bleeding having ingested the *Cap Kaki Tagi* analgesic powder out of a total of 107 patients with upper gastrointestinal haemorrhage. 4 of the 68 developed perforated gastric ulcers. Most patients were ages between 41-65 years and there were 5 times more males than females. The peak seasons these events occurred were the rice planting season in November and December and harvesting season in March to May.

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MARIJUANA

Marijuana, or *Cannabis indica* is more commonly called ganja locally. It grows in the natural state in Malaysia and has been used by various sections of the indigenous people for medicinal purposes such as the relief of asthma, or even as a herb for cooking. In a number of hospital and prison surveys in the 1970s, ganja was the drug abused in between 3% to 12% of all drug addicts. It is often a link in the chain of drugs used which starts with cigarettes and progresses to heroin. The same young single male as for narcotic abuse is the typical ganja victim. But more Malays and Indians relative to Chinese have been found in the case of ganja abuse.

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OPIUM AND ITS DERIVIATIVES

The origins of addiction to opium in Malaysia has to be understood in the context of the history of European colonial expansion into the Far East in the early 18th century. Greedy for commercial gain British and other European traders sold opium to China and other eastern nations, creating a habit and demand that was not previously there. The European political powers refused to see any moral wrong in this enterprise and Britain went as far as to fight two wars with China to defend its power to sell opium to the Chinese. The sufferings that arose from the abuse of opium have been immeasurable and the European powers deserve our full condemnation.

Wu Lien-Teh writing in 1926 to plead that the medical profession take a greater interest in the problem of this narcotic abuse, wrote that 2.5 million pounds of opium was consumed in 1923 in Malaya contributing 24% of the total government revenue by way of tax on it. This amount was in fact already lower than that for the period from 1900-1920 where the opium tax provided almost half the total revenue. In 1923, the opium sold amounted to 33gms. of opium for every person, or since it was mainly the Chinese that were involved, there was 96gms. for each Chinese person in Malaya. The number of registered opium smokers in Malaya was actually 52,313 in 1929. The problem was no less in East Malaysia. In that year Sabah and Sarawak consumed 250,000 and 600,000 pounds of opium respectively. This was for Sabah, 105 gms. and for Sarawak, 216 gms. per Chinese person. Contrary to the belief that most of the addicts came from China with the habit, Wu showed that a big majority (60-80%) acquired the habit after they landed here.

Persons in responsible positions and positions of authority then were even heard to say that opium was good for the East as Easterners needed such a sedative in place of alcohol! Many misconceptions about opium were prevalent. It was at times held to be protective to plague, tuberculosis or malaria. It was also misused by mothers to keep their babies quiet. Nevertheless, the deleterious effects on society were always obvious and that the world's conscience was active as manifested in a succession of Opium Conferences held in Shanghai, the Hague and Geneva - a total of 7 between 1909 to 1925. The political will of the nations involved was however wanting. Little decisive action was taken; as a result many nations today are still paying for their sins.

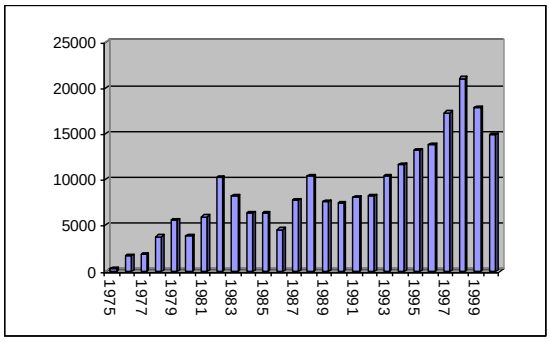
The Post War Period

Up till the end of the Second World War opium continued to be traded legally with a few traders holding the monopoly in Malaysia. It was immediately after the war that the colonial government banned the trade in opium. Despite this, the established addicts must have somehow continued to get their drug as illegal contraband. However, the image of the opium addict was that of an effete, useless old man and so the spread of opium abuse was largely checked from spreading as it was a social disgrace.

Wagner and Tan noted in 1970 that there was no attraction for opium among the young in Malaysia. However, through the 1960s in the West drug abuse started to spread like wild fire among the rebellious young. Figures in the late sixties showed an alarming trend in the U.S.A. and Britain. It became a fashionable thing closely linked to cigarette smoking as the next and more daring thing to do.

With the network of illegal drug suppliers probably already established for the old opium addicts in Malaysia the new market of young drug abusers was easily exploited. In the early 1970s local expert opinion was divided. Some contended that the threat was minimal but some felt that it was rapidly getting out of hand. Surveys among hospitals admission and prison populations did not find large numbers, although this said nothing about the epidemiology in the population at large. The studies did however define the person at risk to drug abuse. In that period drug abusers were mainly urban and therefore mostly Chinese. Women were involved in less than 2% of the cases. Youth usually got involved after the age of 15 years, with the peak age group being those between 20 to 35 years. They tended to be single, with poor educational attainment and of low socio-economic status. They mainly caught their habit from friends. Opium was used mainly in the form of morphine and heroin. Marijuana abuse was common but alcohol, amphetamine and barbiturate abuse did not appear to be a serious problem in the population.

Figure 6.1 Number of new drug addicts reported in Malaysia from 1975-2000



Source: Criminal Investigation Department, Royal Malaysian Police

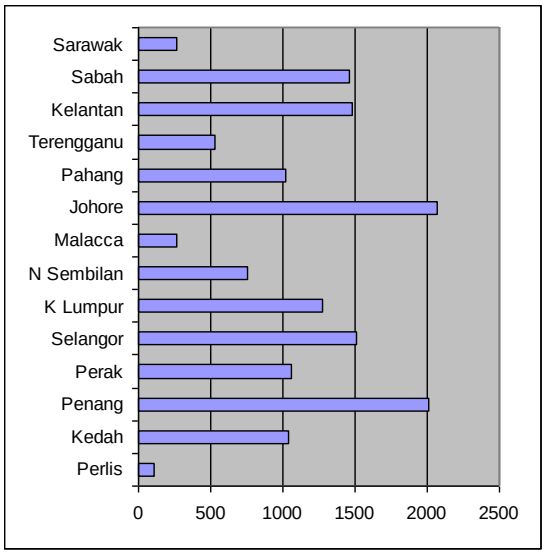
In 1970 there were 711 estimated drug addicts in Malaysia, but this was probably an underestimate. The explosion of the problem is seen the rise in the number of identified cases the next few years. By 1979 a total of 46,778 drugs addicts had been registered. Rough estimates of what the unreported 'iceberg' below the surface amounted to was put at 200,000 to 500,000. The government very rightly took note

of this as a security problem and has been very active in its efforts of identification and rehabilitation through agencies such as "PEMADAM". As of 1986 the total number of drug abusers registered stood at 110,363. The estimated total number 'outside' was about 500,000. Sabah and Sarawak were largely unaffected in the 1970s, but in the late 1980s the number seems to be increasing.

The number of new cases recorded each year remains high, usually above 10,000 but there is hope that the trend is perhaps now turning after reaching the peak. Nevertheless, it may be years before we see the end of this drug tragedy. Our hospitals are still seeing a large number of intravenous drug users seriously ill with septicemia, pneumonia and endocarditis commonly due to *Staphylococcus*. Serum hepatitis is rampant and lately AIDS is multiplying in very alarming numbers among these drug addicts. Though probably rare, even neonates with narcotic drug withdrawal occur as a result of mothers who are abusing narcotics.

The problem which was originally mainly among urban Chinese is now a multi-racial one. Large numbers of Malays are involved and the rural areas are not spared. Of the total reported number of reported addicts from 1970 to 1986 48%, the largest group, were Malays. Indians in proportion to their population account for slightly more than 10% of the total. The immigrant workers also pose a risk. It still remains that males who are unemployed or labourers and are single between the age of 20 to 29 years are the typical group at risk. The number of drug abusers employed as labourers has increased over the years with a corresponding fall in the unemployed. Together these people account for about 75% of drug dependants. A majority (73%) of dependants report less than 5 years of drug use. They probably account for most of 60% who report spending RM10.00 or less on drugs a day in 1986. The 18% who spent above RM16.00 daily are likely those who have a longer habit.

Figure 6.2 Number of drug addicts reported by state in Malaysia 2000



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PAAN or BETEL-NUT CHEWING

The habit of chewing a quid of betel leaf, areca-nut and lime dates from antiquity and was

recorded by chroniclers who travelled with Magallen when he landed in the Philippines in 1521. Paan, to use its local name is the chief factor responsible for oral cancers in Malaysia. The habit has been prevalent from South Asia across all of Southeast Asia and was especially prevalent in the lower social class among the Indians. Investigating Tamil rubber tappers in 1968 Ahluwalia and Ponnampalam found that the habit was more strongly entrenched in those who immigrated from India. Among this group the prevalence of the habit was greater than 80%. 50% of women and 25% of the men who chewed betel-nut started the habit between 10-20 years of age. Most said they picked up the habit from co-workers or their parents. Reasons given for adopting the habit included to relief toothache, to remove residual taste or smell after a meal or to offset toilet or body odour. Tobacco was often added to the quid. Tobacco increases precancerous oral lesions.

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TOBACCO

SMOKING

The catalogue of diseases tobacco smoking induces is formidable. They include lung cancer, chronic bronchitis, lung emphysema, coronary artery disease, neonatal disease, oral cancer, laryngeal cancer, peripheral vascular disease and bladder cancer. It is appropriate to think of it therefore as a form of drug abuse and chemical poisoning.

The National Morbidity Survey of 1986 involving 38,521 persons, found that 41% of the male population above 15 years old smoked. On the other hand only 4.1% of females smoked. 72% of smokers consumed more than 10 cigarettes a day. For every 10 smokers there were 2.2 people who were former smokers. Among these previous smokers 18% had stopped smoking for 1 year or more.

The Second National Morbidity Survey of 1996 involving 32,991 persons, found that 49% of males and 3.5% of female adults above 18 years old were current smokers. The overall rate of smokers (25%) was higher among Malays (28%) and among those with only primary education (28%). On average an adult smoker consumed 13 cigarettes a day. The mean age for starting to smoke was 20 years. 44% of smokers had tried to quit smoking but were unable to. Heavy smokers tend to be those who start younger. The survey also showed that 17% of adolescents smoked and this was more common in the rural area (18%) compared with urban areas (15%). Kelantan (32%), Pahang (30%) and Sabah (29%) were the states with highest prevalence rates. Penang (21%) had the lowest.

University Students

There have also been a number of small surveys of the smoking habits of several different groups in Malaysia. University students have been the focus in a number of studies as they are potentially trend setters. In 1967 Patrick reported that among university students only 2 of 77 women smoked compared to 30% of 322 men. Almost all the male smokers had either one or both parents who were smokers. About half of the non-smokers had parents who smoked.

Pathmanathan repeated such a survey among medical students in 1972 and found that 25% of males and 1.6% of females were current smokers. 18% of males said they were ex-smokers. The smoking habit increased over the years in university. 16% were smokers in the first two years. In the third year 26% and in the final years 29% were smokers. Malays were more often smokers. Wong and Chen also did a study among medical students in 1987. They found to 17% of males and 0.8% of females smoked. 2.6% were ex-smokers.

From a sample of 209 university students surveyed in 1992, UKM workers found 32% of males in local universities smoked compared to 23% of Malaysian males in Australian universities. Only 2% of all the females smoked. Fewer medical students smoked, compared to students in other fields. 70% of smokers said they started smoking before they entered university, which was similar for the students in Malaysia and Australia. About 7% were ex-smokers. From these studies it would seem that over the past 30 years the smoking habit is neither losing ground nor gaining support among university students. Malaysian women are, unlike women in the West, resisting the trend of smoking quite well.

Doctors

In a study of 120 doctors in USM in 1991, Yaacob found that 18% were smokers, 13% were ex-smokers and 69% never smoked. 19 of the 21 smokers only indulged when they felt they could not be seen by the public. 81% of non-smoking and 43% of smoking doctors had advised healthy people to stop smoking. 92% of non-smoking doctors supported the ban of in the hospital compared to 52% of the smoking doctors.

The Armed Forces

Among 103 doctors in the armed forces, questioned in 1980 Supramanian found that 50% were smokers, and 11% were former smokers. 18% started in their teens, 59% in their early twenties and nobody started above the age of 35 years. Teenage starters appear to become heavier smokers.

Community Surveys

Pathmanathan has reported in 1974 that in a rural Negeri Sembilan community, 34% of adults were smokers with a male:female ratio of 2:1.

Teoh found in a heath-screening survey in Ipoh held in 1985, 38% of males and 3.5% of females among 1,800 admitted to being current smokers. Teo and Chong found that 37% of male executives smoked in voluntary survey of 406 respondents in KL in 1985. 23% smoked more than 10 cigarettes a day. The percentage of smokers were quite similar in all the races. These voluntary surveys have an obvious bias inherent in them.

In a general practice survey of 562 adult respondents in a business district of Kuala Lumpur, Maniam found that 63% of Malay men, 36% of Chinese men and 26% of Indian men were current or former smokers. Only 3% of females ever smoked. Malays who smoked averaged 14 cigarettes a day, more than Chinese (9 a day) and Indians (10.6 a day). Those who drank alcohol also smoked more. Heavy smokers drank more alcohol. Smokers who drank usually began smoking at an earlier age than when they started on alcohol.

Minors

Although the Control of Tobacco Product Regulations 1993 prohibits the sale or supply of cigarettes to a person below 18 years, Zulkifli and Rogayah found that six minors aged 15-17 years were successful in 114 out of 177 attempts to purchase cigarettes in Kelantan. They also found that although cigarette companies advertise non-cigarette products, 29% of 12 year old children identified the advertisement as promoting cigarettes.

The Ministry of Health realises that failure to act aggressively in the 1970s has made effective action more difficult in the 21st century.

CHEWING

Like chewing betel nut, tobacco chewing is popular among some communities. Gan found that in a survey of 472 Kadazan women in Keningau, 59.5% chewed tobacco. The habit can lead to oesophageal, pharyngeal and laryngeal cancers, cancers of the pancreas and urinary tract, and nicotine has its cardiovascular effects.

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CHRONIC ENVIRONMENTAL POISONING

INSECTICIDES

Farmers and agricultural workers who spray pesticides are exposed to these chemicals repeatedly over a long period of time. In our hot equatorial climate many do not adequately cover themselves with protective clothing.

Organophospates

Serum cholinesterase levels give an indication of toxic exposure to organophosphate insecticides. Using a Kit cholinesterase by Boehringer Mannheim (CHE MHE 1 1447297) some UKM workers have found normal controls recorded levels of 5160±600U/l while a sample of 66 padi farmers from Kedah, using organophosphates pesticides had a mean level of 4480±1130U/l. Taking a value of 3500U/l as a cut off point, 25% of farmers had abnormally low values. Nerve conduction studies also demonstrated that many farmers suffered from chronic organophosphate exposure. As a group the farmers had a significantly lower current perception threshold with stimulus especially at the 2000Hz frequency.

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LEAD POISONING

High levels of lead in the blood can produce IQ deficits and neurobehavioral changes especially in children. It was formerly thought that levels above 40μg/dl was the level harmful to humans. It has now been realised that even levels above 10μg/dl can be harmful.

Lead has been used as an additive to petrol to improve engine performance and vehicle exhaust fumes had been increasing the level of lead in the cities to unhealthy levels in the past. In 1982 Lim *et.al*. reported that the mean blood lead level in pregnant women in the Klang valley was 17.3μg/dl. Unleaded petrol was introduced in

1992. Hisham *et.al*. reported that in 1996 the mean blood lead level in a sample of 97 pregnant women had decreased to 7.7µg/dl. However 28% had levels above 10µg/dl.

In cases of lead poisoning, unlike the other chronic poisons above, the victim is characteristically an innocent inadvertent sufferer. It is mainly peculiar to the car battery industry in Malaysia. In 8 factories with a total of 251 employees, Lim and Abu Bakar found that 88% of the female workers and 62% of the males in the smaller factories had a blood lead concentration of above the proposed limit of 40 µg/dl for females and 70 µg/dl. for males. In subsidiaries of larger multinational only 7.6% of male worker had blood levels exceeding the proposed limit. It was found that corresponding to this, the lead-in-air levels were higher in the small factories.

A case of a 20 month old child with encephalopathy due to lead poisoning was reported, by Nasir *et.al*, the source of which was in the dwelling place which was within a factory compound. The parents had similarly high levels of lead in the blood.

Ming, Surif and Abdullah used urine delta-aminolevulinic acid as an indirect indicator of lead exposure in a study of primary school children in Kajang and Sepang in a study in 1997. They did not find any excessively high lead exposure. The Ministry of Health monitors food items for lead and has found about 3% of samples from fish to eggs contravening the legal levels.

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PNEUMOCONIOSES

See Respiratory diseases

ANIMAL BITES AND STINGS

FISH

A handful of local fish can sting.

1. Cat fish

Commonest and most well known poisonous fish is the common cat fish, 'ikan sembilang' or 'ikan tapah' (*Paraplotosus albilabris*). Its two relatives, 'ikan sembilang karang' (*Plotosus anguilaris*) and 'ikan kelara' (*Plotosus canias*) are even more poisonous. The poison is secreted by glands on each side of its dorsal and pectoral spines. The cat fish normally lies at the bottom of muddy areas where they can be stepped on or they may sting when carelessly handled by 'fishermen'. The poison has been classified as a toxalbumin, but comparatively little is known about it. It produces immediate agonising pain. This may lead to necrosis if severe, resulting in the loss of a limb or may be fatal in the exceptional case.

2. Sting-rays

There are three main groups of sting-rays in the seas and river mouths surrounding Malaysia. Firstly the whip-tailed sting-rays (genus *Trygon*) of which there are a few species. Secondly the eagle rays of the genus *Myliobatis*. Thirdly, there are the cow-nosed rays of the genus *Rhinoptera*. It is commonly known that the barbed spines of the sting-rays can inflict a pain that is out of proportion to the size of the

wound. Necrosis may follow with loss of limb or life.

3. Scopion fish

The scopion or goblin fish (*Scopaenidae*) inhabit open water on rocky coasts and coral reefs and have a mottled appearance which affords them a camouflage. These fish have a most highly developed poison mechanism, with a reservoir at the base of the poison gland. All these fish have dorsal fin spines on the head that are exceedingly poisonous and living fish should be handled with great care. The most poisonous is the "ikan lepu" (*Synanceia verrucosa*). Another related fish is the *Synanceia horrida*. Another example, the "ikan semaram" (*Apistus cottoides*) is a smaller fish. Stings produce immediate pain, followed by nausea. There is usually great swelling of the affected limb and ulceration in the vicinity of the wound. Cardiac and respiratory difficulty may follow and death probably ensues without treatment.

Reference

Le Mare DW. Poisonous Malayan fish. Med.J.Mal. 7:1-8 1952.

JELLY FISH

Many bathers at the seaside have experienced jelly fish stings. In view of their abundance in our shores it is a good thing that besides the intense pain their stings inflict they are not more lethal. The exception is when anaphylaxis develops. The chemical involved in the sting is acidic and some relief is afforded by washing with a weak solution of ammonia or soda.

SNAKE BITES

There are about 500 species of poisonous snakes worldwide but less than 200 have been known to cause envenomation in man. Southeast Asia is a region with one of the highest incidence of snake bites with at least 38 different species of venomous snakes. Malaysia has about 16 of these venomous snake out of about 110 species of snakes found here.

Reid estimated that the yearly mortality in Peninsula Malaysia from snake bites was 0.5 per 100,000 between 1958 to 1961. He counted 2,114 cases of snake bite in Peninsula Malaysia of which 34 (1.6%) were fatal. Over 67% of medically treated cases occurred in Northwest Malaysia. As many as 14% were treated only as outpatients. With the growth of the population, the number of cases of snake bites rose, although the incidence did not. Lim and Abu Bakar recorded 15,919 snake bites from 1960 to 1968, an average of about 1,700 a year. There were 122 (0.8%) victims who died. From 1979 to 1983 Ambu and Lim recorded 26,733 instances of medically seen snakebites, ranging from 5,077 to 5,492 a year.

Perlis and Kedah are the states with the highest incidence of snake bite, 260 and 180 per 100,000 respectively. The East coast states of Kelantan Terengganu and Pahang have incidences in the range of 38 to 50 per 100,000. Perak, Negeri Sembilan and Penang have about 30 cases per 100,000 and the Southern states of Selangor, Malacca and Johore have the lowest incidences in the order of 10 to 17 per 100,000.

Snake bites are largely a rural and occupational hazard. The typical patient is a Malay farmer in Kedah. The risk to males is twice that to females and the group between 11 to 30 years are mostly affected. Two- thirds of the bites occur in daylight and 76% of the victims are bitten below the knees. It is commonly assumed that bites from venomous snakes are frequently fatal. This is not so. At least half of those bitten by proven poisonous snakes escape without any significant envenomation. The locally important venomous snakes can be grouped into three families.

1. Viperidae

The Malayan Pit Viper (Agkistrodon rhodostoma)

This snake is responsible for 85% of the cases in Perlis and Kedah. It is however, not so common outside the Northwest of Malaya and not found in Borneo. Pain and swelling start within a few minutes of the bite and may involve the whole limb. Blistering may be seen. There may be bruising. Local necrosis occurs in 11% of patients. If systemic envenomation occurs, the most outstanding symptom is haemorrhage due to a clotting disorder. Haemoptysis is the commonest manifestation and may be seen as early as 20 minutes after the bite. Severe haemorrhage from multiple sources can lead to death. Anti-venom is indicated when the bleeding diastesis is seen. Bleeding symptoms in its natural course lasts less than a week but persisting coagulation defects last up to 4 weeks.

Pit Vipers

There are a number of local species including the mountain pit viper (*Trimeresurus monticola*), the shore pit viper (*T. purpureomaculatus*), the flat-nosed pit viper (*T. puniceus*), and the Wagler's or Temple pit viper (*T. wagleri*). Only the latter two are found in Borneo. Like the Malayan pit viper these snakes are more common in the Northwest of Malaysia. Reid has documented over 76 cases. He observed one death.

2. Elapidae

The Common Cobra (Naja naja)

Outside the Northwest of Peninsula Malaysia, this is probably the commonest snake to bite man, especially in the East coast of the Peninsula. Rarely death may occur as rapidly as 15 minutes if the poison, a neurotoxin, is directly injected into a vein. In just under 50% of cobra bites there is envenomation marked always by pain and swelling with blistering. Swelling usually starts from 1 to 3 hours after the bite and reaches a maximum in 24 to 48 hours. There is a dusky discolouration around the bite marks which deepens and extends each day. Local necrosis is the rule and the area is wider than the surface changes suggest.

Choo KE *et.al*. noted that elapid snake bites were more common than viper bites in a series of 83 children with snake bites in Kelantan over 5 years. 11 required antivenom, 3 of them developed minot adverse reactions to the antivenom. 4 children required ventilatory support. 2 children died.

Neurotoxic effects occur in only about 13% of cases. The earliest symptom is drowsiness. Difficulty in opening the eyes, speaking moving the lips, tongue and in swallowing follows in 1 to 4 hours. Onset of weakness in the large trunk and limb muscles occurs latest and is also the last to clear on recovery. Death may result from aspirating saliva or respiratory paralysis usually within 24 hours. In those who survive the neurotoxic symptoms resolve in 2 to 3 days.

Kraits

The Malayan krait (*Bungarus candidus*), and the banded krait (*B. fasciatus*), are the two local important species. Only the latter occurs in Sabah and Sarawak. Krait bites typically do not cause local swelling. They are relatively uncommon. The systemic poison these snake have is a neurotoxin. Abdominal pain may be severe but fatality is rare.

Coral Snakes

Bites by the two local species, the blue Malaysian coral snake (*Maticora bivirgata*), and the banded Malaysian coral snake (*M. intestinalis*), are uncommon. Typically they are

also painless and do not cause swelling. The IMR has recorded one death in a 2 year old girl one hour after being bitten in 1956.

The King cobra (Ophiophagus hannah)

This is not a common snake although it has a notorious reputation. In cases of systemic envenomation death is usually quite fast, ranging from 20 minutes to 6 hours.

3. Hydrophiidae

Sea Snakes

A survey by Reid and Lim in 1957 showed that fewer than 15% of fishing folk bitten by sea snakes sought treatment at government hospitals. They form less than 1% of the medically treated snakebite cases. The commonest sea snake is *Enhydrina schistosa*. Clinical features of envenomation may look like neurotoxicity but it is in fact a myotoxin. Myalgia especially on movement is seen 1 to 3 hours after a bite and myoglobinuria occurs in 3 to 6 hours. Hyperkalaemia is a potentially lethal complication.

In a five year review in Kelantan in 1990, Choo KE *et.al*. did not record any sea snake bite.

References

Reid HA, Thean PC and Martin WJ. Epidemiology of snake bite in North Malaya. Brit.Med.J. i 992-997 1963

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Muthusamy E. Snake bite: experience in Bukit Mertajam District Hospital, Pulau Pinang. Sing.Med.J. 29:383-386 1988.

Tan KK. Choo KE and Ariffin WA. Snake bite in Kelantanese children: a five year experience. Toxicon 28:225-230 1990.

SPIDERS

Reports of poisonous spider stings are rare. In 1951 Wolfe investigated one case reported in the newspaper. A 10 year old girl in Kedah died following a sting by a large spider of the suborder *Mygalomorphae*, possibly *Lampropelma violaceopedae*. She was bitten on the finger and became unconscious after an hour and died after fits after 7 hours.

Reference

Wolfe EDB. Death from the bite of a spider. Med.J.Mal. 5:375 1951.

BEES AND WASPS

Ramanathan and Hwang documented 2 cases who developed acute renal failure following beestings and Thiruventhiran et.al. have reported the same following wasp stings.

References

Ramanathan M and Hwang SL. Acute renal failure due to multiple bee stings - case report. Med.J.Mal. 45:344-346 1990.

Thiruventhiran T, Goh BL, Leong CL et.al. Acute renal failure following multiple wasp stings. Nephrol Dial Transplant 14:214-217 1999.

CHAPTER 7

CANCERS

Without reports from a population based cancer registry, the epidemiology of cancers in Malaysia can only be roughly guessed at. From medically certified deaths, which form about 30-40% of all deaths, we note that as a group cancers have risen from forming 6.7% of deaths in 1966 to 8.9% in 1976 and then 10.3% in 1986. In 1998 cancers as a group were the second largest group of medically certified deaths behind cardiovascular diseases accounting for 10.8% of the total.

The most useful source of information on which are most likely the commonest cancers come from the few hospital pathology based studies that have been reported. Unfortunately, these form only a fraction of the true total number of cancers. An urban bias will probably exist in view of the location of the major hospitals. Furthermore, cancer statistics based on biopsy records are inherently biased in favour of sites more accessible to biopsy. There would be some underdiagnosis of malignancies that are relatively inaccessible to biopsy.

Peninsula Malaysia

The earliest series comes from Marsden whose report in 1958 was based on 4,650 consecutive specimens of cancers sent to the IMR. The next 2 series, by Kutty and Balasegaram (1964-1970) and by Armstrong and Ahluwalia (1969-1971), were also bases on biopsy specimens at the IMR. Lim in 1982 reported a series of all cases seen at the UH from 1972 to 1974 including those in which diagnosis was only clinical. Leukemia may not have been included as a cancer in some the earlier reports.

Two overlapping series, one by Chong and the other by Thanaletchimy cover cancers at GH KL for the years 1980-1984 and 1981-1985 respectively. The former are cases from the UKM pathology laboratory, the latter the GH laboratory. Some specialities, like urology go only to one laboratory, so a combined total of these two series gives a better picture of the spectrum of malignant disease at our largest hospital. The commonest malignancies from these combined series are given in the tables below. Only the five commonest are given because incomplete data does not accurate addition.

From Penang, Hooi and Devaraj reviewed Penang Hospital admissions for 1995 and found 1333 patients admitted with cancer an average of 2.2 times (range 1-17) per patient that year. They accounted for 6.6% of total admissions, and accounted for 13.8% of inpatient deaths.

It can be roughly seen that over the years the pattern of cancers has changed a little. Skin cancers, for example, have taken a lower rank and lung cancer have risen among men. The cause for this is that probably more biopsies of internal sites such as the lung and bladder have become more widely available. Therefore, it is difficult to be really certain what the commonest malignancy was in the past and whether the pattern has in fact really changed today, especially among men. Among women however, there is little doubt that the two most important cancers are those of the uterine cervix and the breast. Cancer of the cervix appears to have been the leading cancer by a wide margin in the 1950s and 1960s. However the gap between it and breast cancer has narrowed and it may be that breast cancer might even have overtaken cancer of the cervix to become the leading cancer among women. Together they form almost one third of all malignancies in women.

Table 7.1 Commonest cancers in Peninsula Malaysia from pathological specimen

a. Males and Females

Kutty and Balasegaram 1964-1970 (n=10,093)	
1. Cervix	12%
2. Skin	9.4%
3. Neck Glands*	8.6%
4. Oral	7.6%
5.Colorectum	7.0%
6. Nasopharynx	6.4%
7. Breast	5.8%
8. Lung	3.9%
9. Stomach	3.8%
10. Oesophagus	3.3%

*** excludes thyroid and parotids**

b. Males

	Marsden (n=2351)		Armstrong and Ahluwalia (n=1704)		Lim (n=1047)		Chong & Thanaletch		Hooi & Devaraj (n=638)
1.	Skin	12.7%	Nasopharynx	15.7%	Lung	13.2%	Nasopharynx	13%	Lung
2.	Oral	9.0%	Skin	12.9%	Colorectum	11.0%	Lung	11%	Nasopharynx
3.	Nasopharynx	9.0%	Colorectum	7.6%	Liver	10.9%	Bladder	11%	Colorectum
4.	Stomach	7.4%	Lung	7.5%	Stomach	10.3%	Colorectum	8%	Leukemia
5.	Colorectum	6.4%	Stomach	5.0%	Nasopharynx	6.0%	Oral	7%	Larynx
6.	Lung	5.8%	Oesophagus	4.9%	Oesophagus	5.2%			
7.	Oesophagus	4.8%	Liver	3.9%	Leukemia	4.9%			
8.	Liver	4.3%	Larynx	3.5%	Skin	4.1%			
9.	Soft tissue	4.0%	Bladder	2.8%	Bladder	2.8			
10.	Penis	3.9%	Penis	2.4%					

c. Females

	Marsden (n=2299)		Armstrong and Ahluwalia (n=1676)		Lim (n=898)		Chong & Thanaletch		Hooi & Devaraj (n=695)
1.	Cervix	20.2%	Cervix	24.9%	Cervix	17.8%	Cervix	24.0%	Breast
2.	Breast	13.2%	Breast	13.8%	Breast	10.7%	Breast	19.0%	Cervix
3.	Skin	8.1%	Skin	7.6%	Colorectum	7.7%	Colorectum	7.0%	Colorectum
4.	Oral	7.2%	Nasapharynx	6.9%	Stomach	6.7%	Ovary	6.5%	Leukemia
5.	Ovary	6.4%	Colorectum	5.9%	Lung	5.6%	Oral	5.5%	Ovary/Lung
6.	Colorectum	5.8%	Ovary	4.8%	Ovary	5.5%			
7.	Nasopharynx	4.8%	Uterus	4.3%	Skin	4.8%			
8.	Uterus	4.3%	Lung	2.7%	Leukemia	3.9%			
9.	Stomach	4.0%	Stomach	2.7%	Thyroid	3.6%			
10.	Choriocarcinoma	3.9%	Thyroid	2.4%					

Significantly, both these cancers are amenable to measures for early detection and treatment. Without doubt therefore, in cancer prevention, greatest effort must be taken in tackling these two in terms of health education, screening and early treatment.

From another angle Lim documented deaths registered due to cancer in Kuala Lumpur for the years 1979 to 1981. In Kuala Lumpur medically certified deaths constituted 98% of all deaths, in contrast to 38% for the rest of the country. The leading cancer causing deaths are given in Table 7.2 . Lung and stomach cancers are the two major cancers that noticeably rank higher among cancers causing deaths than in the biopsy based studies.

Table 7.2 Commonest cancers causing deaths in Kuala Lumpur.

Males (n=1529)		Females (n=995)	
1. Lung	24.1%	1. Lung	13.9%
2. Liver	12.8%	2. Cervix	9.7%
3. Stomach	11.1%	3. Stomach	9.1%
4. Leukemia	8.1%	4. Leukemia	8.9%
5. Colorectum	6.8%	5. Breast	8.3%
6. Nasopharynx	6.0%	6. Colorectum	7.5%
7. Oesophagus	4.7%	7. Liver	6.5%
8. Pancreas	2.9%	8. Ovary	3.7%
9. Lymphoid tissue	2.7%	9. Nasopharynx	3.1%

Racial Differences

An interesting feature about many cancers in Malaysia is that they show a very distinct difference in incidence among the various races. In many cancers Chinese show a higher incidence. It seems likely that this is not only apparent, due to their higher utilisation of hospitals, but a real phenomenon. As Malaysians share the same weather and environment, it leaves lifestyle and genetic constitution to account for the differences. The ranking of common cancers for the various races is given in Table 7.4 and 7.5.

Nasopharyngeal cancer constantly ranks higher in Chinese men than in other races. Oral cancers rank higher in Indian men and women compared with others.

Sarawak

In a histopathology base series of specimens from all over Sarawak, Andrew analysed 1,326 malignancies for the years 1981 and 1982. The Chinese again accounted for the highest rates of cancers. It may partly be due to the fact they stay mainly in the towns and have greater access to the hospitals. Chinese had the highest number of cancers of the nasopharynx (36%), cervix uteri (44%) and breasts (42%). Malays contributed most to skin cancers, including melanomas (41%) and thyroid cancers (36%). The highest number of lymphomas were observed among the Ibans. Excluding secondary and unspecified malignancies in lymphnodes the commons cancers in males and females are given below.

Table 7.3 The commonest cancers in Sarawak 1981 and 1982

Males (n=670)		Females (n=656)	
1. Nasopharynx	11.2%	1. Breast	15.4%
2. Skin	7.9%	2. Cervix	14.5%
3. Stomach	7.3%	3. Skin	5.8%
4. Liver	6.1%	4. Thyroid	5.6%
5. Lymphoma	5.7%	5. Uterus	5.0%
6. Rectum	4.8%	6. Nasopharynx	4.9%
7. Leukaemia	4.8%	7. Ovary	4.1%
8. Lung	3.7%	8. Stomach	4.0%
9. Thyroid	3.3%	9. Lymphoma	3.4%

Sabah

In an old paper covering the years 1963 to 1966, Muir, Evans and Roche analysed the distribution of 380 specimens sent for pathological examination. The specimens were actually sent to the British Military Hospital in Singapore and then to the Royal Army Medical College, London for confirmation. More recently, Ganesan, Pillai and Gudum analysed all the histologically diagnosed cancers in the state of Sabah from November 1983 to October 1988. There was a total of 1,574 specimens.

Table 7.4 Commonest Cancers among Men of different races from biopsy specimens

	(IMR) Marsden		(IMR) Armstrong and Ahluwalia		(UH) Lim		(GH KL) Chong & Thanaletchimy	
Malays								
	(n=513)		(n=388)		(n=110)			
1.	Skin	21.8%	Skin	19.3%	Lung	14.5%	Bladder	15.0%
2.	Nasopharynx	10.6%	Nasopharynx	11.1%	Liver	11.8%	Haematological	15.0%
3.	Soft tissue	7.4%	Colorectum	10.3%	Leukemia	10.0%	Nasopharynx	11.5%
4.	Lymph nodes	6.5%	Bladder	4.1%	Stomach	5.5%	Colorectum	11.5%
5.	Oral	5.7%	Lymph nodes	4.1%	Rectum	5.5%	Lung	9.0%
6.	Nose and sinuses	3.7%	Lung	3.3%				
7.	Colorectum	3.7%	Prostate	3.1%				
8.	Lung	2.9%	Stomach	2.8%				
9.	Stomach	2.9%	Bone	2.8%				
10.	Bone	2.9%	Oesophagus	2.8%				
Chinese								
	(n=1306)		(n=1020)		(n=713)			
1.	Nasopharynx	11.5%	Nasopharynx	20.0%	Lung	14.9%	Nasopharynx	17.0%
2.	Skin	11.4%	Lung	10.9%	Liver	12.6%	Lung	15.0%
3.	Stomach	8.9%	Skin	9.0%	Stomach	9.8%	Stomach	10.5%
4.	Lung	7.8%	Colorectum	7.0%	Nasopharynx	7.7%	Bladder	10.5%
5.	Colorectum	7.1%	Stomach	5.5%	Rectum	6.9%	Rectum	6.5%
6.	Oesophagus	6.5%	Oesophagus	5.4%				
7.	Liver	6.3%	Liver	4.4%				
8.	Oral	4.8%	Larynx	2.7%				
9.	Penis	3.5%	Bladder	2.6%				
10.	Soft tissue	3.4%	Penis	1.7%				
Indians								
	(n=532)		(n=253)		(n=201)			
1.	Oral	22.1%	Skin	14.2%	Stomach	15.9%	Oral	20.5%
2.	Skin	9.4%	Penis	8.7%	Oesophagus	9.0%	Oesophagus	13.0%
3.	Stomach	8.3%	Colorectum	7.5%	Skin	8.5%	Stomach	13.0%
4.	Penis	7.9%	Stomach	7.5%	Lung	7.0%	Larynx	12.5%
5.	Colorectum	7.3%	Larynx	7.5%	Hypopharynx	6.5%	Bladder	8.0%
6.	Lungs	3.8%	Oesophagus	6.7%				
7.	Oesophagus	3.4%	Nasopharynx	5.9%				
8.	Lymphomas	2.8%	Liver	4.7%				
9.	Hypopharynx	2.6%	Prostate	2.8%				
10.	Soft tissue	2.3%	Bone	2.8%				

Table 7.5 Commonest cancers among Women of different races from biopsy specimens

	(IMR) Marsden		(IMR) Armstrong and Ahluwalia		(UH) Lim		(GH KL) Chong & Thanaletchimy	
Malays								
	(n=473)		(n=451)		(n=86)			
1.	Skin	16.5%	Cervix	21.1%	Cervix	15.1%	Breast	22.0%
2.	Breast	12.9%	Breast	14.6%	Breast	10.5%	Cervix	13.0%
3.	Cervix	8.2%	Skin	9.7%	Liver	7.0%	Ovary	10.5%
4.	Ovary	7.2%	Ovary	9.1%	Leukemia	7.0%	Thyroid	8.0%
5.	Oral	4.8%	Colorectum	6.0%	Skin	5.8%		
6.	Thyroid	4.6%	Uterus	4.2%				
7.	Nasopharynx	4.2%	Thyroid	3.5%				
8.	Soft tissue	3.6%	Nasopharynx	2.9%				
9.	Bone	3.0%	Lymphoma	2.7%				
10.	Colorectum	2.8%	Stomach	2.0%				
Chinese								
	(n=1282)		(n=976)		(n=625)			
1.	Cervix	22.8%	Cervix	23.8%	Cervix	18.4%	Cervix	27%
2.	Breast	15.2%	Breast	13.9%	Breast	10.9%	Breast	17%
3.	Skin	6.1%	Nasopharynx	9.3%	Stomach	7.4%	Colorectum	9%
4.	Nasopharynx	6.0%	Skin	6.9%	Lung	6.7%	Nasopharynx	7%
5.	Ovary	5.8%	Colorectum	6.6%	Ovary	5.8%	Stomach	6%
6.	Colorectum	5.3%	Uterus	4.8%				
7.	Uterus	3.6%	Lung	3.8%				
8.	Stomach	3.0%	Ovary	3.5%				
9.	Choriocarcinoma	2.8%	Stomach	2.9%				
10.	Oral	2.5%	Thyroid	2.1%				
Indians								
	(n=544)		(n=213)		(n=171)			
1.	Cervix	24.6%	Cervix	40.4%	Cervix	17.5%	Cervix	28.0%
2.	Oral	19.5%	Breast	12.2%	Skin	12.9%	Oral	17.5%
3.	Breast	8.8%	Skin	5.2%	Breast	9.9%	Breast	13.0%
4.	Skin	5.7%	Colorectum	3.7%	Stomach	6.4%	Oesophagus	10.0%
5.	Colorectum	4.1%	Nasopharynx	2.8%	Oesophagus	5.8%		
6.	Ovary	3.7%	Stomach	2.8%				
7.	Stomach	3.1%	Uterus	2.8%				
8.	Uterus	2.2%	Oesophagus	2.3%				
9.	Thyroid	1.8%	Ovary	2.3%				
10.	Soft tissue	1.8%	Lung	2.3%				

Table 7.6 The commonest cancers in males and females in Sabah

Males				Females			
Muir (n=220)		Ganesan (n=776)		Muir (n=160)		Ganeson (n=798)	
1. Skin	18.6%	1. Nasopharynx	13.7%	1. Cervix	13.8%	1. Cervix	18.0%
2. Nasopharynx	9.1%	2. Stomach	12.6%	2. Breast	10.0%	2. Breast	18.0%
3. Stomach	9.1%	3. Colorectum	11.6%	3. Ovary	9.4%	3. Ovary	9.2%
4. Colorectum	4.5%	4. Skin	10.1%	4. Skin	8.1%	4. Thyroid	6.9%
5. Liver	4.5%	5. Lung	9.3%	5. Thyroid	7.5%	5. Skin	5.9%
6. Connective tissue	4.5%	6. Liver	8.1%	6. Uterus	6.9%	6. Stomach	5.8%
7. Oral	4.1%	7. Lymphoma	7.1%	7. Lymphoma	6.9%	7. Colon	5.4%
8. Bladder	3.6%	8. Bladder	4.4%	8. Connective tissue	6.9%	8. Oral	4.4%
9. Testis	2.7%	9. Oral	4.3%	9. Colorectum	6.3%	9. Nasopharynx	4.4%

Table 7.7 Most Common Cancers reported in the Penang Cancer Registry

CHINESE		**MALAY**		**INDIAN**	
MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
lung	*breast*	*lung*	*breast*	*lung*	*cervix*
nasopharynx	*cervix*	*bladder*	*cervix*	*larynx*	*breast*
larynx	*lung*	*rectum*	*lung*	*esophagus*	*mouth*
rectum	*nasopharynx*	*nasopharynx*	*rectum*	*rectum*	*lung*

Kadazans and Chinese had higher percentages of cancers relative to their hospital utilization rates. Nasopharyngeal cancer was common in these groups and accounted for a large number of their cancers. The most commonly found malignant neoplasms is given in Table 7.6

Cancer Registry

The Ministry of Health has supported the principle of maintaining a cancer registry in Malaysia for more than a decade. In practice, however, poor reporting has produced only false starts nationally. It is hoped now that cancer registries may be successfully implemented regionally. Penang has been most promising in this regard.

Initial efforts over the period 1987-1990 collected 1,762 cases. Based on estimates from the Singapore Cancer Registry 1,561 cases were expected for the year 1989, whereas only 496 were noted. 85% of the case notifications were from one hospital, namely the Mount Miriam Hospital. Table 7.7 show the most frequently reported cancers in that study.

Following this the registry has produced annual statistical reports for 1994, 1995 and 1996. The age-standardised incidence for cancer in Penang those years are given in Table 7.8 and the incidence rates of the 10 most common cancers are given in Table 7.9.

Table 7.8 Age-standardised cancer incidence (per 100,000) in Penang 1994-1996

	1994	1995	1996
Males	115.9	108.3	130.9
Females	119.7	95.4	114.6

Table 7.9 Age-standardised incidence for cancers in the 10 most common sites in Penang, 1996

Cancer Type	Incidence Rate (per 100,000)	
	Males	Females
Lung	30.7	8.3
Breast	-	23.8
Cervix	-	16.2
Colon	8.8	7.3
Stomach	10.9	4.5
Nasopharynx	11.2	3.1
Liver	7.6	2.3
Rectum	4.3	2.1
Other Skin	2.6	3.1
Ovary	-	5.3

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A SYSTEMIC REVIEW

The cancers that affect the different body parts are reviewed below. Benign tumours are not included here. The different body systems are taken roughly in order of the most frequently affected by cancer in a descending order.

The Alimentary System

ORAL CANCERS

Were it not for the habit of chewing betel quid, oral carcinomas would hardly need to be mentioned. But oral carcinomas were formerly the second commonest histologically confirmed malignancy in Malaysia at the IMR in the 1960s (next to carcinoma of the cervix). However the incidence of oral cancers is on the decline, judging from the number of cases collected at the IMR, although we do not have figures from a national registry to prove it. This is in accordance with the decline of the habit of betel quid chewing, which thankfully never had the support of advertising that cigarette smoking enjoys. As for deaths due to cancer, Lim found that for Kuala Lumpur between 1979 and 1981 oral cancers did not rank among the top ten except among Indians. It was fifth among Indian women and sixth among Indian men.

One point prevalence study of a

representative sample of 11,707 adults above 25 years from throughout Malaysia has been done over 5 months from 1993 to 1994. In that study Zain *et.al*. found that the prevalence of oral cancer was 40 per 100,000.

Since 1967, Ramanathan and his co-workers at the Department of Stomatology at the IMR have collected over 2500 cases of malignant oral tumours. In a review of patients with carcinomas totalling 898 from 1967 to1972, they found that 60% were Indians, 22% were Malays and 18% were Chinese. As Indians accounted for only 11% of the national population then, they had a relative risk of greater than ten times that of either Malays or Chinese of developing oral carcinoma. In a follow up study covering 1978 to 1984 they recorded 749 cases, a fall in absolute terms. 64% were Indians, 20% Malays and 17% Chinese, which is an increase in the proportion of Indians.

The peak age group affected are adults between 50-59 years. Among Chinese and Malay men however the peak occurred in the 60-69 age group. The ratio of men to women affected was 1:1.1 among Indians and Malays which is unusual when compared to the pattern seen in Western countries, China and even India. Only among Chinese is there a male preponderance (3.5:1) like most foreign figures.

The commonest site for the carcinoma was the buccal mucosa (43%) followed by the tongue (15%), gums and alveolus (14%), palate (13%), lip (6.4%) and floor of the mouth (4%). The site of tumour corresponds to the habit of betel quid chewing, especially that of parking the quid in the buccal sulcus of the jaw.

Histology

Although Chinese and Malays had a lower frequency of oral carcinoma, they had a higher proportion of anaplastic (Grade III) tumours. Anaplastic carcinomas were especially common among Chinese(14%). It was seen in 6% of tumours among Malays and in less than 2% of tumours among Indians. A follow up report on 100 anaplastic carcinomas in 1981 confirmed its higher frequency among Chinese.

In another report in 1981 they noted that 1.8% of carcinomas were verrucous. These were usually found in betel quid chewers.

Other Histological Tumours

In 1979, Ramanathan and Ng reported that out of a collection of 2,263 cases then, 207 or 9.1% were malignancies other than carcinomas. Of these, 88 were tumours of the minor salivary glands. Mucoepidermoid tumours and adenoid cystic carcinoma were the most common. 71 were lymphomas, of which 43% were reiculosarcomas, 30% Burkitt's lymphoma and 25% lymphosarcoma. 35 were other sarcomas and these were a few melanomas and metastatic carcinomas.

Oral precancerous conditions

From a national registry of precancerous conditions maintained at the IMR between 1967 and 1977, Ramanathan studied a total of 194 lesions. Homogenous leukoplakia (56%) was the commonest condition. Submucous fibrosis accounted for 27 (17%) cases but curiously occurred exclusively in Indians. Speckled leukoplakia (14.5%) and erythroplakia (2.5%) were the other ominous precancerous histological features but were seen only in a few patients. Oral lichen planus, smokers' keratosis and keratosis of the floor of the mouth do not appear to be precancerous conditions in Malaysia.

Ramanathan made a hypothesis that submucous fibrosis could be the Asian form of sediropenic dysphagia, that follows a prolonged period of chronic deficiency of iron and/or B complex vitamins. Yaacob in a study of 54 cases

of oral lichen planus suggested emotional stress may be an important underlying factor. Their patients, 70% of whom were white collar workers did well with reassurance to eliminate fear of cancer.

Indians (72%) accounted for the largest number of patients with oral precancerous conditions. Males represented just over half the total. The peak age group for these lesions was the sixth decade. These features correlated well with the distribution of oral carcinoma and also of the habits of betel quid chewing, smoking and drinking of alcohol.

The 1993 study by Zain *et.al*. confirmed that Indians (4%) have the highest prevalence of precancerous oral lesions including, leukoplakia, erythroplakia, submucous fibrosis and lichen planus, from a sample of 11,707 adults above 25years old. The indigenous peoples of Sabah and Sarawak also had a high prevalence rate of 2.5%, as they too have a habit of chewing betel nut and tobacco. Chinese had the lowest rate of 0.5%.

In a house to house survey of 486 elderly subjects above 60 years old, Ali *et al*. found that 23% had at least one oral mucosal lesion and 3.3% had an oral lesion considered precancerous. Leukoplakia was the commonest oral precancerous lesion. The prevalence of oral mucosal and oral precancerous lesions was highest among the Indians and lowest among Chiense. All except one of the 16 with oral precancerous lesions either smoked or chewed betel quid. 2 subjects, both Indians, had oral cancer.

Risk Factors

There are few other cancers to compare with oral carcinomas in Malaysia in which the main causative agent, betel quid chewing or, is as obvious. However in addition to it, alcohol and smoking increase the risk. The IMR group have found that 85% of patients with oral cancer chewed betel quid, 55% had a habit of consuming alcohol and 29% smoked.100% of Indian women and Malay women with oral squamous cell carcinoma chewed betel quid as did 78% of Indian men.

In a 1973 survey of 407 workers of the lower socio-economic group at government medical and health facilities, Ramanathan found precancerous oral lesions in 7% of Malays, 8% of Chinese and 25% of Indians. In the sample, over 80% of Indians, both men and women, indulged in some form of oral habit, which was either chewing betel quid, smoking or drinking alcohol. Betel quid chewing was most popular. 60% of Malay and Chinese men also had one or more habits. In the majority it was smoking. Few Malay women and no Chinese women indulged in such oral habits, although they not well represented in the sample.

45% of those who chewed betel quid had a precancerous lesion. Those who smoked had a 9% chance, while those who drank alcohol stood a 7% chance of having a precancerous lesion.

Clinical Features

In 1998, Khoo *et.al*. examined the way patients with oral cancers present and reach a diagnosis. They found that from being aware of the lesion, the mean delay due to the patient presenting himself or herself was 29 weeks. 50% of patients delayed seeking professional help for more than 3 months. On the doctor's side the mean time from consulting a medical practitioner to diagnosis was 10 weeks. Misdiagnosis at first presentation is a serious concern.

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SALIVARY GLAND CANCER

In a series of operations for parotid swellings, Arshad reported that 25% of parotid tumours were malignant. There are many varieties of parotid cancers. In his series of 24 cancers the commonest was adenoid cystic carcinoma (6), ex-pleomorphic adenoma carcinoma (5), mucoepidermoid carcinoma (4), acinic cell carcinoma (3), squamous cell carcinoma (2) and one each of adenocarcinoma, malignant lymphoma, haemangiopericytoma and a malignant schwannoma. Recurrences were seen in 5 patients following surgery.

As a note to surgeons, Myint *et.al*. have investigated the branching patterns of the facial nerve, the nerve which is in danger or injury during parotid operations, in Malaysian patients. Classifying them into six types, they found that the classical textbook pattern is one of the least common locally.

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PHARYNGEAL CANCER

Balasegaram has described his surgical experience in 6 cases of patients with carcinoma of the hypopharynx between 1962 and 1967 in Seremban. A 64 year old man died from post-operative staphylococcal pneumonia, another died after 2 months from myocardial infarction and a third died after 8 months with widespread metastases. 3 however were alive and well 5-10 months after surgery.

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OESOPHAGEAL CANCER

Before the 1950s oesophageal carcinomas were considered inoperable and untreatable. After the Second World War a number of surgeons began to report success with surgical excision. Locally in 1952, Mekie in Singapore

noted that it was the 6th most common malignancy seen and formed 9% of all cancers. Of 35 cases seen in 4 years he found that all were Chinese except for 2 Indians. He reported 3 cases where he resected the cancer. 2 patients who had a thoracoabdominal operation survived. 1 who had a 2 stage operation, via an abdominal then thoracic approach (after Lewis) made a satisfactory post-operative recovery but died of bronchopneumonia. Balasegaram reported that between 1962 and 1967 he performed 16 surgical resections and 10 palliative bypass operations on patients with oesophageal carcinoma in Seremban. 3 had tumours in the upper third, 9 tumours in the middle third and 14 tumours in the lower of the oesophagus. There were 18 males and 8 females and they ranged in age from 30 to 77 years. Of the 16 with resections done, there were 3(19%) post-operative deaths, 8(50%) died of metastases and recurrences within several months but 5(31%) were alive 6 months to 3 years after the operation. In the palliative bypass group there were 2 post-operative deaths.

In data from abstracts, UKM experience over 10 years from 1990 showed Indians (46%) were the race most commonly affected race with squamous cell carcinoma of the oesophagus, followed by Chinese (28%) then Malays (23%). Males and females were about equally represented among the 117 patients. A history of smoking and alcohol was noted in 70% of patients. Among Indian women betel nut chewing was a common risk factor. Among 388 patients with carcinoma of the oesophagus seen in the UH over 11 years from 1987, Chinese formed 47%, Indians 41% and Malays only 12%. Relative to the population distribution of their hospital admissions, Indians had a relative risk of oesophageal carcinoma 7.2 times greater than Malays while Chinese had a 5.8 times greater risk than the Malays. The mean age in all races was 63 years and median 62 years. Among Chinese males were 2 times more likely to get the cancer than females whereas among Indians the sexes were equally affected. The ratio of males to females among Malays (1.4:1) was in between. There were 17 operable cases of oesophageal carcinoma at the UH between 1993 and 1997. The were 2 post-operative deaths (12%) and the crude 1 year survival rate was 65%.

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GASTRIC CANCER

The Ministry of Health listed stomach cancer as the fifth commonest malignancy in Peninsula Malaysia by discharges from and death in government hospitals in 1998. With a total of 1,164 cases the overall national incidence was 5.3 per 100,000, though the figure is probably an underestimate. There were 164 deaths recorded in government hospitals giving a mortality rate of 0.7 per 100,000.

Although a common malignancy, we do not know its true incidence. King and Kutty tried to study its epidemiology by examining all histological gastric carcinoma specimens from 6 large state hospitals and the UH from 1965 to 1968. They found 222 cases among Chinese, 58 among Indians and only 24 among Malays. Men were 2-3 times more commonly affected than women in all races. They reasoned however that the incidence in the racial groups may not be very different as the numbers of patients who were willing and had surgery for peptic ulcers and the hospital utilisation rates for the different races showed the same pattern. They failed to consider that peptic ulcers are commoner in Chinese and stomach cancer also probably is. In a report in 1968 Balasegaram noted that out of 326 cases with upper gastrointestinal bleeding seen over 46 months in Seremban, 11 (3.4%) cases were due to gastric carcinoma.

In another series by M.Bahari, Ti and Yong

114 patients with gastric cancer were seen over 5 years at the UH KL in 1976. Patients without histological diagnosis were excluded. Gastric cancer, they noted was predominantly a disease of the Chinese in Malaysia. Chinese formed 78% of their patients compared to 55% of the hospital admissions. In contrast there was only one Malay patient in the series; Malays form 15% of hospital admissions. Indians accounted for 20% of gastric carcinomas and 26% of admissions. The reasons for these racial differences which have also been observed in Singapore have been speculated upon. Environmental factors such as urbanisation, ingestion of liquor, hot food and drink and especially food cooked in superheated fats and oils are prime suspects. The age at diagnosis ranged from 31 to 74 years. The peak occurred in the seventh decade. The male to female ratio was 1.7:1. There was no predilection for the blood group A.

Other data from abstracts report a similar racial distribution in cases seen in Ipoh between 1988 and 1998. Malays, it was estimated, had an incidence 8-9 times less than Chinese and Indians. USM workers in Kelantan calculated that the incidence of gastric carcinoma between 1997 and 1999 was 1.2-1.4 per 100,000 and hence among the lowest reported in the world. They postulated that the low prevalence of *Helicobacter pylori* might be an important factor. In both regions males were more than twice as likely to have gastric cancer as females and the median age was the seventh decade.

Histology

All the tumours in the 1976 UH series were adenocarcinomas, well differentiated in 49%, moderately differentiated in 5% and poorly differentiated in 30%. Colloid adenocarcinoma occurred in 13% and the sclerosing variety in 2.6%.

Clinical features

Epigastric pain, weight loss and anorexia were the commonest presenting symptoms in the UH series. More than half the patients had physical signs of advanced disease such as cachexia, an epigastric mass or Virchow's node. Out of 109 patients subjected to laparotomy, 58% had resectable lesions. But 72% had lymph node metastases, 64% had invasion of adjacent structures, 24% had peritoneal dissemination and 22% had liver metastases, underlining the fact most are advanced disease at presentation. The site of the tumour was in the antrum in 53%, in the lesser curve in 17%, the cardia and fundus in another 17%, in the body and greater curvature in 11% and the remaining 3% there was diffuse infiltration of the entire stomach.

The Ipoh series of 250 patients from 1988 to 1998 found similar features. 82% had stage IV disease and a further 11% had stage III disease. Only 67% (166) were offered surgery at which 148 (60%) were found to have resectable lesions.

Survival

The operative mortality was 14% in the UH series. Follow-up information was incomplete but 28 were known to survive one year and 2 to survived 5 years. The Ipoh series recorded a 1 year survival of 86% for stage I and 80% for stage II and II patients. Even a 50-60% survival from stage IV patients survived 1 year.

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COLORECTAL CANCERS

Like many parts of the world, colorectal carcinomas are common in Malaysia in both men and women. They are the commonest cancers of the alimentary tract. Taken separately, colon cancer and rectal cancer both consistently ranks among the top ten cancers. Taken together cancers of the colon and rectum probably rank as the second most common cancer. However the true incidence has not been documented adequately in Malaysia and we do not have a really good estimate of its incidence and whether there are any local peculiarities.

In a survey of biopsy specimens from 6 large state hospital and the UH over 4 years from 1965, King and Kutty noted 135 colon cancers among Chinese, 22 among Indians and 17 among Malays. There were 221 rectal cancers among Chinese, 28 among Indians and 45 among Malays. In that era rectal tumour could be biopsied in clinic but specimens of colon cancers could only come from surgical resections, hence the numbers seen would be affected by the willingness of patients to have surgery. They suspected a lower frequency of colorectal carcinoma among Indians who normally have high hospital utilisation rates.

UKM workers have reported that in their experience rectal bleeding was the reason for colonoscopy that yielded the a diagnosis of colorectal cancer most often (11/88). This was followed by altered bowel habit (5/56).

Lim *et.al*. reported their experience with adjuvant chemotherapy for colorectal cancer in 98 patients referred to the Institute of Oncology, KLGH between 1986 to 1994. These accounted for 31% of colorectal cancer patients actually referred to the centre. All had primary surgical treatment elsewhere. The mean age of the 98 patients, 55years, was relatively low. 5% were under 30 years old. Chinese formed 65%, Malays 27%, Indians 6% and others 2%. 34% were rectal tumours. Rectosigmoid and sigmoid tumours accounted for another 28.5%. By Duke's stage only 2% were stage A, 43% stage B and 47% stage C. In 8% the stage was not known.

It has been mentioned in abstracts that in UH 33% of colorectal tumours occurred in the rectum, 24% in the sigmoid and 16% in the caecum in a 5 year series from 1993. In HUSM, over 3½ years from 1995 it was noted from 58 patients undergoing surgery that 28% had rectal cancers, 52% cancers in the left colon, 10% in the transverse colon and 12% in the right colon. In UH Chinese accounted for 69% of 199 patients, Malays 20% and Indians 10%. In HUSM Malays formed 72%, Chinese 24% and 3% were Thais. Considering the local population for these hospitals, it appears that the incidence is higher among Chinese. Males slightly outnumbered females in a ratio of 1.1-1.3:1. In HUSM 5% had stage A disease, 48% stage B, 38% stage C and 9% stage D disease at surgery. In UH 82% of patients received surgery, 2% were deemed inoperable and 18% refused surgery. It has also been noted that there were 120 cases of colorectal carcinoma operated on in UKM over 6½ years from 1990 with a post-operative mortality of 6.7% and the crude survival rate was 80% with recurrences occurring in 38%.

Familial Polyposis coli, the autosomal dominant chromosome abnormality located on chromosome 5q, does occur in Malaysia. It causes adenomatous polyps to develop throughout the colon that inevitably turn malignant. Tay *et.al.* described a 45yr old patient who presented with a rectal carcinoma who had additional features that fit Gardner's syndrome. Surgeons in the public hospitals in KL and Seremban have identified at least 16 families, 10 Chinese, 4 Malay and 2 Indians, with the condition.

A case of a 14 year old Malay boy who had 3 benign adenomatous colonic polyps and who presented with acute intussusception from a mucinous adenocarcinoma in the transverse colon which acted as the lead point has been reported.

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ANAL CANCER

Over 12 years from 1970, Krishnan and colleagues at the UH reported seeing 18 anal canal cancers, compared with 430 colonic carcinomas in the same period. Anal cancers seen there thus accounted for 4% of large bowel tumours which is higher than the figure of 1-2% mentioned in the West. Males and females were equally affected, but males had anal margin tumours more often, whereas females usually had anal canal tumours, the dividing line being the dentate line. All races were represented but Indians may be slight more commonly affected. The majority of patients (78%) were over 50 years. The mean age was 57 years.

14 tumours were squamous or basosquamous, 2 were adenocarcinomas and 2 were melanomas. 72% presented late with either inguinal nodes involved or metastases present. 67% had surgery, which consisted of abdomino-perineal resections. Some received chemotherapy and radiotherapy which has more recently become the first choice of treatment.

Four cases of anorectal melanomas have also been reported among Malays from UH.

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LIVER CANCER

This is another major cancer more common among the Chinese. Curiously, it is also very common among the Senoi, although the other races in this region also have a high incidence. It carries a very poor prognosis like lung and stomach cancer. It was the third most frequent cause of death from cancer among men and fifth among women in KL between 1979 and 1981.

Numerically Chinese account for most cases of hepatocellular carcinoma (HCC). But among the Orang Asli HCC is their most common malignancy, accounting for 36% of malignant neoplasms in an autopsy series between 1967 and 1975, and its presentation exhibits a few differences. It tends to occur among the Senois, in a younger age group and there is a greater male preponderance than in Chinese. The tumours in Senois generally present in the presence of cirrhosis, as multiple nodules studding both lobes of the liver instead of being one large solitary tumour as in Chinese.

Risk factors

There is an extremely close relationship between Hepatitis B virus (HBV) infection, and HCC in Senois reaching nearly 100%. In the other races Sumithran reported that Hepatitis B antigen was positive in between 72-82% of Chinese, Malay and Indian patients with HCC. He found that healthy individuals and cirrhotics seen in the same period at the UH KL were positive for the HBsAg in about 10% and

45% of cases respectively. Among non-Senois where the link between Hepatitis B and HCC is not so close, a role for aflatoxin as an additional carcinogen has been argued.

In 1994, Lopez *et.al*. however noted that although only 75% of 80 patients with HCC had HBsAg, 99% had evidence of HBV infection. Only 6 (8.6%) of these patients had anti-HCV of whom 4 were also positive for HBsAg. None of those tested had anti-HDV.

Clinical features

Yap and Peh report that they found a serum alpha-fetoprotein level (>20iu/ml) in 70% of 50 patients. In 28 of these 35 the level was greater than 500iu/ml. Alpha-fetoprotein production did not correlate with tumour differentiation. Balasegaram reported that 85% of a series of patients with primary liver cancer in 1977 had raised urinary ascorbic acid. Normal individuals had urine ascorbic acid concentration of 1.5-2.5mg/100ml, whereas 65% liver cancer patients had concentrations of 7-75mg/100ml and 25% had concentrations between 2.5-7mg/100ml.

Balasegaram, who had a special interest in liver surgery collected a series of 1,011 patients at the KL General Hospital. In his book published in 1982 he recounted he performed major hepatic resections in 111 (11%) patients. 190 had various types of palliative surgery sometimes in combination with other treatment modalities. 395 received either chemotherapy, radiotherapy, immunotherapy or a combination of these. In 315 the disease was too advanced and no therapy was given.

Long term survival was only seen in those who had surgery. 22 were alive and well at the time of reporting but only 3 had survived more than 5 years. Postoperative mortality, considered as deaths before discharge from the hospital, was 13.5% for major hepatic resections. Of 96 discharged from hospital 38 died more than one year after the operation.

Paediatric liver cancer

Childhood liver cancer does not appear to be more common in Malaysia in comparison to the European, American and Australian experience, either when liver cancers as a percentage of admissions to hospital or as a percentage of all neoplasms are studied. 5 cases were seen in the UH KL between 1967-1969. Three were hepatoblastomas, one was hepatocellular carcinoma and the other a cholangiocarcinoma. In a very rare case, Ramanujam *et.al*. reported a case of a malignant mesenchymoma in a 6 year old child who had a previous resection at 18 months old for a mesenchymal harmatoma. In a 7 year period from 1980, Cheah *et.al*. at the UH noted that in the 6 cases of hepatocellular carcinoma they had, 5 were seropositive for HbsAg. The youngest of these patients was 7 years old.

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BILIARY CANCER

Jalleh, Mukherjee and Krishnan collected an experience of 24 cases of biliary malignancy at the UH over 5 years from 1981. Most were Chinese (67%). Their ages ranged from 20 to 73 years but the peak age group was the 60 to 69 year olds who comprised 46%. One third of the tumours were in the gallbladder. Upper duct (17%), intrahepatic carcinomas (13%) and extensive tumours (25%) where the site of origin could not be identified formed other large groups.

20 patients had surgery. For 7 only a biopsy was performed. 4 others had paliative drainage only. 7 had a cholecystectomy and 2 had extensive resective. But even in those who had tumour resction there were no known long term survivors.

Lim and Sellaiah have observed 2 cases of extrahepatic cholangiocarcinomas with coincidental biliary ascariasis. In other reports of Asiatic Cholangiohepatitis which typically affect rural Malay women above 50 years old, Khan in USM observed 2 out of 20 cases with periampullary carcinoma and Din in KL GH noted 1 out of 49 cases with a similar situation. These cases commonly have large soft brown bile duct stones and occasionally *Ascaris* worms were found. It appears likely that the worms and the stones and the cholangiocarcinomas might be aetiologically linked in this rural population setting. The worms being migratory might not be found as often as they are actually present. Though thought to be benign, their presence might cause irritation that leads to inflammation. Perhaps when they die in the bile ducts they initiate the formation of the large bilirubinate stones. Infection may set in from time to time and in certain circumstances the chronicity perhaps leads to a malignancy.

Other rare tumours seen include one case report of a carcinosarcoma of the gall bladder.

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PANCREATIC CANCER

In his personal series of 87 cases presenting with jaundice, pain and weight loss seen over 10 years in Seremban and KL from 1965, Balasegaram observed that cancer of the head of the pancreas formed 76% of the group termed periampullary carcinoma. Carcinoma of the ampulla of Vater, formed by the union of the bile and pancreatic ducts, formed another 16% while the remainder 8% were carcinomas of the duodenum and common bile ducts. The overall 30 day mortality for all these patients was 39%, 34 deaths, including all 10 who had no surgery or only exploration and drainage operations. Mortality rates for those who had tumour resection was 33%, for those who had internal drainage of bile, 63%, and for those who had external T-tube drainage of bile, 20%.

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LYMPHOMAS, CARCINOIDS AND OTHER BOWEL TUMOURS

The assortment of other gastrointestinal malignancies are difficult to treat separately.

In a 6 year study of malignant lymphomas at the UH beginning 1967, Ti, Murugasu and Yong

noted 17 cases. These formed 4.8% of all gastrointestinal tumours. All were adults with an average age of 49 years. There were 10 males to 7 females. Malays and Orang Asli were found in numbers higher than their normal hospital utilisation rates although the numbers involved are small.

Carnoid tumours are rarer yet findings. Dutt and colleagues presented a few case reports in 1969. Leiomyomas are usually considered benign but an aggressive leiomysarcoma in the duodenum in a 45 year old Malay woman has been reported by Ho *et.al*.

There were two case reports of an intra-abdominal desmoplastic small round-cell malignancy. One was a 16 year old Malay boy in Kelantan with the tumour in the jejunal mesentry reported in 1996. Another such case was in an 11 year old boy, in UH KL, reported in 1997.

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The Respiratory System

NASAL CANCER

Besides carcinomas a few unusual malignancies of the nasal cavity and sinuses have been recorded. Indudharan *et.al*. reported a case of a 78 year old woman with a rare nasal septum chondrosarcoma. She underwent surgical excision and was disease free at 26 months. Sharma *et.al*. reported a 74 year old man with a teratocarcinosarcoma of the nasal cavity and another patient with a malignant paraganglioma.

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Sharma HS, Madhavan M, Othman NH et.al. Malignant paraganglioma of frontoethmoidal region. Auris Nasus Larynx 26:487-493 1999.

NASOPHARYNGEAL CARCINOMA

Nasopharyngeal carcinoma (NPC) has been probably the best studied form of malignancy in Malaysia as a result of interest in the incidence of the disease among Southeast Asian populations. As early as 1955, Lawley had studied a collection of 170 NPC cases pathologically. Armstrong *et.al*. recorded all known cases of histologically confirmed NPC in Malaysia for 10 years from 1968. Special efforts in case finding were made in Selangor where conditions are optimal. They found an age-adjusted incidence among Chinese males and females of 16.5 and 7.2 per 100,000 respectively and an incidence of 2.3 and 0.7 per 100,000 among Malay males and females respectively. Among Indian males the incidence was 1.0 per 100,000. There was no significant changes in the incidence rates over the 10- year period, nor did Yadav, Tan and Singh note a change in a study from 1981 to 1983, for sex and ethnic groups, or for Chinese subethnic groups.

In Chinese subethnic groups, rates were highest among Cantonese, moderate among Khek(or Hakka) and lowest among Hokkien and

Teochiu. Judging from the incidence figures obtained for Selangor there appears to be considerable under-reporting in the less urban states of Malaysia, particularly among females. In Selangor, incidence rates were similar for urban and rural residents, but the incidence was higher among Chinese working in the industrial sector and living in poor neighbourhoods. Armstrong noted that 94% of NPC patients were bread winners or homemakers in the households they came from. 80% had key roles as parent of dependent children.

In a study similar to Armstrong's of 10 years from 1968, Prasad and Rampal attempted to trace every case of NPC in 1988 throughout Peninsula Malaysia. They had 365 cases. The mean age was 47 years, with the incidence increasing with age up to the 40-49 year bracket, after which it plateaued. They noted an incidence of 40.1 per 100,000 among Chinese males and 14.9 per 100,000 among Chinese females in the 40-49 year age group. The numbers were too small to comment on the incidence in the other races.

There have also been a number of reports of NPC from Sabah where it is one of the commonest malignancies. Rothwell calculated that the age-adjusted incidence was 18.6 and 8.4 per 100,000 among Chinese males and females and 15.9 and 8.7 among Kadazan males and females, in whom NPC is also very common. In Sarawak, it seems that the Bidayuhs also have a high incidence of the disease. In a survey of malignancies in 1981 and 1982, Andrew Kiyu noted an incidence rate of 9.0 per 100,000, higher than that for Chinese.

In Kelantan, Indudharan *et.al*. reviewed all the cases seen in the two major hospitals managing NPC over 10 years from 1986. There were 122 cases in a population of just over 1,000,000. They noted that Chinese had a relative risk of 6 times compared to Malays of getting the disease. The ratio of males:females was 2.9:1.

The peak incidence of NPC in the studies in the 1970s was the fifth and sixth decades. The series in the 1980s suggests that the peak age may have shifted about 5 years earlier. A small but important group of patients however, develop the disease before the age of 20 years. Yadav *et.al.*, reviewed 52 juvenile and adolescent patients who accounted for 2.5% of the total number of cases in one series. Young Chinese formed 1.1% of the NPC observed among the Chinese and the ratio of males:females with NPC and were under 20 years was similar to that of adults. In contrast, young Malays with NPC formed a significantly larger group; that is, 11% of all Malay females and 3% of all Malay males. The sex ratio in this age group was 1:1 instead of males being 3 times the number of females seen in adults over 20 years old. The study also found that young Kadazans and Sarawakians grouped together formed 10% of all females and 8.5% of all males, consistent with the earlier findings of Rothwell, although the incidence he reported for 1969 to 1975 was higher. Taken together the Malay-Kadazan-Sarawakian group display the bimodal age distribution, which is also seen in Caucasians. Young Chinese do not have a similar high juvenile incidence peak. The incidence of NPC in young Chinese is similar to the other races although Chinese adults have a much higher incidence. Hence the Chinese show a unimodal age distribution with a peak in the fifth decade.

Risk Factors

Investigators in the late 1960s established that sera of patients with NPC all over the world contained antibodies to the Epstein-Barr virus (EBV) often in much higher titres than normal. These studies firmly implicated the Epstein-Barr virus in the aetiology of NPC but exactly how it causes this is not clear. Viral infection of cells in the nasopharynx is not a regular feature of the normal EBVcarrier state. It may be that it is when the virus invades the nasopharynx that carcinoma can occur. Further observations have indicated that anti-EBV antibodies are useful in the diagnosis and prognosis of patients with NPC. In Malaysia,

Yadav *et.al*. have shown that 90% of NPC cases have IgA anti-viral capsid antigen (VCA) as compared to 2-4% of controls and antibodies like it increase with the stage of the disease in Chinese, Malays and Kadazans. The practical value of this is that the presence of IgA and IgG anti-VCA antibodies, in combination with CT scanning, can be used as a means for early diagnosis of NPC.

Armstrong and Chan implicated consuming salted fish as a cause of NPC in a case-control study in Selangor and obtained similar findings in Hong Kong. Salted fish consumption during childhood was a significant risk (relative risk = 3.0) with a higher risk for daily consumption. Consumption during adolescence was less significant, and consumption in adulthood, not at all. Exposure to fumes and smoke, cigarette smoking, together with the frequent use of herbal drugs and nasal balms have also been implicated. In an other case control interview study of 55 dietary items in 1998, Armstrong again found that consumption of salted preserved food such as fish, vegetables, egg and root were positive risk factors. Other foods that increased the risk of having a nasopharyngeal carcinoma were fresh pork or beef organ meats, beer and liquor consumption. On the other hand, consumption of a number of fruits and vegetables lowered the risk of NPC. In the study of 282 Chinese patients in Selangor and KL between 1990-1992, Armstrong found that after adjustment for food and smoke, wood dust remained statistically significant as a risk factor.

Since carcinogenesis is a multistaged process several levels of genetic interactions can be expected. The HLA complex, which is closely linked to the loci coding for antigen recognition ability of T-lymphocytes, has been studied to identify individuals at risk of a given disease. The HLA-A2 and BW46 antigen has been associated with NPC in older Chinese patients. In all Chinese NPC and especially in the young the AW19 and B17 is more frequent. There is also an association with HLA-B17 among Malays who in addition show a correlation between B18 and the disease.

Histology

In the first reported local series of 100 patients in 1972, Prasad found that squamous cell carcinomas accounted for 60% of cases, anaplastic carcinoma for 15%, lymphoepithelioma for 16% and 6% were transitional cell carcinomas. The histological classification proposed by the WHO grouped tumours into:

WHO type I - well differentiated squamous cell, keratinising
WHO type II - poorly differentiated, non-keratinising
WHO type III - undifferentiated, non-keratinising

Type I tumours which account for about 20% of cases in low risk regions like Europe and America, accounted for only 1% of cases in Malaysia. Type II tumours formed 55% of our cases and the Type III tumours formed about 44%.

One case of a nasopharyngeal papillary adenocarcinoma has been reported in a Chinese female with Turner's syndrome and 2 cases of craniopharyngioma mainly in the nasopharynx have been noted.

Clinical Features

In the series of 100 patients by Prasad in 1972, in 40% the first symptom was a neck swelling, underlining the fact that the typical case is a late one in which the disease has already spread to the lymph nodes. 50% of patients had their first symptom for at least one year.

The situation has not changed much over the years. In 1997, Indudharan *et.al*. also found that patients presented late in Kelantan, with 72% having palpable cervical lymph nodes and 15% with evidence of distant metastases. Writing in 1993 Prasad still remarked that 80% of patients at the UH were at stage IV at diagnosis. Studying

100 consecutive cases beginning in 1994, he determined that 73% of patients actually presented to a doctor within 2 months of their first symptom, nearly 50% visiting a doctor on the first day they noticed a symptom. The median delay on the doctor's part, on the other hand, was 4 months (127days). For those with a nasal symptom the median doctor's delay was 26days, but it was alarming to find that the median doctor's delay for those with a neck swelling was 94 days.

Treatment and Outcome

2032 patients were seen between 1978 and 1982 at the Institute of Radiotherapy, Oncology and Nuclear Medicine, then the only facility for treatment of NPC in Malaysia. From the incidence figures above, this would account for about 60% of all cases in the country. The shortfall may be due to those too advanced and living far from KL to go for treatment. It also suggests that many were not receiving treatment. There are today many more facilities for management so the level of unmet treatment is harder to determine.

Prasad noted in the year 2000, that in the previous 10 years at the UH 100% of those who presented with UICC I & II tumours have survived, but they formed only 9% of the 380 cases seen. For those with non-metastatic UICC stage IV tumours, combination radiotherapy followed by chemotherapy gave a survival rate of 80% at 3 years. However, there is room yet for improvement in the management of NPC. The challenge is especially with regards to early diagnosis.

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MAXILLARY SINUS TUMOURS

31 malignant tumours of the maxillary sinus have been reported in a series of four years at the UKM by Lokman, Said, Hakim and Yusop. 58% were squamous cell carcinomas, 23% were non-Hodgkin's lymphoma, 12% were adenoid cystic carcinomas and the rest were undifferentiated. Presentation was generally late.

The nose was involved in 61% of cases, the palate in 52% but the cervical nodes were not usually involved (6.5%). Non-Hodgkin's lymphomas were treated with radiotherapy and chemotherapy while other cases usually had surgery and/or radiotherapy. Indudharan, Das and Thida reported one rare case of a verrucous carcinoma. The patient presented with an advanced tumour but responded dramatically to radiotherapy and chemotherapy, and was tumour free 28 months after treatment.

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LARYNGEAL CANCER

Laryngeal carcinoma causes a change in voice and has a chance to present early. It ranked among the 10 commonest cancer in KL GH between 1980-1984. Sani *et.al*. reported a series of 137 cases seen between 1981 and 1988 at the KLGH. The male to female ratio was 7.6:1. Patients were mainly in the seventh decade of life. Chinese formed 54% of patients, Indians 23%, Malays 19% and others 4%. There was transglottic involvement in 55% of patients, 30% involved the glottis and 14% were supraglottic. Supraglottic carcinoma presented differently from the others in that significantly more patients presented with dysphagia (33%) and neck nodes (42%). They also had the poorest 3 year survival of 50%. Overall 3 year survival was 68%, and was 76% for glottic tumours. Among T2 and T3 patients survival was better with surgery than primary radiotherapy. Aside from supraglottic tumours, more than 90% of other tumours presented with hoarseness of voice, however quite a number present late with neck nodes (20%) and stridor (26%). Squamous cell carcinomas (87%) were the commonest histological type. Others were nonspecified, spindle cell, verrucus or mucoepidemoid.

Reference

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TRACHEAL CANCER

Said, Phang and Gibb have reported a mucoepidermoid tracheal carcinoma which is extremely rare, successfully resected. Archuna also reported a case of an adenoid cystic carcinoma of the trachea in a 35 year old Indian women who was well and disease free at 6 months after radical surgery and radiotherapy.

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LUNG CANCER

The Ministry of Health lists cancer of the trachea, bronchus and lung as the commonest malignancy in Semanajung Malaysia as well as Sabah and Sarawak with an incidence of 19 per 100,000 in 1998 based on the number of government hospital discharges, which is probably an underestimate. Lim, in a survey of cancer fatality in Kuala Lumpur from 1979-1981 reported lung cancer as the leading cancer accounting for 24% of cancer deaths in men and 14% in women. By ethnic breakdown it was first in men of all races. But although it was first among Chinese women, among Malay women it ranked second behind leukemia and it was sixth among Indian women

There have been two fairly large hospital series of lung cancers in Malaysia. Both were from Kuala Lumpur. Many very similar results were observed. In a series of 388 patients from UH from 1967 to 1976, Menon and Saw

observed that 89% of their male patients and 57% of the female patients were smokers but did not take ex-smokers into account. Gopal, Iyawoo, Hooi and Parameswary who collected 589 patients at the National Tuberculosis Centre, KL between 1978 and 1986 found smokers formed 87% of their patients including 8% who were ex-smokers. The rate was 94% for males and 53% for females.

In both studies, Chinese accounted for a higher percentage (82% and 87%) than would be expected from the racial composition of hospital admissions and the local population. The relative risk of lung cancer among Chinese was about 3 to 7 times higher than among Malays and Indians respectively. Indians seem to have the lowest incidence of lung cancer. It is not easy to explain the preponderance of Chinese patients. There are no statistics on differences in smoking habits of the ethnic groups in the general population.

Menon and Saw observed that most of their patients were from the lower socio-economic groups and there was a male to female ratio of 2.8:1. Gopal *et al*. reported a male to female ratio of 4.8:1. Both found that the peak age group affected was the sixth and seventh decade of life. They accounted for over 60% of the total. Fewer than 5% of patients were under 40 years old. Menon has reported a further series of 48 patients under the age of 40 years collected over 20 years from 1967. He found that Chinese were less predominant, accounting for 65% of the total, while Malays accounted for 25%. The sex ratio was similar but the history of smoking was contrasting. 62% were non-smokers. Liam *et.al*. found 36 patients with lung cancers under the age of 40 years over 8 years from 1991 accounting for 6% of lung cancer patients at the UH. 58% never smoked.

Ismail, Zulkifli and Zainol has more recently reported a series with very similar findings from Kelantan, covering the period 1984 to 1989. Theirs was also a hospital rather than community based study at the HUSM. In 119 patients 84% of their males and 26% (this is comparably lower than in KL) of their female patients smoked. Chinese had a relative risk of getting lung cancer of 3 times than Malays and other races. Males outnumbered females by 2.8:1. Another very similar feature was the mean age of patients which was 60 years.

Histology

The type of cells seen on histology in the three series mentioned above are summarised in a table below (Table 7.10). In all studies, women had a higher proportion of adenocarcinoma. Malays also had a higher proportion of adenocarcinoma. In Menon and Saw's series it was commoner than squamous cell carcinoma among Malays. The ratio of smokers to non-smokers was 5.5:1 for squamous cell, 1.6:1 for adenocarcinoma and 10:1 for oat cell carcinaoma in that study. According to Gopal *et.al.* the ratios were 9.5:1 for squamous cell, 3.5:1 for adenocarcinoma, 15.5:1 for oat cell, and 5.3:1 for anaplastic/large cell carcinoma.

In young patients adenocarcinoma was the commonest cell type seen in 44% of the cases in Menon's series and 67% in Liam's series.

Table 7.10 Distribution of histological types of lung cancer.

	Authors		
	Menon & Saw	Gopal *et.al.*	Ismail *et.al.*
% of series with histology	72	91	90
Squamous cell carcinoma	34%	55%	41%
Adenocarcinoma	25%	28%	27%
Small/Oat cell	12%	12%	13%
Large cell/Undifferentiated	12%/15%	4%	19%
Other	2%	1%	-

Clinical features

70-88% of patients with lung canceer had symptoms of disease for less than six months. Gopal *et.al* noted a past history of tuberculosis

in 55 patients. 24 patients had concurrent pulmonary tuberculosis. Over 70% of these comprised of those with squamous cell tumours.

Menon and Saw considered the lesion inoperable in 89% of cases. Gopal *et. al.* considered 68% of their patients inoperable because of advanced disease and 6% inoperable because of poor general condition and in 199 patients operability could not be determined from data available. In that series 27 patients had surgery at which 4 were found to be unresectable. Only 3 who underwent resection were still on their follow-up at the time of reporting. Both do not have a comprehensive study of survival but considered that almost all would have died soon.

Given the grim outlook of this common disease the only rational line of action to take is prevention by way of anti-smoking measures.

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The Reproductive system

BREAST CARCINOMA

Breast cancer is now probably the commonest cancer among women in Malaysia. It was clearly second to cancer of the uterine cervix before the 1970s but narrowed the gap and recently appears to have even taken the lead.

Most breast lumps however, are benign. Between 1971 to 1980 Chan received 1,172 specimens of breast lumps sent for pathological study in the Johore Bahru GH. 81% were benign lesions leaving a total of 228 cases of breast carcinoma. Jayaram, Alhady and Yip recorded the UH experience with 780 cases of making a cytological diagnosis for breast lumps over 1 year in 1996. These included 745 samples of fine needle aspirates and 35 samples nipple smears. 12% were found malignant and 70% were found benign on cytology. In 7% the sample was inadequate and in 3.3% (26 cases) the cytological study was suspicious for malignancy or equivocal. 17 of these (65%) proved to be cancerous on excision biopsy.

Over 7 years from 1982, Soon, Ariffin and A.Aziz reported a series of 90 cases of breast carcinoma at the Alor Star GH. 79% of their patients were aged between 41 to 60 years. 71% were Malays, 23% were Chinese and 6% Indians, probably reflecting the racial composition of the locality in Kedah. Only 40% of their patients presented with early cancer (Stage 1 or 2). 14% presented with metastases already evident.

Lim reported similar characteristics in 125 patients with breast cancer seen in the Kuantan GH from 1984 to 1990 where only 42% of the patients had early cancer. Over the mean age of women was 48 years being slightly younger (46 years) in Malays compared to Chinese (50 years). Chinese women had a higher relative risk of 2 to 3 times greater than Malay women of getting the disease. The incidence of breast cancer for the Kuantan district was 23.5 per 100,000 but patients who never presented for treatment would have been missed.

In a spate of cases over 2 years, Yip *et.al*. at the UH had 6 cases of women with breast cancer

during pregnancy. With a total of 266 new breast cancer cases during that period that gave a rate of 2.6%. The 6 had a mean age of 37 years, 3 of them primigravids and the rest had only one child before. All but one were seen between 25 to 32 weeks of gestation. 2 had been diagnosed with breast cancer before they became pregnant but refused treatment. 4 were already in late stage at presentation. All 6 died of the disease 14 to 42 months after presentation. Histology showed infiltrating ductal carcinoma in all cases. Estrogen receptor status was determined in 3 cases. All were negative.

Receptor Status

From 200 breast tumour specimens from various hospitals Shaharuddin found that 20% were receptor positive. 60% were negative while another 20% was either only cytosol fraction or nuclear fraction positive and not both.

Mutation of the BCRA1 gene has been found locally, and even a novel mutation (E879X), has been detected in a Chinese patient.

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OVARIAN CANCER

Marsden listed ovarian cancer as the third most common malignancy in females in 1958. Chong reviewing cancers at the UKM found ovarian cancers to be the fourth commonest site of malignancy in females in 1986.

Siti Aishah, Tham and Samy have described a series of 147 consecutive malignant ovarian tumours seen at the UKM Pathology Department from 1980 to 1987. They constituted 31% of ovarian tumours studied. The fourth and fifth decade was the peak age compared to benign tumours which peaked in the third decade.

50% of their patients were Malays, 37% Chinese and 11% Indians. These percentages were in keeping with the racial distribution of the overall hospital admissions. There is however, a suspicion that as seen in studies in Singapore ovarian cancer may be the only cancer where Malays had the highest rate.

Histologically 45(31%) were cystadenocarcinomas. 26(18%) were malignant germ cell tumours and another 26(18%) were metastatic carcinomas principally from the breasts, intestinal tract and the uterus.

Reference

Siti Aishah MA, Tham KY and Samy M. Ovarian tumours: a retrospective study. The Family Physician. 2:30-32 1990.

ENDOMETRIAL CARCINOMA

Endometrial carcinoma or cancer of the body of the uterus does feature among the ten most common malignancies in women in Malaysia. They appear to be relatively less common than in the West.

One known risk factor of tamoxifen adjuvant therapy for breast cancer is an increased risk for endometrial carcinoma. Omar has noted this in Malaysia in 2 cases.

Reference

Omar SZ and Sivanesaratnam V. Endometrial carcinoma can develop in patients on tamoxifen therapy. Med J Mal. 54:280-282 1999.

CHORIOCARCINOMA

Marsden remarked from his series in 1958 that choriocarcinoma appeared more common in Malaysia than in the West. It seemed to be not just due to the higher number of pregnancies women here had. Compared with the number of live births, the number was a third more than would be expected, in the West, and even then he felt his figures were incomplete. He believed that there was no evidence that hydatidiform moles here were more malignant, but that they were just more numerous.

Cheah, Looi and Sivanesaratnam observed 2 cases of choriocarcinoma and 1 invasive mole among 39 cases of gestational trophoblastic diseases. Tharmaseelan estimated that invasive moles and choriocarcinoma occur in 10% of molar pregnancies at the Seremban GH. Choriocarcinomas seemed most common among Chinese. Choriocarcinoma is preceded by a molar pregnancy in 85% of cases but it can also occur following an abortion or a normal pregnancy.

Khoo reported a rare case that occurred 18 years after the last pregnancy in a 63 year old lady whose last pregnancy was a hydatidiform mole.

Outcome

6 of 36 cases of choriocarcinoma in the UH between 1980-1984 were found to have cerebral metastases. 2 did not respond to intrathecal methotrexate and combination chemotherapy and died. The other 4 achieved remission. Sivanesaratnam and Sen reported a patient who subsequently had two uneventful pregnancies, who had presented with choriocarcinoma and cerebral metastases.

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CARCINOMA OF THE CERVIX

Cervical cancer was the commonest cancer among women in Malaysia although it appears to be decreasing in incidence as breast cancer appears to be increasing relative to it. It is still the commonest cancer among Indian women, but is second to breast cancer among Malay and Chinese women. However in terms of hospitalisation even when cancers of both sexes are counted, as in the Ministry of Health figures of discharges from government hospital (1998), carcinoma of the cervix ranked as the second commonest cancer with a rate of 12.3 per 100,000 for the whole country. Therefore in terms of disease burden the two leading cancers among women are probably equal.

Among the Orang Asli, Sumithran has noted that carcinoma of the cervix is rare. There were only 3 cases, among 81 cases of cancer found in women over a 13 year period, recorded in the Gombak Hospital. There were 18,000 female admissions in that period.

Risk Factors

96% of a small series of cases studied were positive for the human papillomavirus (HPV). HPV 16 occurred in 74%, HPV 18 in 65% HPV 31 and 33 were found in 17%. These confirm findings all over the world that this virus is important in the development of cervical

carcinoma.

Screening

A 5 year cervical smear screening study was done at the UH in KL between 1968 to 1973 covering 11,283 patients. No women under 25 years old were positive. The 'pick-up' rate (0.2%) was also low in the 25-29 year age group. The yield was between 1.4% -1.8% in women over the age of 40 years. Of the 75 positive cases 67(89%) had carcinoma-in-situ, the remaining 8 had early invasive squamous cell carcinoma of the cervix. Allowing for variations due to selection of the screened population these findings are not unlike those from other countries.

In 1985 there were 34,627 women who had the Pap smear screen. In 1987 there was an increase to 73,868. This is a good trend, but we are still a long way off from having all the women in the group at risk screened.

Clinical Features

An important factor for the lower mortality in developed nations is the impact of cervical smear screening which detects cervical cancers early. A local study between 1977 and 1979 in GHKL found 80% of the series of 1,000 women presented at an advanced stage (Stage IIB-IV). This series by Azhar and Lopez consisted of patients seen at the Institute of Oncology and Radiotherapy referred there for treatment from all over the country, and as such is a selected group.

In this series the peak age group affected was the 5th and 6th decades (more than 60% of total) as in most Western series. The lower socio-economic groups were much more commonly affected. Two thirds of the women had a parity of five or more. 96% of the tumours were squamous cell cancers while the remaining were adenocarcinoma.

Siti Aishah and Tham reported a clinic based series at the UKM covering 1987. They found 77 cases in one year of whom 30 had carcinoma-in-situ and 47 had invasive cancer. They mean age, they noted, was younger (37 years) in the carcinoma-in-situ group compared with those with invasive cancer (47 years).

Histology

In the UH in 2 years from 1991-1992, 121 cases of invasive cervical carcinoma were noted. In another 2 years from 1996-1997 there were 145 cases. Squamous carcinomas formed 76% of cases in the first period and 66% between 1996 - 1997. Adenocarcinomas formed 16% between 1991-1992 and 26% between 1996-1997. Other epithelial tumours accounted for the rest.

Outcome

Sivanesaratnam reported the 10 years follow up of the experience in UH of 239 patients with stage IB and IIA cervical carcinoma who presented over 7 years from 1983. The 10-year survival for patients without risk factors was 97.2% following radical hysterectomy. 108 patients (45.2%) had various poor histological features (lymph node/parametrial metastases, lymphatic tumour permeation) and received adjuvant chemotherapy. Those who received adjuvant chemotherapy had a higher 10-year survival rate (86%) than those who refused adjuvant chemotherapy (74%). Those who had squamous cell carcinoma did better on a mitomycin C and 5-fluorouracil regime while those who had adenocarcinoma did better on a cisplatin, vinblastin and bleomycin regime. Recurrent tumour, when found to occur, all happened within 23 months of surgery except for one case where it occurred 8 years later.

Sivanesaratnam also noted in 1993 that 4.5% of the early cervical carcinoma patients undergoing radical hysterectomy in the UH were pregnant. There were 18 cases and this gave a rate of 1 in 4077 pregnancies. The overall 5-year survival rate was 78% but of the 3 of the patients

who succumbed within 27 months of presentation presented in the puerperium and had poor prognostic histological features. The 5-year survival for those who presented antepartum (93%) was similar to that in non-pregnant patients.

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CARCINOMA OF THE VULVA

Carcinoma of the vulva is a relatively rare tumour. Between 1968 and 1980, 16 cases were managed at the University Hospital in KL. Of these 12 were initially seen in other hospitals all over the country.

Clinical features

The mean age of the women was 60 years, and ranged from 42 to 82 years. The racial distribution followed very closely that of all gynaecological patients admitted to the hospital in the same period. The majority were housewives of the lower socio-economic group. Diabetes, hypertension and leukoplakia vulvae were common associated conditions. 56% had symptoms for less than six months. Another 25% had symptoms for less than a year.

A large group (75%) presented in the middle stages; that is FIGO stage II and III. Two patients in Stage IV were considered too advanced for surgery. The other 14 had radial vulvectomy performed. Follow-up information was available for 9 patients. All 5 without lymph node involvement were alive and disease free ranging from 3 - 6 years. Of 4 patients with inguinal and pelvic node metastases, one died and two had recurrences within a year. The fourth was disease free at one year.

Sivanesaratnam also reported one case where carcinoma of the vulva occurred in early pregnancy in a 28 year old woman.

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OTHER GYNAECOLOGICAL MALIGNANCIES

Relatively rare tumours of which there have been cases reported include carcinomas of the vagina and of the fallopian tube.

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TESTICULAR TUMOURS

The main testicular malignancies, namely the teratomas and seminoma, are not particularly common or rare but there are no large series about them in Malaysia. Koh has reported 5 cases of seminoma in men ranging from 29-58 years old who had undescended testes. They presented with abdominal tumours from 8cm to 20cm in largest diameter. 4 were known to be well 1 year after presentation but one died 5 years after presentation.

Adenocarcinoma, a rare low grade malignancy was reported in 4 infants, who were all Chinese between 1962 and 1968.

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CARCINOMA OF PENIS

Carcinoma of the penis was the more important cancer of the male reproductive system in Malaysia. It was the tenth most common malignancy in male in two series. The incidence was high in Chinese and even higher among Indians, but extremely low in Malays. This shows that circumcision is a strong protection against this disease, but proper hygiene is probably the key.

The Blood and Circulation

THE LEUKAEMIAS

ACUTE LEUKAEMIAS

Leukaemia is the commonest form of childhood cancer in Malaysia and its epidemiological and clinical features in Malaysian children appear to be similar to Caucasian children according to by Sinniah and Lin in descriptive reports in the 1970s and 1980s. Lin estimated that there must have been at least 100 new cases a year in Malaysia in children under 13 years in 1985. The peak age group is between 2 and 7 years. Most have acute lymphoblastic leukaemia (ALL). Boys outnumber girls slightly in a ratio of about 1.3:1.

In a series of 168 cases seen at the UH from 1967 to 1980 Sinniah and Lin noted that 75% were ALL, 17% were acute myeloid leukaemia (AML), 4% were chronic myeloid leukaemia (CML) and 4% were other types of leukaemia. From 1980 to 1984 ALL accounted for 66% of acute leukaemias and 31% of all haematological malignancies in the UH. 56% of the 172 ALL cases were Chinese, perhaps a slightly higher percentage in relation to hospital utilization rate (41%).

Lin and co-workers had a series of 104 children with ALL treated over 7 years at the UH between 1976 to 1982. Remission was achieved in 82 (94%) patients. However, overall disease free survival at 3 years and 5 years was only 40% and 25% respectively. 9.1% of boys had testicular relapse. The median time from diagnosis of ALL to relapse was 28 months. Menon *et.al.* in HUSM also collected a series of 65 children with ALL over a period of 7 years from 1991 to 1997. The racial distribution of their patients corresponded to the region and they found boys in the majority by 1.4:1. They noted a high proportion (48%) of their patients presenting with a high white cell count of 50 $x10^9$ or more. (18/26) 69% of these children, who had immunophenotype data available, and who had a high white cell count had B-linage CD10 positive ALL.

In adult ALL, Bosco and Teh have compared the outcome of therapy in Malaysians with a German study, as some reports have suggested Asians tend to respond less favourably to treatment. Using a similar chemotherapy protocol they studied 74 patients aged 15-69

years diagnosed from 1986 to 1990. They obtained complete remission in 73% with a probability of continuous complete remission at 5 years of 29% which were comparable to the German study. They found that age, sex, ethnic group and immunophenotype did not affect leukaemia free survival. Only an initial white cell count of less than 30 x 10^9/l gave a significantly better prognosis than those with a count above that level.

Immunophenotyping

In Kelantan, Menon, Dasgupta and Jackson immunotyped 45 childhood acute leukaemia cases seen over 3.5 years from 1994. 80% were ALL. Of these 3% were of B-cell origin, 22% of T-cell origin. 96% of the B-lineage ALL were CD 10 positive. The remainder 20% of the 45 were AML. All these AML cases expressed CD33 and 78% expressed CD 13. Of the ALL cases, 5 had myeloid antigen co-expression (My+ ALL) and of AML cases 1 had lymphoid antigen co-expression (Ly+ AML), overall giving a total of 6 (13%) mixed lineage leukaemias.

In the UH, Ng *et.al*. studied 151 of their ALL patients with available immunophenotype data over 41months from the start of 1992 to see if there was a difference in outcome between those with and without myeloid antigen co-expression (My+). Myeloid antigen co-expression was defined as B-lineage ALL where more than 30% of isolated leukaemic cells were positive for CD13 and/or CD33. 39(23%) had myeloid antigen co-expression. These patients were similar in clinical features with the rest and the overall 2 year survival rate of 62% was not significantly different from others (which was 77%).

In a cytogenetic study of 30 patients with ALL, Chin *et.al.* noted that none had major breakpoint cluster region (M-bcr) rearrangement on chromosome 22. Workers in HUSM looked at the ABO blood group of acute leukaemia patients in view of the excess of males always seen. Among 109 male patients 39% had blood group O which is the same as the normal control population. However among 79 female acute leukaemia patients only 24% had blood group O, which is significantly less. They postulate that there may a "sex-responsive" gene near the ABO gene locus on chromosome 9 which relatively protects group O women against acute leukaemia.

A pair of monozygotic twins have been diagnosed with ALL within 2 weeks of each other at the age of 4years at the UH. Similar immunophenotyping suggests the blast cells were derived from the same clone and must have arisen in utero.

The **acute promyelocytic form of leukaemia** (PML) is due to a translocation involving chromosome 15 and 17 which fuses the gene for retinoic acid receptor alpha (RARα) on chromosome 15 with the PML gene on chromosome 17.It is designated M3 by the French-American-British co-operative group. It has a relatively good prognosis as it responds to all trans-retinoic acid (tretinoin) therapy. There were 13 (5%) cases of PML out of 262 cases of acute leukaemias in the UH between 1980 and 1984. In 7 cases seen over 10 months, 6 were typical M3 and one was 'microgranular' or M3 variant. Patients ranged from 6-51 years, there were more males. Leong has reported a case of a 21 year old primigarvid at 33 weeks gestation with PML who achieved remission and delivered a healthy baby with tretinoin.

Clinical Features

Reddy and Menon studied the ocular manifestations of acute leukaemia in 82 children in HUSM prospectively. Although only 3 (3.6%) presented with eye symptoms, 14(17%) had ocular lesions, including, proptosis, retinal/macula/vitreous haemorrhage, cotton wool spots, subhyaloid haemorrhage, papillodema, cortical blindness, sixth nerve palsy and exudative retinal detachment with choroidal

infiltration.

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CHRONIC LYMPHOCYTIC LEUKEMIA

This is rare locally. Only 7 patients, which constituted 0.9% of the total of 747 cases of leukaemia patients, were diagnosed over a 5 year period in the UH. They had similar haematological profiles as Western patients though most of them had advanced disease at presentation. Treatment of such patients was palliative and should be reserved for symptomatic patients and/or patients with progressive disease.

References

Ng SC, Bosco J and Teh A. Chronic lymphocytic leukaemia: a review of 7 case from University Hospital, Kuala Lumpur. Med.J.Mal. 45:23-28 1990.

HAIRY CELL LEUKAEMIA

This is a rare variety of leukaemia that has gained interest partly because it has been found to be sensitive to interferon therapy. Ainoon and colleagues at UKM recorded a case in a young Malay woman in 1988.

Reference

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CHRONIC MYELOID LEUKAEMIA (CML)

This is not uncommon and presents in adults like in other countries. Studying the chromosome arrangements in 50 Malaysians of different ethnic groups with a 1.2-kb 3'bcr probe, Bosco and Dyck found the molecular features consistent with that of Western countries. In another study using another DNA probe they confirmed the presence of gene rearrangement indicating the presence of the Philadelphia chromosome in all 20 CML patients studied. This consistent acquired specific genetic abnormality has made CML the best understood of all blood malignancies. The Philadelphia chromosome, which is a translocation of chromosome 9 and 22 results in a novel fusion transcript arising from the BCL gene on chromosome 22 and the ABL (which encodes a tyrosine kinase) gene on chromosome 9. The resultant fusion protein (BCR-ABL) an active tyrosine kinase accelerates growth and differentiation of haemopoeitic cells. This knowledge has been seminal in understanding other haemotogical malignancies.

Both Ng and Kuperan at UH and Hamidah *et.al*.at UKM found the mean age at diagnosis of CML in the 1980s to be 35 years which was about 8 years younger than European and North American reports

In 13 years from 1967, out of 168 cases of childhood leukaemia, Sinniah *et.al*. found 7 cases of CML. 5 children ranging in age from 3-10 years were adult type CML with the hallmark Philadelphia chromosome. 2 children ranging from 5 months to 3 years in age had juvenile CML. Prognosis was poor and only one of these children was alive at the time the report was written.

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Hamidah NH, Cheong SK, Ainoon O and Hoe TS. Age at diagnosis of chronic myeloid leukaemia. Mal J Pathol. 13:123 1991.

PLASMA CELL LEUKAEMIA

Described as multiple myeloma without bone involvement, Ng and Lee have written a report of one case.

Reference

Ng SC and Lee MK. Plasma cell leukaemia - a case report. Sing.Med.J. 30:408-409 1989.

THE LYMPHOMAS

BURKITT'S LYMPHOMA

Working in Uganda in the 1950s Burkitt elucidated the link between this lymphoma which usually attacks children very aggressively and certain geographical areas in Africa. It has subsequently been shown that this tumour is caused by the Ebstein-Barr virus (EBV) in the setting of malarious and malnourished regions. The lymphoma characteristically appears around the jaw. In Malaysia, Ramanathan and Ng noted that Burkitt's lymphoma was the commonest malignant oral tumour in children in 1979. They collected a total of over 20 such cases from 1967. The peak age of children affected was 4 years, and most were between 3 to 8 years. Indians seemed to be free from Burkitt's lymphoma. Among East Malaysian patients seen in the UH over 3 years from 1981, Chai *et.al*. noted that Burkitt's lymphoma was the commonest lymphoma in children accounting for 7 of 13 cases (54%). 60% of the tumours tested positive for the presence of EBV.

In a rare case Samani, Syed Noori and Tan described Burkitt's lymphoma in the appendix.

Table 7.11 Number of Children and Adults with Hodgkin's Disease and (percentage with EBV)

		Children (age<15years)	Adults
Classical Hodgkin's	Nodular Sclerosis	8 ⎫	33 (22%)
	Mixed Cellularity	16 ⎬ (93%)	24 (86%)
	Lymphocyte Depleted	1 ⎭	2 (50%)
Lymphocyte Predominant Hodgkin's		9 (0%)	6 (0%)
Unclassifiable			1 (100%)

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Chai SP, Peh SC, Kim LK et.al. The pattern of lymphoma in East Malaysian patients as experienced in the University Hospital, Kuala Lumpur. Mal J Pathol. 21:45-50 1999

HODGKIN'S LYMPHOMA

Peh, Looi and Pallisen have reported a series of 100 consecutive cases of Hodgkin's disease in Malaysia. 34 patients were children the rest were adult. Their results are given in Table 7.11. 85 patients had classical Hodgkin's disease and their racial distribution of Malays:Chinese:Indians was 23:32:30. There 15 cases of lymphocyte predominant Hodgkin's and the racial ditribution of Malays:Chinese:Indians was 4:10:1. There appears to be a significant predilection of classical Hodgkin's disease cases in ethnic Indians patients. They examined the association of EBV in 81 cases. Overall EBV was detected in 61% of those with classical Hodgkin's, the percentage for the subtypes given in parentheses above. None of the lymphocyte predominance Hodgkin's disease showed the presence of EBV.

Reference

Peh SC, Looi LM and Pallesen G. Epstein-Barr virus (EBV) and Hodgkin's disease in a multi-ethnic population in Malaysia. Histopathology 30:227-233 1997.

NON-HODGKIN'S LYMPHOMA

Non-Hodgkins lymphoma (NHL) are commoner than Hodgkin's in Malaysia, numbering 100 against 49 cases of Hodgkin's in the UH between 1980 to 1984 and 49 versus 8 in a UKM series between 1983 and 1987. The highest frequency of Non-Hodgkin's lymphoma occurs in Chinese. They formed 67% of cases compared to a hospital utilization rate of 41% at the UH. There was no marked male:female difference. 97% of the NHL were diffuse in type. The UKM series found B-cell NHL 4 times more common than T-cell NHL. There was a high incidence of extranodal primary NHL. Most NHL was high grade disease. Another series of 47 cases in the UH over 2½ years from 1993 found B-cell NHL twice as common as T-cell NHL. Of the 29 B-cell tumours 3 had lymphoblastic lymphoma, 14 diffuse large B-cell lymphoma, 5 had Burkitt's lymphoma and 7 had other variants. Of the 15 with T-cell NHL, 10 had peripheral T-cell lymphoma and 5 had lymphoblastic lymphoma. Overall 47% of patients had marrow involvement. The authors examined but did not finding any distinguishing features in the blood counts of any particular type of NHL except that atypical lymphoblasts were common in lymphoblastic lymphoma.

In children, Sinniah, Tan and Lin noted 10 NHLs compared to 14 Hodgkin's Lymphomas in 13 years. Their series of children had a median age of 2-3 years. 8 were males, 7 were Chinese. Among a series of East Malaysian patients Chai *et.al*. reported that there were 9 times more NHL lymphomas than Hoddgkin's lymphomas in 107

patients over 3 years from 1981 to 1983. There were 80 cases of Bcell NHL and 16 cases of Tcell NHL.

Peh, Sandvej and Pallesen have demonstrated the presence of EBV in 11 of 13 T-cell NHLs (85%) but in only 1 of 16 B-cell NHLs (6.3%). The EBV were all of the type-A virus. EBV was detected in 56% of Tcell-NHL and only 3% of Bcell-NHL in the East Malaysian patient series.

In many cases, NHLs, present with lymph node enlargement but just as often they produces masses in about any part of the body. They can occur in almost any site and have been reported locally in the nose and paranasal sinuses, oral cavity, in the spleen, lingual tonsil. It has also been reported in bone and brain. A number of cases of NHLs have been reported in the maxillary sinus. These were noted to be more common among Malays.

Bosco and colleagues have noted one case of a rare type of T-cell lymphoblastic malignant lymphoma.

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X-LINKED LYMPHOPROLIFERATIVE DISEASE (XLP)

XLP was first described by Purtilo in 1975 when he observed 6 out of 18 related males dying of the disease. Affected males produce an abnormal proliferation of transformed B-cells following a primary Epstein-Barr virus (EBV) infection which cannot be controlled by suppressor T-cells, leading to deranged immune function. A world-wide registry for XLP was established in 1978. UH paediatricians have found the disorder in 2 brothers, one presented at the age of 2years with EBV meningoencephalitis but recovered and was discharged after about one month with some residual neurological deficit and remained well till the age of 7 years when he fell ill with abdominal tumour and systemic infection following which he succumbed to the disease. The elder brother presented with infectious mononucleosis at age 5 years just a few days after 2 year old brother fell ill and died 24 days later.

Reference

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HISTIOCYTOSIS

Dutt *et.al*. reported a case in 1969 where transition from eosinophilic granuloma of the bone to, Letterer-Siwe disease, the severest form of the disease, was observed. Thong *et.al.* also reported a case of Letterer-Siwe disease in association with histiocytic medullary reticulosis and monocytic leakemia.

A case of a 3 year old Chinese girl who had the Hand-Schuller-Christian variation of histiocytosis X in the inner skull and pelvic bones has been reported. She obtained remission with chemotherapy but at the age of 13 years developed a recurrence in the form of a non-healing vulvar ulcer.

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Wong KK, Lin HP and Looi LM. Histiocytosis X and vulvar ulceration. Int J Gynaecol Obstet 39:131-134 1992.

CAROTID BODY TUMOURS

Carotid body tumours are rare. Locally, Loh and Devaraj reported a case involving a 39 year old Chinese woman, in 1972. Another case, in a 45 year old Chinese man, was reported by Rajapaksa and Ng in 1977. Both these patients were not operated on but remained well. Rarer still are bilateral carotid body tumours of which Krishnan, Fareeda and May reported what they said was 1 of only 10 cases Ever known in the world.

References

Loh TG and Devaraj TP. A case of glomus jugulare tumour. Med.J.Mal. 27:69-72 1972.

Rajapaksa ACP and Ng KK. Carotid body tumour. Med.J.Mal. 31:73-74 1976.

Krishnan MMS, Fareeda A and May J. Bilateral carotid body tumours. Southeast AsIan J.Surg. 7:173-176 1984.

HEAMANGIOENDOTHELIOSARCOMA

Dutt remarked in 1969 that this rare malignancy was seen in a considerable number of cases at the IMR. He reported 4 with unusual presentations where the tumours were respectively in the mediastinum, perinephric space, attached to the femoral artery and attached to the bladder.

Reference

Dutt AK. Hemangiothelioendotheliosarcoma. Med J Mal. 24:161-163 1969.

HAEMANGIOPERICYTOMA

A haemangiopericytoma is a rare neoplasm of unpredictable malignant potential that can occur anywhere in the body. Saw and Prathap reported 3 cases presenting in different ways.

Reference

Saw HS and Prathap K. Haemangiopericytoma: problems in diagnosis and management. Aust NZ J Surg 49:350-354 1979.

The Skin and Sense Organs

SKIN CANCERS

Because they are easily noticed and biopsied skin cancers ranked high in early reports of cancers in Malaysia for example in the study by Marsden. Squamous cell carcinomas are commonest, unlike in the West where basal cell carcinomas were commonest. Squamous cell carcinomas form about two-thirds of skin cancers here similar to what is found in Africa. This is because chronic skin irritation from sepsis is common. Neglected sores in the legs

and groins, constantly exposed to minor trauma undergo malignant change. Mohamed described an example of this in trophic ulcers in leprosy patients. Jaafar and colleagues described three cases of squamous cell skin cancers in 3 Malay patients from Sentul with hyperkeratotic lesions believed to be due to chronic arsenic poisoning. Arsenic is present in the drinking water in tin mining areas.

Basal cell carcinomas form about one-sixth of skin cancers. The incidence appears to be the same in all races and in both sexes.

The incidence of melanoma does not appear to be high forming the remaining one-sixth of skin cancers. No clear cut racial difference of incidence has been reported. Over a period of 12 years from 1972, Ismail and Looi reported 23 cases of malignant melanoma in the UH. 19 were cutaneous and 4 were from the eye and orbit. Males were slightly in the majority. Although Chinese were the majority this might be expected from the population base. Of the skin melanomas the sole (6/19) was the commonest site. Nodular melanomas (13/18) were the commonest histological type of primary skin melanoma.

Lacrimal gland tumours: Reviewing this uncommon tumour, Sivanesan and Chandran reported that there were 3 cases over 12 years in the UH. All were women, ranging in age from 16 to 32 years. Two were adenoid cystic carcinomas and one an adenocarcinoma. One case of adenoid cystic carcinoma was unusual in that the patient developed metastases to the lungs.

Sweat gland tumours: These are uncommon but when found usually occur in the face and neck. Tan and Khong noted a rarity of a sweat gland tumour of the toe in 1964.

References

Tan KK and Khong BT. A sweat gland tumour of the mixed-salivary type of the right middle toe. Med.J.Mal. 19:128-133 1964.

Sivanesan S and Chandran S. Lacrimal gland carcinoma. Med.J.Mal. 37:257-260 1982.

Mohamed KN. Malignant transformation of plantar ulcer in leprosy. Sing.Med.J. 28:432-435 1987.

Ismail R and Looi LM. Malignant melanoma in Malaysia – a report of 23 cases. J Dermatol. 15:168-171 1988.

Kandiah R, Sukumaran K and Chandran S. Malignant conjunctival melanoma. Med.J.Mal. 43:178-180 1988.

Jaafar R, Omar I, Jidon AJ, Wan-Khamizar WK, Siti-Aishah MA and Sharifah NASH. Skin cancer caused by chronic arsenical poisoning - a report of three cases. Med.J.Mal. 48:86-92 1993.

KAPOSI'S SARCOMA

Kaposi's sarcoma was a rare skin condition first described by the Hungarian, Moritz Kaposi, that occurred among elderly men of Jewish or Eastern European origin. In the 1980s it became the stigma of young men with AIDS. It produces vascular nodules in the skin and mucous membranes eruptions. It has been associated with the newly identified Human Herpes virus type 8. The cell of origin of the tumour is most likely a mesenchymal cell of the lymphatic or vascular endothelium. Choon and Khoo described two cases, in a 29 year old Malay man and 51 year old Chinese man in Johore without HIV infection but positive for syphilis. It has not been commonly observed in Malaysia AIDS patients.

Reference

Choon SE and Khoo JJ. A report of two non-AIDS associated Kaposi's sarcoma in Malaysia. Med.J.Mal. 52:437-440 1997.

RETINOBLASTOMAS

38 retinoblastomas were reported by Sukumaran in the UH between 1968 and 1988. 85% of patients were between 1½ years to 3½ years old. The ratio of males:females was 16:11. There was no racial preponderance. 4 patients refused any form of treatment. 20 cases of unilateral retinoblastomas received enucleation

of the involved eye. 12 patients survived a mean period of 4.5 years (range 1-19 years). 7 patients with bilateral disease had enucleation of the worse eye. None survived beyond 5 years (mean 2.5 years).

Reference

Sukumaran . Retinoblastoma - a 20 year review from the University Hospital Kuala Lumpur. Med.J.Mal. 46:129-135 1991.

The Urinary System

WILMS' TUMOUR

14 children with nephroblastomas were seen in the UH over 10 years from 1968, according to Sinniah, Muthiah, Lin and Somasundaram. This formed 5.4% of childhood malignancies. There were 6 boys and 8 girls and all the races were represented. The mean age at diagnosis was 2 years, and ranged from 6 months to 4 years. From the first 5 years of 7, only one patient who had stage 1 disease survived more than 6 years. From the second 5 year period, 3 of 4 with Stage 1 and 2 disease had survived 2½ to 4 years and 2 of 3 with Stage 3 disease had survived over 1½ years.

Reviewing the UH experience over 22 years from 1968 a later report noted 37 cases. 19 patients were Chinese, 13 Malay, 4 Indian and 1 Anglo-asian. 21 were boys 16 girls. 70% of patients were below 2 years of age. One had bilateral tumour. By histology, 53% showed a mixed pattern, 21% were epithelial predominant, 18% were blastemal predominant, 7.8% were stromal predominant and 5.3% were anaplastic. Wilms' tumour has been reported in one 2 year old girl with an unusual association involving Fanconi's anemia, mental subnormality and dysmorphic features.

Clear Cell Sarcoma of Kidney. This is a childhood tumour frequently confused with Wilms' tumour, but it has a characteristic histology, a marked predilection for metastasis to bone, an aggressive clinical course and a high relapse rate despite surgery, chemotherapy and radiotherapy. Over a 16 year period from 1973, 8 cases were recorded in the UH. 5 were males 3 female. 6 were Malay, and one each Chinese and Indian. The victims ranged from 8 months to 3 years. Six were initially diagnosed as Wilms' tumour. Recognizing this entity opens up the prospect of intensified chemotherapeutic regimes.

References

Sinniah D, Muthiah M, Lin HP and Somasundaram K. Review of Wilms' tumour in Malaysian children. Sing.Med.J.22:24-27 1981.

Cheah PL, Looi LM and Lin HP. Clear cell sarcoma of kidney: a clinicopathological study of eight cases from Malaysia. Histopathology 21:365-369 1992.

Cheah PL, Looi LM and Lin HP. Wilm's tumour in Malaysian children: a histopathological study of cases encountered at the University Hospital, Kuala Lumpur over a 22-year period. Mal J Pathol 14:111-115 1992.

Ariffin H, Ariffin WA, Chan LL and Lin HP. Wilms' tumour and Fanconi anaemia: an unusual association. J Paediatr Child Hlth. 36:196-197 2000.

BLADDER TUMOURS

Zakriya and Hussain at the Institute of Urology reviewed 150 cases of bladder tumours at the institute between 1978 and 1981. Being a referral centre patients came from all over the peninsula and little can be said about the incidence of the disease.

Patients ranged in age from 25 to 87 years with a peak in the eighth decade. Males outnumbered females 5.25:1. 88% of patients presented with invasive tumours which had gone beyond the mucosa which contrasts sharply with the 20% invasive cancer normally seen in the UK. The biggest group of patients (46%) presented with Stage C (Marshall's classification) tumour which are tumours which have gone beyond the bladder wall.

Only a few patients agreed to total

cystectomy and urinary diversion and many are lost to follow-up.

Reference

Zakriya M and Hussain A. Bladder tumours - a review of 150 patients treated at the Institute of Urology and Nephrology General Hospital Kuala Lumpur. Med.J.Mal. 38:4-8 1983

The Skeletal System

OSTEOSARCOMA

Bovill, Silva and Subramaniam conducted a survey to trace all cases of osteogenic sarcoma in Malaysia between 1969 and 1972. Using records of the Department of Radiotherapy and Pathology in the Kuala Lumpur GH and the Pathology departments of the IMR and University Hospital they reckoned they covered all the histologically diagnosed case. In addition they sent letters to all general hospitals and visited most of them. They detected 68 cases, of which 5 were not biopsy proven because the patient did not allow it. They estimated that this was 85% of the predicted minimum total based on the rate recorded in the Singapore Cancer Registry.

Clinical features

The age, sex and primary site characteristics fitted the established pattern for the disease. Two thirds of the patients were in the second decade of life. Less than 5% were more than 50 years old. Males outnumbered females in a ratio of 1.4:1. The calculated incidence was highest in Penang (0.47 per 100,000) and low in Kelantan, Johore, Sabah, Pahang, Perak and Sarawak (<0.14 per 100,000). They suggested that with the operating medical and health services in the country it seems unlikely that a patient with osteogenic sarcoma would not reach a hospital at some stage of the disease and receive preliminary diagnostic evaluation. Hence, the argue there is a true 'urban' versus 'rural' difference in the incidence of the disease. Grouping the seven least densely populated states as rural and the others as urban, the incidence (cases per 100,000) they found was 0.09 for rural and 0.22 for urban Malays. For Chinese it was 0.18 and 0.31 respectively. There were too few Indians to divide them as such; put together their incidence rate was 0.23.

The youngest case on record is a 16 month year old boy in whom the disease was aggressive and the course fatal.

Prognosis

Silva and Teo in 1978 reviewed a series of 21 patients with osetosarcoma seen at the University Hospital KL. 12 were known to have died, 8 were lost to follow-up and only one was alive and well at the time of reporting.

Occurrence of a rare extraskeletal osteosarcoma of the thigh as been reported locally. Metastases to the ethmoid causing epistaxis and proptosis has also been noted.

References

Bovill EG, Silva JF and Subramaniam N. An epidemiologic study of osteogenic sarcoma in Malaysia. Clin.Orthop and Related Research 113:119-127 1974

Silva JF and Teo WS. A review of cases of osteosarcoma admitted to the University Hospital, Kuala Lumpur. Med.J.Mal. 32:225-231 1978

Dhillon KS. Suntharalingam S and Maurer HJW. Extraskeletal osteosarcoma of the thigh. Med.J.Mal. 48:453-456 1993.

Sharma HS, Reddy SC, Mohamad A et.al. Metastatic osteosarcoma of the ethmoid: an unusual cause of recurrent epistaxis and proptosis. J Laryngol Otol. 110:676-678 1996.

Ibrahim S, Sundari MN. Masir N. Osteosarcoma in a sixteen-month old boy. Med J Mal. 54:261-263 1999.

OSTEOCLASTOMA

Although most of these tumours are benign some behave malignanly. This is probably the second commonest tumour of bone in Malaysia after osteosarcoma, according to a series by Peh,

Cheah and Sengupta. Sambandan and Pathmanathan recorded 41 histologically proven cases at the UH from 1967 to 1985. Patients ranged in age from 15 - 50 years with a mean age of 29 years. Males slightly outnumbered females and Chinese formed the largest group. The femur and tibia were the leading locations for the lesion.

Razak and Fazir have reported a rare case of osteoclastoma of the axis (2nd cervical vertebra).

References

Sambandan S and Pathmanathan R. Clinicopathological correlation in osteoclastomas: The University Hospital experience. Sing.Med.J. 28:537-541 1987.

Peh SC, Cheah PL and Sengupta S. The pathology of tumour and "tumour-like" lesions of bone in the University Hospital, Kuala Lumpur. Mal.J.Pathol. 10:45-50 1988.

Razak MA and Fazir M. Neurological recovery in a patient with recurrent aggressive giant cell tumour of the axis – a case report. Med J Mal. 55sC:97-100 2000.

EWING'S SARCOMA

9 cases of Ewing's sarcoma were diagnosed in the 6 year period from 1980 - 1986 reviewed by Peh, Cheah and Sengupta at the UH KL. The tumour affects the young, the mean age being 11.6 years with boys outnumbering girls 3.5 times. Very curiously no Chinese were seen although they are the majority in most other bone tumours.

CHONDROSARCOMAS

6 cases of chondrosarcomas were seen from 1980 -1986, one fifth the number of osteosarcomas, in the review by Peh, Cheah and Sengupta. The patients' mean age was 41 and the male to female ratio was 5:1. Wong and Tan have presented a report of 2 cases of large chest wall chondrosarcomas successfully resected.

Reference

Wong PS and Tan GP. Resection of large primary chest wall chondrosarcoma with reconstruction: 2 case reports. Med J Mal. 55:516-519 2000.

MYELOMA

Although this tumour is reported to be the commonest bone malignancy in Western countries, it is uncommon in Malaysia. There were only 7 cases of myeloma accounting for 5% of primary tumours in bone in the review by Peh, Cheah and Sengupta. The IMR workers however collected a larger series of 175 cases studied over 1980 to 1984 from all over the country. 54% of the cases were Malays, 27% Chinese and 12% Indians. There were 101 cases of IgG, 38 cases of IgA, 15 cases of IgM, 7 cases of IgD, 1 case of IgE and 12 cases of light chain myelomas.

Wong *et.al.* reported a series of 37 cases from the UH seen from 1980 to 1987. The mean age was 60 years. Males and females were equally common. Bone pain and pallor were the commonest clinical features.

Waldenstrom's macroglobulinnaemia, a malignancy of B cells that produces IgM has once been reported. One 67 year old Malay woman has been found to have synchronous AML and multiple myeloma. Anti-myeloma chemotherapy resulted in progression of the AML.

References

Ng SC, Teh A and Lee MK. Waldenstrom's macroglobulinaemia - a case report. Med J Mal. 44:167-170 1989.

Wong KT, Ng SC, Kuperan P, Yap SF, Menaka N and Bosco J. Multiple myeloma in the University Hospital: a retrospective study of biodata, clinical, laboratory and radiological profiles, 1980-1987. Med.J.Mal. 45:136-143 1990.

Saw MH and Bosco JJ. A patient with two haematological malignancies. Med.J.Mal. 51:292-294 1996.

METASTATIC TUMOURS IN BONE

Because of its great total mass and blood supply the skeleton is one of the commonest sites for metastatic cancers. These are bone tumours only in the sense that they happen to be in bone. Nevertheless, they constitute the largest group (25%) of malignant lesions in bone in Malaysia as elsewhere. Although they were unable to verify the sites of primary tumour in some cases, to Peh, Cheah and Sengupta it appeared that the lung, breast and thyroid were the 3 most frequent primaries which metastasised to bone. The bones most commonly involved were the femur and vertebrae.

Razak and Sappani, reported a series of 45 patients who underwent decompressive laminectomy for secondary malignancy in the spine. The commonest primary tumours metastasising to bone were nasopharyngeal (24%), lung (13%), breast (13%) and renal (6.7%), but there were an assortment of 7 others besides these and a further 20% where the origin was unknown. Those with less severe power loss (weakness and incontinence) tended to regain more function from the surgery. Overall improvement was seen in 27%.

References

Peh SC, Cheah PL and Sengupta S. The pathology of tumour and "tumour-like" lesions of bone in the University Hospital, Kuala Lumpur. Mal.J.Pathol. 10:45-50 1988.

Razak M and Sappani K. Neurological recovery following posterior decompression of spinal secondaries. Med.J.Mal. 53s:6-11 1998.

The Muscles and Connective Tissues

RHABDOMYSARCOMA

Sinniah and colleagues collected a series of 11 children with rhabdomyosarcomas over 13 years from 1967. They ranged in age from 4 months to 8 years. 5 had tumours in the head and neck region, 3 in the extremities, 2 in the genitourinary tract and one on the trunk. Histologically, 6 were embryonal, 3 alveolar and 2 pleomorphic.. The most important determinant of outcome was the extent of disease at presentation. A high defaulter rate contributed to a poor outcome.

Said and colleagues, have reported 3 cases in boys ranging from 3 to 8 years old seen roughly over 2 years from 1984 to 1986 with rhabdomysarcomas in the region of the ear. One survived, following treatment. Ariza has reported one encouraging case of a girl who was treated at age 14 years for a vulval rhabdomyosarcoma who survived to marry, undergo vaginoplasty then have a baby in 1997, 11 years after her disease.

References

Sinniah D, Tan HM, Lin HP and Looi LM. Rhabdomyosarcoma in childhood. A 13 year review from the University Hospital, Kuala Lumpur 1967 - 1980. Sing.Med.J. 22:158-165 1981.

Said H, Phang KS, Razi A, Khuzauah R, Patawari PH and Esa R. Rhabdomyosarcoma of the middle ear and mastoid in children. J.Laryngol.Otol. 102:514-519 1988.

Ariza M, Rafaee T, Adeeb N et.al. A successful pregnancy outcome in treated vulval rhabdomyosarcoma. Med J Mal. 54:371-373 1999.

CONNECTIVE TISSUE SARCOMAS

Besides rhabdomysarcomas, a number of less common sarcomas occur. In 10 years, Sinniah *et.al*. noted a couple of fibrosarcomas, leiomyosarcomas, liposarcomas and haemangioendotheliosarcomas each. These add up to about equal the number of rhabdomysarcomas in children.

References

Sinniah D, Lin HP and Prathap K. Soft tissue sarcoma in childhood. Sing.Med.J. 21:487-489 1980.

Kuppuvelumani P, Rachagan SP, Syed N et.al. Rare case of huge retroperitoneal liposarcoma presenting as a gynaecological problem. Eur J Obstet Gynecol Reprod Biol 48:220-222 1993.

MALIGNANT FIBROUS HISTIOCYTOMA

Malignant fibrous histiocytomas are composed of a mixture of cells resembling fibrobalsts, myofibroblasts, histiocytes and mesenchymal cells. They are thought to arise from primitive mesenchymal cells. Most of these tumours develop on the limbs. They can however also occur in the abdominal cavity as described in a report of 4 difficult cases by Sim, Razack, Parthmanathan and Jalleh. Rathakrishnan also reported one from the stomach.

References

Rathakrishnan V, Arianayagam S and Kumar G. Primary malignant fibrous histiocytoma of the stomach: a case report. Australas Radiol 33:302-304 1989.

Sim PH, Razack AHA, Pathmanathan R and Jalleh RP. Retroperitoneal malignant fibrous histiocytoma with renal involvement. Med.J.Mal. 50:189-191 1995.

The Nervous System

GLIOMAS

According to a review of radiologically diagnosed neurological tumours at the UH by Wastie and Chawla, gliomas were the commonest intracranial tumours. This corresponds to experience in other countries. In cases diagnosed over one year gliomas constituted 52% of neurological tumours. Assessing size of brain tumours in general for suitability for radiosurgery in Kelantan between 1990-1996, Abdullah and Ridzuan found that 73% were less than 4cm.

Glioblastoma multiforme is a rare but very malignant form of glioma found in children. Arumugasamy and Tarkington have report one case.

References

Arumugasamy N and Tarkington JA. Primary glioblastoma multiforme of the spinal cord in infancy and childhood. Med.J.Mal. 27:136-141 1972.

Wastie NL and Chawla JC. Radiological investigation of neurological disorders. Med.J.Mal. 27:271-274 1973.

Abdullah J and Ridzuan MY. Incidence of tumour suitable for radiosurgery in a developing country like Malaysia: retrospective study done before the decision to start a radiosurgery programme. Stereotact Funct Neurosurg 69:152-155 1997.

PITUITARY TUMOURS

One of the common intracranial tumours, pituitary tumours constituted 3 out of 25 neurological tumours seen by Wastie and Chawla over one year at the UH. Pituitary tumours are usually known for their endocrinological manisfestations.

Ngan and coworkers have a series of 30 patients with prolactinomas ranging from 1 to 15 years on followup. 26 are females 4 males all aged between 17 - 46 years. 7 (23%) had tumours less than 10mm. 14 (47%) had macroadenomas (>10mm) which were confined within the sella. 9 (30%) had suprasella lesions with visual defects.

Reference

Ngan A, Zaini A, Singh J, Satkunasingam N, Colheart GJ and Wong WP. Prolactinoma, natural history and therapeutic options. J.Asean Fed.Endo.Soc. 3:61-67 1983.

MENINGIOMAS

Meningiomas are probably the second commonest intracranial tumours in adults after gliomas, excluding metastatic tumours. Djavadkhani and Halili reported a collection of 13 cases at the UKM Neurosurgical unit in just 9 months in 1982. The peak age of patients was the fourth decade. There were 10 females compareed with 3 males, the female preponderance being in keeping with other reports. There were 9 Malays, 3 Chinese and 1 Indian. All these patients had extripation of their tumour. There was no operative deaths.

Chee reported a cauda equina meningioma

that caused syringomyelia in the UH.

References

Djavadkhani K and Halili R. Intracranial meningiomas: a report of 13 cases. Med.J.Mal. 40:321-324 1985.

Chee CP, Tan CT and Nuruddin R. Syringomyelia associated with a cauda equina meningioma involving conus mudullaris. Br J Neurosurg 4:529-533 1990.

PARAGANGLIOMAS

Tumours from paraganglionic tissue of neural crest origin can arise in a wide area around the head and neck. Sharma *et.al*. have report a sinonasal nonchromaffin paraganglioma which was initially surgically removed and treated with radiotherapy but recurred 22 years later with rapid growth and malignant transformation which they believed was due to radiotherapy.

Reference

Sharma HS, Madhavan M, Othman NH et.al. Malignant paraganlioma of frontoethmoidal region. Auris Nasus Larynx 26:487-493 1999.

NEUROMAS

Intracranial neurinomas of the auditory nerve are well known in medical texts. Neurinoma involving the hypoglossal nerve is rarer but two such cases have been reported locally by Arumugasamy and colleagues.

A rare case that has been reported is of a malignant schwannoma of the orbit, by Fathilah and Sivanesan.

References

Arumugasamy N, Sarvananthan K, Rudralingam V and Pillay RP. Intracranial hypoglossal neurinomas - a report of two cases. Med.J.Mal. 26:168-172 1972.

Fathilah J and Sivanesan S. Metastatic malignant schwannoma of orbit: a case report. Med.J.Mal. 41:356-360 1986.

NEUROBLASTOMA

After leukemia and nephroblastoma, the neuroblastoma is probably the next most common malignancy in childhood. At the UH, Sinniah, Choo and Somasundram recorded 16 cases over 10 years from 1968 while Looi and Cherian reported an overlapping series of 37 cases over 15 years from 1970. Neuroblastomas made up 13% of all malignant solid tumours in children and accounted for 0.65 per 1,000 hospital paediatric admissions. 89% were below the age of 5 years which is similar to the pattern in other countries. There was little sexual predilection. Of the series of 37, 17 were Chinese, 12 Malays, and 8 were Indians.

68% of tumours were abdominal and 30% were mediastinal. About 14% were undifferentiated neuroblastomas, 54% differentiated neuroblastomas and 30% were ganglioneuroblastomas. Urinary vanillymandelic was detected in 86% of cases where screening was performed. At time of biopsy 80% had metastatic disease, 65% included evidence of marrow infiltration (where marrow aspiration was done). Overall survival was less than 2 years in 78% and more than 5 years in 17%. Sinniah, Lin, Kwan and Somasundram recognised 6 cases of Stage IV-S disease out of 20 cases which is generally thought to have a good prognosis even without treatment.

In another series from UH, overlapping the previous one by 4 years, Ng *et.al.* found 78 children with neuroblastomas between 1982 and 1997. This might appear to be an increase in incidence but it might just reflect the centre receiving more referrals. The median age of these patients was 3 years. In 83% the tumour originated in the adrenal gland which was more than in previous reported studies. Most patients unfortunately presented late, 22% in stage III and 66% in stage IV. The overall 2 year disease free survival rate was 39%. 4 patients underwent bone marrow transplant of whom 3 (75%) achieved a 2 year disease free survival.

Neuroblastoma is rare in adulthood but a case has been noted by Cheah *et.al*. at the UH.

References

Sinniah D, Choo M and Somasundram K. Neuroblastoma in Malaysian children. Med.J.Mal. 34:149-152 1979.

Sinniah D, Lin HP, Kwan PW and Somasundram K. Stage IV-S neuroblastoma. A review from the University Hospital, Kuala Lumpur. Sing.Med.J. 22:254-258 1981.

Looi LM and Cherian R. Childhood neuroblastoma in the University Hospital, Kuala Lumpur: a study into features of prognostic value. Mal.J.Pathol. 8:49-56 1986.

Thajunnisa HM and Yip CH. Cystic neuroblastoma with colonic fistula. Pediatr Radiol 18:406 1988.

Cheah PL, Jayalakshmi P, Jeyamalar R and Kuperan. Adult neuroblastoma: a case report. Mal J Pathol 11:69-71 1989.

Ng SM, Abdullah WA, Lin HP and Chan LL. Presenting features and treatment outcome of 78 Malaysian children with neuroblastoma. Southeast Asian J Trop Med Pub Hlth. 30:149-153 1999.

HAEMANGIOBLASTOMA

An important childhood malignancy Wastie and Chawla noted one case at the UH in a review covering one year.

METASTATIC TUMOURS IN BRAIN

Next to gliomas, metatases are the commonest neurological tumours. In the small series by Wastie and Chawla they accounted for 16% of neurological tumours.

Reference

Wastie NL and Chawla JC. Radiological investiGation of neurological disorders. Med.J.Mal. 27:271-274 1973.

The Endocrine System

THYROID CARCINOMA

Thyroid malignancies form a small percentage of all cancers in Malaysia as in the West. Surgeons removing solitary thyroid nodules have reported low rates of carcinomas locally. Out of 100 cases in Penang, Hari Rajah found 2 (2%). Thambi Dorai in Taiping found 5 (7%) out of 75 cases.

By selecting only cold nodules on isotope scan which were solid nodules on ultrasound for operation, Ahmad and Meah found malignancy in 25% of 69 patients. In their patients papillary carcinoma, follicular carcinoma and anaplastic carcinoma were seen in a ratio of 17:2:1. In a 10 year series of 152 cases Meah and colleagues found the ratio of papillary, follicular, anaplastic and medullary carcinoma to be 63:28:5:4. Females outnumbered males in a ratio of 4:1. In a further study by Thambi Dorai in Taiping, on the efficacy of fine needle aspiration, it was found that in 73 cases where satisfactory samples were obtained 13 (18%) were malignant. The ratio of papillary, follicular and anaplastic carcinoma was 9:3:1. They had no false negatives on aspiration cytology and only one false positive. Jayaram *et.al*. collected an experience of 1853 fine needle aspirates from thyroid lesions over 6 years from 1992 at the UH. 67% were found to be benign nodular goitres.

In a retrospective review of 107 patients operated on for multinodular goitre in the UH, Koh and Chang noted that 8 (7.5%) harboured incidental carcinomas. 4 were papillary carcinoma, 2 were follicular carcinoma and one each were squamous cell carcinoma and medullary carcinoma.

In 31 cases of thyroid cancer seen in Kelantan at the USM from 1985 to 1989 Sothy, Mafauzy, Wan Mohamad and Mustaffa noted 17:10:2:2 cases of papillary, follicular, medullary and anaplastic carcinomas. There were 25 women and 6 men. All the patients with follicular carcinomas were women. The mean age for these cancers were 53 years, 48 years, 49 years and 75 years respectively in the order the tumours were mentioned above. Treatment

was in general unsatisfactory because of the patients' non-acceptance of surgery and radioactive iodine.

Occasionally more histologically unusual malignancies may be found in the thyroid. Jayaram, Wong and Jalaludin MA noted a case of a mucoepidermoid carcinoma.

References

Ahmad KA and Meah F. Ultrasound of the cold thyroid nodule. Med.J.Mal. 39:123-126 1984

Thambi Dorai CR. Solitary thyroid nodule - experience in a district hospital. Med.J.Mal. 43:55-58 1988

Pillay RB, Thambi Dorai CR, Sharma K and Yap SK. Solitary thyroid nodules - an evaluation by fine needle aspiration. The Family Physician. 2:33-35 1990.

Sothy K, Mafausy M, Wan Mohamad WB and Mustaffa E. Carcinoma of thyroid - clinical presentation and outcome. Med.J.Mal. 46:212-217 1991.

Koh KB and Chang KW. Carcinoma in multinodular goitre. Br J Surg 97:266-267 1992.

Meah FA, Abdullah T, Wan Khamizar WK and Jasmi AY. Thyroid carcinoma - a 10 year experience in Malaysia. J ASEAN Fed Endocrine Soc 13:29-34 1994.

Jayaram G, Wong KT and Jalaludin MA. Mucoepidemoid carcinoma of the thyroid: a case report. Mal J Pathol. 20:45-48 1998.

Jayaram G, Razak A, Gan SK and Alhady SF. Fine needle aspiration cytology of the thyroid – a review of experience in 1853 cases. Mal J Pathol 21:17-27 1999.

PARATHYROID CARCINOMA

A rare entity, a case presenting with hyperparthyroidism has been reported.

Reference

Chng SL, Krishnan MMS, Ramachandran, Chan CH and Zain Z. Parathyroid carcinoma with steroid-suppressible plasma immunoreactive parathyroid hormone and human chorionic gonadotrophin. Sing.Med.J. 31:83-84 1990

ADRENOCORTICAL CARCINOMA

Meah *et.al* at UKM have recorded a series of 12 cases of adrenocortical carcinomas, among 130 cases of surgically treated adrenal tumours between 1978 to 1993. More than 50% of these were non-functioning tumours. The prognosis was poor.

Reference

Meah FA, Abdullah T, Jasmi AY et.al. The surgical treatment of adrenal diseases Ann.Acad Med. Sing. 25:251-254 1996.

Germ Cell Tumours

ENDODERMAL TUMOUR

Tumours from germ cells may present as malignancy in early life. Ahluwalia and Sharma reported a rare case of an endodermal sinus tumour believed to resemble the allantois and yolk sac, in a 3 year old child in Penang in 1973. Sivanesartanam reported a patient with stage IV endodermal sinus tumour of the ovary who conceived and delivered a normal child 5 years after surgical excision and cyclophosphamide therapy. In 1988 Sinniah noted that the UH had seen 11 cases over 15 years, 4 arising in the testes, 2 in the abdomen, 2 in the sacrococcygeal region, 2 in the mediastinum and one in the ovary.

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TERATOMAS

Teratomas are a heterogenous group of tumours and may be discussed under the organ where they arise, for example, in the ovary or testes, but they can also occur elsewhere. They may be benign, malignant or potentially malignant, hence making teratomas a special topic.

In a 10-year review of paediatric cases at the UH from 1968 Sinniah *et.al*. collected 19 cases of teratomas. This accounted for 6.6% of all their paediatric tumours, which was not unlike what is reported in Caucasian children. There were 12 Chinese, 5 Malays, 1 Orang Asli and 1 Indian. There were 11 boys and 8 girls. There was no significant association of the incidence for either race or sex. There were 6 ovarian teratomas, 6 sacrococcygeal and 5 retroperitoneal ones. They noted that the retroperitoneal tumours were more frequent in their series compared to other countries. Besides these site, teratomas were also found in the abdomen, mediastinum, parotid gland and testes. 9 tumours had malignant histological features. Hussein reported 1 case and Bahari and Abdullah reported 3 cases of mature, benign retroperitoneal teratomas which they also remarked seemed unusually common in that site.

In their series 9 cases of immature ovarian teratomas in the UH, Sen *et.al*. found 6 patients in Stage 1 and 3 in Stage 3. The majority has grade 2-3 tumours. After surgery and adjuvant chemotherapy 7 patients survived up to 9 years disease free.

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CHAPTER 8

VIRAL INFECTIONS

Viruses probably account for more human infections than any other infectious agent and probably quite a number of viral agents are not yet identified. They are the smallest and simplest life-forms whose nature began to be understood only from 1892 from the work of the Russian scientist Ivanovsky. They are capable of reproduction but are not free- living. As such, it is still debated if they should be classed with biological organisms. Usually they are given to occupy a special taxonomic position; a separate kingdom, Monera, apart from plants, animals and prokaryotic bacteria. Viruses are classified into about 18 families, plus other viriods that do not fit the definition of classic viruses, but for simplicity here they are just listed alphabetically.

ADENOVIRUSES

Adenoviruses were named such following their discovery from the work of Rowe and co-workers in 1953 where the virus was found to be disrupting attempts to culture human adenoid tissue. It was once called the 'adenoidal-pharyngeal-conjunctival virus' aptly describing the area where it is pathogenic. There are over 46 serotypes but they share some common antigens.

They are worldwide in distribution. A notable problem they cause is epidemic kerato-conjunctivitis. Although adenoviruses causes kerato-conjunctivitis endemically together with many other agents, when an epidemic breaks out the cause is very often the adenovirus.

Subgenus B. A spate of alarming paediatric death from cardiomyopathy and encephalitis, following a very short severe febrile illnesses occurred in Sarawak between April and September 1997. The outbreak began in Sibu, against a backdrop of hand, foot and mouth disease and spread to other towns in Sarawak resulting in at least 34 deaths. A few similar cases were seen in Peninsula Malaysia, especially around KL where UH workers isolated the enterovirus-71 (see Enterovirus). Much uncertainty surrounded the aetiological agent in the outbreak. Enterovirus –71 (EV-71) was isolated in many cases but no single virus or other pathogen could be easily isolated consistently from the victims. Cardosa *et.al*. studied the 20 deaths that occurred in Sibu, the epicentre of the outbreak and found a fastidious agent in 10 of the 16 fatal cases examined, which was shown to be a subgenus B adenovirus whose genome is not exactly like any known subtypes. The virus was isolated from serum, tissues of the central nervous system and heart. It was also isolated in the cerebrospinal fluid of a few patients who survive an illness of acute flaccid paralysis.

Adenoviruses are now suggested to be important causal agents of myocarditis. Cardosa has suggested that the temporal association of the deaths with an EV-71 related hand, foot and mouth disease season indicates that dual and synergistic infection may have been responsible for the severe illnesses and deaths.

Abubakar in UH KL later reported detecting the new subgenus B adenovirus in some of their patients. Although there was much similarity in the fatal Sarawak and KL cases, Lum *et.al*. however, disagreed that myocarditis was present in their patients in KL, arguing that brainstem involvement resulting in neurogenic pulmonary edema and secondary myocardial dysfunction instead was evident.

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CHIKUNGUNYA VIRUS

The Chikungunya virus (CHIK), is another mosquito borne virus endemic in Africa and Southeast Asia. It gets its name from an African tribal word meaning 'to bend up' which was used to describe an epidemic in Tanzania in 1952-1953. The virus is an alphavirus and it is borne by the culex mosquito and transmitted mainly in urban areas. An outbreak occurred in the Port Klang area in 1999. At least 17 people were tested positive serologically.

COXSACKIEVIRUS

Dalldorf and Sickles first described the Coxsackie group of viruses and the disease of 'epidemic pleurodynia' named Bornholm disease after the island on which it occurred in 1949. Together with the poliovirus and echovirus, the coxsackie virus are known as the `enteroviruses'. Besides pleurodynia they can cause herpangina, hand foot and mouth disease, conjunctivitis, myocarditis, pericarditis and meningoencephalitis.

In perhaps the first case documented in Malaysia, either a Group B or A9 Coxsakie virus was isolated in 1956 in a case with pleurodynia. One of the investigators was himself the patient. In a survey in the early 1970s of preschool children in Health clinics in KL, Tan and Lam detected a prevalence rate of Coxsackie viruses of nearly 8%. They were the commonest enteroviruses. Coxsackie A accounted for 42% and the various Coxsackie B viruses together accounted for 24% of the enteroviruses detected.

Tan, Yin-Murphy and Kandiah documented an epidemic of acute conjunctivitis in KL in 1978 where 2,133 cases were involved. The virus concerned was Coxsackie A24 which had gained notoriety as the cause of an epidemic in Singapore in 1970 during which Malaysia was also involved, and then in Hong Kong the next year.

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CYTOMEGALOVIRUS

Cytomegaloviruses are ubiquitous agents that commonly infect people throughout the world. Clinical disease is uncommon and the high prevalence is accounted for by subclinical infection. Its importance lies in the fact it can cause congenital abnormalities from intrauterine infections and its opportunistic malfeasance in the immunocompromised patient.

The prevalence of CMV infection in Malaysia lies in between that of developed countries where the prevalence is less than 30%, (where infection occurs in the elderly and immunocompromised patients and are life threatening infections) and places like Tanzania where it is reported that virtually all children are

infected before the age of 15 years.

In 1976 Tan reported that 83% of women in the childbearing age in KL showed antibodies against CMV. Ten years later Madhavan, Ong and Anuar found a rate of 26% in the 11-20 year age group increasing to 59% in those above 50 years old, among 838 sera in Penang from blood donors and patients whose blood was sent for other serology tests.

Maternal humoral immunity does not always protect the foetus against congenital CMV infection. Reactivation or secondary infection of the virus can cause congenital foetal abnormalities. Of 1,688 infants with congenital abnormalities, tested by IMR workers, 11.4% had IgM against CMV. This was greater in number than those positive for congenital syphilis (4.0%), rubella (3.7%), toxoplasmosis (1.0%) and herpes simplex (0%). Sabah and Selangor had significantly higher rates of congenital abnormalities due to CMV than other states. There was no racial differences and no difference in the number or boys or girls affected. Of the 193 infants with CMV congenital abnormalities 80% had liver involvement while only 10.4% had the more severe CNS defects.

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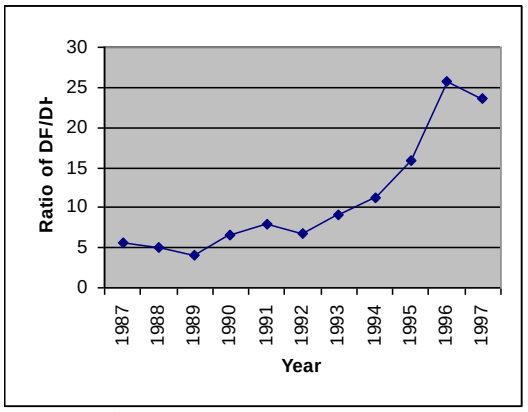
DENGUE FEVER

Dengue fever has been endemic in Malaysia for a long time. As early as 1902 Skae recorded the disease in Penang. However, the classical disease attracted little attention. In young children it may be just an undifferentiated febrile illness. Older children and adults may have the classical high fever, headache, back, muscle and joint pains, orbital pain and rash or just mild fever. The case fatality is very low. Four serotypes of the causative dengue virus have been identified in Malaysia. Any one of these may be responsible for the haemorrhagic form of the disease.

Figure 8.1 Ratio of number of cases of dengue fever (DF) to dengue haemorrhagic fever (DHF) in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Dengue Haemorrhagic Fever: The haemorrhagic form of the disease is of more recent advent first seen only after the Second World War and it has been confined to South East Asia. Its first ever appearance was an outbreak in Penang in 1962. 41 cases were detected. In several cases the virus was isolated and identified as the Dengue type II virus. There were 5 deaths in the outbreak. Shock has been identified as the important bad prognostic sign. Also called the Dengue Shock Syndrome, it is due to loss of plasma from the vascular compartment through increased vascular permeability. In addition disorders of haemostasis like thrombocytopenia and coagulopathy occur concurrently. In the 1980s

dengue haemorrhagic fever was 4-5 times less common than dengue fever itself. In the late 1990s, the incidence of dengue fever has greatly increased while the haemorrhagic form appears

Figure 8.2 Incidence of dengue fever in Malaysia per 100,000 population

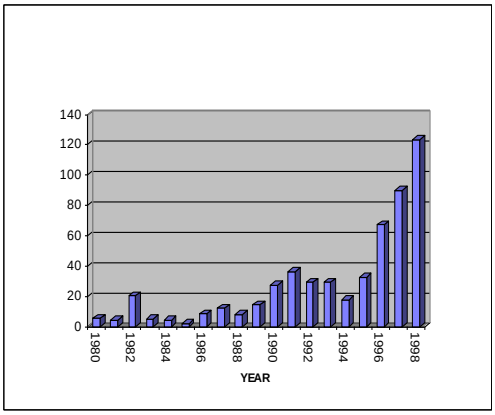
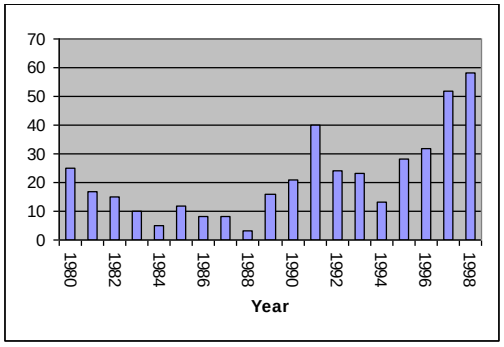


Figure 8.3 Number of deaths from Dengue in Malaysia

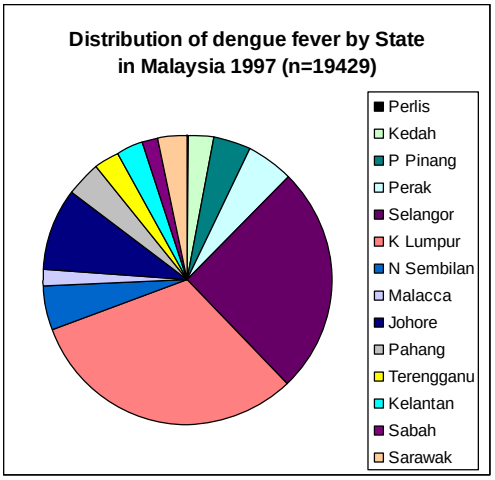


Source: Information and Documentation System Unit, Ministry of Health, Malaysia

not to have risen as much. The total number of dengue haemorrhagic fever still stands at less than 1,000 and is now more than 20 times less common than non-haemorrhagic dengue fever.

Between 1963 and 1972, 194 cases of dengue were reported. In 1971 dengue fever and dengue haemorrhagic fever were made a notifiable diseases.

Figure 8.4 Distribution of dengue cases by state 1997



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

An alarming outbreak occurred in 1973, starting in Kuala Lumpur and spreading to involve mostly the urban centres in West Malaysia. Including Dengue Haemorrhagic Fever, which was more common than the classical form, there were 1,487 cases that year with 54(3.6%) deaths. The majority of patients were children and the peak age was between 6 and 7 years. July was the month with the highest number of cases. The outbreak carried over into 1974 where there were 2,200 cases and 104(4.7%) deaths. The incidence of dengue fever in 1973 was 5.4 cases per 100,000, but was higher in Chinese (9.0 per 100,000) than in Malays (2.9 per 100,000) and Indians (2.4 per 100,000). Males suffered a higher attack rate, (M:F among Chinese was 1.1:1) especially among the Malays and Indians (M:F among Malays and Indians 1.5:1). The incidence of dengue haemorrhagic fever in 1973 was 10.1 per 100,000 with a fatality rate of 6.4 per 100 persons. Again the Chinese appeared more prone and males more vulnerable than females.

After this the incidence declined with about 600 to 900 cases a year with a small peak in 1978.

The next big outbreak was in 1982 with 3,006 cases. The main serotypes involved were Dengue type I and III. An analysis of the 1982 outbreak showed that most cases occurred between the months of July to September and almost half the total for the year happened in August, the peak month. The urban states of the West coast, namely Penang (incidence 49 per 100,000), KL (38 per 100,000) Selangor (28 per 100,000) and Malacca (29 per 100,000) were the main centres but Perlis (39 per 100,000) and Kelantan (34 per 100,000) actually had the highest incidences after Penang. Sabah, Kedah, Terengganu and Sarawak had low incidences (3 to 10 per 100,000) the disease only making a recent appearance in these states. Instead of children, young adults were now most often affected. 56% in this epidemic were above 15 years old, and instead of being largely confined to Chinese, Malays increased in number. In this outbreak several mild unusual symptoms were noted, including cardiac arrhythmias and neurological manifestations including fits which were all reversible. Deaths from dengue were rare but since 1982 over 50% of deaths have occurred in patients over 15 years.

The next peak occurred in 1986 running into 1987, when 1,408 and 2,025 cases were recorded respectively, roughly following a 4 year cycle. 63% of these clinically diagnosed cases were supported serologically. In these last few years the fatality rate dropped to about 0.5%. It may partly reflect better case detection. In this period it was noted that more infants were affected and severe manifestations including gastrointestinal bleeding, extensive pleural effusions, neurological derangement and hepatic failure were appearing. Selangor, including Kuala Lumpur, Perak and Penang are the principal states affected numerically.

In recent years Sarawak has risen to be the state most affected after these four. The first reported case in Sarawak was in 1973 but Surtees claims it has been endemic before that. When notification was started in 1973 the number of cases initially remained low with only 17 reported up to 1980. The first large epidemic occurred in Lawas in 1982 going on to 1983 with over 100 cases each year. In 1987 Sarawak recorded 343 cases and over 600 in 1989.

When first the possibility of importing the disease into Sabah was studied a survey in 1978, only 2 of 20 sera from patients with febrile illness were positive for arbovirus B likely to be dengue. Sabah however has the mosquito vectors but of late only 10 to 20 cases are found yearly.

Since 1987 the cyclical pattern of 4 years seems to have been lost. 1989 and 1990 recorded a high number of cases. However over the next few years the incidence declined till 1994. 1995 saw a rise in the incidence of dengue that continued to escalate till 1998 when the incidence of dengue notified was 6 times that of 1994.

In the light of the current situation, a vaccine would be very welcomed.

Virology

In different years different dengue virus serotypes predominate. One serotype accounting for up to 80% of all isolates. In 1985 when the outbreak was mainly due to Dengue type III the case fatality was high whereas when Dengue type I was predominant the case fatality was low. The fatality rate in 1987 and 1988 when Dengue type I predominated was 1.86%. Between 1989 and 1991 with serotype II predominant the fatality rate increased to 4%. In 1993-1994 outbreak was due mainly to the Dengue type III virus which was shown by cDNA studies to have originated from Thailand. The fatality rate rose to 5.1% in 1994 and 7.3% in 1995.

Clinical features

Dengue fever may be asymptomatic but classically dengue fever in a non immune person consists of a severe headache, retro-orbital pain,

backache, fever with other variable manifestations. With dengue haemorrhagic fever or the dengue shock syndrome there is usually some respiratory and alimentary symptoms, like anorexia, vomiting and abdominal pain, some myalgia and then circulatory complications. However uncharacteristic manifestations are not unusual.

Of late the clinical spectrum of dengue has been changing and multisystem involvement with more severe manifestations being seen. Lum *et al*. reported 8 cases of fulminant heapatitis and liver failure in 8 children with dengue fever in 1990-1991. There was one death and one survivor with hemiparesis due to an intracerebral bleed but the rest recovered fully. In another report they noted 3 cases with adult respiratory distress syndrome. Reye's like syndrome has been seen. Children have presented with adult respiratory distress syndrome.

Chye *et.al*. have observed 2 cases where dengue fever in two mothers just before they delivered resulted in the disease in the newborn. One of the neonates died due to intracerebral haemorrhage and multiorgan failure. Both these cases involved the Dengue virus typeII.

The Vectors

Aedes aegypti is the most efficient mosquito vector for dengue fever. It was first studied as a potential vector for yellow fever but it has become more important for dengue. It is an indoor biting mosquito active in the morning and evening. It breeds in natural and artificial water containers such as ant-traps and coconut shells and is associated with built-up urban areas. In Malaysia *A. albopictus* is a proven, though less efficient secondary vector. It may have had a role in the rise in the number of rural dengue cases very recently.

Since 1983 the control of dengue fever has come under the Vector Borne Disease unit. Control measures include fogging in affected urban areas, surveillance, educating the public about preventing mosquitos breeding around dwellings and enforcing fines for houseowners found with mosquito breeding grounds.

Foo, Lim, Lee and Fang from the IMR found relatively strong statistical evidence relating rainfall to dengue outbreaks in analysis the pattern in Selangor from 1973 to 1982. The lag time between onset of heavy rain and dengue outbreak was about two to three months. A 120% increase in number of cases was observed when the monthly rainfall exceeded 300mm. This can serve as a useful warning for mosquito control measures.

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EBSTEIN-BARR VIRUS

Infectious mononucleosis is very rarely observed in Malaysia. Tan, investigating 401 Malaysians with clinical features suggestive of infectious mononucleosis from 1954 to 1966 found that not one had a positive Paul-Bunnell serological test. Norhanom *et.al.*, in surveying 1,881 serum sample from all parts of Malaysia found that not one was seronegative to the Ebstein-Barr virus. Devaraj *et.al.* reported similar findings in Sabah.

The vast majority of Malaysian children acquire antibodies to the Epstein-Barr virus (EBV) in the first year of life. Yadav, Malliga and Ablashi reported in 1987 that 71% of infants less than 3 months old had maternal IgG to the EBV capsid antigen, but by 7-9 months only 26% retained the maternal immune protection. Primary infection, denoted by the emergence of EBV IgM antibody occurred at 4-6 months. By 8 years old all children were seropositive. Thus in Malaysia very few if any are susceptible when they reach adolescence when infectious mononucleosis is the likely result of delayed primary EBV infections.

The EBV is nevertheless an important disease agent in Malyasia implicated as an aetiological factor in nasopharnygeal carcinoma and Burkitt's lymphoma which are not uncommon. Besides that, it may be present in some types of lymphoma as an aetiological factor as well.

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ECHOVIRUSES

Echoviruses can cause aseptic meningitis, conjunctivitis, coryza and febrile illness. They occur in all parts of the globe. Tan and Lam in a survey before and after polio vaccination in the early 1970s found echoviruses in about 1% of children in a preschool health clinic.

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ENTEROVIRUSES

Although echoviruses, coxsackieviruses and the polioviruses are also known as enteroviruses, this section deals with the other enteroviruses not in those groups. These are, in particular, enteroviruses types 68-71.

The Enterovirus type 70 has been found to be responsible for a conjunctivitis outbreaks in Malaysia since 1969. Like the coxsackievirus it differs slightly from the adenovirus in that the cornea is not usually badly involved.

Haemorrhage however may occur. An ourtbreak of enterovirus 70 acute conjunctitivis was recorded in November 1980, thought to have started in Pahang and spread throughout the peninsula.

More notorious is Enterovirus type 71(EV-71). It was detected in the brain of 4 fatal paediatric cases between April to October 1997 in UH, where it was seen to cause extensive damage to the pons and medulla. Clinically these children presented with sudden cardiopulmonary collapse causing death within a few hours of admission. Overwhelming neurological signs and symptoms were absent. The outbreak was thought to be linked to an outbreak of hand-foot-mouth disease (HFMD) but two of the four children who died did not have cutaneous or mucosal exanthemata. Abubakar *et.al*. detected EV 71 in 51% of 57 samples from patients with suspected HFMD. Genetic sequencing studies suggest that 2 potentially virulent strains were co-circulating in Malaysia in 1997. A similar outbreak occurred in the summer of 1998 in Taiwan where 50 children with preceding HFMD died of pulmonary edema or haemorrhage.

Concurrent with the cases reported at the UH, and the initial cause of public anxiety between April and September 1997, was an outbreak in Sarawak where at least 34 children, aged between 5 months and 7 years, died with an acute febrile illness complicated by cardiomyopathy and encephalitis against a backdrop of HFMD. In fatal cases, all had fever, 66% had oral ulcers, 62% had extremity rashes, 28% rapidly progressed to seizures, 17% to flaccid limb weakness and 83% had cardiopulmonary symptoms. There was much uncertainty about the viral agent responsible and it was initially known as a Coxsackie outbreak in the media. In a number of these patients EV-71 was isolated. Cardosa *et.al*. however isolated other viruses including a subgenus B adenovirus (see Adenovirus). A synergistic interaction of EV-71 and the Adenovirus could have caused the severe illnesses observed.

Using genetic sequence studies Abubakar has found that several enteroviruses, including Echovirus 1 and Coxackievirus A9 were also circulating in Malaysia during the 1997 outbreak of HFMD but these did not cause fatal infections.

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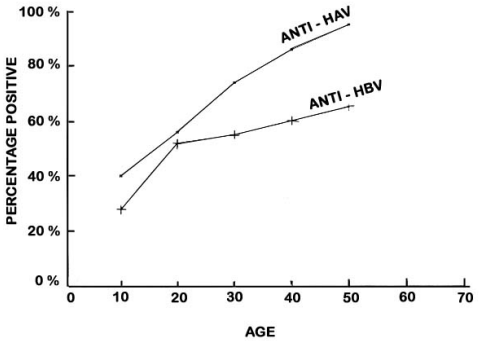
HEPATITIS A

Hepatitis A (HAV), which is transmitted by the faecal-oral route is a common cause of morbidity but causes little mortality. Infection produces long-lasting immunity indicated by the presence of IgG antibody. In a survey of 110 normal, healthy adults in KL, Ton, Thiruselvam, Lopez and Noriah found that at the age of 20 years about 67% had been exposed to the virus. The proportion rose to 92% in the over 40 years age group. These findings probably reflect the situation elsewhere in Malaysia. Of hospital patients diagnosed as having viral hepatitis 88% had IgG to Hepatis A, which is like the rate in the general population, and 33% were positive for the IgM antibody,

suggesting the Hepatitis A probably causes one third of the admissions for acute viral hepatitis second in number to leptospirosis. In a survey hospital in Terengganu and Kelantan from 1994-1997, it was also noted that Hepatitis A accounted for 48-66% of acute hepaptitis cases. Hepatitis B and C accounted for a further 6.8%, and Hepatitis D and E were detected in less than 1%.

Figure 8.5 Age specific prevalence of anti-HAV and anti HBV markers in Malaysia 1983



Tan, Fang, Collett and Ooi found a similar rate of previous exposure to HAV among 494 people surveyed. Indians (81%) had the highest rate followed by Malays (70%) then Chinese (56%). As could be expected rural folk (75%) had a higher rate than urbanites (66%).

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HEPATITIS B

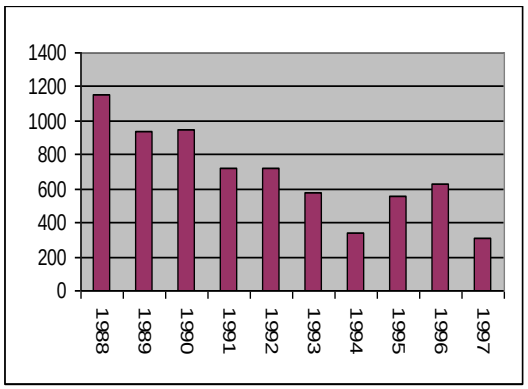
Worldwide, it is estimated that 350 million persons are carriers of the hepatitis B virus (HBV). 0.8 to 1.7 million of these are Malaysians.

In 1987 Ross, Dass, Thavarasah and Noor estimated that in Malaysia about 2% of children are infected with HBV per year. The infection rate is highest during the first 10 years of life. At the age of 50 years, 62% of males and 50% of females have been exposed to the HBV. The difference between the sexes occurs because males have a higher rate of infection than females after the age of 15 years. A prolonged carrier state that lasts many years or even a lifetime develops in about 1% of infected adults in this region. Infection during childhood may have a higher chance of producing a carrier state.

The first population survey of carrier status of HBV in Malaysia was carried out in 1971. The overall prevalence of the HbsAg was 1.7% among 2,962 male blood donors. The rate was highest among Chinese (3.4%) and lowest among Indians (0.5%). The rate was 1.3% among Malays and 2.7% among 110 individuals from other races. The rate was fairly even among the various age groups in Chinese but among the other races it was noticeably higher among those under 30 years old. In 1984 a study of a sample of 24,747 blood donors in KL indicated that 3% of the Malaysian adult population were carriers of the HBV. A study 6 years later in 1990 of 191,340 blood donors found that 3.7% were HbsAg positive. The rate appears to be rising.

Similarly, in Sarawak, among blood donors, 3% of 12,793 were found to be HBsAg positive in 1983, but just two years later 6% of 15,160 were positive in 1985.

Figure 8.6 Number of acute Hepatitis B cases in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

In a survey of non-icteric medical patients Tan *et.al.* found that Indians (9%) had lower carrier rates than Chinese (19%) and Malays (20%) in 1986.

In a 1986 paper, Mangalam *et.al.* reported that among 200 drug addicts aged 17 to 45 years 52% had been exposed to the virus but only 5.5% were HBsAg positive carriers. This is surprisingly low and comparable to the general population. Duraisamy *et.al* noted however in 1994, that 12.3% of 3,138 intravenous drug users screened were HBsAg positive. In a study of recipients of blood products in HUSM, it was found that 22% of 55 children who had malignancies and received blood products were HBsAg positive.

The infection rate of HBV among 370 prostitutes in KL was found to be 66% in 1990. Similarly, the rate among Chinese patients with sexually transmitted diseases who had multiple partners in a clinic was reported to be 64% by Gan *et.al*. A control group who did not have multiple partners had an infection rate on only 39%. However in the these two groups the carrier rate of the infection (HBsAg) was 9.2% for the multiple partner groups and 6.8% in the non-multiple partner group.

Man is the only natural host of the HBV. The acute illness is self limiting and irequently not serious. Many infections go unrecognised because they are mild and non-specific. The importance of the disease lies in its carrier state which can lead to hepatocellular carcinoma and/or cirrhosis. It has been estimated that the life time risk of death from these conditions is about 25% to 30% for carriers. The risk is higher for those who contract the disease early. What is striking about hepatocellular carcinoma in Malaysia is that among the Orang Asli, in whom this is the commonest malignancy, virtually 100% are associated with the HBV carrier state. Hepatocellular carcinoma is associated with 70 to 80% of cases among the Chinese, Malays and Indians.

Looking at the infectiousness of 330 HbsAg carriers in Malaysia, Ton and others found that 22% of them had HBV-DNA. The prevalence of HBV-DNA was higher in Chinese HbsAg carriers than in Malays.

It is held that vertical transmission from mother to child but not in-utero, is the most important form of spread. As such infants ought to be protected and it is now possible with a vaccine. Since 1989 the vaccination programme for HBV has been extended to all children born in Malaysia. The immunisation coverage has increased from an initial 86% in 1990 to 91% in 1998. Studies in the future to see its impact will be hopefully encouraging.

Serotypes

In a study of frozen sera at the UH, Ng and Saw found that 25% of their patients had untypable HbsAg. 50% had the *adw* subtype, 18% had the *adr* subtype and 4.5% the *ayw* subtype. One sample reacted to both the *adw* and *adr*. 23 (77%) of the 30 Chinese had the *adw* subtype. The *adr* subtype however, was the commonest among Malays (4/11).

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HEPATITIS C

Between 1970 and 1987 there were more than 50 agents purported to be the Hepatitis C virus responsible for the non-A non-B hepatitis. But it was in finally in 1987, when its genome was sequenced, that the right candidate to take the name Hepatitis C virus was discovered. Though not isolated, it could be shown to be flavivirus type of virus 50-60nm. in size. The largest population surveys were done in Japan and showed a prevalence rate of 1.1%. It has been reported as 0.6% in the U.S.A. The Japanese experience is that about 70% of post transfusion non-A non-B hepatitis was due to Hepatitis C. 81% of such patients went on to chronicity. It is thought to be more carcinogenic than Hepatitis B. More than 80% of those with acute hepatitis C become chronic carriers.

In a study between 1985 and 1991 Sinniah and Ooi at the IMR screened several risk groups for the anti-HCV antibody by ELISA. Their results are given in Table 8.1. In hepatocellular carcinoma patients, HBV was the viral agent, present in 75%, while in 10%, HCV was detected together with HBV.

Table 8.1 Prevalence of HCV antibodies in special Malaysian groups

Group	Number Screened	Number Positive (%)
Intravenous drug users	190	162 (85%)
Haemophiliacs	14	9 (64%)
Dialysis patients	356	192 (54%)
Liver Cirrhosis patients	25	7 (28%)
Hepatoma patients	65	9 (14%)
Homosexual males	37	4 (11%)
Female prostitutes	100	9 (9%)
Chronic liver disease	108	7 (6.5%)
Blood donors	363	11 (3%)
Dialysis unit staff	53	0
Laboratory personnel	123	0
Total	1,434	410 (28.6%)

In a series of 3,540 blood donors in GHKL in 1991, 1.5% of males were reactive to anti-HCV by ELISA. None of the 53 female donors were positive. The rates in Malays was 1.63%, in Chinese 1.6% and 0.5% in Indians. The UH reported that 1.9% of 504 blood donors were anti-HCV positive in a study the same year. 30% of intravenous drug users tested were positive as were 9.1% of patients on haemodialysis, 8% of patients with cirrhosis and 17% of patients with hepatitis. Hepatitis C accounted for 33%(19/57) of post-transfusion hepatitis.

Detecting acute hepatitis C is important because in Asians more than 80% of patients with acute hepatitis C become chronic carriers. However, up to 64% of them can be prevented from the chronic infection by antiviral therapy.

In a study of recipients of blood products in HUSM, it was found that 29% of 55 children who had malignancies and received blood products were anti-HCV positive. In the Nephrology Unit in GH KL antiHCV was positive among 56% of those have Centre Haemodialysis, 42% of those doing Home Haemodialysis and 19% of those on CAPD. Isahak *et.al*. found in 1993, that 5.8% of 52 thalassaemics who had received multiple transfusions were positive.

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HEPATITIS D

As a defective virus requiring helper functions of the hepatitis B virus (HVB), the hepatitis delta virus (HDV) can only develop and infect patients with hepatitis B surface antigen in whom it aggravates the course of the underlying infection.

Worldwide estimates indicate that more than 5% of HBV carriers are infected by the HDV but it varies greatly geographically. The ratio of HDV to HBV is about 90-100% in some Pacific islands and parts of the Amazon but 0% among some Eskimos who have a high prevalence of HBV. In countries like China and Saudi Arabia there is variation of its prevalence between regions.

Nearly all studies confirm that HDV is a significant cause of chronic hepatitis leading to cirrhosis and liver failure as well as a major cause of fulminant hepatitis. However, its role in oncogenesis is debated. Drug addicts sharing needles are the prime group at risk from HDV transmission.

How *et.al*. suggested that the delta agent had not yet been introduced to Malaysia prior to 1985 from screening 176 HBsAg positive blood samples. Dimitrakakis *et.al*., however, detected the virus in 4 out of 27(15%) Malaysian HBsAg positive in intravenous drug users in study in 1985. Just a year later Sinniah, Dimitrakakis and Tan found 7 out of 35 (20%) similar subjects positive.

The same group writing in 1989 had found only one asymptomatic blood donor with the delta agent out of 125 HBsAg carriers tested. Among male homosexuals and prostitutes HBsAg carriers the positive rate for HDV was 3 out of 22(14%). In 1994 Duraisamy *et.al*. detected anti-HDV in 15 out of 34(34%) of HBsAg positive drug addicts. It appears the rate is increasing in this specific risk group.

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HEPATITIS E

The existence of Hepatitis E came to scientific attention through Khuroo from epidemics in Khasmir between 1978 and 1982 and was known first as epidemic non-A non-B hepatitis. It is a 7.6kbase RNA virus and was characterised in 1987 as Hepatitis E by Balayan who incidentally, swallowed the virus himself in his efforts to study it. It is transmitted oro-faecally. It is not easily transmitted from person to person, usually the source is a contaminated water point source. Children seem to be spared but adults, especially pregnant women are commonly affected. On hindsight the first large outbreak was thought to be in New Dehli in 1955. It is probably more common in the tropical and semitropical regions.

In Malaysia, a seroprevalence study of 315 women attending antenatal clinic in the UH in 1996 found no cases of Hepatitis E. A year later however, Ng *et.al*. found that among 145 HIV-1 infected subjects, 10.3% had anti-HEV IgG and 4.1% had anti-HEV IgM, giving a total prevalence of 14.4% in this group. The prevalence was not significantly different between ethnic groups, all adult ages and across HIV risk groups. Seow reported in 1999 that 2 of 100 (2%) of healthy urban blood donors and 60 of 132 (45%) of Orang Asli in Pahang and Perak had anti-HEV IgG.

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HERPES VIRUSES

CHICKENPOX and HERPES ZOSTER

Chickenpox (or varicella) and zoster, is highly endemic in Malaysia like most places in the world. The varicella virus has no prediliction for any group nor does it leave anybody exempt. Mortality is very rare in the normal population. Therefore it is of interest that even if one case such as that of a 19 year old Malay male in 1991 is reported in the press.

In the immunocompromised, varicella is potentially life threatening. The pediatric oncology department in GH KL reported 12 cases in children with haematological malignancies over one year, of which 2 died, despite aggressive antiviral and supportive therapy. Gangaram and Cheong have also reported a fatal case involving a 14 year old girl with nephrotic syndrome receiving immunosuppressive therapy. Lau in Sarawak, on the other hand has reported a severe case of varicella pneumonia who required ventilatory support but survived.

Morbidity, however, for chickenpox and zoster can be serious, as in two examples of zoster by Loh or troublesome as in the Ramsay-Hunt syndrome.

Chan and Goh have reported a case of life threatening pancreatitis in a 2 year old child following vaccination with the Oka strain of live attenuated varicella vaccine.

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HERPES SIMPLEX

The Herpes simplex virus is fairly ubiquitous. Tan found antibodies to the virus in 79% among 365 women of child-bearing age in 1976. Besides cold sores this virus is usually considered in the context of genito-urinary infections. Of specimens of urine and vaginal swabs examined at the IMR for suspected cases about 10% turned out to be positive. From a study of genital ulcers in 249 patients at the Loke Yew clinic, IMR workers have reported that Herpes Simplex type II (19%) was the commonest cause of ulcers, followed by *Haemophilus ducreyi (9%)* and syphilis (7%) in 1991.

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HUMAN HERPESVIRUS-6

Human herpesvirus-6 (HHV6) was first isolated in 1986 but it was given its current name and established as the cause of exanthema subitum in 1988. Clinical features of this childhood viral infection, however, had been described and called roseola by Zahorsky in 1913 and called exanthema subitum by Veeder and Hempelmann in 1921. Chua *et.al*. have shown that the prevalence is high in Malaysia. 84% of 600 randomly collected serum samples of children were positive. There is high transplacental transfer of antibody against HHV6 and 82% of infants have the antibody. The rate drops in those between 1-2 years. After that infection occurs very early in life. 80% of children between 2 to 5 years were positive and this rate remains till the ago of 60 years. There was no significant difference between the sexes and among the major ethnic groups. Yadav *et.al*. have however noted that the Orang Asli in Peninsula Malaysia and East Malaysian tribes like Ibans, Kadazans and Bidayuhs have lower prevalence rates.

Five children 2-8years old from Assunta Hospital have been reported to have HHV6 infection clinically similar to infectious mononucleosis. They had fever, neck swelling, cevical lymphadenopathy, enlarged tonsils with exudates, periorbital swelling and hoarseness of voice. They all had EVB-IgG as expected. In addition they had HHV6-IgM and a 4 fold rise of HHV6-IgG.

Chua and colleagues from the UH have also reported the HHV6 was the cause of fever in 5 of 31 children with febrile convulsions. These 5 all had uvulo-palatoglossal ulcers which the other children did not. These ulcers are an early sign that appear before the macropapular rash and have a very high correlative value for exanthema subitum (χ^2= 1810, p<0.001 Chua KB 1999).

Over in Sabah, Yadav *et.al*. have noted a low prevalence of the HHV-6 virus. Only 34% of 95 blood donors were serologically positive, while they noted the EBV was ubiquitous.

Yadav *et.al*. have detected the HHV-6 virus in 80% of squamous cell carcinoma cells and in 67-100% of cases of lichen planus and leukoplakia. The role of HHV-6 in oral mucosal tumours however, remains to be determined.

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HUMAN HERPESVIRUS-7

Human herpesvirus 7 (HHV 7) was isolated from a healthy adult CD4 lymphocyte by Frenkel in 1990 and was shown to be a cause of exanthema subitum in Japan. Similar reports have not been noted outside Japan but Chua *et.al*. confirmed one such case in a 7 month old child in UH in 1996.Yadav *et.al*. showed that the virus could be very frequently detected in archival salivary gland tissue, the site evidence suggests it replicates in and persists in for potential transmission of infection.

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HUMAN HERPESVIRUS-8

In a study of Southeast Asian countries including Malaysia, Ablashi *et.al*.found a low prevalence of human herpesvirus-8 (HHV-8) in both healthy individuals and HIV patients. This correlates with the fact that hardly any Kaposi's sarcoma has been reported here.

Reference

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HUMAN IMMUNODEFICIENCY VIRUS (HIV)

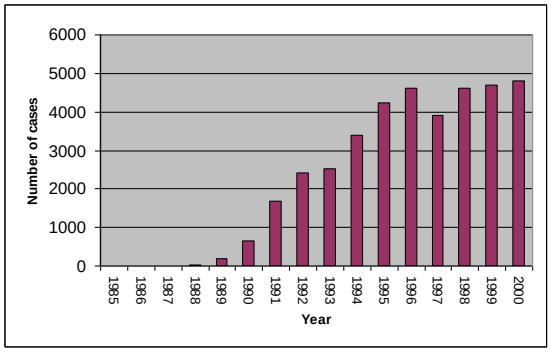
It is believed that the Human Immunodeficiency Virus (HIV) that causes AIDS probably originated from a virus in the African green monkey and was first transmitted to man in central Africa, probably a few years before 1969, where it remained confined for some time. It was eventually transferred to the Carribean from where it was carried to the United States. In the United State it came to worldwide notice, first affecting principally the male homosexual community.

The awareness of HIV infection arose from the devlopment of the end-stage of the disease, AIDS, in a report of 5 men in Los Angeles with the unusual infection of *Pneumocystis carini* in the morbidity and Mortality Weekly Report on 5 June 1981. A few months earlier 3 young homosexual men in New York had presented with *Kaposi's* sarcoma. The term 'gay related immune deficiency', GRID was coined to label the syndrome. Within a year the disease appeared in IV drug abusers and in a haemophiliac. In late 1983, the French scientist Montagnier first identified the virus and called the lymphadenopathy associated virus, LAV. The American Gallo also identified it and called it HTLV III. Finally in 1986 the International Committee on Taxonomy of Viruses decided is should be called HIV.

AIDS became a notifiable disease in Malaysia on 22 May 1985. That year however no cases were detected in a nationwide serosurveillance covering 4,913 blood donors and 1,067 samples from identified high risk groups. In the subsequent 2 years less than 10 victims were diagnosed. But the number shot up

to 177 HIV carriers in 1989 following another screening survey and to 650 in 1990. By 1990, 5 years after the first case in Malaysia, 26 patients had developed the full blown syndrome of AIDS and of these 17 had died.

Figure 8.7 Number of reported HIV cases in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

The largest number of patients initially were from the border states of Kelantan, Kedah, Johore and Terengganu. In 1990 Johore took over the lead with most cases. 96% were males and 77% are Malays. The age group most affected are the 16 to 35 year olds. The risk groups identified are intravenous drug users (IVDU), recipients of blood products and homosexuals. In 1994 IVDU accounted for 77% of HIV patients. Mandatory tests upon entry to detention camps contributes to a high pick up rate. In 1991 the first infected baby born to an infected mother who was a drug abuser was found in GH KL. Four cases have been reported of patients receiving living unrelated renal transplants in India acquiring HIV.

From 1995 to 2000 there has been gradual change in the profile of the Malaysian HIV cohort. The number infected through the sexual route now form at least 12% of HIV infections, and could be as high as 24%. The number of infections among women is increasing. While new infections among men has stayed level at about 4,300 cases a year, new cases among women increased from 297 in 1998 to 459 in 2000, an increase of 54%. As a result there were 221 cases of perinatal HIV infections in 2000.

Clinical Features

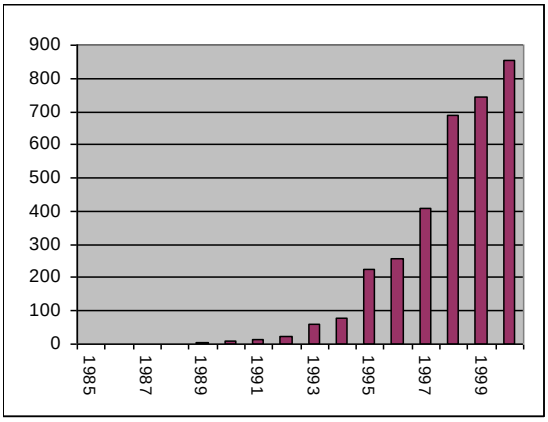
In the UKM experience of 334 HIV patients between 1987 and 1995, 48%(159) were Malays, 32%(108) were Chinese and 19%(64) were Indians. 96% were males. 66% were between the ages of 26-45 years. IVDUs constituted 77% of the patients, although many of them had more than one risk behaviour. 41(12%) presented with full blown AIDS. A further 25 progressed to AIDS on follow-up. The two commonest AIDS defining events were tuberculosis (56%) and *Pneumocystis carinii* pneumonia (23%). The mean CD4 count at progression to AIDS was 130/mm^3. All patients with AIDS were male. UKM workers also reported in 1998 that in HIV patients who were IVDUs, tuberculosis (40%) and bacterial pneumonias (33%) comprised most of the lower respiratory infections whereas in patients with 'other' risk behaviours *Pneumocystis carinii* pneumonia (40%) was the most common. IVDUs also had a much higher rate of hepatitis B and C co-infection and developed chest infections at higher CD4 counts. 100% were co-infected with hepatitis C, 12% with hepatitis B, 73% with cytomegalovirus and 59% with toxoplasma.

Pneumocystis carinii (33%) was the commonest AIDS defining event in the UH experience of 66 patients between 1986 and March 1994, followed by esophageal candidiasis (16%).

In a review of 145 Chinese HIV patients (96% men), most of whom already had an AIDS defining event, seen in UH and GH KL over 1 year in 1997, Jing and Ismail noticed that 104 (72%) had mucocutaneous disorders. 36% had generalised hyperpigmentation, 30% had nodular prurigo, 28% had xerosis, 21% had seborrheic dermatitis and 8.3% had psoriasis. The most common infections were oral candidiasis (36%),

tinea corporis and onychomycosis (19%) and herpes (5.5%). Kaposi's sarcoma was rare.

Figure 8.8 Number of deaths from AIDS in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Virology

IMR workers, studying the HIV virus in 60 Malaysian intravenous drug users reported in the year2000 that the predominant subtype was HIV-1 B accounting for 92% of specimens. Subtypes B and E were also found.

With no certain cure for HIV infection, prevention of spread is of major importance in disease control. Measures to create public awareness have been carried out in Malaysia extensively and health professionals made aware of counselling patients about the disease. A study in Kelantan showed AIDS awareness was high among drug abusers but there was little change in risk behaviour.

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HUMAN PAPILLOMAVIRUS (HPV)

The human papillomaviruses (HPV) infect epithelial or fibroepithelial tissue causing proliferating lesions varying from warty condyloma to flat condyloma and low grade dysplasias. These lesions do not cause significant morbidity. The significance of HPV is mainly that in the female cervix. These lesions progress to become carcinoma. In a study of 60 samples of cervical carcinoma from patients from Seremban GH between 1986 and 1988, HPV was detected in 80% of the samples by polymerase chain reaction and 80% by immunohistochemistry. However there was a discrepancy in 13% of the cases and 95% were positive in at least one technique. Dual infection with HPV 16 and 18 was noted in 40-52%, HPV 16 alone in 13-35% while HPV 18 alone accounted 5-15%. The virus was not associated with any particular histological type of cervical carcinoma. HPV was present in a lower percentage of Malay patients (60%) compared to

Chinese (80.5%) and Indians (78.6%).

Condylomata acuminata, due to HPV has been reported in an 18 month old girl. Its mode of transmission was not established.

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HUMAN T-CELL LEUKEMIA VIRUS-I (HTLV-I)

A serological survey of 1,664 unselected people and patient done in the UH reported in 1992 found that 1.6% were reactive to an ELISA test. However, only 2 of these were confirmed positive on Western blotting indicating that a low prevalence HTLV-I in our population.

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INFECTIOUS MONONUCLEOSIS

(see EBSTEIN-BARR VIRUS)

INFLUENZA

Influenza is well known for its epidemic, and occasionally pandemic outbreaks which have claimed millions of lives, but generally the influenza virus is not very lethal. People tend to blame the flu for many mild febrile illnesses. Though it is a common virus we do not really know what percentage of the flu-like fevers the influenza virus actually causes. The causative agent for influenza is a group of myxoviruses of many strains and three types described as A,B and C. Immunity is type specific and relatively short lived. And because the viruses change their antigenic properties rapidly, work in developing useful vaccines is difficult.

The antibody pattern in the elderly population of Malaysia indicates that the country had been affected by the ancient Asian(H2) pandemic of 1889-1890, the 1918-1919 pandemic caused by the swine virus and possibly also by the ancient Hongkong flu strain presumed to have circulated around 1900 or even prior to that.

The influenza virus was first isolated locally in February 1954 at the IMR and the US Army Medical Research Unit following an outbreak in a rubber estate near KL. The virus was identified as the A-prime virus. The next outbreak occurred a year later in 1955 at the Malay College Kuala Kangsar. 140 (35%) of the 401 boys were affected with a type B virus.

In 1968 the pandemic of Hongkong flu hit Malaysia in July that year. Many were affected, but the actual number of cases is not known because of inadequate returns of epidemiological data. It continued into 1970. Surveys of influenza Hi antibodies pre- and post- epidemic show a rise of anitbodies against the A/Hongkong/68(H3N2) virus rose from 8% to 81%. There has not been a major epidemic or pandemic since.

In a country highly endemic for dengue fever, it should be noted that influenza may be mistaken for dengue. Tan noted in 1979 that 30% of 245 paired sera taken for dengue test were negative but were in fact positive for influenza.

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JAPANESE ENCEPHALITIS

The virus that causes Japanese encephalitis was isolated in 1924, although records of very likely epidemics in Japan go back as far as 1871. Japanese encephalitis occurs in a wide area from India to Japan and the Pacific islands. In Japan, Taiwan and Korea serious epidemics occur from time to time. In Malaysia, parts of Thailand and south-east India the disease is considered to be endemic and enzootic.

It is due to a flavivirus transmitted by at least 7 species of *Culex* mosquitos, and affects a number of vertebrate hosts. Cruikshank suspected an outbreak among British prisoners of war in 1951 but this was not confirmed by laboratort tests. In 1952, Paterson first described a fatal human case in Malaysia confirmed to be Japanese encephalitis , by demonstrating neutralising antibodies to the virus in human and equine sera, following an outbreak of equine encephalitis among imported race horses. Pond, McCrum and Simpson found the virus in pigs, cattle, dogs, goats and sheep in 1954. Vythiliongam found that the vectors *Cx tritaeniorhynchus* and *Cx gelidus* were the most abundant, accounting for 63% of mosquitos collected in a pig farm in Selangor in 1992.

Oda *et.al* carried out a cross-sectional serosurvey for Japanese encephalitis specific antibody from animal sera in Malaysia in 1993 and found the disease widely distributed in many animals. By Haemagglutination-inhibition 88% of pigs (177), 41.5% of cows (576), 45% of buffaloes(347), 18% of sheep(492), 13.8% of goats(449) and 1% of birds(111) were positive. By the more sensitive neutralization test 99.4% of pigs, 98.5% of cows, 98% of buffaloes, 90% of sheep, 87.7% of goats and 55.4% of birds were infected.

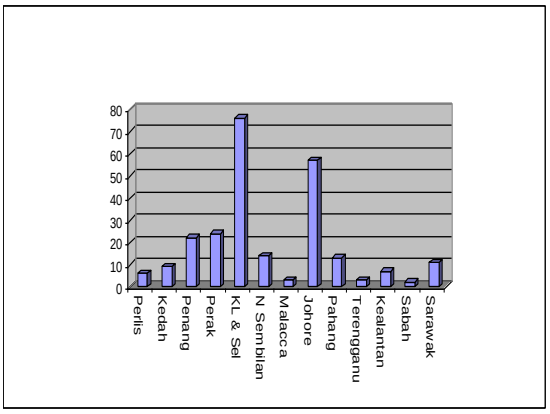
Japanese workers, together with IMR collaborators have identified 3 different genotypes among the strains of the Japanese encephalitis viruses from different parts of the country from 1992-1994. One genotype was found in Sarawak and Sepang, another in Ipoh and a third in Sabak Bernam.

Japanese encephalitis is not a notifiable disease but is included among viral encephalitis which is notifiable. Japanese encephalitis forms 20% to 60% of viral encephalitis cases notified to the Ministry of Health. The IMR however does serological tests for Japanese encephalitis on suspected cases and records of confirmed cases at the IMR show that the incidence is low. The yearly figures do not vary far between 10 to 35 cases. From 1968 to 1980, out of 21,985 cases examined only 308 (1.4%) were positive by serology or virus isolation. One outbreak in that period was in Pulau Lankawi in 1974 where there were 10 cases and 2 deaths.

Almost all the cases of Japanese encephalitis are in the age group from 5 to 14 years. The majority are Chinese and males. Inhabitants of coastal regions especially of Penang, Perak, Selangor, Johore and Sarawak have higher antibody rates than those living in inland hilly areas. Tan reported that from 1985 to 1993, 273 cases were detected although the actual number could be more. There was an outbreak of 9 cases and 4 deaths in Pulau Pinang in 1988 and another with also 10 cases and 3 deaths in Serian, Sarawak in 1992. From a serological study conducted in Perak and Penang from 1989-1990, Cardosa, Choo and Zuraini also suggested that there is more Japanese encephalitis infections in Malaysia than the notified figures of viral encephalitis suggests.

The disease is enzootic.

Figure 8.9 Distribution of cases of Japanese encephalitis confirmed by the IMR in Malaysia between 1977-1988.



Focusing on admissions over 16 months, in the Penang General Hospital, Cardosa, Hooi and Kaur, found that in 5 of 13 (38.5%) of children with a discharge diagnosis of viral encephalitis, Japanese encephalitis virus (JEV) was the agent responsible. This was based on the presence in serum of CSF of IgM determined by IgM capture of ELISA. JEV was also detected in 4 of 195 (2.1%) of children admitted with CNS symptoms and 2 of 482(0.4%) of children with non-specific febrile illnesses.

The largest and most perplexing outbreak, though there is uncertainty whether Japanese encephalitis really was involved, began in October 1998 in Tambun, Ampang and Ulu Piah in Perak where 25 cases and 15 deaths occurred. A small cluster of cases appeared in Sikamat in Negeri Sembilan in December. The outbreak then spread to Bukit Pelanduk, Kampung Jawa and Sungai Nipah in Negeri Sembilan and Malacca in January 1999. By March there were 32 deaths out of 62 cases. The victims were all from pig farming communities. Although it was initially thought to be an outbreak of Japanese encephalitis, on the basis some had IgM antibodies to JEV indicating a recent infection, it became obvious Japanese encephalitis could not be solely responsible for the. Instead of children most fatalities were adults (44/48). Only those who were in direct contact with pigs were affected while their family members who lived but not worked in the pig farms were spared. Even those who received the full course of Biken JE vaccine were not protected. Pigs were also dying. Public anxieties led to a drastic decline in pork consumption and economic ruin for many pig breeders. The government announced plans for culling over 800,000 pigs, mass vaccination of pigs and 300,000 people in the affected areas. Vaccination of all pigs against Japanese encephalitis was made a legal requirement. On March 11th, Chua KB identified a different virus particle on electron microscopy which was later named the Nipah virus (see Nipah virus). It was recognised that this new virus was responsible for most of the encephalitis and mortality in this outbreak but controversy about the role of the Japanese encephalitis virus remained.

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KOREAN HAEMORRHAGIC FEVER

It was during the Korean War when thousands of United Nations troops were afflicted with this disease that attention was focused on the viral infection that came to be known as Korean Haemorrhagic fever. About 400-800 persons are hospitalised with the disease every year in South Korea. A similar form of disease occurs in the area from Japan, through the Soviet Union, China, Eastern Europe and Scandinavia. The disease has come to be called the Hantaan virus disease. The field mouse is an animal reservoir for the virus. It has been found now that Hantaan viruses occur throughout the world, the niche in different continents being occupied by different species of the virus.

In Malaysia rats trapped in the port area of Penang have been found to be serologically positive for the virus. There have however not been any proven human cases although one has been found with clinical and serological features.

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MEASLES

In recent years, somewhere between 400 to 800 cases of measles are notified to the Ministry of Health annually. However, this forms only the tip of the iceberg. Even at the UH KL a survey showed that only 4% of measles cases were notified. Among general practitioners the rate is probably as low. Government clinics probably do most of the reporting. Based on an overall 5% reporting rate there would be between 100,000 to 200,000 cases a year at about 1990. On top of this some cases may never be seen by the medical profession. An IMR survey of Kelantan in 1990 found that 89% of the population screen had measles antibodies.

At the UH, the age distribution of patients seen, as reported by Chen, was similar to that of other developing countries. There is a peak from 6 months to 4 years. 44% were under 1 year. Even where there is good housing, 10% developed measles before the age of one year. In a follow-up serological study it was noted that it was from the twelfth month onwards that the infection rose sharply and hence they recommended that immunization should optimally be done at 11 months.

Studying 185 cases, Chen noted that 54% had complications, not including febrile fits which were common. Most complications involved the respiratory system (39%), followed by gastroenteritis (8%), and meningitis (4%) with septicemia, conjunctivitis and stomatitis accounting for the few remainder. Children who suffered such complications sometimes took as long as one year to regain their place in the weight percentile chart. The complication of subacute sclerosing panencephalitis is rare but nevertheless, has been reported locally.

Although measles is so widely endemic in Malaysia, the mortality statistics show that it accounts for only 0.5% of toddler deaths. This is almost certainly due to under-reporting. Chen found that even in the UH, among children who died of bronchopneumonia, in 15% the

underlying cause was measles but it was not certified as such. It is therefore hard to guess at the true mortality of measles. But it is clear that the morbidity and mortality of measles easily justifies mass immunisation against it. In view of the local pattern it should be given to children before they reach one year.

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MUMPS

Mumps occurs endemically and mostly unremarkably. Mumps encephalitis however can be serious and one case involving a 7 year-old Indian girl has been reported. She required respiratory support and was on a bladder catheter for 21 days. She was however completely recovered at follow up in 3 months.

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NIPAH VIRUS

The Nipah virus is Malaysia's own virus, discovered here in March 1999 by Chua KB. It is a 200-300nm virus, morphologically a paramyxoviruses. It is serological related to the Hendra virus. It was isolated in what was first thought to be an outbreak of Japanese encephalitis which began in Perak in October 1998 (see Japanese encephalitis). It spread as a result of illegal movement of pigs to the Eastern corner of Negeri Sembilan where the largest concentration of pig farms in Southeast Asia was located. It is spread to humans by direct contact with infected pigs. It is from one of the affected villages there, Sungai Nipah, that the virus takes its name. Up to 19th April 1999, the outbreak had taken a toll of 256 cases and 111 deaths (43%), including 25 cases and 15 deaths in Perak. Almost all the other cases were from the Negeri Sembilan. area. The epidemic tailed off after this. Not surprisingly the majority of cases were Chinese and activities related to direct exposure to sick pigs the most important predisposing factor.

Whether the Nipah virus was solely responsible or whether there were two overlapping viral outbreaks was at first a contentious issue. A WHO statement released said that of the deaths for which completed tests were available, 40 were due to Nipah, 8 to Japanese encephalitis and 17 had dual infection. It was reported that the fatality rate for double infection was 52% compared to 38% for Nipah virus alone and 36% for JEV alone.

The origin of the Nipah virus has not been clearly established. It was suspected that it mutated from the Hendra virus that might have been in horses imported from Australia to Ipoh, and transmitted to pigs via fruit bats. Genome analysis of the viruses however show that there are far too many differences between Nipah and Hendra for one to be a mutant of the other. In addition, horses are a dead end host, they do not spread the disease among themselves or to other animals. They just get the infection and die. Fruit bats however show evidence of having the infection. When the virus first appeared is another interesting question. Looking retrospectively, a few pig farm workers who suffered from viral encephalitis as early as January and October 1997 might have been ill and died with the Nipah virus. The more important question however, is whether the virus still lurks in some animal reservoir.

Clinical Features

The illness was characterised by 3-14 days of fever and headache followed by drowsiness, dizziness, vomiting and disorientation that can progress to coma within 24-48 hours. A few patients had respiratory illness, as had the affected pigs. Those who survived the illness may have memory lapses and some neurological deficit but the number who have permanent neurological damage is small. It is unclear whether they or those who became serologically positive but had few symptoms can suffer a relapse of the disease.

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POLIOMYELITIS

General opinion about the epidemiology of paralytic poliomyelitis, which is borne out by the American and even the Singapore experience, is that when the socio-economic conditions and health standards of a country improve, the opportunity for acquiring immunity through natural infection in early childhood decreases. As a result a susceptible population builds up and opens up the risks for large scale epidemics.

Malaysia has been fortunate in that when socio-economic and health factors improved, as indicated for example when the infant mortality rate fell below 75 per 1,000 live births in the 1950s, no epidemic outbreaks of poliomyelitis occurred. The morbidity rate of poliomyelitis in West Malaysia remained low right into the 1960s at a level of 1.7 to 2.9 per 100,000 population. Except for minor increases at 5 to 8 year intervals, there was a general decline in the number of notified cases until in 1965 a small outbreak was experienced.

The epidemiological pattern of poliomyelitis was that of an endemic disease showing small peaks every few years. No seasonal incidences could be observed. Neither was there a sex difference in incidence. However, racially, Indians constantly had highest incidence followed by Chinese, with Malays having the lowest rates. Most poliomyelitis cases are children under the age of 5 years and the most susceptible are the very young of the six months to three year age group.

Virology

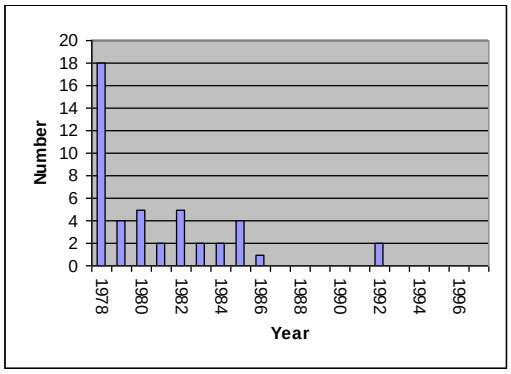
Out of 411 polioviruses isolated from 1960 to 1965, 90% were Poliovirus Type 1. 7.8% were Type 2, and 1.5% Type 3. 0.7% were mixed infections. A subsequent antibody survey confirmed the distribution of virus types as well as the higher susceptibility of Indians.

Polio control and eradication

Since the mass immunisation with Sabin live virus in the 1960s, poliomyelitis has come under control and is almost eradicated in Malaysia. In the 1980s less than 5 cases a year were reported including from Sabah and Sarawak with some years with no cases. A serological survey in Kelantan in 1990 by the IMR found that 90% of the population had antibodies to all 3 serotypes of poliovirus including 31% of 400 subjects who

were not vaccinated or incompletely vaccinated against polio. In 1992, however, two case of polio were found in non-immunized children following 6 years without polio in Malaysia. Malaysia was finally declared free from polio together with 37 countries in the West Pacific region in October 2000. The last case of polio in the region was in Cambodia in 1997.

Figure 8.10 Number of reported polio cases in Malaysia



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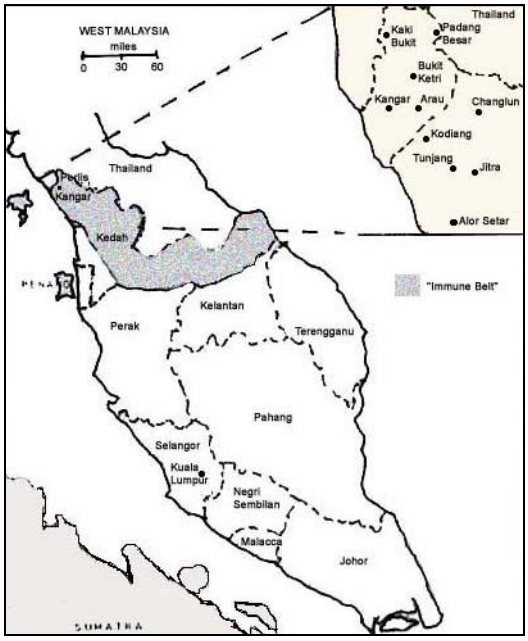
RABIES

Rabies has been known to occur in Malaysia as long ago as in 1884 but it was only since 1924 that records of its occurrence has been kept. It is not a disease transmitted from man to man and requires the bite of an infected dog or wild animal. As such human rabies has never been rife as measures to control the disease in animals have been fairly effective.

Sporadic outbreaks were recorded in the states bordering Thailand from 1924 to 1944. However, at the end of the Second World War, in 1945, a major outbreak occurred in Perak and Province Wellesley through army dogs brought from India and Burma. Over a hundred cases were recorded in animals each year until 1952. The disease was recorded even in cattle, buffaloes, goats and cats. The outbreak came to a peak in 1952 when Selangor was worst affected with over 100 recorded cases. This prompted the National Rabies Eradication Programme which involved licensing of dogs and shooting of all stray dogs. These measures were so effective Malaysia was declared rabies free in April 1954. Following that, an "immune" belt along the Thai border was established. In this 30-50 mile wide area registration and continual compulsory vaccination of dogs and destruction of strays is imposed to prevent the spread of rabies introduced through dogs infiltrating in from Thailand. Movement of dogs out of the immune belt into the rest of Malaysia requires certification of rabies vaccination.

Figure 8.11 "Immune belt" for rabies across the north of peninsula Malaysia



However sporadic outbreaks of rabies still occur. In 1970 there were 11 human cases in Kedah and Perlis. Over the next ten years 6 sporadic human cases were recorded and about twice the number of infected dogs found. However, from 1981 to 1989 there were no rabies cases in humans in the country.

Ganesan and Sinniah reported the case of a 7 year old boy who died in Alor Star from rabies in 1990. Between 1992 and 1998, six more fatal cases occurred in Kedah. The 3 deaths in 1997 resulted from one dog attacking all three victims on the same day. In all these cases rabies was not suspected and neither rabies vaccine nor immunoglobulin was given.

Terengganu experienced a sporadic outbreak between 1996 and 1997, where 9 rabid dogs were found. The outbreak occurred in a coastal district a great distance from the Thai border. It is likely that rabid dogs were brought in by road or sea. However, endogenous transmission of rabies probably occurred given the time spread of the cases and the fact two cattle were also confirmed to have rabies. There were 9 human dog bite victims in the outbreak but all of them received rabies vaccination and none of them succumbed to rabies.

No cases of rabies has ever been reported in Sabah and Sarawak although they share a common border with Kalimantan where rabies is enzootic.

However our recent history reminds us that sporadic outbreaks can occur anywhere in the country and we must constantly be vigilant for rabies in any case of dog bite.

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RESPIRATORY SYNCYTIAL VIRUS (RSV)

Ong reported finding serological evidence that the RSV was the pathogen in 22 out of 101 children in KL suffering from respiratory illnesses in 1975. It was the commonest pathogen found in the battery of serological tests used.

In a review of 5,691 children under 2 years admitted to the UH between 1982 and 1997 for a lower respiratory tract infection Chan *et.al*. found a viral cause in 22%. Respiratory viruses were identified by indirect immunofluorescence, viral culture or both from nasopharyngeal secretions. The RSV accounted for 84% of the viruses isolated. Parainfluenza virus (8%), influenza virus (6%) and adenovirus (2%) accounted for the rest. They also observed that among 185 children with RSV infection between 1993 and 1995 63% had mild disease, and 8% had severe disease requiring intensive care of whom 80% required assisted ventilation. 8% of patients had diarrhoea and 7% had seizures.

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ROTAVIRUS

Rotaviruses were first isolated from the duodenum of some children in Australia and implicated as the cause of diarrhoea by Bishop and Flewett in 1973. Since then it has been recognised that it is probably the leading cause of acute gastroenteritis worldwide.

Yap, Dahlan and Paranjothy reported in 1984 that 46% of childhood diarrhoeal disease was due to rotaviruses, based on a year long study of diarhoeal cases in KL GH. They noted that the peaks occurred with the wet months of March and September. They noted a higher incidence of vomiting in rotavirus disease compared to non-rotavirus disease, but the number of vomiting episodes was not different. The mean duration of diarrhoea was 5 days.

In a longitudinal community based study of 156 children for diarrhoeal disease in 1992, Yap *et.al*. found that rotaviruses were responsible for 12% of diarrhoea in children in the Klang Valley. 3.2% of asymptomatic children also had the rotavirus. In another report the same year the same group found rotaviruses in 28% of 973 hospitalized children with diarrhoea in 1988 and 1989. All isolates were group A rotaviruses but there were 22 strains. Re-examining the same hospital 7 years later the same workers reported that 179(20%) group A rotaviruses were detected from 870 children. They found that the electrophoretic pattern of the viruses, classified into 14 types, had not changed over that time. Besides group A rotavirus, Rasool has reported finding one group C rotavirus among 9 rotaviruses isolated in 1987 in GH KL.

In a study of 69 cases of paediatric gastroentiritis in Sarawak, Barker and co-workers found that 51% were associated with rotaviruses. It was more common in the 6-24 month age group.

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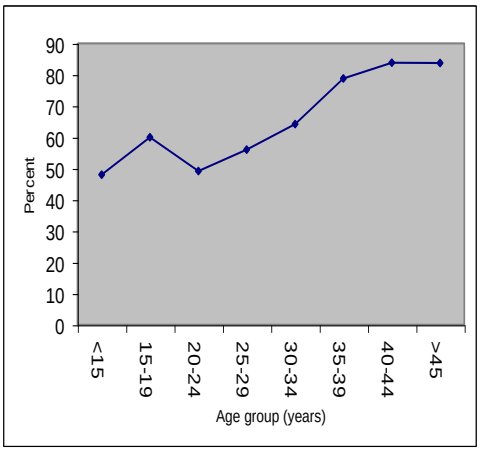
RUBELLA

The medical importance of rubella lies not in the morbidity of the acquired acute infection, but in its ability to cause congenital malformations in the foetus of a woman who is infected in early pregnancy. This was first recognised by Gregg in Australia in 1941.

Rubella is endemic in Malaysia, but its incidence and trend is not known as it is not a notifiable disease. Lam found the rubella antibody rate in women of child bearing age to be 60% and and Tan found a rate of 64%. The Ministry of Health survey done in 1985 prior to launching the national immunisation programme however recorded at rate of 48% for such women and a rate of 21% for school girls. Ilina, Salleh, Dahlan and A.Shukor studied 452 nurses in KL and found an overall prevalence of rubella antibody of 65%. It was highest in intensive care and maternity ward nurses and lowest in the opthalmology ward. They believed that nurses were occupationally at risk.

Fig 8.12 Distribution of Rubella antibodies in women according to age in 1972 (Lam)



Of the five prenatal infections generally recognised as causing congenital defects, namely, toxoplasmosis,rubella, cytomegalovirus, herpes simplex and syphilis, rubella was said to be the most important in Malaysia according to Tan in 1985. She had noted that among children with clinical features of the congenital prenatal infection 87% had rubella-specific IgM or IgG, compared to only 1.3% in normal children. She considered those with raised IgG to be genuine cases contending that maternal IgG disappears by the age of six months and normal children up to 5-6years are largely sero-negative. Looking at which congenital defect rubella contributed to, she found the sero-positive rate of 71% among children with congenital heart disease, 64% among those with congential cataract, 60% among those with deafness, 17% among those with hepatomegaly and 4% among those with mental retardation. By IgM alone, Balasubramaniam V *et.al*. however found a higher prevalence of congenital cytomegalovirus infection among infants with congenital abnormalities than rubella in 1994. In a survey of 165 children in a school for the deaf, Elango *et.al*. noted that 35% deaf children had ocular manifestations of rubella making rubella the commonest cause for deafness in these children.

These findings makes a very strong case for the need for rubella immunisation in Malaysia. A Selective Rubella Vaccination Programme for primary six schoolgirls was adopted in the early 1980s. Chua *et al*. have studied done a serologic study of rubella among students and outpatients at the UH as well as babies delivered there between 1993 and 1999 to review the impact of the Selective Rubella Vaccination Programme. Overall he found that 51% of clinically suspected rubella was confirmed by serology. He found the number of positive cases of rubella the same among males and females aged 14-48 years. He noted that there appeared to be a periodic pattern of rubella activity with increased incidence of rubella cases at 2½ to 3 year intervals. Peaks of rubella cases also appeared to be followed by an increase occurrence of congenital rubella syndrome cases 6-9 months later. The rate of congenital remained the same at an average of 48 per 100,000 deliveries over a 6 year period. They suggest that the selective vaccination programme should be replaced by a universal one.

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SINDBIS

The Sindbis virus is a Group A arbovirus, or flavivirus, known to occur in Asia. It is transmitted by the culex mosquito. Low activity in serological tests have been noted to this virus in tests at the IMR and one clinical case was

reported in 1972 in the routine investigation for dengue infection.

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SMALLPOX

On the 9 December 1979 the Global Commission for the Certification of Smallpox Eradication signed a declaration that the whole world was free from smallpox. They were satisfied that the conditions set, that two years must elapse without a case being detected by a system of surveillance sufficiently sensitive to have detected a case had it occurred, had been met. The reason for this is that since there is no animal or inanimate reservoir for the disease, experience had shown that once human transmission of the disease had ceased the virus would be extinguished.

The last area to be free of smallpox was the Horn of Africa and the last ever person to contract the disease was Ali Maow Maalin who fell ill in Merca, Somalia on 26 October 1977. He had variola minor and recovered. Smallpox is now a disease for the history books but it is hoped that the lessons learnt in its eradication will help mankind in the fight against other diseases.

The history of smallpox in Malaysia was not very remarkable compared to other countries. Early records show that there were over a hundred to three hundred cases a year in about 1920 when the population of the peninsula stood at about 3 million. The vaccination programme was well established and over 100,000 people were vaccinated each year. Within the decade the number had fallen to an average of less than a hundred with epidemics taking the total above that only on a few years like 1927, 1930, 1931 and 1935. This is largely due, as elsewhere, to the practice of vaccination Jenner discovered in the 18th. century. When the Second World War interrupted progress endemic smallpox had nearly been eradicated. However in the two years after the war when statistics became available there were over 7,800 cases with over 1,000 deaths. However, by 1950 control measures had curbed the disease again and for a few years no cases were detected. But one imported epidemic followed in 1959 (338 cases) running over to 1960. That was then the end of smallpox in Malaysia. Patient may still be seen today with smallpox scars and it will be possible to place them by history whether they belonged to the war period or to that rare epidemic after.

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YELLOW FEVER

One of the greatest epidemiological enigmas is why; although men, animals, and mosquitos suitable for transmission of yellow fever exist in Asia, the disease has never spread here. Two probable explanations are that there is some ecological barrier in East Africa and that the presence of several viruses serologically related to yellow fever, namely Japanese encephalitis and dengue, in Asia confers some degree of cross immunity on the population. However, there is no evidence that if yellow fever were to be introduced to tropical Asia it would not cause a catastrophic epidemic. It is therefore incumbent upon us that we be always vigilant against the importation of yellow fever, especially through international air travel.

DISEASES OF UNKNOWN BUT PROBABLY VIRAL CAUSE

KAWASAKI'S DISEASE

This acute febrile mucocutaneous lymph node syndrome in children was first recognised by Kawasaki in Japan in 1967. The first three cases in Malaysia were diagnosed by Sinniah, Nagappan and Choo from 1977 to 1979. By 1984, 19 more cases had been seen at the University Hospital KL.

In Kelantan, 7 cases were observed in HUSM over 8 years, according to Malik. Perhaps only the more characteristic cases were noted because 5 of these had all 6 criteria for diagnosis. The mean age of the children affected was 29 months and 4 of the 7 were boys. Reviewing other reported cases of Kawasaki disease in Malaysia it appeared to him that the incidence of cardiac complications was low in Malaysians.

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CHAPTER 9

RICKETTSIAL, CHLAMYDIAL AND MYCOPLASMA INFECTIONS

Rickettsiae and Chlamydiae are now widely accepted as bacteria. In previous editions of Bergey's manual they were considered an order named Rickettsales. In the taxonomical dispute in the past they were sometimes put in a class together with viruses called Microtatobiotes. Comparisons on the ultrastructure and biochemistry with bacteria however show that they are closer to bacteria although they are very small and are obligate intracellular parasites.

CHLAMYDIAL INFECTIONS

CHLAMYDIAE PNEUMONIA

Seroprevalence studies in many adult populations indicate that *C. pneumoniae* infections are ubiquitous and subclinical. *C. pneumoniae* can be grown in a variety of cell cultures. The first strain TW 183 was isolated in Taiwan in 1965. It is, however, considerably more difficult to culture than other chlamydiae hence knowledge of its epidemiology is principally derived from serologic studies.

C. pneumoniae can produce sinusitis, pharyngitis, bronchitis and pneumonitis. Ngeow *et.al*. looked for *C. pneumoniae* among 87 children aged 3 years and under admitted to the UH for lower respiratory infection over one year by culture, serology and immunoassay. They found only one case, and one of *C. trachomatis*. They have also published a case report of a respiratory infection of a 5 year.

C. pneumoniae infection has also been implicated in the pathogenesis of atheroscelrosis. In a study of 110 patients with acute myocardial infarction or coronary disorders and 137 healthy blood donors in 1994 in KL, Naidu et.al reported that 27% of the myocardial infarct patients, 62% of chronic coronary disorders and 47% of healthy individuals were serologically positive for *C. pneumoniae.* By a polymerase chain reaction test however, 25% of those with myocardial infarction, 48% of those with coronary disease and 12% of the controls were positive.

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PSITTACOSIS

Psittacosis or ornithosis, which is an infectious disease due to *Chlamydia psittaci*, was first recognised in Malaysia in Grik, Perak. In May 1959 a German missionary lady-doctor reported fever, headache and cough in a Chinese family of seven who were rearing pigeons, of which several birds were also ill. Investigation revealed that although the human cases were negative, all the three pigeons examined were positive for complement fixation antibodies at titres of 1:20. However, no viruses were isolated from the pigeon faecal samples.

A 1970 study of 119 randomly selected patients with pyrexia of unknown origin revealed 2 positive cases. A history of bird contact was obtained from one but not the

other. Of 5 birds tested in association with the first case, 2 were positive.

Of 12 pigeons from the rapidly increasing number at the Batu Caves tested in 1972, 8 were positive although no evidence of transmission to human contacts was found. However, human ornithosis should always be considered in patients with pyrexia who are in contact with pigeons.

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TRACHOMATIS

Chlamydia trachomatis infection is probably not well known by its own name. Instead it is more well known as non-specific urethritis, lymphogranuloma venerum and only in its infection of the eye is it known as trachoma.

Deva and Ngeow found that between 1984 and 1990, 28% of 184 patients seen in the Eye Clinic in UH with acute conjunctivitis were positive for chlamydial infection by direct immunofluorescence. The rate was same in men and women and among the 3 ethnic groups. The rate was higher among sexually active adults.

In urethritis *C. trachomatis* was reportedly the cause of up to 30-40% of sexually transmitted genital infection in the 1970s in some Western countries. However, one survey at the UH looking into the importance of *C. trachomatis* produced an isolaton rate of only 2.5% of 197 specimens of genital exudates. In another a survey of women attending the KL GH gynaecological clinic Ngeow *et.al*. found that the prevalence of *C. trachomatis* was only 1.8%(3/164) in women with a vaginal discharge. But Ramachandran and Ngeow detected chlamydial cercivitis in 26.5% of 370 prostitutes and Ng, Sarvananthar and Cheong found 17% of women with salpingitis to be infected with *C. trachomatis* using an ELISA technique.

In other serological studies Rachagan and Ngeow (1990) reported that chlamydia infection was more prevalent among asymptomatic infertile women (33%) than women selected as controls from a family planning clinic (8%). The study showed a strong relationship between *C. trachomatis* infection and infertility due to tubal pathology. In another report, the same year, using a single antigen (LGV2) indirect immunofluorescence test they found a prevalence of 10% -16% among children, increasing with age and sexual activity to 25%-43% in adult women and men and 72%-94% in men and prostitutes attending a sexually transmitted disease(STD) clinic. Intrauterine and perinatal infection occurred as seen in 6 of 46 infants under 6 months of age being IgM positive.

In Seremban, Ravindran, Tan and Ngeow, in 1998, found that 23% of 44 women with pelvic inflamatory disease compared with 2.3% of control were serologically positive for *C. trachomatis* using a microimmunofluoresence technique.

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RICKETTSIAL INFECTIONS

Q FEVER

Q fever is an acute infectious disease caused by *Coxiella burnetti.* Clark *et.al*. recognised the first case of Q fever in man in Malaysia in 1951. Reports from several investigators in China, Sri Lanka, India, Japan and Vietnam in the 1950s established that Q fever is endemic in this region. It exists in many small Malaysian jungle mammals and their tick ectoparasites.

However, in 1970 when 119 febrile patients were examined serologically for Q fever none of them showed significant complement fixation antibody increases in their paired sera. It is thus unlikely that Q fever is an important disease in Malaysia.

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TYPHUS

Three types of typhus are seen locally. They exhibit similar clinical features but are distinct entities transmitted by different vectors and do not confer cross-immunity for each other. Despite these differences, in treatment, all these rickettsia respond to the same chemotherapeutic agents, mainly doxycycline, and hence are considered here together.

Between 1995 and 1997 the IMR conducted a seroprevalence survey for the 3 types of typhus in rural Peninsula Malaysia. Among 1,596 febrile patients seen in 8 different health centres 51% had antibody against at least 1 of these rickettsia. 31% actually had antibodies against more than one species of rickettsia suggesting co-infection, previous exposure or cross-reactivity. Males and females were similarly affected and adults more frequently affected than children. Those working in the agricultural sector had a significantly higher a seroprevalence than others.

Scrub Typhus.

Scrub typhus is the most important form of rickettsial disease in Malaysia. Its origin can be traced back to as far as the third century when a disease resembling it in description was mentioned in China, according to a report in 1885 by Li Shih-Chen. In well recorded history Hashimoto is said to have first described the disease in Japan in 1810 where it became known later in Japanese as "shima mushi" meaning "flood fever". It was in Japan that the infective agent was first isolated around the 1920s but there is controversy about the details. The organism was first designated *Rickettsia orientalis* but now accepted as *R. tsutsugamushi* or *Orientia tsutsugamushi*.

The disease occurs in a geographical region bounded roughly by India, Japan and North Australia. It is also called rural typhus. It is transmitted by the larval mite of the *Leptotrombidium akamushi* (formerly Thrombicula akamushi) and *T. delinsis* species. Scrub typhus was a significant problem in the Pacific Theatre during the Second World War and in the Vietnam conflict. For that reason the US Army had a unit attached to the IMR actively studying the disease.

Typhus was first serologically diagnosed in Malaysia when in August 1924 a Punjabi woman and her daughter from Kepong, who were patients of Travers, were found to have blood specimens positive for the Weil-Felix test. It was thought on hindsight then that several puzzling cases in the past may have been the same disease.

768 cases of scrub typhus were recorded in Malaysia between 1929 and 1933. Serologically the Weil-Felix reaction agglutinates the OXK type of *Proteus X* strains, but not the OX19. All these patients were connected with the country-side by either domicile, work or recreation. In rural Malaysia today scrub typhus is still one of the commonest causes of a febrile illness.

Prior to 1975, available information indicated that scrub typhus was not a major problem in Malaysia. During the 1967-1974 period an average of only 55 cases of scrub typhus was reported per annum. Serological surveys though, demonstrated a high prevalence of antibody in some rural areas, indicating a high rate of infection that it was suspected was not reported. In early 1975 workers at the US Army MRU showed that scrub typhus was a very common cause of febrile accounting for as high as 23% of the fevers at the Mentakab hospital. Among oil palm workers admitted with fever to the Mentakab hospital, about 80% were due to scrub typhus. In an oil palm plantation of 10,000 people it was estimated there were 400 cases of scrub typhus annually.

In a study, reported in 1984 of 1,629 febrile cases around Mentakab, where a laboratory diagnosis was made for the fever, in 63% (1,025), scrub typhus was the leading diagnosis, accounting for 19% of all cases or 31% of the diagnosed cases. It was followed in frequency by typhoid and paratyphoid, flaviviruses, leptospirosis and malaria.

Studies at oil palm plantations indicate that human infection rates could possibly vary according to the stage of oil palm growth, with the highest rates occurring in young plantations. This is related to the ecological changes of the *R. tsutsugamushi* vector. The highest number of chiggers (trombuculid mites) per host, the rat *Rattus tiomanicus*, was found in 2½ year oil palm trees. The majority were of the known vector species, *L. deliense*. In older oil palm schemes the chiggers were mainly *A. indica* a non-vertor mite, while *L. deliense* made up less than 1 % of the chigger population.

IMR workers have developed an IgM dot immunobinding assay for the diagnosis of scrub typhus infection. In seroprevalence studies conducted by IMR workers between 1995 and 1997, 25% of 1596 febrile patients seen in 8 rural health centres had antibodies to *R. tsutsugamushi*. It was estimated that the annual attack rate of scrub typhus was 18.5%. Among 300 rubber estate workers the seroprevalence was 23% in December, a wet month. Indians had the highest seropositive rate among the different races.

In view of its importance as a cause of undiagnosed febrile illness in rural Peninsula Malaysia a random cross-sectional survey was conducted across Sabah. In a report in 1986, by Taylor and colleagues, of 837 blood samples collected only 7 (0.8%) had *R. tsutsugamushi* significant specific antibody titres. None of 383 febrile patients studied had evidence of rickettsial infection. It is important to note that although Sabah fall within the endemic Pacific region, scrub typhus is apparently not a problem in Sabah.

It has been shown that doxycycline is an effective prophylaxis against scrub typhus for people at risk like soldiers in jungle operations. In the future it is hoped that a vaccine against scrub typhus can be developed. The need is seen in estimates from epidemiological studies that half a million people, mainly in the rural areas, are affected by scrub typhus yearly in Malaysia.

Murine Typhus.

Lewthaite and Savoor at the IMR demonstrated in 1936 that this was a separate entity from scrub or tick typhus. Murine typhus or urban typhus is also sometimes known as ‘endemic typhus’. It is caused by *R. mooseri*, also called *R. typhi* and borne by rat fleas (*Xenopsylla cheopis*. Marchette in 1966,

reported that 10% of rats trapped from urban areas in West Malaysia had murine typhus. Besides man and rats, animals like dogs in urban areas are infected by murine typhus.

In the same period between 1929 to 1933 that 768 cases of scrub typhus were recorded there were 204 cases of murine typhus. Most patients had indoor occupations. Many handled food or grain. Serologically the patients is positive to the OX19 type of *Proteus X* and not to the OXK.

In the seroprevalence survey conducted between 1995 and 1997, IMR workers found 28% of 1596 febrile patients seen in 8 different rural health centres had antibodies to *R. typhi* . Among 300 rubber estate workers the prevalence of *R. typhi* was 3.0% in December, a wet month, but rose by 12.3% in March, dry month.

In KL, UH workers report that endemic typhus accounted for 8.5% of acute infective febrile illnesses between 1991 to 1997. Men were nearly twice more likely to be affected than women and the peak age group were those between 21-40 years old. There was no seasonal pattern. The more socially disadvantaged Indians were more greatly affected than Malays and followed by Chinese. There was a sharp rise noted in 1997.

Tick Typhus

Tick typhus belongs to the spotted fever group of rickettsioses of which the Rocky Mountain Spotted Fever is the classical example. Serologically patients react to the OX2 antigen of Proteus X. The niche for this disease appears to be filled by several similar agents in various parts of the world. In Malaysia the rickettsia most prevalent is the Thai tick typhus which is detected by the TT-118 antigen.

There were no reports of tick typhus in South-east Asia before the early 1950s. The IMR first detected the disease serologically in jungle animals in 1955. The first human case in Malaysia was in 1958 when a patient suspected of having scrub typhus was found to have tick typhus complement-fixing antibodies for the OX2 type of *Proteus X*. The following year additional cases were found. In 1986, Taylor *et. al.* reported that in Sabah 17% of forest dwellers showed serological evidence of tick typhus, whereas the other forms of typhus were uncommon in Sabah.

Seroprevalence surveys by IMR workers between 1995-1997 suggest that tick typhus is actually the commonest type of typhus in Peninsula Malaysia. In December, the wet season the seroprevalence of TT-118 among 300 rubber estate workers was 57%, 15% of whom were dually positive for *R. tsutsugamushi* as well as TT-118 antibodies. Rubber tappers had the highest seroprevalence rate compared with other occupational groups. In a survey of 1596 patients seen in 8 different rural health centres 42.5% had antibodies to TT-118.

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MYCOPLASMAL INFECTIONS

The mycoplasma are flexible-walled, non-motile cells with highly variable shapes that do not retain the dye-iodine complex of Gram's stain. As such they are innately resistant to all the penicillins. They are apparently intermediate between rickettsia and eubacteria.

MYCOPLASMA

The first isolation of *Mycoplasma pneumoniae* in Malaysia was reported in 1985 by workers at the IMR although it must have been around before this. Following that in the Acute Respiratory Infection project involving children under 5 years admitted to the paediatric wards in the Kuala Lumpur, Ipoh and Kota Bharu general hospitals from 1984 to 1985 it was found that of 550 nasopharyngeal aspirates cultured for *M. pneumoniae* 17(3%) were positive.

Chua *et.al.* in UH have noted a cervical colonisation rate of *M. hominis* of 18% among 60 healthy pregnant women in 1998. The transmission rate to their babies was 30%.

A serological tests kit for *M. pneumoniae* antibodies which detects both IgM and IgG, SERODIA-MYCO II, has been evaluated in at least 3 studies.15-45% of healthy controls show levels of ≥1: 40, the recommended positive titre level, suggesting previous exposure is common. In view of this it is suggested that a level of ≥1:80 or higher is used to make a diagnosis of mycoplasma pneumonia for patients with pneumonia in Malaysia. With this level 15-28% of patients with pneumonia probably have myoplasma pneumonia. As in other countries, the incidence of mycoplasmal infection is higher in children (>20%) than adults (<5% among 30-39year olds).

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UREAPLASMA

Once known as 'T' strain mycoplasma, *Ureaplasma urealyticum* is one of the causes of non-gonococcal urethritis. In some surveys it is isolated in about 5% of urethritis cases. It is more common than *Chlamydia*.

Cheong *et.al* have found in a study of women attending a Malaysian gynaecological clinic that the prevalence of *Ureaplasma* was as high as 47% in women with vaginal discharge and 38% in women without complaints of discharge. Chua *et.al*. noted a cervical colonisation rate of 57% among 60 healthy pregnant women and a transmission rate of 88% to their infants. The significance of this lies in neonatal respiratory illnesses. In a study of 182 neonates with respiratory distress requiring ventilatory support *Ureaplasma urealyticum* was isolated in the tracheal aspirates of 39 (21%) of cases. Other bacteria isolated in that study include Gram

negatives in 17 cases, Staphylococci in 8, group B streptococci in 3, and one each of *Haemophilus influenzae* and *Mycoplasma homonis*. Ten *U. urealyticum* isolates were available for antibiotic susceptibility tests. All were sensitive to erythromycin, one was resistant to minocycline and tetracycline. Two were resistant to ciprofloxacin.

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CHAPTER 10

SPIROCHAETE INFECTIONS

The order of *Spirochaetales* are made up of spiral cells that swim by flexion, and are all parasites on man and other animals. Three members, causing leptospirosis, syphilis and yaws are important locally. Relapsing fever, caused by *Borrelia*, though known to occur in the Far East has not been reported in Malaysia.

LEPTOSPIROSIS

Galloway was the first to draw attention to the existence of leptospirosis in Malaysia when he reported four patients in whom leptospirae were isolated in 1926. These were all severe icterohaemorrhagic forms of the disease in which all the patients died. His report was accompanied by one from Staton, from the IMR, who also proved four fatal cases who all happened to be Punjabis. These discoveries proved to be only the tip of a large iceberg.

Leptospirosis is probably the most widely prevalent zoonosis in Malaysia. About 30 different pathogenic serotypes of leptospires have been isolated and clinical cases have been extensively reported. The main animal reservoir are rodent species although some serotypes are more commonly found in dogs, pigs and cattle. Infections are incurred by contact with urine of carriers or streams, ponds or wet soil contaminated with urine. Leptospires can survive for 3 months or longer especially in alkaline waters. Acidic clay soil types help render leptospires less virulent.

A serological survey from 1960 to 1961, using Sensitised Erythrocyte Lysis (SEL) antibody, of 4,819 afebrile indivuduals in West Malaysia reported by Tan revealed an overall antibody prevalence rate of 12%. A similar survey also by Tan running from 1961 to 1971 of 4,646 individuals found a 13% rate. Males (83%) were much more commonly infected than females (17%). SEL antibodies were acquired as early as 4 to 6 years of age in rural areas and these antibodies persist through the all older age groups at much the same levels. As these antibodies last for about only two years, this indicates constant re-infection throughout life, even up to 60 years and above; the repeated booster effect conferring a higher state of immunity to the general population. Rural residents had a higher antibody rate (16%) compared to town residents (6%).

In a study of 1,437 unselected febrile patients in a community rural setting in 1976, 86(6%) were found to have leptospirosis. The illness was mild in most cases and apparently goes unnoticed often. Jaundice was observed in only 2 patients. There were no deaths. The season in which the highest number of leptospirosis cases occurred is the last quarter of the year which corresponds to the period of heaviest rainfall.

Between 1991 and 1997, Sekhar *et.al*. found 104 cases of serologically diagnosed leptospirosis in UH. They found more males than females affected and adults more than children. The peak season was March to May and August to November corresponding to the inter-monsoon period.

Risk Groups

Of the different occupational groups studied, oil palm and rubber estate workers, labourers in forest and rural areas and hospital staff had the highest rates (25%-30%). But antibody rates in different estates varied from 43% to 46% in some, to less than 4% in others. Military personnel, farmers and padi planters, rural school children and tin miners had

moderately high rates between 13% to 18%. Teachers, housewives, office workers and fishermen had the lowest rates (less than 10%). Racial difference in the rates of antibody prevalence is accounted for by the differences in occupations.

Table 10.1 SEL antibody distribution among 18 occupational groups in Peninsula Malaysia in 1961-71.

Group	No. examined	% Positive
Oil palm estate workers	92	32.6
Hospital Staff	47	25.5
Rubber estate workers	427	23.2
Town cleaning labourers	459	17.9
Malaysian armed forces	290	17.2
School children	176	17.0
Alluvial tin miners	122	16.4
Farmers	204	14.7
Padi planters	259	14.2
Anti-malarial labourers	246	13.0
Shop owners	172	12.2
Policemen	154	11.7
Veterinary staff	463	11.6
School teachers	53	9.4
Housewives	1201	5.3
Office workers	120	5.0
Lode tin miners	136	1.5
Fishermen	25	0

Differences were seen in infection rates in different localities. Clinical leptospirosis is uncommon among padi planters in Kelantan, who account for only 2.6% of positive cases. This may in part be due to avirulent strains because of the clay soils. But in Perlis, padi farmers formed 41% of the total confirmed cases of leptospirosis. Although urban areas over all have only a 6% positive antibody rate, it ranged from 0 to 12% as shown in Table 10.2

Clinical features

Based on an antibody reversion rate of 42% per annum, it is estimated that the population of West Malaysia suffers an annual attack rate of about 5%. The ratio between silent infection and clinical illness is unknown, but it is potentially a serious cause of morbidity and mortality.

Table 10.2 SEL antibody distribution in the urban centres in Peninsula Malaysia 1970

Urban Area	No. examined	% Positive
Georgetown	224	12.0
Seremban	277	7.2
Kuantan	45	6.6
Kuala Lumpur	527	6.3
Malacca	398	4.8
Butterworth	320	4.4
Alor Star	94	4.3
Kota Bharu	199	4.0
Ipoh	36	2.8
Kuala Terengganu	203	2.5
Johore Bharu	66	0

The commonest presumptive infective serogroups in West Malaysia are *javanica, pomona, pyrogenes*, together with the better known *canicola* and *icterohaemorrhagiae*. The *autumnalis* and *hebdomadis* serotypes were commonest in an earlier study.

Out of 584 cases of fever of unknown origin between 1958 and 1962 30% were positive for leptospirosis. In a later report in 1970 Tan again observed that of 1,993 suspected cases 28% were positive. In contrast, over ten years from 1969 to 1978 of 1,738 fever cases suspected to have leptospirosis, 20% were confirmed positive. Leptospirosis can produce the clinical picture of acute hepatitis and is the commonest cause for acute hepatitis when the cases of unknown causes are excluded. It accounts for as many cases as all the viral hepatitis put together. The age, sex and occupation of patients seen are consistent with those of the antibody survey which indicates that the group most highly exposed to leptospirosis were governed mainly by occupation.

Clinical symptoms of leptospirosis do not give a characteristic picture and do not greatly help in making a diagnosis. The few commonest features are, fever (100%), chills and rigors (85%), headache (76%), muscle pain (67%), back pain (58%), cough (49%) and vomiting (47%). Jaundice occurs in about 40%. Renal involvement by way of proteinuria was seen in 25% and raised blood urea in 20% of Tan's series from 1958 to 1968. Renal failure is the commonest cause for death in leptospirosis but with full nephrological support, including dialysis, mortality is low.

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SYPHILIS

An indication of the prevalence of syphilis can be obtained from surveys of serological markers of the disease. Jegathesan, Fan and Ong obtained a large series of 8,574 blood donors and 10,096 expectant mothers between 1973 and 1975. A higher than expected rate (for example, in comparison to Britain) was noted. The rate was 2.0% in expectant mothers and 4.7% among blood donors. These were reactors to both VDRL and FTA-ABS tests. A further 1.3% and 1.2% in each of the two groups were only VDRL positive and considered biological false positives, due to causes such as collagen diseases, viral infections and malaria. Yaws could be part of the reason for the high rate of apparent syphilis but it is unlikely as it could add very little more than a small percentage to the figures. The higher rate among blood donors may be due to the fact most donors are young males and about 20% of them are from the Armed Forces reflecting a true higher prevalence of syphilis. Among prostitutes, Ramachandran and Ngeow recorded a rate of syphilis of 13.6% in 1990.

Unlike gonorrhoea where the annual number of reported cases appears fairly constant, the number of notified syphilis cases rose from about 500 at the beginning of the 1980s to nearly 2,000 in 1987. Since then the number reported annually has remained about the same with 2,460 cases reported in1 998. Syphilis, being a common disease with diverse manifestations, one would expect a great source of local information about the history of the disease in Malaysia. Unfortunately there isn't much. Because it is a social embarrassment, many patients suffer and get treated in the quietest possible way so that reliable records are not available.

The spectrum of late complications of syphilis has been of great worldwide interest. No doubt these features are encountered locally but such case reports are not common. Loh and Tan have described a series of 25 cases of

neurosyphilis seen in the UH over 10 years from 1970. They note that with the advent of penicillin the classical forms of neurosyphilis has declined, however neurosyphilis is more likely to present in unusual forms.

The rate of congenital syphillis has not been clearly determined but UH reported an incidence of 48 per100,000 livebirths between 1990-1993. 13 babies accounted for this rate. Over 85% had hepatospenomegaly and all but one were low in birth weight. The initial diagnoses in these babies was septicaemia and they received penicillin. Only one baby with hydrops died. The mothers of these babies were housewives, none were single mothers. 75% were from the lower socio-economic group, and were from all races. None of them received anti-syphilitic treatment and antenatal care was inadequate.

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YAWS

Yaws is a classical tropical disease found mainly in the hot wet regions of the earth. It is largely a rural disease. The aetiological agent, *Treponema pertenue* is morphologically indistinguishable from the causative agent of syphillis and pinta. It causes granulomatous lesions in the skin and less often in bones. Transmission of the disease is usually from skin to skin although indirect transmission by flies is possible. There are no animal reservoirs for the disease. Although yaws is rarely fatal it causes morbidity and paves the way in malnourished patients for other lethal diseases. It has long been prevalent in Malaysia and is known among rural Malays as *puru*. Viswalingam estimated that in the 1920s, 60 out of every 100 people in Malay kampongs suffered from it.

The first effective agent against yaws to be found was Norvarsenobillon. It was the drug used in the first anti-yaws campaign in Malaya led by Viswalingam which began in 1920. It was limited only to the Federated States of Perak, Selangor and Pahang. A peak of 31,135 cases were detected and treated in 1921 which dropped to 16,455 in 1929. A high defaulter rate, due to the multiple injections required, incomplete coverage of the peninsula and a waning of effort over the years resulted in failure to achieve the goal of the eradication of yaws. However it succeeded in bringing the disease under control in some areas.

The Second World War interrupted all treatment causing a recrudescence of yaws throughout the country. MacGregor remarked in 1949 that in some parts of the country particularly in the East Coast, almost every child was affected. But in the post-war period, the introduction of procaine penicillin dramatically changed the prospects of yaws eradication. It made only one injection necessary. Built upon this discovery, between 1954 and 1963 the Malayan Government with the assistance of the WHO and UNICEF carried out the Yaws Elimination Campaign. It was started in Kelantan and Terengganu where the prevalence was greatest and subsequently extended to other endemic states including Pahang, Kedah and Perak.

The campaign consisted of planning, mass treatment of open cases, latent cases and contacts and a consolidation stage of resurveys and treatment. Initial surveys showed that in the districts of Besut in Terengganu and Pasir Putih in Kelantan the most affected areas, about 20% of the population had yaws. A peak of

104,202 cases were treated in 1948 which declined to 43,822 in 1953. In resurveys in 1962 and 1963 the incidence rates had dropped to less than 0.5% in all areas.

However the enigma of 'the last yaws case' remains. Clinicians today are still picking up the odd one or two. As recently as 1989, Elango and Palaniappan reported a case of the disfiguring facial manifestation of 'gangosa' and 'goundou', which were common in Africa a century ago, in a patient with yaws who also had nasopharyngeal carcinoma. Patients with yaws tend to be the very rural Malays and Orang Asli. The day of yaws eradication still lies in the future.

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CHAPTER 11

THE GRAM POSITIVE BACTERIA

Gram-positives do not form a clear order of bacteria. However, the Gram stain property of bacteria appears to be a fundamental one, for example, determining sensitivity to antimicrobials and correlated with many other morphologic properties. Like Gram negative bacteria, Gram positives are free-living, rigid-walled, may be spore forming, coccoid or bacciloid, and may grow in chains or clusters. As in other sections the bacteria are listed here alphabetically according to 'genus'. Different 'species' then, though they may cause different infections like gas gangrene and tetanus, are found under their genus *Clostridia*.

CLOSTRIDIA

GAS GANGRENE

Very little appears to have been written about this notorious disease in Malaysia, classically caused by *Clostridium perfringens* originally known as *Bacterium welchii*. It is the dreaded complication of soiled traumatic wounds and such wound are common in our hospital admissions. Usually the diagnosis has to be made clinically as it progresses rapidly and radical surgical treatment cannot wait for bacteriological confirmation. Penicillin is usually the antibiotic of choice when the crepitus of gas in tissues and characteristic smell is detected. It has been noted though, that in diabetic patients with traumatic wounds *Klebsiella aerogenes* instead may be the more common organism. It would require different antibiotic treatment.

PSEUDOMEMBRANOUS COLITIS

This acute exudative infection of the colon was found to be caused by *Clostridium difficile* in 1977 after its enterotoxin was assayed in the faeces of patients with pseudomembranous colitis. Almost all the anti-bacterials except vancomycin and the anti-mycobacterials can cause the disease. It has been described in Malaysia but we can comment little on the local prevalence of the bacteria. In a report of 3 cases, Goh, Peh and Wong had two patients who died. One was moribund with ovarian carcinoma and had not received antibiotics. The second patient who died had been on multiple antibiotics. The patient who survived had received cotrimoxazole. In all these cases the diagnosis was based on sigmoidoscopy and biopsy findings and culture of the bacteria and assay for the toxin was unsuccessful.

Parasakthi, Puthucheary, Goh and Sivanesaratnam in a paper in 1989 reported 7 cases of pseudomembranous colitis isolating the bacteria in 5 cases and showing the presence of its cytotoxin in 6. Four of these patients died but in the 3 survivors they described what they believe is a different syndrome. These patients did not have pseudomembranous plaques on sigmoidoscopy and their disease ran a rather benign course. Boey, Ramanujam and Looi have described a case in a child associated with Henoch-Schonlein purpura.

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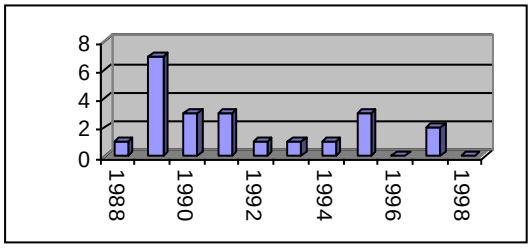
TETANUS

Neonatal tetanus was and perhaps still is the most important form of tetanus in Malaysia. It was common in the past usually due to unhygenic midwifery techniques of traditional birth attendants. The incidence of neonatal tetanus has however declined progressively over the years. The credit goes to the improved maternity services and antenatal immunization programme.

The drop in incidence of neonatal tetanus has also been accompanied by a decline in the mortality of babies affected. With the introduction of total paralysis with intermittent positive pressure ventilation the mortality of serious cases has dropped from about 90% to about 20% in some of our local centres. The UH in KL had 62 cases over eight and a half years ending 1977. The overall mortality was 16%, and among the survivors 16% had significant neurological sequelae.

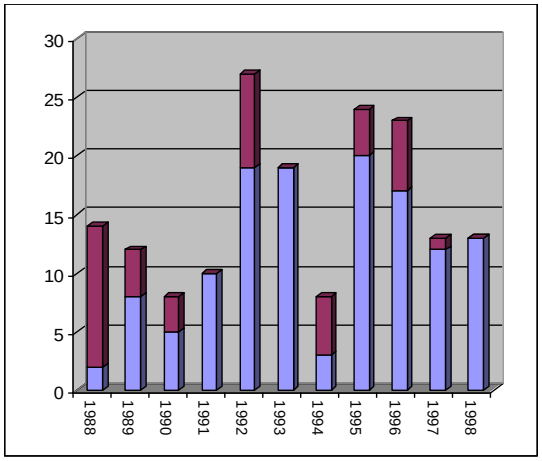
Tetanus is a notifiable disease but as with all such diseases in Malaysia under-reporting most likely occurs. However, cases that get admitted to hospital often need prolonged management in the ICU and do not get missed. The Epidemiological Unit of the Ministry of Health has detected between 30 to 80 cases annually the last 20-30 years. Neonatal tetanus forms the majority of cases but in some years the adolescent and adult group have occasionally outnumbered the neonates. People, particularly rural farmers, whose nature of work exposes them to a higher risk, ought to be better covered with booster doses of tetanus toxoid. Miranda and Miranda noted that Kelantan, principally a rural state recorded 38% of all the cases in Peninsula Malaysia during 1979 to 1984. But since then, in the 1990s it is Sabah that has stood out most significantly, accounting for almost all the cases of neonatal tetanus.

Figure 11.1 Number of neonatal tetanus cases (note: no deaths) in peninsula Malaysia and Sarawak



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Figure 11.2 Number of neonatal tetanus cases (whole bar) and deaths among them (upper part of bar) in Sabah



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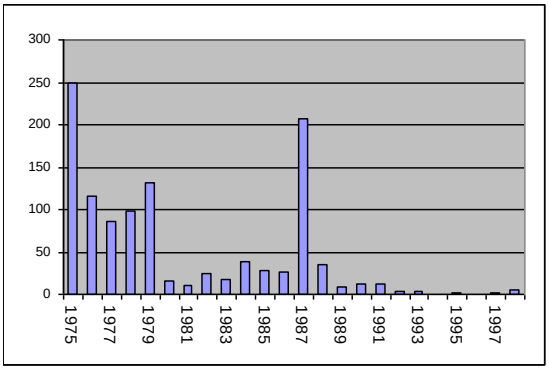
DIPHTHERIA

Routine immunisation and improved in health and living conditions have resulted in a drastic decline in the incidence of diphtheria in Malaysia. Before immunization, which began in the mid 1960s, there were over 150 deaths annually from diphtheria in Malaysia. A dramatic decline in the number of cases and deaths from diphtheria was seen in the 1970s. The number of notified cases dropped below 100 in the 1980s. Nevertheless, these figures may have underestimated the true incidence of diphtheria. In 1988 an outbreak occurred in Selangor which resulted in a jump of 187 cases being reported that year. Since then the number of notifications of diphtheria have dropped below 10 annually and there have been a few years in which no cases were reported. However in 1997,

Figure 11.3 Number of diphtheria cases in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

when only 2 cases were reported one was fatal and in 1998 Lee *et.al*. reported a spate of 3 cases in Kuala Terengganu over 4 months. These children had not completed their diphtheria immunisation. One case was fatal.

The causative bacteria *Corynebacterium*

Figure 11.4 Number of deaths from diphtheria in Malaysia 1960-1980

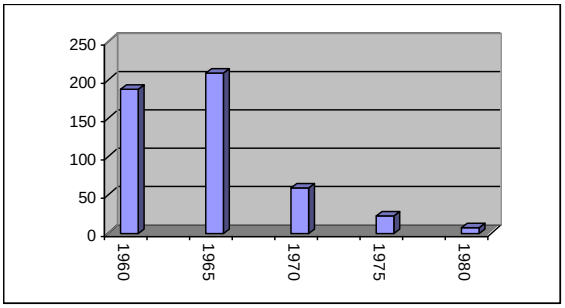
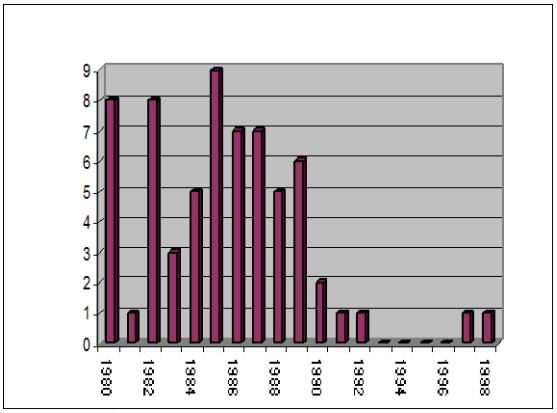


Figure 11.5 Number of deaths from diphtheria in Malaysia 1980 onwards



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

diphtheria comes in different strains. Singh in 1955 reported that most of those cultured here have been of the less severe *mitis* group. The cases in Terengganu in 1998 were of the toxigenic *mitis* biotype. Contact tracing in Terengganu in 1998 surprisingly found 10 cases of the non-toxigenic biotype gravis. *Corynebacterium diphtheria* has been recorded as the cause of endocarditis complicating cyanotic heart disease.

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ENTEROCOCCUS

These bacteria were formerly known as Lancefield Group D streptococci, the non-haemolytic group. They have the unique feature of being resistant to all the cephalosporin antibiotics and deserve being classified as a separate genus. They are an important 'blind spot' to remember because they can escape the coverage of the broad spectrum cephalosporins commonly used in abdominal sepsis. *Enterococcus faecalis*, and *En. faecium* cause wound infections, septicaemia, endocarditis and intra-abdominal sepsis. *Str. bovis* is an uncommon cause of endocarditis, but nevertheless has been reported locally. In relation to abdominal sepsis it is important also to remember that aminoglycosides alone have poor action on the entrococci, but they act synergistically with penicillin on many strains.

Riley, Parasakthi and Teh have reported one case of vancomycin resistant *En. faecium* in a 21 year old male from Sabah with aplastic anemia in 1996.

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LISTERIA

Listeria monocytogenes, a gram-positive rod is an uncommon cause of meningitis. It was only first reported in Malaysia in 1982 by Halim and Lim. Although it can be found widely in the environment, such as in soil, it is an uncommon human pathogen. Even in the United States less than 200 cases of listerosis are reported each year.

One study in 1991 has found between 19-50% of our retail beef and poultry sold in wet markets and supermarkets were contaminated with *Listeria monocytogenes*. A 1992 sample study of fresh vegetables in Kuala Lumpur found 5 out of 280 samples contaminated. *Listeria monocytogenes* was found in lettuce, 'sengkuang' and 'selom'. *Listeria innocua* was detected in 'sengkuang' and 'pegaga'.

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MICROCOCCUS

Micrococcus species resemble staphylococci and are found free living in the environment or as commensals. A case of *M.luteus* causing multiple intracranial abscesses in 37 year old woman in Kelantan with no obvious immunosuppression has been reported.

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STAPHYLOCOCCI

Microscopically staphylococci appear as spherical cells arranged in grapelike irregular clusters stained deep blue with the Gram stain. Three types of staphylococci are important human pathogens. The most notorious is the *S. aureus* that naturally inhabits the skin and the nares of about 50% of the public and 75% of hospital workers. The *S. aureus* is one of the most successful human pathogens. It is common both in community acquired infections and nosocomial ones. It is the commonest organism cultured from pus drained from abscesses. It is a common agent in all sorts of infections of the upper and lower respiratory tracts and commonly cultured from almost any sort of clinical specimens. In nosocomial septicaemia it ranks with *E. coli*, *Klebsiella* and *Pseudomonas* as the commonest pathogens.

Staphylococci more than other types microbes have been able to develop antibiotic resistance. Its development of resistance to penicillin was the classic example of the problem. As early as 1950 in the West the majority of hospital strains of *S. aureus* were penicillinase producing resistant organisms. Resistance subsequently appeared in certain strains to all the major antibiotics. A report in Malaysia by Puthucheary, Chen and Dugdale in 1971 showed also that over 60% of hospital Staphylococci were then penicillin resistant. From a school health service in Petaling Jaya however, only 24% of strains were found to be resistant. In 1986, Tan, Ngeow and Farida reported a study of community acquired *S. aureus*. They found 73% resistant to penicillin. Cephalexin and tetracycline were also ineffective. They suggested that erythromycin (resistance 18%) and cotrimoxazole may be more appropriate. A large 6 hospital survey (6642samples) of antibiotic resistance in 1991-2 found 77% penicillin resistant, and 19.4% methicillin resistant.

Methicillin Resistant S. aureus

The problem of methicillin resistance (MRSA), arose first in the UK in 1961. It is usually a plasmid mediated resistance. In the late 1960s it rose to rates as high as 40% in Denmark but in most places declined a little in the 1970s before recrudescing in the 1980s through to the present. As early as 1969, MRSA were isolated in the UH in Malaysia. The percentage of *S. aureus* that were MRSA in UH was 12% in 1979, 13% in 1981, falling to 6.6% in 1983 but rising to 19% in 1985. A survey of nosocomial infections in the KL GH in 1982 revealed that 25% of the *S. aureus* were methicillin-resistant. In 1990 a rate of 35% was reported. The Special Care Nursery in GH KL had a 6% rate of MRSA in 1987. In the 6 hospital study although the overall rate of MRSA was 19.4%, it ranged from 6.7% in the Kuching and Kuantan hospitals to 31.7% in Johore Baru. In general the larger the hospital the higher the rate is likely to be. These strains are now found probably in all district hospitals as well but probably not in the community. For example, Cheong *et.al*. found that none of 218 strains of *S. aureus* were methicillin resistant in a 2 year study of 2,823 specimens from general practice in the Klang valley from 1991.

The problem MRSA pose is that they are no less virulent and are multiple antibiotic resistant with more than 85% resistant to the aminoglycosides, erythromycin, tetracycline and chloramphenicol. There are a few antibiotics that have activity against most MRSA, and vancomycin shows the lowest rate of resistance (0.5% in the 6 hospital study).

Hanifah studied the characteristics of 50 MRSA isolates in the UH in 1992. The predominant strains there produced Type IV coagulase. All the isolates that could be phagetyped were susceptible to Group III phage, with 77% of these susceptible to phage 85. At least 10 different patterns were distinguishable by plasmid typing.

Assessing the impact of MRSA on morbidity and mortality, Lee *et.al*. found on review that 148 patients treated by the surgical department in the UH were either infected or colonised with these organisms in 1988. 47%, they considered, were just colonised. 53% they considered were infected. 28 (19%) patients died but only 5(3.4%) as a direct result of the infection.

Over 6 months in 1994, Cheong reported that MRSA bacteraemia were encountered in 25 patients in GH KL. Most had severe underlying illnesses and long hospital stay. Sensitivity studies found 100% sensitive to vancomycin, 96% to fusidic acid, rifampicin and ciprofloxacin, and 28% to perfloxacin. 13 patients eventually died. In 9 the deaths were directly attributed to MRSA bacteriamia.

Enterotoxic S. aureus

S. aureus is also a known cause for enterotoxic gastroenteritis. In a study of *S. aureus* 130 isolates in 1982, Lim *et.al*. found that 21% produced enterotoxin. The most common enterotoxin from *S. aureus* from human isolates was enterotoxin C, whereas the most common enterotoxin from *S. aureus* strains from food sources was enterotoxin B.

Besides *S. aureus* the two other clinically important staphylococci are *S. epidermidis* and *S. saprophyticus* both labelled as coagulase negative staphlococci. The former is often cultured as a commensal but in the intensive care setting is becoming more often recognised as a nosocomial pathogen. The latter is recognised now as a fairly common urinary pathogen but its status in the Malaysian context is not well determined.

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STREPTOCOCCI

The Gram positive streptococci are widely distributed in humans. Classically they are divided up according to the type of haemolysis they cause on blood agar plates and their Lancefield antigens.

The α Haemolytic Streptococci

The Pneumococcus, a diplococcus, is as the term suggests usually seen in pairs. Its proper name is *Streptococcus pneumoniae*. By far the most important disease caused by the pneumococcus is pneumonia. The clinical uniformity of its lobar involvement is pathonomonic. This used to be the commonest

form of pneumonia but it is no longer so. Uncommonly, the pneumococcus can cause meningitis, endocarditis and peritonitis. In a series of 90 cases in KL over 4 years, Farida noted that 34% were pneumonic, 21% had meningitis, 18% had conjunctivitis and 14% had septicaemia. Nallusamy has reported 2 cases of fatal neonatal sepsis due to *Streptococcus pneumoniae* that is typically associated with the Group B Strep.

The problem of penicillin resistance among pneumococci was first noted in the 1970s. It first appeared in New Guinea and was noted only a few years later in the U.S. and Britain. Penicillin resistance in Malaysia was first reported by Farida, Motilal and Zaiton in 1983 after having been on the lookout for it several years. Its is not widespread and the degree of resistance is moderate. In 1987 Cheong *et.al.* reported resistance rates of 2% to penincillin, 0.8% to erythromycin, 0.4% to cephaloridine but 18% to tetracycline. About the same time Farida reported a 4% resistance to penicillin, 4.5% resistance to cefuroxime and 6.5% resistance to chloramphenicol. The large 6 hospital study found no penicillin resistant strains but 6% resistance to erythromycin and 18% to tetracycline. In Kota Bharu, a community survey of pharyngeal swabs of 355 children in 1998 obtained growth of *Streptococcus pneumoniae* in 36 (10%) of subjects. Only 1 (3%) was penicillin resistant.

Rohani *et.al*. have noted that serotypes 1 and 19B were the commonest serotypes associated with invasive infection, among specimens sent to the IMR in 1996. 72% of the infections were due to serotypes covered in the 23 valent polysaccharide vaccine. They found a resistance rate of 7% to penicillin and 1% to erythromycin.

The Viridans Group; formerly thought to be one species, now encompasses a few species such as *Str. sanguis* and *Str. mitior*. They are of low virulence and mainly important for subacute bacterial endocarditis. Like the pneumococcus these streptococci do not have the Lancefield antigens.

The ß Haemolytic Streptococci

In a cross-sectional study of 286 children between 6-8 years old in Petaling Jaya in 1969, Chen found a ß haemolytic streptococcal carrier rate of 36%. The commonest type was Group A streptococci accounting for 45% of all streptococci. In a one year longitudinal study of 30 of these children where throat and nasal swabs were taken every 2 weeks, it was found that all the children had streptococci isolated from them at least once. There was however no cyclical or seasonal pattern. At an individual level, one child had a positive culture only 9% of the time whereas another had a positive culture 77% of the time. Group A and G accounted for 42% and 30% of the isolates respectively. Group C and Group B were found infrequently.

Lancefield Group A, also known as *Streptococcus pyogenes*, is the commonest group of streptococci and account for 90% of human streptococcal infections. It is found in the nasopharynx of asymptomatic carriers. Farida and coworkers estimated the carrier rate among 6-8 year olds at 9.4% in 1986. It causes pharyngitis, tonsilitis, impetigo, scarlet fever, erysipelas, wound infections and septicaemia. It two well known sequelae are post-infective acute glomerular nephritis and rheumatic fever. As in other countries resistance to sulphonamides and tetracycline has developed, as reported for instance, by Ampalam and Cheng in 1971. *Str. pyogenes* however, appears incapable of developing resistance to penicillin. Norazah found streptococcal impetigo common among Orang Asli children affecting 8 (20%) out of 41 children in a community survey in 1995. Group A streptococci was isolated from all cases.

Lancefield Group B: In the early 1970s, the Group B streptococci emerged in the West as the cause of a much dreaded, yet common virulent infection among neonates, that was fatal in up to 50 to 70% of cases. As many as 2 per

1,000 babies contracted the infection from mothers who had the organism in their genital tract. They could develop symptoms of septicemia within 12 hours of birth or present as meningitis as late as a few weeks after birth. Evidence suggests that neonates are particularly affected because they lack IgG that act as opsonins to facilitate phagocytosis. In this regard intravenous immunoglobulin therapy seems promising.

In Malaysia, the first case where the Group B streptococcus was isolated in a neonatal infection was in 1979. One survey of vaginal swabs put the carrier rate at 21% of women, another found the rate to be 11% (18/164) in women with a vaginal discharge and 14%(27/188) in controls which was similar to that in other countries. Over one year in 1979, in which the bacteria was actively looked for in the KL General Hospital, six cases were found. There were 2 deaths. In 1994, 30 cases of early neonatal group B streptococcal septicaemia were recorded, giving an incidence of 0.4/1000 livebirths. 40% were preterm babies and 47% were low birth weight babies. 80% had symptoms within 6 hours of birth. 80% were respipratory symptoms. Meningitis was uncommon. 6 (20%) cases died. All the bacteria isolates were sensitive to penicillin.

In 1987 Ngeow and Puthucheary found that from 350 strains locally, 51% were serotype III and a further 36% were Serotypes II and Ic.

Lancefield Group C and G, can be found in the throats of healthy individuals. They are said to a common cause of impetigo in the tropics but the local experience is uncertain. They also cause other infections like *Str. pyogenes* but is much more rare.

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CHAPTER 12

THE GRAM NEGATIVE BACTERIA

The Gram-negatives constitute the largest group of medically important bacteria. They are free-living, rigid-walled, coccoid or bacilloid, sometimes in chains and sometimes motile by flagella. They form a number of recognisable groups, such as the Enterobacteriaceae that inhabit the mammalian gut, the Pseudomonads, the Vibrio and so forth. Although they can be grouped into families it is perhaps simpler here to just list them in alphabetical order here according to their genus.

ACINETOBACTER

Acinetobacter are ubiquitous in the environment and usually found in water. Like most gram-negative bacteria they are mainly nosocomial pathogens. It is not as common a pathogen as *E. coli* and *Klebsiella* but in most laboratories the acinetobacter is in the second tier of organisms frequently isolated alongside *Pseudomonas*. Sometimes they are disregarded as contaminants but the clinician ought to be wary of it in the ill hospitalised patient. A 9-month study on neonatal bacteraemia in Maternity Hospital KL in 1991 found that *Acinetobacter* (32%) was the most common isolate, followed by *Klebsiella* (30%), *S. epidermidis*(9%) and *Enterobacter*(8%). This study recorded a 30% mortality in affected neonates. The antibiotic sensitivity studies in this study found resistance of over 50% to the aminoglycosides and third generation cephalosporins among *Acinetobacter* and *Klebsiella*. Only imepenem and ciprofloxacin had less than 10% resistance to these two pathogens. Lim and Sulaiman have recorded a case of *Acinetobacter* causing neonatal meningitis. Malik recorded a case of *Acinetobacter* endocarditis in an infant with Fallot's tetralogy and an absent pulmonary valve. an found that *Acinetobacter* was the commonest cause of peritonitis in patients having peritoneal dialysis in the Nephrology Unit in 1981 occurring in 52% of patients with positive cultures or 6% of occasions peritoneal dialysis was performed.

Acinetobacter is highly resistant to many antibiotics. In the large 6 hospital survey of various body fluids of 1991-2 the only antibiotics that had a resistance rate to *Acinetobacter* lower than 20% were ceftazidime (16.4%), amikacin (18.9%), norfloxacin (10.5%), perfloxacin (5%), imipenam (3.7), aztreonam (15.8%) and amp/sulbactam (15.1%).

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ACHROMOBACTER

Achromobacter xylosoxidans was first described by Yabuuchi and Ohyama in 1971. It is not a common gram-negative aerobic bacillus, but can be responsible for some nosocomial infections, especially in compromised patients. They can cause septicaemia, wound infections otitis media and

meningitis. Some 30 strains were isolated in the UH from 1977 to 1983. They appear sensitive to the penincillins but resistant to most aminoglycosides.

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AEROMONAS

Aeromonas hydrophilia is one of about ten bacterial pathogens that cause gastroenteritis. It can be found in water and soil. It has also been found to be carried by flies in KL. Though it is not mentioned in some studies, when it is particularly looked for it may account for nearly 6% of all gastroenteritis, or about 25% of cases where a bacterial pathogen was isolated. UH workers reported that in 86 clinical isolates of *Aeromonas hydrophilia* at least one of four exotoxins was produced by 80% of the enteric and 96% of the non-enteric isolates.

In addition, *A. hydrophilia* can cause a wide range of other infections, including wound infections, hepatobiliary infections and septicaemia. Puthucheary reported 23 such cases at the UH over a 5 year period. Most were adults and the majority were compromised hosts. The overall mortality in this series was 71%. Almost all strains were resistant to ampicillin, but nearly all were sensitive to the newer cephalosporins and quinolones. Sambandan noted *A. hydrophilia* complicating an open fracture, which is a rare occurrence.

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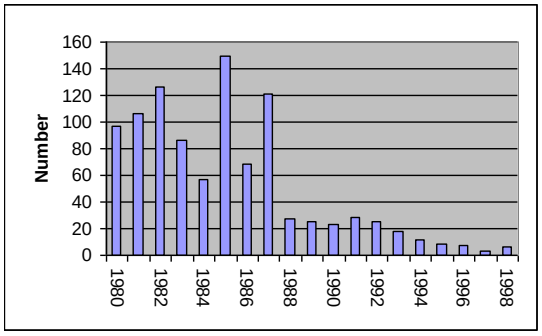
BORDETELLA (WHOOPING COUGH)

Reed produced perhaps the earliest record of whooping cough in Malaysia in 1950 when he documented a limited outbreak of 20 cases, with no fatalities in an estate. It usually occurs sporadically and continues to do so. An epidemic outbreak however occurred in 1967 among Orang Aslis in Pahang and Negeri Sembilan. This involved 346 cases and there were 19 deaths, all in children under 5 years of age.

Figure 12.1 Number of Whooping cough cases in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Whooping cough, or 'batuk kokol', is a notifiable disease. In the last two decades the number of cases notified annually ranged between 70 to 160 without any change in the trend. One or at most two deaths occurred in some years. Under the national Acute Respiratory Infection project in 1984, 1678

nasopharyngeal aspirates from children admitted with acute respiratory infections in Ipoh, Kota Bharu and Kuala Lumpur were examined by direct immunofluorescence for Bordetella organisms. 45(2.5%) were positive for *B. pertussis* and 15(1%) were positive for *B. parapertussis*.

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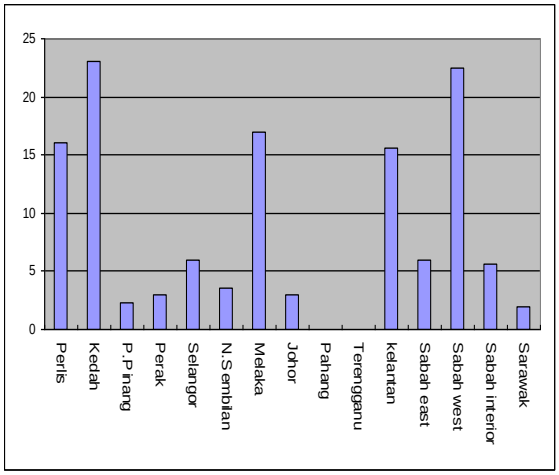
BURKHOLDERIA (MELIOIDOSIS)

Melioidosis ought to be recognised as a fairly common disease in Malaysia. It is caused by *Burkholderia pseudomallei* formerly known as *Pseudomonas pseudomallei* a gram negative aerobic motile bacillus, which is a saprophyte widely found in soil and water in both East and West Malaysia. The rate the bacteria is isolated from soil is especially high in land cleared for rice fields or oil palm (15% - 30%). Isolation rates from mining pools, primary and secondary forests in comparison are less than 2%. *B. pseudomallei* thrives best in high moisture and grows best at 37C. It is nutritionally versatile and can remain viable for months even in tap water. Melioidosis is contracted by soil contact of skin abrasions. Person-to-person transmission of melioidosis can occur but is rare. Other animals can suffer an infection similar to man but there is no evidence to suggest that animal hosts are necessary. Studies on flies in KL have found that *Burkholderia pseudomallei* was the dominant bacteria carried on the *Chrysomya megacephala* species of fly.

Melioidosis was first recognised as a Glanders like disease in Burma in 1911 by Whitmore and Krishnaswami, and initially thought to be a zoonotic disease involving rodents. The first case in Malaysia was recognised by Stanton in 1917. Between that year and 1927, Stanton and Fletcher at the IMR had detected 39 cases. Malaysia lies in the centre of the area endemic for melioidosis which covers South East Asia and stretches to East Asia, India and Australia. There have also been some cases in Africa.

Figure 12.2 Anti- B. pseudomallei antibodies among Malaysian army recruits from different states 1964-1966.



Clinical features

Four clinical forms of the disease are recognised, latent or unapparent, sub-acute, acute fulminating and chronic suppurative.

Unapparent infection

Using a haemagglutination test on 1,592 persons f om to 1966, Strauss *et. al.* found significant antibody titres reaching 20% in healthy army recruits from the rice growing states of Kedah, Perlis, Kelantan and Malacca. Orang Asli forest dwellers in surprising contrast and estate workers were positive in less than 5% of those sampled. Embi *et.al*. found that among 420 soldiers serving in Sabah and Sarawak in 1992, 54% had antibodies to *B. pseudomallei* exotoxin and 66% had antibodies

to the whole cell antigen.

Sub-acute and acute infection

The largest number of documented cases of melioidosis comes from the University Hospital in KL where, in an early series Puthucheary noted a male preponderance of 3:1. Associated diseases included diabetes melitus (38%), carcinoma (26%), trauma, tuberculosis and renal disease. The mortality rate was 30%. In reviewing 50 septicaemic cases in 1992 Puthucheary found them ranging in presentation from fever to septicaemic shock. 58% had pulmonary involvement and 24% had sepsis in the skin and soft tisuue. The mortality rate in this series was 65%.

The septicaemic form of the disease with either an abrupt onset, or with prolonged fever, with or without a demonstrable infection site, has been the commoner form of the disease (about 60%). Of 7 acute septicaemic cases, who had associated disorders, rendering them more susceptible, at the UH between 1976 to 1979, 6 died. There have been reports from HUSM of fatal melioidodis in neonates in 1993 and 1998 from septicaemia and meningitis. Liam in the UH reported one case with cutaneous pustules in 1993.

Many melioidosis patients are already debilitated in some way, and in fact, the first cases in which melioidosis was discovered were seen in vagrants and morphine addicts in Rangoon. The fatality rate then noted was about 95%.

In the 1970s, tetracycline and chloramphenicol were established as the most useful chemotherapeutic agents. Studies in the late 1980s of clinical isolates showed that 58% were sensitive to tetracycline, 84% to chloramphenicol and 86% to cotrimoxazole. Relapses can occur even with prolonged therapy due to intracellular survival of the organism. Of late the new B-lactams have surpassed these as the choice for treatment especially in the acute phase. In-vitro tests have shown cefoperazone-sulbactam to have MIC_{90} of 4mg/l in 50 strains locally.

Chronic infection

Melioidosis may present as multiple abscesses, sometimes in unusual parts in the chronic form. Pit, Cheah and Farida have reported an example of a brain abscess in a 48 year old Malay woman. Lee and Chua reported another. Kareem, Aiyar and Marshal found a patient with chronic osteomyelitis of the foot and tibia. Elango and Sivakumaran report a diabetic patient with parapharyngeal space infection. Kan and Kay found it was the cause of prostatitis in a man in Sabah allegedly from a fly excreting some fluid in the eye. Koh reported it as the cause of epididymo-orchitis. Physicians have not infrequently found it to be responsible for puzzling cases.

In 6 years beginning 1981, Yee *et.al*. at the UH noted 10 cases of melioidosis, 6 patients had underlying diabetes mellitus, three of them also had tuberculosis. Other predisposiding factors noted were corticosteriod therapy, renal impairment and malnutrition. One patient had acute septicaemia, the remainder presented with a diverse range of abscesses, in the supraspinatus, psoas, brain, liver, suppurative skin lesions, chronic lymphadenitis and three forms of pulmonary disease.

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CAMPYLOBACTER

First described as curved rod-like vibrio related bacteria, *Campylobacter* has been recognised to cause infection in man only since 1947. It became increasing clear that one species *C. jejuni* was the major cause of bacteraemic enteritis in the West in the 1970s. The first report of this in Malaysia was in 1982 by Puthucheary and Lin. Lim, Jegathesan and Wong in 1984, reported a study looking into its prevalence in diarrhoea patients and found that it was the third commonest bacteria after *Salmonella* and *E. coli*. They recovered the bacteria in about 4% of diarrhoeals stools.

80% of *Campylobacter* isolates were identified as *C. jejuni* in 85 clinical and 15 poultry specimens by Tay *et.al*. The remaining strains were *C doylei* (5), *C coli* (7), and *C lari* (3) and a few were untypable. The similarity of clinical and poultry isolates suggests that chickens are the most common source of *Campylobacter* infections. Approximately 57% clinical and 33% poultry isolates examined produced cytotoxin. 83% of *Campylobacter* isolates from watery diarrhoea cases were cell-invasive by means of the gentamicin HEp-2 invasion assay.

Reviewing 137 children with *Campylobacter* diarrhoea at the UH in 1994, Puthucheary *et.al*. noted that 61% were between 2-12 months and 95% were under 5 years old. Half of these cases presented with fever and bloody diarrhoea. Vomiting was seen in 28% and abdominal colic in only 8%. 37% had a history of a recent or concurrent illness. Other bacterial enteropathogens were isolated in 15% of the children. Erthyromycin was the most useful antibiotic.

In a special group of patients, the splenectomised, the *Campylobacter* can be more virulent. Jackson *et.al*. have described a case of fatal septicaemia in a 35 year old man in Kelantan who had undergone splenectomy 9 years previously because of HbE/β^o thalassaemia.

Campylobacters have rather unusual antimicrobial sensitivities. Most strains are

resistant to penicillin and the B-lactams have low activity towards them. Erythromycin, chloramphenicol and the aminoglycosides are the most active compounds.

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CHROMOBACTERIA

Chromobacterium violaceum is a soil saprophyte, a facultative anaerobe, that may be a contaminant on culture but is known to cause septicaemia, urinary tract infection and abscesses. Hassan *et.al*. reported the case of one young Malay man who succumbed to septicaemia from this organism.

Reference

Hassan H, Suntharalingam S and Dhillon KS. Fatal Chromobacterium violaceum septicaemia. Sing Med J. 34:456-458 1993.

CITROBACTER

The *Citrobacter* is one of the lesser members of the *Enterobacteriaceae* and account for less the 2% of hospital bacterial isolates (1.5% in the 1991-2 study of 6 hospitals).

Reference

Cheong YM, Lim VKE, Jegathesan M and Abu Bakar S. Antimicrobial resistance in 6 Malaysian general hospitals. Med.J.Mal.49:317-326 1994.

ENTEROBACTER

The *Enterobacter* is a *Klebsiella* related member of the *Enterobacteriaceae* family but of lesser importance. It can cause infections in similar situations like the other coliforms, but is usually a nosocomial infection. It constituted 4.8% of all bacterial isolates in 6 general hospitals. *Serratia* is a related bacteria, also usually found in nosocomial infections, but less often encountered, constituting 1.1% of isolates in the said study.

Reference

Cheong YM, Lim VKE, Jegathesan M and Abu Bakar S. Antimicrobial resistance in 6 Malaysian general hospitals. Med.J.Mal. 49:317-326 1994.

ESCHERICHIA COLI

The *Escherichia coli*, or *E. coli* as it is more commonly called, is the characteristic Gram negative, non-spore forming bacteria of the *Enterobacteriaceae* family that inhabits the intestines of mammals. It is the commonest bacteria to be cultured in most clinical laboratories. Often it may be a contaminant but it is the commonest cause of many infections, such as urinary tract infections, abdominal sepsis like cholecystitis, wound infections and septicaemia.

E. coli comprised 20.7% of all bacterial isolates in the large 6 hospital study in 1991-2. The resistance rate to cotrimoxazole was

35.5% and to gentamicin it was 10.2%. Clinicians need to bear this in mind when choosing an antibiotic in infections such as urinary infections where *E. coli* is likely to be encountered. The resistance rate to second and third generation cephalosporins and the quinolones were under 10%. Nitrofurantoin was another useful antibiotic (resistance rate 4.7%). A study of bacterial isolates in general practice in the Klang Valley over 2 years from 1991 found that the resistant rate to ampicillin was 50%, to cotrimoxazole 33%, to ampicillin-sulbactam 21% and to ampicillin-clavulinic acid 18%. *E.coli* was the second commonest organism cultured after *S. aureus* and was the commonest cause of urinary infection.

The subgroup of *E. coli* that cause gastroenteritis need a special mention. A few different groups have been described.

Enteropathogenic E. Coli. (EPEC): As early as 1895, Escherich a German paediatrician after whom the bacteria takes its name, implicated *E. Coli* as the cause of infantile diarrhoea. However, it was only in the 1940s with the advent of serology that it could be established that particular strains, and not just any ubiquitous *E. coli* was responsible. These strains do not produce any toxin nor do they invade the bowel mucosa. Their form of pathogenesis is unclear. Jegathesan *et.al.* reported in 1975 that EPEC was responsible for 9% of diarrhoeal cases in children under 10 years. Salaswati and colleagues found, in a survey of healthy pre-school Malay children in Selangor, a prevalence of EPEC of 6.7%.

Enterotoxigenic E. Coli. (ETEC): Some *E. coli* produce either or both a heat labile (LT) and a heat stable (ST) enterotoxin that acts somewhat like cholera toxin. They are responsible for what has been termed travellers' diarrhoea. ETEC is ubiquitous in the environment in Malaysia. In a survey of water, weaning foods, food preparation surfaces, fingers and stools of children in 20 households in a Malaysian village, Vadivelu found ETEC in at least one location in each household.

Cheong *et.al.* in 1990 found that ETEC was present in 3.7% diarrhoeal cases of all ages, which is in the low in the rates reported among countries of the region. In 1997 Samuel *et.al* reported that in 107 diarrhoeal cases in children, bacteria was isolated in 71(66%) cases. In 11 cases more than one bacteria was cultured. In 65 cases ETEC was found, most commonly STa2 toxotype.

Iyer *et.al.* found that 21 out of 310 *E. coli* isolates from 62 children under the age of 5 years with diarrhoea in the UH produced enterotoxins in 1995. 15 isolates produced ST only, 2 produced LT only and 4 produced both ST and LT. None demonstrated the known colonisation factor antigens.

Enteroinvasive E. Coli. (EIEC): This group of *E. coli* invade the colonic mucosa and cause ulceration like *Shigella* and cause a diarrhoea like dysentery.

Enterohaemorrhagic E.coli. (EHEC): *E.coli*O157:H7 was the first of several strains recognised in 1983 to produce Shiga toxins and post-diarrhoeal haemolytic uraemic syndrome (HUS), which is defined by acute renal injury, thrombocytopenia and microangiopathic haemolytic anemia. EHEC is now believed to account for over 90% of all cases of HUS in industrialised countries today. The *E.coli*O157:H7 strain has also become well known and has featured in newsmagazines having been responsible for illness in over 5,000 Japanese schoolchildren in 1996 and the recall of 25 million lbs. of ground beef in the USA in 1997 and the death of over 20 people in Scotland in 1998. Malaysia needs to keep on the look out for this bacteria but it has yet to be reported locally.

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FLAVOBACTERIA

Flavobacterium meningosepticum is a nonfermentative gram-negative bacillus which became recognised as the cause of outbreaks of neonatal meningitis in about 1958. It is not an uncommon cause of such meningitis in Malaysia. Often it is the cause of a hospital outbreak and can have a very high mortality. Such an example was seen in the Kota Bharu GH in 1980 where over 14 babies born in the labour room were affected and the microbe was initially mistaken for *Pseudomonas* as it is also a gram-negative bacillus.

In a series of 18 cases, Boo *et.al.* reported in 1989 that there were 4 deaths, and 8 neonates that required insertion of entriculo-peritioneal shunts for progressive hydrocephalus. It is difficult to treat antimicrobially because it has very unusual antibiotic sensitivities, and requires these drugs to penetrate the blood brain barrier well. Usually antibiotics such as rifampicin, moxalactam, piperacillin, erythromycin, and vancomycin are used in some combinations.

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GARDNERELLA

Gardnerella vaginalis (formerly called *Corynebacterium vaginale* and *Haemophilus vaginalis*) is a Gram negative to Gram variable pleomorphic rod isolated from the normal female genitourinary tract and also associated with vaginitis. Ngeow *et.al.* found that it was present in 15% (25/164) in women with a vaginal discharge and 13% (25/188) controls in a survey of women attending a the gynaecological clinic in GH KL. It is sensitive to metronidazole and covered in the treatment of tricomoniasis.

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HAEMOPHILUS

DUCREYI

Soft chancre or chancroid may be presumptively diagnosed by the exclusion of syphilis but is only proven be the isolation of *Haemophilus ducreyi*. Annual reports from the IMR suggests that the bacteria can be isolated from about 2-3% of penile ulcers. It is a notifiable disease and the number reported has

risen from below 50 in the early 1980s to 171 in 1987. This is probably through a greater awareness of its presence.

INFLUENZAE

H. influenza is one of the important bacteria causing serious infections, especially in children. The organism may occur asymptomatically in the upper respiratory tract. In some conditions it appears not to be the cause but plays a secondary role. However, in the typical acute, usually severe, pyogenic conditions where the organism is isolated there is little doubt *H. influenza* causes the disease. There is a wide range of clinical entities it can produce. Meningitis and pneumonia are the most serious and common. Acute epiglotitis, otitis media, septic arthritis, osteomyelitis, peritonitis, cholangitis, abscesses and cellulitis are also encountered but less frequently. In Malaysia, studies on pyogenic meningitis in childhood, *H. influenza* has usually been the commonest bacteria isolated.

In a series of 40 acute cases, where *H. influenza* was isolated over nearly 8 years in the University Hospital, 22 had meningitis, 14 had pneumonia inclusive of 4 who had both these features. Of these 40 cases 37 were children. The various entities are believed to be the local manifestations of *H. influenza* bacteremia, hence two or more local manifestations may be present in one patient at the same time. In a series from HUSM between 1985 to 1994, 65 children had invasive *H. inf luenza* disease. The peak age was from 7-12 months. 64% had meningitis, 29% had pneumonia, 5.4% had septicaemia and 1.3% had abscesses.

There has been one case report of *H. influenza* causing fatal endocarditis in an 8 month old child with a ventricular septal defect from Kealantan, a rare event.

It has been said that the frequency of recovery of *H. influenzae* from clinical specimens is directly related to the interest and experience of the investigator. In routine hospital isolates in Malaysia it usually accounts for less than 2% of bacteria, and often none at all. In the large series of 6 hospitals it accounted for only 0.1% of isolates.

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HELICOBACTER

Although spiral and curved bacteria had been observed in the human stomach in the 19th century it has only been recently that their significance have been brought to light. Warren, at the Royal Perth Hospital became interested in the bacteria, initially called *Campylobacter pylori*, in 1979. Together with Marshall he demonstrated a strong link with gastritis by 1981. It is now accepted that the bacteria has a causal role in gastritis and is responsible for nearly all peptic ulcers.

The pathophsiology of peptic disease can be simply put as gastric acid eroding the alimentary mucosa due to the breakdown of the normal mucosal barrier. But the underlying aetiology was under debate for a long time. What caused an increased acid output and a deficient mucosal barrier? It was even argued that it was psychosomatic. There was initial doubt the

bacteria discovered by Warren and Marshall, now named *Helicobacter pylori,* could be responsible for such a well studied and common disease. However there are still a few sceptics left today.

A few studies of the prevalence of *Helicobacter pylori*, have been done in Malaysia. In 1989 Nafeeza *et.al* reported a rate of 34% by H&E stain and culture among 60 patients with non-ulcer dyspepsia. The prevalence was highest among Indians (75%), followed by Chinese (45%) and only 8% among Malays. Goh *et. al.* reported that in 399 patients seen over 15 months, 51% of patients with dyspepsia had the organism. It was found in 96% of patients with histological changes of chronic active gastritis. It was present in 88% of patients with duodenal ulcers and gastric ulcers. In a 1997 report of 1,060 patients seen at the UH, Goh found that the prevalence of *Helicobacter pylori* was 91% in duodenal ulcer patients and 74% in those with gastric ulcers. Chinese were 2.5 times and Indians 4.9 times more likely than Malays to be affected. Other factors associated with a high relative risk of infection after multiple logistic regression analysis were, male gender (1.6), smoking (1.6), age above 45years (1.5) and a low level of education (2.3)

There appears to be a distinct racial difference in the prevalence rates of *H.pylori* infection. Malays are consistently reported to have lower rates. Mazlam found that 56% of Indians, 45% of Chinese but only 11% of Malays gastroscoped with non-ulcer dyspepsia were infected. In a seroprevalence study of 514 children aged 0.5-17 years, Boey *et.al*. noted an overall rate of 10.3%. They also noted that Indians had the highest rates and Malays the lowest.

Kelantan appears to show some regional peculiarity. In 1994 Uyub and Raj showed that *H.pylori* infection was seen in only 9% of patients with non-ulcer dyspepsia, 5% of patients with gastric ulcers and 50% of patients with duodenal ulcers. Serological surveys in blood donors (496) and people attending health clinics (921) also show a low prevalence rate of 4.2% to 4.8%. It reflects the low prevalence seen in Malays. Of all patients endoscoped 63% of non-Malays were positive compared with only 5% of Malays. In another series reported from 1996-1997, in 124 patients with endoscopically seen lesions, the presence of *H.pylori* was determined by using 5 different tests. The infection rate was 20% in patients with duodenal ulcers, 21% in patients with gastric ulcers, 17% in patients with duodenal or gastric erosions. The low incidence is accounted for by the fact that Malay form the great majority in Kelantan. Among them the infection rate in patients with endoscopic lesions was only 7%. Among non-Malays, on the other hand the rate was 47%.

Goh and Parasakthi reported the largest serological survey of 2,381 subjects in 2001 from KL, Kota Bharu, Kota Kinabalu, Sibu and Kuala Pilah. The racial difference in prevalence in every location was striking. Prevalence rates in Malays ranged from 12-29%, while in Chinese it ranged from 28-58%. Indians had rates of 49-52%. The highest rates were recorded in the indigenous races in Kota Kinabalu. There was no difference between males and females. An increasing prevalence was noted with age.

Reinfection is a concern in the management of *H.pylori.* Goh reported that after successful eradication no reinfection was seen in 35 patients when they were studied 2 years later.

Complications

Ulcers

The early recorded history of peptic ulcer in Malaysia goes back at least 80 years. In the 1920s the chief surgeon in Perak records having performed 21 gastroenterostomies for Chinamen with gastric and duodenal ulcers, of whom 20, left hospital apparently cured enough to resume their occupations.

It is hard to be certain what proportion of the

population suffer from dyspepsia at any one time or have a ulcer in their lifetime. But in any ordinary endoscopic service about 20% of those submitted to the test have an ulcer, another 30% have features labelled non-ulcer dyspepsia and 50% are normal and probably have another cause for their pain, and this is true in Malaysia. Duodenal ulcers outnumber gastric ulcers in a ratio of about 2.5:1. We do not have accurate data of the incidence of the complications of peptic ulceration locally but a few reports give us some picture of the situation.

Perforation

Perforated peptic ulcers form a fairly common surgical emergency. The number of cases reported in several hospitals are given in Table 12.1. Although the true incidence cannot be deduced from these figures, it may serve as a rough guide to the incidence of the disease. Should a significant drop in the incidence occur as a result of changes in the management of peptic ulcer it may be reflected in the number of cases these institutions see in the future.

Table 12.1 Number of cases of perforated peptic ulcers in selected hospitals in Malaysia

Years	Author	Hospital	Number Of Cases	
1959-1964	Alhady	Klumpur GH	124	
1961-1967	Balasegaram	Seremban GH	133	
1969-1975	Leela et. al	Klumpur GH	94	
1972-1974	M Yusof	JohorBharu GH	72	(1:200 surgical admission)
1968-1972	Ti & Yong	UH Klumpur	73	

All these series found that Malays and other races were not as commonly affected as Chinese, who often account for more than 80% of cases. It is also the experience on the East coast of Peninsula Malaysia where Uyub and Raj reported a low rate of 1.5 per 100,000 person years from a study of all the records ofoperations and endoscopy done in the state between 1991 and 1992. In most series males outnumber females by 5 to 10 times, and the peak age group of sufferers are between 40 to 69 years old. In Kelantan however 71% of patients were above 60 years old. The oldest patient on record is a 103 year old woman in KL who survived a simple closure.

Balasegaram reported that duodenal perforations were more than 2 times as common as gastric ones. He performed definitive operations, mainly partial gastrectomies, in 125 cases and simple closures in only 8, mainly on the very old and ill. He had 2 post-operative deaths in those with definitive surgery compared to 3 in the ill ones who had simple closure. At 2 years follow-up only 6% of patients had mild epigastric pain. Ti and Yong also found twice as many had perforated duodenal ulcers as gastric ulcers. Of their 73 patients 4 had conservative treatment, 50 simple closures. In this pre-antihistamine-2 era, because of problems getting patients to a second operation, they chose whenever possible to do definitive procedures. This was done in 19 cases. They had 5 deaths from the group with simple closures. M.Yusof found that gastric perforations were 7 times more common than duodenal ones. Surgical treatment in all cases was a simple closure and there were 3 deaths in the series.

Haemorrhage

In a series of 326 patients with haemetemesis or melaena over 46 months from 1963, Balasegaram in Seremban found that 63% were due to peptic ulcers and erosions. Duodenal ulcers (34%) were more common than gastric ulcers (25%) and 4% more were erosions and stomal ulcers. Only 42 patients had endoscopy with a Herman Taylor gastroscope and barium radiologic studies were the main stay of investigations. Chinese who formed 38% of the population accounted for 79% of cases, Indians who formed 10% of the population accounted for 20% of cases while Malays who formed 46% of

the population only accounted for 1% of cases. 57% of the 206 patients with bleeding peptic disease were operated on. In 52 patients (25%) diagnosis of the peptic ulcer was made only at surgery. The overall mortality rate for bleeding peptic ulcers was 3.4%. There were 3 deaths in the operated group and 4 in the non-operated group.

With the advent of flexible gastroscopes management of gastrointestinal bleeding underwent a big step forward. From a series of endoscopies for upper gastrointestinal haemorrhage in the UH, beginning in 1985 Jalleh, Goh and Wong reported that duodenal ulcers accounted for 43%, gastric ulcers for 23% and erosive gastritis a further 15% of the causes. Together these peptic ulcer causes make up 81% of the patients with upper gastrointestinal haemorrhage. The endoscopists were able to diagnose the source of bleeding in 96% of their patients. In 1995 Lakhwani reporting a similar series from GH KL, found that duodenal ulcers accounted for 32%, gastric ulcers for 30% and erosions for a further 22% of upper gastrointestinal haemorrhage, together adding up to 84%. Only 60% of these patients required blood transfusion. In an earlier series where diagnosis was based on barium meals, Leela, Joshy and Balasegaram reported that of 138 bleeding ulcers, 75% were duodenal compared to 25% gastric.

In the pre-antihistamine-2 era from 1968 to 1972, Ti and Yong studied patients with bleeding from peptic ulcers serious enough to warrant emergency surgery. They formed 22% (124/ 562) of all patients admitted with acute upper gastrointestinal haemorrhage. They found that Chinese patients accounted for 91% of such cases while they only accounted for 55% of all patients utilising the hospital. The distribution of lesions was similar to the endoscopic series mentioned above. The overall mortality was 10.5%; being lower in gastric ulcers (7.5%) than in erosive gastritis (12.5%) and duodenal ulcers (12.5%). In his series of 79 patients with either duodenal or gastric ulcers Lakhawni found that 11% needed surgery after endoscopic treatment. There was no significant racial predominance but males greatly outnumbered females. There were 5 deaths out of the 107 patients with bleeding peptic ulcer disease giving a mortality rate of 4.7%. 3 of these were post-operative deaths. In addition to these deaths there were 6 patients who died of torrential bleeding before gastroscopy was done and the diagnosis established. Though not common in children Balasegaram has recorded a case in a 15 year old boy with a bleeding peptic ulcer in 1963.

In Kelantan Uyub and Raj have reported a duodenal ulcer bleed incidence of 4.3 per 100,000 and gastric ulcer bleed incidence of 2.3 per 100,000 in 1991-1992.

Stenosis

Leela, Joshy and Balasegaram reported that in their series stenosis was the least common complication, more than 4 times less common than perforation and more than 6 times less common than bleeding. This follows the Western experience and is unlike Africa where stenosis is said to be common.

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KLEBSIELLA

The experience of most local hospitals suggests that closely following *E. coli*, *Klebsiella* is the second most commonly isolated hospital pathogen. There are over 5 species of *Klebsiella* but *K. aerogenes* is by far the commonest. Although in most patients the source of the bacteria is endogenous, it being an intestinal organism , most *Klebsiella* infections are hospital acquired ones and affect all the common body sites, such as wounds, the respiratory tract, urine, blood and pus. *K. aerogenes* can cause gas gangrene resembling clostridia and is the commoner agent in diabetic limb infections. The importance of the Gram stain in this situation should be emphasised.

Klebsiella spp accounted for 17.4% of bacterial isolates in the 1991-1992 study of 6 hospitals, just behind *E.coli*. Its resistance to antibiotics followed the pattern of *E.coli* but in general *Klebsiella* tended to be slightly more resistant to the cephlosporins and aminoglycosides compared to *E.coli*. Resistance to the different third generation cephalosporins ranged from 8.5-16.6%. Resistance rates to the quinolones were however under 2% and surprisingly resistance rates to cotrimoxazole (28.1%) and tetracycline(27.2%) were lower than those for *E.coli*.

Multidrug resistant *Klebsiella pneumonia* (MRKP) is a scourge like MRSA (methicillin resistant *Staph. aureas*) that surfaced in the 1980s. It is usually inferred that these bacteria produce extended spectrum beta-lactamase (ESBL). Over 2 years from 1996 to 1997, Ariffin prospectively studied febrile neutropenic children in the oncology unit of the UH and found that 52% of *K. pneumonia* isolates were resistant to amikacin and ceftazidime. Children who had been hospitalised longer and who had recently received antibiotics were more likely to have MRKP. Sepsis related mortality was 50% in this group. The UH reported an outbreak of MRKP in the year 2000. It was first isolated

from the blood and wound of a boy with necrotizing fasciitis but in the following 2 weeks phenotypically similarly MRKP were found in blood cultures of 4 patients and rectal swabs of another 3 patients. Furthermore MRKP was cultured from 2 liquid soap samples from the same ward. Analysis of plasmids however, demonstrated 6 different DNA profiles showing they were not from the same clone. The MRKP were all resistant to amikacin and ceftazidime but sensitive to imipenem and ciprofloxacin

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LEGIONELLOSIS

Legionella pneumophilia live in natural and man-made aquatic environments. It gained notoriety for growing in water cooling towers in air-conditioning systems causing outbreaks of respiratory disease in hotels and other buildings. In 1989 Ngeow *et.al*. sampled 30 cooling towers on one or more occasions (46 samples) in 3 building complexes and grew the organism on 12 occasions. *L. pneumophilia* serotypes 1 and 7 were the commonest. None belonged to Pontiac 1a subgroup.

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NEISERIA

MENINGITIDIS

Neisseria meningitidis seem conspicuous by its absence in this country in annual reports from most hospitals and the IMR. An example showing its absence is the study of 59 children with purulent meningitis by Lee, Puthucheary, Khoo and Thong at the UH.

Reference

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GONORRHEA

Gonorrhea has been known as a sexually transmitted disease for centuries and was described in ancient literature, but the causative bacteria, *Neisseria gonococcus* was only discovered by Neisser in 1879.

As far back as 1926 Hariharam had noted that gonorrhoea was the most prevalent venereal disease in the estates in Malaysia. Venereal disease as a whole was second to malaria as a cause for hospital admissions. Like any other place in the world it is hard to estimate the true number of cases encountered each year. Especially since the antibiotic era, any sufferer can find treatment quietly and escape being reported even though it is a notifiable disease. In a short report in 1958, Holmes obtained the co-operation of government doctors as well as private practitioners in Ipoh in a one month study. He reported that in one month 123 patients, including 108 males, 10 females and 5 children were treated for gonorrhoea in Ipoh. 94 (76%) were treated by private practitioners.

In the 1980s the number of gonorrhoea cases reported to the Ministry of Health was about 5,000 a year. A large number, over 1,000 each came from Sabah and Sarawak. It outnumbered syphilis by 5 to 8 times. However, the number

of cases reported has been declining. Less than 2,000 cases have been reported annually since 1996. This however, does not mean we can conclude that the incidence of gonorrhoea is declining.

Lim and Ridzwan found that in a genitourinary disease clinic in KL that gonorrhoea accounted for 80% of urethritis in males. In addition to urethritis annually about 90 to 130 cases of opthalmia neonatorum are notified. Gonorrhoea may also cause arthritis, uveitis and Deva has described a case where it threatened iris prolapse. Deshmukh reported one case of gonococcal sacro-iliitis.

In a survey of 370 prostitutes in 1990 Ramachandran and Ngeow found gonorrhoeae in 14% which was about only half as many as those whom had chlamydial cervicitis. Ismail reported that in the UH between 1977-1982, out of 422 cases, 16(3.8%) were in girls less than 12 years old. Parents of the girls denied knowing their daughters had any sexual contact, but 9 of these girls were linked to culture-positive adults.

From a study of all bacterial specimens collected by general practitioners in the Klang Valley in 1991, it was noted that *N. gonorrhoeae* was the 4th most common organism isolated accounting for 9.3% of positive specimens.

Antibiotic Resistance

Since early 1976, many countries have been reporting strains of penicillin resistant gonococci. The first time such resistance was encountered in Malaysia was in July 1977, from a case believed to be from Thailand. Surveillance at the UH showed in 1978 that 11% of gonococcal infections were due to penicillinase producing *N. gonorrhoeae*. Ismail noted that beta-lactamase producing strains of *N. gonorrhoeae* rose from 5% in 1977 to 49% in 1985. Lim and Ridzwan at the UKM noted in 1981 that 36% of gonorrhoea urethritis failed to respond to ampicillin. Lim from Penang also reported a similar rate of penicilinase producing gonococci there in 1983. Gururaj *et.al*. reported that between 1985 and 1988, in 58 cases of gonococcal ophthalmia neonatorum seen in Kelantan, 26% were penicillin resistant.

Since 1988 the IMR has set up a surviellance to detect antibiotic resistance in gonorrhoea. They have found the percentage of penicillin resistance varying from 12% to 49% in different parts of the country. Tetracycline resistance appears to have increased rapidly in recent years, the percentage of tetracycline resistant *N. gonorrhoeae* increased from 28% in 1992, to 42.5% in 1993 and to 52% in 1994.

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PLESIOMONAS

Plesiomonas shigelloides was isolated in the faeces of a child in 1947 by Ferguson and Henderson and implicated as the cause of diarrhoea.

Ampalam and Fang first isolated it in Malaysia in 1971. Lim, Young and Balakrishnan isolated it as the cause of diarrhoea in 2% of patients in Johore Bahru. It appears to be less common than in Thailand where it formed up to 37% of bacterial agents causing acute gastroenteritis. Singapore on the other hand does not seem to have pathogenic cases of the bacteria.

P. shigelloides may also be responsible for a typhoid like illness and may cause septicaemia, meningitis and other infections very rarely.

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PROTEUS

The genus *Proteus* is the gram negative bacteria characterised by their active motility in spreading on solid growth media. Being part of faecal flora and present also in the soil, it infects wounds and can cause peritonitis and urinary tract infections. It is also found in other places like in ear infections.

It accounted for 4.5% of bacterial isolates in the 6 Hospital study in 1991-2. The related bacteria *Morganella morganii* accounted for a further 0.7% of isolates. The resistance rates of third generation cephalosporins, quinolones and aminoglycosides were under 10% except for gentamicin which had a resistance rate of 13.9%.

Reference

Cheong YM, Lim VKE, Jegathesan M and Abu Bakar S. Antimicrobial resistance in 6 Malaysian general hospitals. Med.J.Mal. 49:317-326 1994.

PSEUDOMONAS

The *Pseudomonas* is a formidable bacteria. It can live just about anywhere: in ponds, soil, drains, steamy hot tubs, shower curtains and even antiseptic solutions. It can also infect a tremendous variety of organisms from plants to man. It is equipped with a genome more than 30% larger than that of the *E coli*.. 10% of its genome, higher than most bacteria, is devoted to regulation, pump systems. This explains why it has a natural resistance to antibiotics that surpasses all its peers. There is no shortage of chemicals capable of killing the *Pseudomonas* but its 10-12 drug-efflux pump system prevent many from being effective.

Clinically the *Pseudomonas* can often be recognised by its characteristic smell and sometimes its colour in exudates. The *Pseudomonas* does not usually cause primary infections in the community, because it not a virulent organism. But because it is naturally resistant to many antibiotics it is one of the most important opportunistic pathogens causing potentially fatal infections in hospitals. In the compromised host such as patients with burns, major trauma or who are endotracheally intubated it often produces septicaemia, and urine, lung or wound infections. However, often when it is isolated, it may not be the infective organism but only a commensal.

The *Pseudomonas* is a worldwide problem but it thrives better in a warm moist

environment. Malaysia is therefore conducive to its growth and if clinical impressions are correct it more prevalent here than in temperate countries. For the past two decades the aminoglycoside compuonds have been the mainstay of antipseudomonal therapy. However, due to widespread use, resistance has developed to many of these drugs, such as gentamicin, which was introduced in 1963. In these cases amikacin, or the third generation cephalosporins, ureidopenicillins, and newer agents such as quinolones have to be employed. Even then, resistance to these compounds has developed.

In the 1991-2 study of 6 general hospitals, *Pseudomonas aeruginosa* accounted for 8.8% of isolates and other *Pseudomonas spp* accounted for a further 2.5% of isolates. Ceftazidime (6.8%), amikacin (6.2%), imipenam (2.3%) and aztreonam (7.1%) were the only antibiotics which had resistance rates below 10%.

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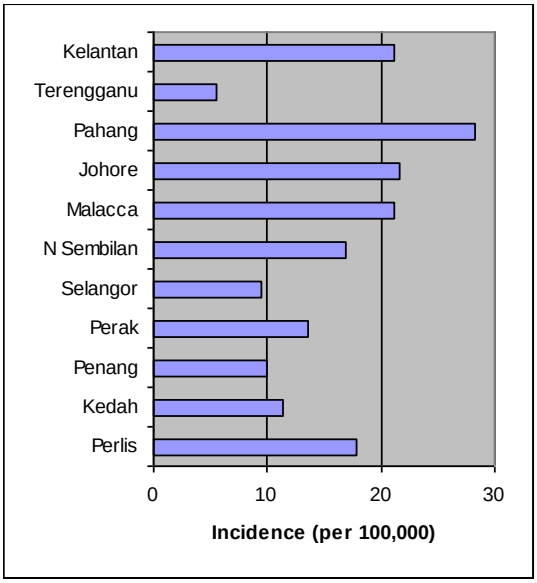
Cheong YM, Lim VKE, Jegathesan M and Abu Bakar S. Antimicrobial resistance in 6 Malaysian general hospitals. Med.J.Mal. 49:317-326 1994.

SALMONELLA

TYPHOID

Typhoid is found all over the world and been clinically described as early as the 17th. century. Eberth was the first to describe the causative agent, *Salmonella typhi* in 1880. Typhoid has long been endemic in Malaysia. Fletcher was probably the first to write about it in 1927. In the pre-antibiotic era the number of cases recorded, which is most probably only a fraction of the real number of cases, rose from about 70 a year in the 1920s to about 800 just before the Second World War. The mortality rate was then between 20 to 40%. In the post-war period up to Merdeka, the mortality rate dropped steadily to about 5% although the incidence of typhoid showed little variation, at about 15 to 20 cases per 100,000 annually, with a total number of between 800 to 1200 cases.

Figure 12.3 Mean incidence rate of typhoid in the various states in Malaysia from 1961-1965



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

In the 1960s typhoid appeared to be common, and outbreaks were prone to occur in every state. But it was mainly a rural problem. Over 60% of patients came from rural areas and just over 65% were Malays. The commonest age group affected were those from 15 to 44 years. Typhoid has a reputation of mimicking other diseases, like malaria. The step-rising-fever, headache, cough, enlarged spleen, change in bowel action and later abdominal complications are classical though other features are reported. Tan has reviewed the clinical features of 100 local cases. Ramanathan and Karim reported a case with life-threatening haemophagocytosis.

In Kelantan, Choo *et.al*. have described the clinical features in a series of 137 paediatric patients who were blood culture positive for typhoid. The commonest features were fever, hepatomegaly, diarrhoea, cough and vomiting. Gastritis, bronchitis, ileus, psychosis, encephalopathy, gastrointestinal bleeding and myocarditis occurred but Rose-spots were rare. A 4-fold rise in 'O' titres occurred in only 50% and if Widal 'O' titres of 1/160 was used for diagnosis, 50% of the blood culture positive patients wound have been missed.

Figure 12.4 Number of typhoid cases in Malaysia

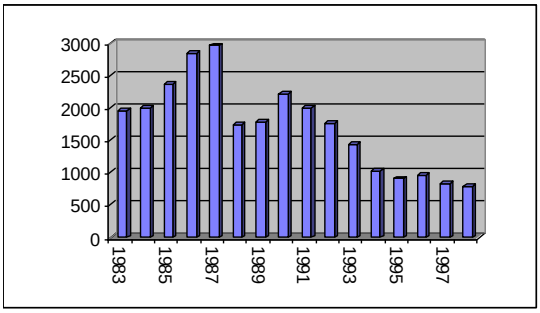
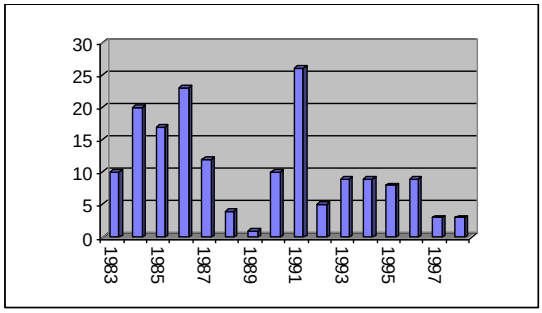


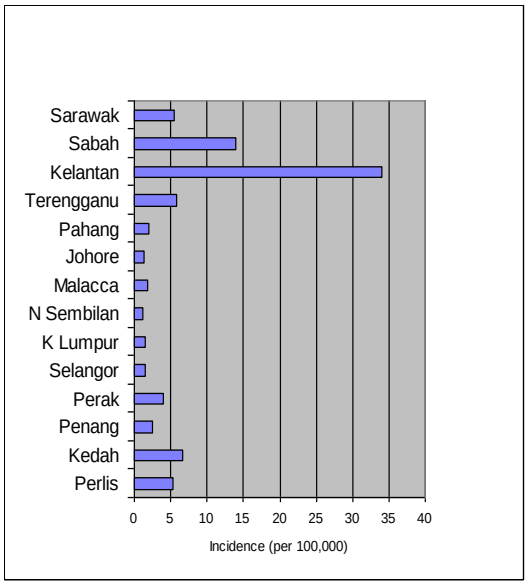
Figure 12.5 Number of typhoid deaths in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Yap and Puthucheary also reviewed clinical features in 54 paediatric patients in the UH in 1998 and reported similar features to that found in Kelantan. They found almost all their patients had a Widal titre of ≥ 1:640 or a fourfold rise in titre.

Figure 12.6 Mean incidence rate of typhoid in the various states in Malaysia from 1992-1996



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Outbreaks today appear less likely to occur than in the past. The number of cases reported annually in Malaysia, including Sabah and Sarawak, ranged from 1,800 to 3,000 in the 1980s and showed a rising trend until 1988 and 1989 when from nearly 3,000 the number dropped rather abruptly to less than 1,600. The number reported continued to drop in the 1990s and since 1995 there have been less than 1,000 cases a year. Kelantan is the state with the highest incidence of typhoid but from time to time outbreaks occur in other states like Penang in 1986 and Johore in 1990.

Bacteriology

In Malaysia, *S. typhi* is the main organism responsible for typhoid. The paratyphoid serotypes are of very little importance. Singh back in 1966 has studied the phage types of *S.*

typhi locally. Jegathesan and Khor reported first finding chloramphenicol resistant strains of *S. typhi* in 1980. Thankfully till now this has never been as widespread as it is across the border in Thailand. 18 cases of typhoid resistant to chloramphinecol occurred in an outbreak in Selangor in 1991. Although investigators did not find a common source for the outbreak, one case was a visitor from Southern India. In 1992 Cheong and Jegathesan reported receiving 13 strains of chloramphenicol resistant from various parts of the country. Pursuing their history they found that 10 of these patients had recently traveled from India or Pakistan, while the travel history of the remaining 3 were not available. 11 of the strains belonged to phage type E1 while 2 strains belonged to phage type O. In view of this, it is important that chloramphenicol resistance be suspected in imported cases of typhoid and that they be properly controlled and notified to the health authorities in order to prevent an outbreak and endemic spread of such strains.

Serology

Workers in HUSM, Kelantan investigated the significance of the Widal test done on 2,382 children investigated for fever in between 1984 an 1987 and concluded that an O and/or H titre value of ≥ 1/40 (sensitivity 89%, specificity 89%) gave the best predictive value. However although a level less than this excluded typhoid well (negative predictive value 99.2% of culture being negative), a positive result at this level was associated with a corresponding positive blood culture in only 50% of cases. By noting corresponding clinical features they felt many typhoid patients would be missed if clinicians relied only on culture.

A rapid dot enzyme immunoassay (EIA) using an outer membrane protein has been found to be as effective as the Widal test.

OTHER SALMONELLOSIS

S. typhi was the first salmonella to be isolated but the list of salmonella serotypes found in Malaysia increased from 23 in 1952 and to 51 in 1966. These salmonella can cause enteric-like fever and they are important also for gastroenteritis (see acute gastroenteritis). They can also cause abscesses, urinary infections cholecystitis and meningitis. But are not very common, making up less than 1% of bacterial isolates in the 6 hospital study. They can also be found in symptomless carriers. UKM investigators reported a prevalence of 0.8% asymptomatic carriers of *Salmonella* spp. among a small sample of pre-school Malay children in Selangor.

Over a 5 ½ year period from 1989, IMR workers found 99 serotypes of *Salmonella* among 6,937 isolates from samples sent to them. The commoest serotypes were *S. weltervreden,* (31.1%) *S. enteritidis* (16.1%), *S. blockly* (9.3%), *S. typhimurium* (5.7%), *S. bareilly* (4.4%) and *S. agora* (4.1%).

In a retrospective review of 131 children with non-typhoid Salmonella gastroenteritis seen in the UH between 1994 and 1996, Lee *et.al*. noticed that infants below 1 year (67%) were most often affected. 7 children had invasive complication: 5 bacteraemia and 2 meningitis. The commonest serotypes isolated were *S. enteritidis, S. paratyphi B* and *S. bovis-morbificans* and almost all were sensitive to commonly prescribed antibiotics.

13 cases of *Salmonella* meningitis was observed by Lee and others from the records of the UH from 1973 to 1997. The patients were between the ages of 3 days to 9 months old. Their symptoms were similar to other bacterial meningitis. *S. enteritidis* was the commonest serotype isolated. The overall mortality was 18% but more than 50% of those who survived had normal long-term outcome. Besides these there were non-typhoid *Salmonella* infections in the blood, urine, synovial fluid, pericardium and

other body secretions in about 85 children at the UH from 1978 to 1998.

Between 1978 and 1998 Lee, Puthucheary and Parasakthi found 98 cases of children admitted to the UH with extra-intestinal non-typhoid Salmonella infections. Bacteriaemia and meningitis were the commonest infections. 50% of the affected children were either severely immunocompromised or had underlying chronic medical disorders.

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SHIGELLA

A number of surveys put the number of acute diarrhoeal cases due to *Shigella* as between 1 to 2%. However, because enrichment mediums are usually not used, the actual figure could in fact, be much higher. *S. flexneri* (about 85%) is the commonest strain, followed by *S. sonnei* (about 15%). Only very rarely has *S. dysenteriae* been isolated. A study in Sabah obtained a similar picture to the Peninsula.

Extraintestinal shigellosis is uncommon. A rare case noted was *S. flexneri* vulvovaginitis in a 3 year old girl.

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STENOTROPHOMONAS

Stenotrophomonas maltophilia has formerly also been known as *Xanthomonas* or *Pseudomonas maltophilia*. It belongs to the low virulent group of bacteria that are highly resistant to antibiotics, that emerge as pathogens only in hospital settings. The important feature of *Stenotrophomonas maltophilia* is that, it has developed resistance to the carbapenems. It has been encountered in intensive care units in Malaysia.

TATUMELLA

Tatumella ptyseos is a newly described member of the Enterobacteriaceae. Studies from the Centre for Disease Control (CDC) USA show that it is chiefly isolated from the respiratory tract, but sometimes also from blood, urine and stools. Tan, Wong, Jegathesan and Chang reported what they believed is the first case in a neonate at GH KL in 1989.

Reference

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VIBRIO

CHOLERA

Man has been afflicted with cholera since antiquity. Although early records are meagre, there is evidence that outbreaks probably occurred in Malacca in the sixteenth century. Being in regional proximity to the Ganges delta, 'the home of cholera' and having trade links with it, Malaysia has been involved in all the seven recorded world pandemics.

In the first pandemic cholera appeared in Malacca in May 1829, two years after the epidemic had ravaged India. We have records of the epidemic from the Durian Daun Hospital in Malacca. It recurred in December that year and continued to February 1830. The disease also appeared in Penang and was said to have been carried overland through Burma and Thailand. Ward and Grant recorded that there were 40 to 50 deaths daily in 1830 mainly among Indians and Malays.

In 1895, according to Rodger, just prior to the installation of the Kuala Lumpur water supply, 126 inmates of the KL prison contracted cholera and, of these 68 died. There was a similar outbreak in the Taiping Jail in 1911.

Sir Hugh Clifford wrote of an episode involving Chinese junks arriving at Port Klang, then called Port Swettenham, in 1896. They had previously been refused admission to port at Deli, Sumatra, due to cholera onboard. With a view to convince the Klang authorities that the junks were no longer carriers of cholera cases, the healthy threw overboard their recent dead, the comatose and many in the early stages of the disease, before reaching Port Swettenham. At this stage, it appears the wind dropped and the current carried the junks into port surrounded by bobbing shark-jostled corpses. It was as if the dead followed silently to accuse the living. Even so, when the seemingly healthy survivors were quarantined on board for six days, a further 57 cases developed and of these, 38 died.

Some history about cholera in Sarawak has also been documented. There was an outbreak in December 1857 in Kuching (the Sarawak Bazaar) that originated from sailors on board a ship returning from Singapore where there had been an outbreak. The Sarawak Gazette in 1873 mentioned an epidemic that year that was also imported from Singapore. Two children of the Raja Brooke also died, possibly of cholera that year though they were on board a ship at sea. The next epidemic was in 1888. Then again in 1902 possibly the most severe outbreak occurred, taking over 1,500 lives. It mainly involved an expedition assembled by the authorities consisting of Dayaks and Malays

who were travelling up the Lupar river to Simanggang to punish a group of Dayaks who were attacking and killing friendly neighbours. After that, small outbreaks occurred only in 1910 and 1911 of only about 100 cases. Following that, it appeare that Sarawak was free of cholera till the *El tor* era.

Since the establishment of the Institute for Medical Research (IMR) in 1900 careful records of cholera have been kept and from time to time reports published. From 1900 to 1927, a total of 2,644 cases, with 1,833 deaths, were recorded mainly from Perak, Pahang and Selangor. Negeri Sembilan appeared to have been relatively free from cholera. In certain years, notably 1910, 1911, 1914, 1918 and 1927, the disease assumed epidemic proportions.

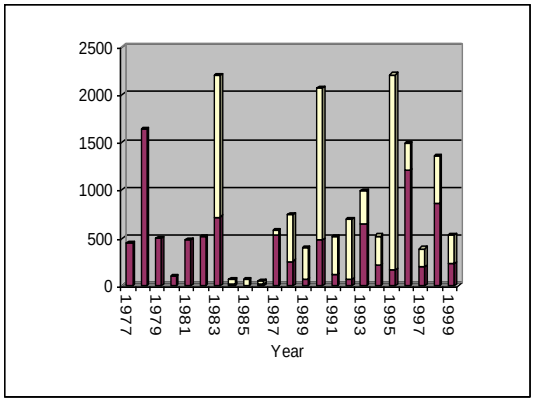
From 1928 the IMR began to produce a cholera vaccine to meet the country's needs. The situation remained calm for a number of years and the next big outbreak occurred only in 1945. Perlis had 287 cases with a death rate of 75%. The following year Kelantan and Terengganu had 221 cases with 182(82%) deaths. From 1947 to 1960, Malaysia was free from cholera.

El Tor Biotype Cholera

Almost like something new, this broke out in 1961. Unlike all previous epidemics which were due to classical *Vibrio cholerae*, this seventh pandemic which started from Sulawesi was caused by *Vibrio cholerae* biotype *El Tor* which has become, in several countries including Malaysia, an endemic problem. Within 4 days of the outbreak in July that year, in a kampong in Kuching across the river from the Sarawak Bazaar 62 cases were found. By October there had been 301 cases. There were over 300 cases in Sarawak over the next 3 years before it waned. Sabah was less affected with just over 40 cases reported in 1961-62.

The *El Tor* cholera first made its appearance in Semenanjung Malaysia in Malacca in May 1963, probably via Sumatra. By July when the outbreak ended, 205 cases had been reported with 14 deaths. Another outbreak occurred in December 1963 and ran on till July 1964 principally in the Northern states of Perlis, Kedah, Kelantan and Terengganu. Over 500 cases were recorded. After a lull of about 5 years Kelantan was hit again in 1969 with 68 cases and 125 carriers. There after its endemic pattern became obvious with cases each year. In the 1970s major outbreaks of over 200 cases occurred in 1972, 1974 and the worst was 1978 with 1,536 reported cases and 62 deaths.

Figure 12.7 Number of Cases of Cholera in Malaysia



(the lighter shade upper portion of the bar shows the contribution by Sabah alone)

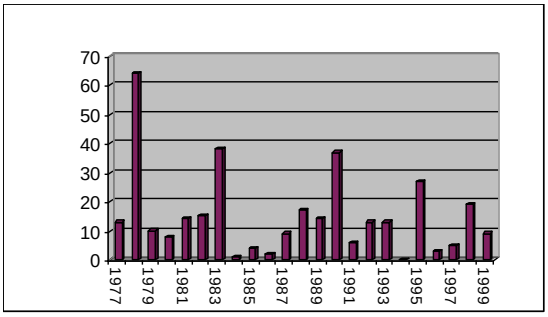
Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Before the annual figures had a chance to come down another huge outbreak occurred in 1983 with 2,195 cases recorded, with Sabah (1,474 cases) the worst affected. It fell to less than 100 cases annually after that. But in 1987 there were 584 cases with Kelantan most affected. 1988 was another bad year with 753 cases mainly in Sabah and also Penang. In 1990 Kelantan again had another outbreak spreading into the neighbouring states. But as Figure 12.7 above shows, in the 1990s Sabah alone accounted for more than half the total

number of cases. Unlike cholera before that was only epidemic, *El Tor* is also endemic because, it is now clear that, it persists indefinitely in aquatic environments indefinitely as free living organisms associated with plankton. It remains in a dormant non-culturalble state but can be detected by DNA studies.

Endemic cholera is largely a rural problem. Outbreaks have tended to occur in the dry season when many are forced to use river water. It more commonly affected adults, aged 20-40 years, engaged in outdoor work. Malays were affected in about 90% of cases. Although tetracycline remains an antibiotic of choice for cholera, tetracycline-resistant strains of *Vibrio cholera El Tor* have been reported in Malaysia.

Figure 12.8 Number of Deaths from Cholera in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

The mortality rate from cholera in the first half of the twentieth century was quite a frightening thing. 60-80% died in outbreaks between 1900 to 1946. From the 1960s onwards however the scourge of cholera has been much less frightening. This is partly due to better medical facilities and treatment these days and partly perhaps to the fact that *Vibrio cholera* biotype *El Tor* is less virulent than the classical *Vibrio cholera*. There were 38 deaths (1.7% of cases) in 1983, a rate which has not been exceeded since.

In the 1990s Sabah has had the most endemic cases of cholera in Malaysia accounting for 50-90% of the notified cases in Malaysia from 1991 to 1995. Immigrants account for the majority of cases, accounting for example, for 60% in the 1990 outbreak. 1995 saw a particularly bad outbreak with 2,046 cases and 26 deaths recorded in the state alone, giving a mortality rate of 1.3%. After that the number of cases reported fell below 300 during the next 2 years, which is lower than figures before the outbreak.

There was however, a bad outbreak in Penang in 1996. The first case was an 11 year old boy from Kg Melayu. Subsequently most cases were from colleges and schools. The bacterium was of the El Tor serotype Ogawa. There were 901 cases and 1 death in Penang and 188 cases in neighbouring Kedah. It was the worst outbreak there in 25 years. Although 1997 saw a decline in cholera cases, cholera broke out again in 1998 following the heels of the dry weather caused by the El Nino phenomenon.

The best safe guard against cholera is vigilance and quick action to contain any outbreak. With cross border travel widespread today Malaysia will not be totally free from cholera the next decade at least but prompt health safety measures can keep the impact of outbreaks to a minimum.

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Hassan H and Teh A. Tetracycline-resistant Vibri6o Cholera El Tor. Med.J.Mal. 48:95-96 1993.

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and Annual Reports. Kementerian Kesihatan Malaysia.

PARAHAEMOLYTICUS

This Gram-negative motile rod is one of the causes of gastroenteritis, albeit responsible for less than 1% of such cases (see acute gastroenteritis). Puthucheary reported isolating 7 strains in the course 1972 and has collected at least 40 strains. It is thought to be associated with eating fish.

Reference

Puthucheary SD. Vibrio parahaemolyticus gastroenteritis in Malaysia. Med.J.Mal. 28:44-46 1973

YERSINIA

ENTEROCOLITICA

Yersinia enterocolitica has joined the growing list of organisms implicated as gastrointestinal pathogens but it has gained prominence mainly in the temperate zone. Studies in the tropical regions suggest that it is very low in incidence. One case has been reported in Malaysia in a female Indian estate worker in Selangor.

Reference

Jegathesan M, Paramasivam T, Rajagopalan K and Lim KL. Yersinia enterocolitica infection: first case report from Malaysia. Trop.Geogr.Med. 36:207-210 1984

PLAGUE

Yersinia pestii, isolated in 1894, is infamous in the West as the cause of Bubonic and pneumonic palgue. As the Black Death in the middle ages it decimated the population of Europe. As such it was on the mind of physicians in Malaysia from the start. Although records of prevailing diseases are available in the Federated States from 1890 plague was not reported till 1901 when there were 5 fatal cases. There was never a high incidence of plague but it was always accompanied by a high case mortality.

Plague was probably brought by immigrants from China. In 1912, the IMR carried out investigations following the occurrence of some plague and rat plague in KL. It was thought that plague was unlikely to occur in endemic form the common as domestic rat and the common rat flea were both small and unlikely to be good zoonotic hosts. This appears to have been proved correct as since 1923 there have not been cases of plague.

CHAPTER 13

MYCOBACTERIA

The mycobacteria are a family in the order of *Actinomycetaceae*. They are the most important pathogenic members in this order and leprosy, tuberculosis and the atypical mycobacteria are well known diseases and are discussed below. Another notable member of this order is the *Streptomycetaceae* family from which penicillin was obtained. The other organisms in this order that are pathogens are the *Actinomyces* and *Norcadia*. These 'higher bacteria' are more often discussed with fungal infections and they have been assigned there in this book.

"ATYPICAL" MYCOBACTERIA

The designation 'atypical' mycobacteria is commonly used to describe mycobacteria other than *Mycobacterium tuberculosis* and *M. leprae*. Of 61 strains isolated at the IMR from 1979 to 1982, 28 were *M. avium-intracellulare.* Almost all were isolated from sputum. There were 16 strains of *M. fortuitum*, 8 of *M. chelonei* and 4 each of *M. scrofulaceum* and *M. gordonae*. Chronic pulmonary disease resembling tuberculosis is the most important problem associated with atypical mycobacteria. A case of meningitis has also been reported. These mycobacteria may be resistant to a large number of anti-tuberculous drugs.

In the IMR series *M. marinum,* which is known to cause swimming pool granulomas, was not isolated. Neither was *M. ulcerans*, which causes Buruli or Bairnsdale ulcers. *M. marinum* though, has been isolated by Chu and Soo-Hoo from a skin lesion of a Chinese hawker who was also a fish fancier. *M. ulcerans* has been isolated by Pettit, Marchette and Rees in 1966 at the Sungai Buloh Research Unit in 3 out of 5 suspected cases. Pettit also diagnosed 3 cases later in 1976 at the Gombak Orang Asli Hospital.

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Khor SY and Jegathesan M. Isolation of atypical mycobacteria from clinical material in Malaysia. Med.J.Mal. 38:158-160 1983.

Chu SM and Soo-Hoo TS. Mycobacterium marinum infection treated with cotrimoxazole. Mal.J.Derm. 1:20 1987.

LEPROSY

The reader interested in the history of leprosy in Malaysia ought to refer to the excellently researched book by Joshua-Raghavar. It would be hard to rival his comprehensive coverage for the disease.

Historians generally believe that leprosy is a very old disease although in the past the word leprosy or 'lepra' or its Indian equivalent 'kushtha' which gave rise to the Malay word 'kusta' may have been used to describe all sorts of skin lesions, probably including malignancies, and not only what we now term Hansen's disease. Leprosy has been perhaps the most badly misunderstood disease for a long time and leprosy patients have suffered much for it.

There are pointers to suggest that leprosy was present in Portuguese occupied Malacca but it is not conclusively evident. The earliest leprosy is specifically mentioned is during the early days of the British Straits Settlements. As early as 1828, the Senior Surgeon's report to the Governor had proposed isolating leprosy sufferers found in the Penang Settlement on the smaller island of Pulau Jerejak. However it was on Pulau Serimbun, off Malacca, that the first 'leper colony' in Malaysia was founded in 1850.

The Era Of Segregation

Leprosy was perhaps one of the diseases that health authorities and administrators were most aware of in the early days of the Straits Settlements. Sufferers were frequently unsightly and economically incapacitated and as such formed the very poor in the migrant population of Chinese, who were rising rapidly in number from the 1820s onwards. It was the health threat that leprosy patients posed that influenced the establishment of 'Pauper Hospitals' in Penang and Singapore, and also the Tan Tock Seng Hospital in Singapore. At the latter it was reported that in the year 1850, 451 patients had been treated, 26 of whom were listed as suffering from leprosy of whom 7 died. There was however still a strong desire in the Strait Settlements to remove all leprosy sufferers "out of sight".

Pulau Serimbun, which was started by the local authorities in Malacca had 21 patients in 1862. It impressed the Senior Surgeon visiting it who found patients "cheerful and contented" and "passing their time fishing and cultivating vegetables". It was perhaps this success that led to the establishment of Pulau Jerejak, off Penang as a leprosy asylum in 1871. Soon it became the centre for all the Strait Settlements supplemented only by collecting stations in Singapore and Malacca. By law, it was made compulsory for leprosy patients to be detained.

Dom Sauton who visited Pulau Jerejak in 1900 quoted the number of lepers at this centre as 280. In 1906 Jeanselme, another visiting French leprologist gave the number as 495. By 1926 when the Brazillian leprologist de Souza Araujo visited the population had risen to 700, and in a year there were some 217 admissions and 201 deaths. As Pulau Jerejak was solely for men there was a female camp at Jelutong in Penang which had 40 inmates in 1926. As for the situation in a 'Collecting Centre' de Souza Araujo wrote; "96 were admitted in 1924, of whom 77 were transfered to Penang, 6 escaped, and 12 died, thus remaining 48". It is clear that treatment for leprosy was not done on a voluntary basis.

With the British influence extending over the Malay states after 1874, and the passing of government enactments on the detention and isolation of known leprosy patients, there came too the establishmant of isolation centres for these states. In KL this was at Setapak (1900) which benefited by being close to the IMR. As a result the staff there such as Travers developed an interest in treating leprosy patients. In Perak, Pulau Pangkor Luat became a centre in 1903 and Tampoi and Tumpat became centres for Johore and Kelantan respectively. Each of the states could count about 100 new cases a year. Many were transferred to Pulau Jerejak leaving only about 20 in each of these places, except Setapak which was a big centre.

A new approach to the treatment of leprosy came with the establishment of the Sungai Buloh Settlement in 1930, which resulted from Traver's idea of a self-contained settlement. It replaced the Setapak and Pangkor centres.

The End Of Segregation

In 1930 it was estimated that there were 1,200 leprosy patients in the Straits Settlements and about 1,600 more in the Federated Malay States and most were in detention centres. Following an editorial in the Malayan Medical Journal in 1931 the matter of compulsory segregation was featured in the newspapers and became a matter disturbing public conscience.

Armaur Hansen of Norway isolated the 'lepra bacillus', now called *Mycobacterium leprea*, in about 1872. Following that, St. Maur Mouritz experimented with inoculating healthy persons with the mycobacterium in Hawaii in 1885 and they failed to be infected. This led to knowledge that leprosy was in fact very lowly infectious. However, it took years before this became widely known and accepted. It was said that in places like the Philippines that the

policy of isolation actually showed no evidence that it reduced the incidence of the disease. It was also pointed out that tuberculosis was at least 5 times as infectious and carried a higher mortality rate yet tubercular patients were not segregated. As a result of the airing of views, provisions for domiciliary treatment and voluntary segregation were implemented by 1933.

Unlike Sungai Buloh which was designed as a treatment centre Pulau Jerejak was from early on a rather over-crowded detention centre and showed comparatively higher death rates. But from the late 20s to 1940 renovations on the island brought gradual improvements to the outcome of patients there. As the mortality of leprosy dropped everywhere, overcrowding became a problem in both centres. Ryrie estimated that in 1935 there were 443 new cases, with a combined population of about 2,000,000 in the peninsula this gave an incidence of 1:5,000. The death rate which was a staggering 20% annually in the 1920s had dropped to 0.3% in 1935. Thus the population of Pulau Jerejak grew to 1,315 in 1939 and Sungai Buloh to 2,178. Adding to this the number in other centres and patients either discharged or absconded there were about 5,400 known leprosy patients just before the war.

The Second World War which hit Malaya very suddenly had an equally sudden impact on the treatment of leprosy. It led to drastic reductions at both leprosariums. A large number of patients were dispersed to their homes. Those who remained behind were in later stages, reduced to eating tapioca and snails. The death rate climbed back up to 30% though not due to leprosy *per se*. Ryrie who remained behind to work was later interned by the Japanese in 1943 and for health reasons was repatriated prematurely after the war. At the end of the war there were 640 left at Sungai Buloh and 360 at Pulau Jerejak.

However, by 1946 the number at Sungai Buloh had climbed back to 1,229 and was 2,401 in 1954. The Pulau Jerejak centre however, was never revamped but carried on till 1969 when it was closed and made a prison centre.

The Sulphone Era

Before the sulphones, Travers who worked at Setapak had tried the Chinese remedy called Tai Fong Chee and from 1922 made it the routine. Ryrie who succeeded him at the Sungai Buloh Centre studied several agents including aniline dyes. But the big impact on leprosy treatment was by the drug diamino-diphenyl-sulphone or dapsone from the U.S.A. It began to be used locally from 1948 and slowly displaced other agents.

This era was also one of much research from the Sungai Buloh "Research Unit". Going back in time the first treatise on leprosy in Malaysia was probably that written by Anderson who had been stationed in Malacca. He published a monograph entitled "Leprosy as met with in the Straits Settlements" containing "coloured photographs"! and "explanatory notes" in 1872. Ryrie, before the war, had built up a foundation for research and from it the "Research Unit" was set up in 1950. In the next 30 years many clinical drug trials, immunological investigations, work on drug resistance and other studies established a worldwide reputation for the centre.

In this post-war period it was estimated that there were about 3,800 leprosy cases in Peninsula Malaysia out of a population of 4,877,678 in the 1947 census. As before Chinese constituted the majority making up 75-80% of the total. Males outnumbered females in a ratio of more than 3:1. This figures however do not take into account the large undiagnosed pool, hence the true prevalence is not known.

Although segregation was no longer compulsory the authorities still continued to treat most leprosy patients in leprosaria. From new admission figures it is estimated that the

number of patients increased to about 6,000 in 1957, of whom 3,357 were in the various leprosaria. Sungai Buloh, the largest had 2,435. The remainder was estimated from the number previously discharged. As segregation was more and more discredited, out-patient clinics for leprosy treatment were opened, beginning in Penang in 1955. But it was only towards the end of the 1960s that treatment of leprosy was fully integrated into the country's medical and health services.

A Leprosy Control Programme

In 1969, Malaysia launched the National Leprosy Control Programme in the Peninsula. The programme was extended to Sarawak in 1974 but Sabah was included only in 1984. The Sungai Buloh Settlement was also re-designated The National Leprosy Control Centre in 1969. With the programme, came the registering of patients and valuable epidemiological data was obtained for the first time. Starting with follow-up cases at all clinics a total of 5,033 were registered first. In 1975, for West Malaysia 8,199 cases had been registered giving a prevalence rate of 78 per 100,000. However, from a sample survey in 1963, a WHO consultant had estimated that the pool of leprosy cases could have been as large as 15,000. For Sarawak, there were 578 cases in 1975 and a prevalence rate of 52 per 100,000. In 1984, 1,099 cases had been registered which gave Sarawak a prevalence of 84 per 100,000 but it was estimated that two others remained for every one reported case.

Registration showed that in West Malaysia, 56% of patients were Chinese, 33% Malays and 10% Indians. Others formed 1%. In Sarawak, 40% were Chinese, 32% Ibans and 17% Malays. In age distribution, 54.5% were between 15-44 years old. 40% were above 45 years and children under 15 accounted for 5.5%. About 45% had lepromatous leprosy. 13% were borderline, 40% were the tuberculoid type and 3% indeterminate. The proportion of lepromatous leprosy was higher in Sarawak being 60% and nationwide the proportion of lepromatous disease is becoming more common latterly.

From 1970 it could be seen that the number of registered cases began a downward trend from above 400 down to just below 300 annually in Peninsula Malaysia in 1980. From a detection rate of 3.8 per 100,000 in 1969 it fell to 1.4 per 100,000 in 1989. In Sarawak the number of cases on the register began to decline in the 1980s. In Sabah an epidemiological study in Tawau in 1983 found the prevalence rate to be 160 per 100,000. In 1987 there were 375 cases registered for Sabah but the incidence rate was high at 7 per 100,000.

Leprosy Today

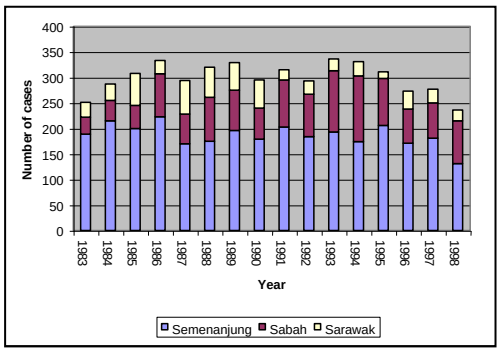
The target of the Leprosy Control Programme, and the WHO target for elimination of the disease, is to achieve an prevalence rate of less than 1 per 100,000. Although overall Malaysia reached that target in 1994 immigrants who constitute a significant proportion of cases in places like Kuala Lumpur and Sabah push the incidence and prevalence rate up. In 1995 30% of new leprosy cases were among immigrants. The Orang Asli also remain at high risk for leprosy and have a prevalence rate more than 20 times higher than the general population in 1995.

The number of registered case in Sabah which ranged from 400 to 440 began to decline in the 1990s. In 1995 the number was 332 and has come down to 232 in 1998.

With a total of 1,125 cases in Malaysia in 1998 the prevalence rate was 0.5 per 100,000. Sabah has a prevalence rate of 0.8 per 100,000 and ironically it is only Kuala Lumpur with a prevalence of 1.2 per 100,000 that was above the WHO target. Among new cases reported 37% were the non-infectious indeterminate and tuberculoid type of leprosy and 63% were the infectious borderline or lepromatous type of

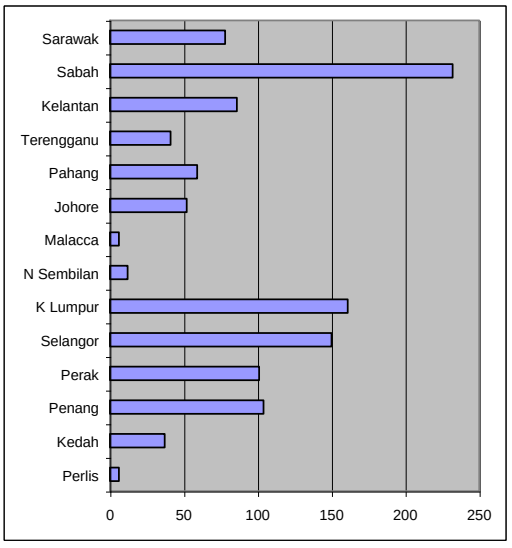
leprosy. Only 3.9% of new cases in 1998 were children, a decline from 10.8% in 1996 and 6.4% in 1997, which is an indication active transmission in the community is declining.

Figure 13.1 Number of new cases of leprosy reported in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Figure 13.2 Number of registered leprosy cases by state in 1998.



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

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TUBERCULOSIS

Writing in the Malayan Medical Journal and Estate Sanitation in 1926, the editor said that unlike the appalling spread of tuberculosis in Europe that decimated the population, tuberculosis was not a great scourge in Malaya, taking a back seat to malaria. He remarked that Malaya then was one of the most thinly populated countries in the world and over-crowding and industrial life that facilitates transmission of tuberculosis was not prevalent. However he described how these unsanitary conditions were growing in the big towns like Kuala Lumpur. As a matter of fact, in the Strait Settlements hospitals between 1920 and 1924 tuberculosis had become the leading cause of death, replacing malaria, although in number of admissions malaria cases was about 5 times as many. Furthermore, whereas malaria was declining, tuberculosis was rising.

A Major Public Health Problem

At about the time of independence several people took cognisance of the fact that tuberculosis had become the major cause of death in Malaysia. Case finding studies put the prevalence at 1% to 3% of the population. That meant that there were 70,000 to 210,000 people living with tuberculosis. The number of deaths from tuberculosis had risen from about 700 in

the 1920s to become the biggest killer in the country, causing more than 5,000 deaths a year, which was about 7% of all deaths. It was the public health problem in the 1960s.

About 25,000 new cases of tuberculosis appeared a year, which meant that for every death five new cases swelled the ranks of the 70,000 to 210,000 already prevalent. It was estimated that of these only about 40,000 cases were undergoing treatment which had a success rate then of 60%.

So large was the pool of infectious cases that one child in every four got infected with tuberculosis before the age of 5 years. By the age of 15 years three out of four were found to be infected, fortunately though, not all these developed the disease.

Although tuberculosis is usually a disease of townsfolk, in Malaysia it was found that our rural areas were affected almost as seriously as our towns. The kampong folk in Kedah, Kelantan and other East coast states had a prevalence as high as in the towns. Even the Orang Asli had a prevalence as high. Malays, Chinese, and Indians contracted this disease with equal facility and spread it as readily as they contract it.

The National Tuberculosis Control Programme

1951 was a landmark in the history of tuberculosis in Malaysia. It was the year the BCG campaign began. It was well received by the public and slowly increased in momentum. Nevertheless it was brought to light that the colonial health authorities had actually failed to appreciate the reports and recommendations about the gravity of tuberculosis then and that tuberculosis patients had come to occupy more than 25% of the hospital beds and consumed almost 10% of the total health budget. Furthermore the prevalence of the infection among children was alarmingly high.

With Merdeka came a sense of responsibility on the part of our own government for tuberculosis control which became a political issue included in the Alliance Party election manifesto. The post for a Senior Tuberculosis Specialist was created and WHO advice was sought. In 1961 the National Tuberculosis Control Campaign was launched. In the same year the National Tuberculosis Centre was opened.

The campaign consisted of a three-pronged attacked. One was a training programme to equip the health services with the technical personnel required, such as chest specialists, nurses, mass X-ray operators, and laboratory technicians. Second was a B.C.G. vaccination drive aiming to protect at least 75% of the population below 20 years. Finally there was a case-finding drive including miniature chest X-rays with a target of detecting at least two-thirds of the infectious sources and rendering at least 95% of them non-infectious with adequate treatment.

In Sarawak, a similar but separate Tuberculosis Control Project was also started in 1961. In Sabah, the tuberculosis control programme began in 1960. These programmes were later integrated into the national programme in 1969 and 1979 respectively. Though tuberculosis was a very serious health problem in East Malaysia it did not reached the proportions it did on the peninsula. In Sabah for example, in the early 1960s the picked up incidence was about 2.5 per thousand population or 1,300 cases a year.

Tuberculosis Under Control

After one decade, in 1970, the number of tuberculosis deaths had dropped to 1,069 or 12 per 100,000. The prevalence rate was estimated at 0.3% or 300 per 100,000.

In 1986, 25 years after launching the National Tuberculosis Control Campaign, there

were 320 deaths from tuberculosis in Peninsula Malaysia, a rate of 2.4 per 100,000. It was estimated that there were 37,162 cases; 28,300 in the peninsula, 4,950 in Sarawak and 3,912 in Sabah. The campaign target of 75% B.C.G. coverage was achieved and exceeded. Over 90% of children all over Malaysia were immunised. However, the case finding fell short of the targeted calculated incidence of the disease except in Sabah. The actual number of cases detected was 3,945 in the peninsula, 963 in Sarawak, and 1,774 in Sabah. A disconcerting observation that emerged was that a large proportion of sputum positive cases (over 80%) were moderate to far advanced stages. Treatment completion also fell short of the 95% targeted. The risk of infection for the population was now less than 1%.

Although tuberculosis has ceased to be a menace it once was it still accounted for much morbidity. Besides the pulmonary disease, practically every part of the body causing illness in a host of different ways. Local reports of the protean clinical manifestations of tuberculosis would be hard to enumerate. Hooi reports in an audit that the diagnosis of tuberculosis was made after death in 17 out of 54 patients in 1993. It was the cause of death in 29 of these 54 patients and a contributory cause in 8 more. Only 41% of deaths from active tuberculosis was correctly certified. Thus the reported death rate of 4.6 per 100,000 for tuberculosis in Malaysia is probably lower than the actual figure.

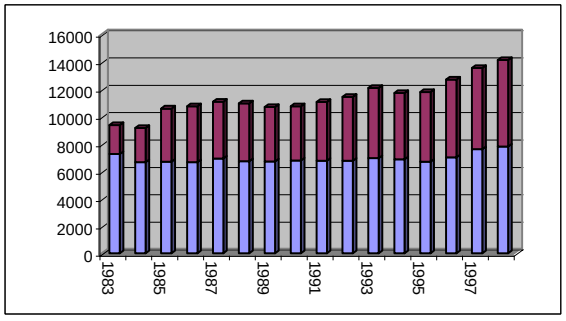
Caseating regional lymphadenitis is a recognised adverse reaction following BCG vaccination of newborn children. An outbreak of this occurred between August 1990 and late 1992. It was documented by Hooi in Penang where 638 infants were recognised in 317 of whom the nodes became suppurative. This was because the strain of BCG used for mass vaccination was changed from the Japan freeze-dried to the Pasteur strain in May 1990. As the change in vaccine affected the whole country thousands of infants were actually affected and could have shaken public confidence in the vaccination programme. The problem was eventually solved when the National Tuberculosis Control Programme changed the vaccine back to the Japan strain in April 1992.

The Re-emergence Of Tuberculosis

All over the world tuberculosis has made a comeback at the end of the twentieth century. It is estimated that of the world's 6 billion population, one third, or 2,000,000,000 people are infected with tuberculosis and that globally tuberculosis causes 3,000,000 deaths annually, or 26% of all avoidable adult deaths. In 1993 the WHO declared tuberculosis a "global emergency". Unfortunately one does not get a sense of this urgency in the popular media. But tuberculosis once earned and should still be remembered as "the captain of the men of death".

Figure 13.3 Number of All forms of tuberculosis (whole bar) and infectious cases (lower part of bar) reported in Malaysia

Source: Information and Documentation System Unit, Ministry of Health, Malaysia



In Malaysia the incidence of tuberculosis in 1997 was 64 per 100,000 and had been holding steady the past 10 years. It is some consolation that the incidence has not risen but it falls short of the target of getting the incidence down below 40 per 100,000. That number in 1997 translates

to 13,539 cases, 57% of which were the infectious form. Sabah (28%) and Sarawak (13%) are the states that account for the most cases, followed by Kuala Lumpur (11.5%). The incidence rate in Sabah runs about 4 to 4.6 times as high as in the Peninsula. The incidence in Sarawak is 2 to 2.6 times that of the Peninsula. Among changes in pattern the recent years has seen are, the 20-45 year old age group now outnumber the over 45year old group who used to be the majority. Males outnumber females nearly 2:1. Tuberculosis with HIV co-infection first appeared in 1990 with 6 cases. By 1997 this had risen to 322 cases with 63 deaths accounting for 9.3% of all tuberculosis deaths. One ominous figure about tuberculosis in Malaysia is the number of deaths and the death rate from tuberculosis has risen over the last decade (figure 13.4).

1,767 tuberculosis patients in 1997 were foreigners, 908 were detected by the agency monitoring foreign workers in 9 months. TB meningitis is declining accounting for 0.4% of tuberculosis cases in 1997. The incidence of tuberculosis remains high among the Orang Asli, being 237 per 100,000 in 1997 in Perak, 5 times higher than the general public there.

Tuberculosis is still a diagnosis doctors must always bear in mind in all unusual illnesses. A commonly used test to help confirm the diagnosis in a doubtful case is the Mantoux tuberculin test. Its value though, remains uncertain. In a study to evaluate its local profile, Ismail and Zulkifli reviewed 468 suspected tuberculosis cases in HUSM. They found that it was fairly sensitive, in that 86% of patients with active tuberculosis had positive reactions but not specific, as 42% of those positive did not have active tuberculosis. From astudy of cohort of student nurses Jeyakumar has suggested that a tuberculin reaction above 20mm warrants preventive therapy. Advanced untreated cases are more common in the less developed areas like in Kelantan. Improved living conditions and better sanitation the are most important measures to further stem the disease and ensure that recrudescence does not occur.

Drug Resistance

In any population of *M. tuberculosis* there will be mutant strains resistant to one or more anti-tuberculous agents. Workers at the National Tuberculosis Centre found 14.2% of isolates resistant to one drug and 1.97% resistant to two drugs from a sample of 856 strains from previously untreated patients from various states in Malaysia between 1984 and 1987. No strain was resistant to 3 or more drugs. This rate of resistance is relatively high and underlines the need for vigilance and monitoring for the development of multi-drug resistant strains.

Jeyakumar has described the alarming case of one patient who was discovered to have sputum positive tuberculosis in 1992 and treated with streptomycin, isoniazid, rifampicin and pyrazinamide. Although his sputum remained positive after 2 months he remained on the standard regime for 11 months after which ciprofloxaxin was added. A culture reported resistance to streptomycin and isoniazid, but sensitivity to rifampicin, ethambutol, kanamycin and cycloserine. In 1994 he was changed to enviomycin, clofazimine ethambutol and rifampicin. He became sputum negative after 2 months but returned strongly sputum positive in another 3 months. He had 2 more changes to his therapy. Resistance to streptomycin, inoniazid, rifampicin and ethambutol was noted. He became very ill in December 1994 and was started on 7 drugs. He was given an irridiation killed *Mycobacterium vaccae* vaccine. He became sputum negative but relapsed in October 1995. He was given another set of 7 drugs but remained sputum positive but fairly asymptomatic. In 1996 he spent a spell of 7 months in Sabah. Sensitivity testing revealed resistance to isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin, kanamycin, amikacin, capreamycin, ethionanamide and clarithromycin but the strain was sensitive to rifabutin, cycloserine, clofazimine and

thioacetone. He was started on another 7 drugs in April 1997 and became sputum negative after 3 months and remained so till last reported in October 1997. The possibility of that this strain of bacteria has spread, which it probably has, is indeed distressing.

Some Unusual/Notable Clinical Features

Tuberculosis occasionally mimicks cancers. Lee reported a patient with laryngeal tuberculosis looking like a carcinoma. Sharma *et.al*. noted a case of chronic granulomatous pharyngeal tuberculosis like that and Pan and Ibrahim, a case of tuberculosis of the distal end of the radius looking like a giant-cell tumour.

Loke reported a young man with tuberculous pneumothorax and an oesophago-pleural fistula. He refused any surgical procedure but was treated with anti-tuberculous chemotherapy. The fistula apparently healed. There has been case reports of tuberculosis causing a liver abscess and presenting with recurrent pancreatitis.

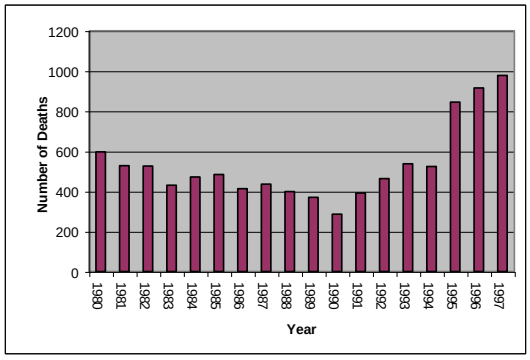
Reviewing radiological manifestations of tuberculosis among 71 patients, Rathakrishnan and Mohd have reported unusual findings of sclerotic bone reactions and periosteal new bone formation. Razak *et.al*. have noted that tuberculosis accounted for 84% of their cases of spinal infection at UKM between 1993 and 1998.

Occasionally patients with tuberculosis present themselves in hypercalcaemic crises as in case of a young man who had a with abdominal tuberculosis reported by Ramanathan and a woman with mediastinal lymphadenopathy reported by Tan. Liam and colleagues at the UH noted that 27.5% of 120 patients with tuberculosis, mainly of the lung and pleura, had hypercalcaemia, although only about half of these showed symptoms of hypercalcaemia. Tan *et.al*. on the other hand reported that in 43 of their newly diagnosed cases only one (2.3%) had hypercalcaemia.

Compliance to therapy

Chuah has looked at factors that affect compliance to anti-tuberculous therapy in 219 patients in Taiping in 1991. Patients with tuberculous adenitis alone especially if male were more likely to default. Patients treated as outpatients from the beginning were more compliant, as were housewives. Patients who defaulted, tended to default early. In the UH Liam reported that only 68% of 118 of their patients treated between 1994 and 1996 completed the full course of tuberculosus treatment.

Figure 13.4 Number of Deaths from Tuberculosis in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

A cohort analysis of patients put on treatment from 1995-1997 by the Ministry of Health showed that 83% were cured, 9% abandoned treatment and 8% died. The defaulter rate in Sabah however, is twice as high that of the Peninsula but this is not the case in Sarawak. Figure 13.4 shows deaths from tuberculosis but these are only cases who died while on treatment. The fate of defaulters are not known and those considered cured might succumb years later with tuberculosis as a contributing factor.

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CHAPTER 14

FUNGAL INFECTIONS

Haeckel in 1866 proposed that microorganisms be placed in a separate taxonomic kingdom from animals and plants. From this arena bacteria were again separated as the kingdom **Prokaryota,** as they were found to be quite different in that they lacked a nucleus. The remaining microorganisms that Haeckel included, which are eukaryotic, namely the algae, fungi and protozoa are now generally regarded as the kingdom **Protista**.

Fungi are non-photosynthetic protists that grow as a mass of branching, interlacing filaments. Many fungi cause plant disease, but only about 100 of the thousands of known species cause human or animal disease.

Actinomycosis and nocardiosis, that can be grouped with higher bacteria, as they are prokaryotic. They are listed here as pseudomycotic infections as they commonly are in medical microbiology. It is however important to remember that they are actually bacteria because when it comes to therapy, we use antibiotics and not the antifungals in such cases. Absent in this chapter are fungal infections so far not seen in Malaysiae including, Blastomycosis, Coccidiodomycosis, Mucormycosis, and Paracoccidiodomycosis.

PSEUDOMYCOTIC INFECTIONS

ACTINOMYCOSIS

Reports of *Actinomyces israelii* and *A. naeslundii* which usually cause chronic multiple draining sinuses in Malaysia are rare. The cervico-facial form has been reported following third molar surgery. Two rare cases of involvement of the spine has been documented. Other unusual case reports include a case involving the breast, a case presenting with a mass in the lung and a case with empyema thoracis.

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NOCARDIOSIS

The granulomatous form of the disease has been reported probably only once in our local medical literature. The patient from Jerantut was seen by Gangaram, Suraiyah and Rajagopalan. He had had a discharging sinus from his left leg for 1½ years and was successfully treated with rifampicin and cotrimoxazole.

Pulmonary nocardiosis has also been documented in one man, a 69 year old Tamil in Klang by Ponnampalam in 1963. The agent, *Nocardia asteroides* was cultured from his sputum on a Lowenstein Jensen medium. Lee *et al*. reported a child with hyperimmunoglobulin E who developed pulmonary nocardiosis and succumbed to the disease in 1999. *Norcadia brasiliensis* has been grown from pus obtained from needle aspiration in a 24 year old man with Hodgkin's lymphoma in the same lung. In another unusual case the fungus was found in a patient with pan-opthalmitis.

As might be expected, nocardiosis might occur more frequently among the immunocompromised. Kong *et.al*. recorded 5 cases over nearly 13 years in the GH KL Nephrology units. 2 were patients with systemic lupus erythematousus, 2 were post-renal transplant patients and 1 was a patient with glomerulonephritis. Tan *et al*. reported a renal transplant recipient with disseminated nocardiosis in the year 2000.

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MYCOTIC INFECTIONS

ASPERGILLOSIS

After candida and crpytococcus, aspergillosis is probably the third most frequent fungus to cause systemic mycosis. Usually, the immunocompromised and those with chronic lung infection are affected. In particular, in Malaysia aspergillosis is to be found in tuberculosis patients. But aspergillosis does not seem to occur as frequently as one might expect in view of the prevalence of tuberculosis locally. Arianayagam, Jayalakshimi and Soon in reviewing 79,363 pathological specimens at the UH from 1972 to 1984 found only 3 cases of pulmonary aspergillosis.

Teoh Yow and Soo-Hoo have reported aspergillus causing keratitis in a patient. A case of orbital abscess due to *S. aureus* and aspergillus complicating ethmoiditis in a neonate has also been reported. Ng *et.al*. reported that molds, predominantly aspergillus, accounted for 35.5% of fungal nail infections. Chin and Jegathesan found it to be the commonest fungus in otomycosis.

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BLACK PIEDRA

Black piedra is an infection of the hair shaft by the ascomycete fungus *Piedra hortai*. It consists of hard dark brown to black nodules 5-10mm in size found at intervals along the hair shaft confined to scalp hair and is known indigenously as 'rambut berbuah'. It was first described by Niven in a Caucasian residing in Malaya in 1936. Adam observed 31 cases in medical students, their relatives, nurses and a few patients, most of whom were unaware of the nodules on the scalp hair. Some were aware of it present in at least 3 generations. 28 of those affected were Malays. The other 3 (2 Chinese and 1 Indian) were medical students who developed the condition while sharing rooms with other students. Those who were aware of the condition, had entire families affected, but

did not seek medical treatment as the fungus caused minimal damage to the hair. The fungus does not penetrate beyond the cuticle of the hair shaft. Infection can be eradicated by keeping the hair short and dry.

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CANDIDIASIS

The yeasts *Candida* is commonly seen causing oral thrush in infants and vaginitis in females. In the compromised patient it can become a life-threatening illness. In one UH study *Candida albicans* accounted for 64% of yeasts isolated for vaginal swabs. Ngeow *et.al*. in a survey of women attending a the gynaecological clinic in GH KL found that the prevalence of *Candida albicans* was 25% (41/164) in women with a vaginal discharge and 9%(17/188) in women without a complain of discharge. In a survey of 2,153 women they found *C albicans* was more common in pregnant women; 27% in those with vaginitis and 14% in those without. In non-pregnant women 15% of those with vaginitis and 3% of those without had *C albicans* isolated from vaginal swabs.

Among yeasts isolated from sputum specimens of patients suspected to have fungal respiratory infections in the UH in 1989, *Candida* species accounted for over 95% of isolates, chiefly *C. albicans* (76%) and *C. tropicalis* (13%). In yeasts isolated from urine these were also the commonest species accounting for 49% and 22% respectively, in one study. The clinical conditions in which yeasts were found in urine included, urinary infections, diabetes mellitus, patients with indwelling catheters, post-operative patients, renal disorders, acute leukaemia, and burns. In 1998, 9 species of *Candida* were identified among 1,114 isolated in the UH. They were *C. albicans* (44%) *C. parapsilosis* (26%), *C. tropicalis* (18%), *C. glabrata* (9.6%), *C.krusei* (1.2%), *C.rugosa* (0.6%), *C. guilliermondii* (0.2%), *C. lusitaniae* (0.08%) and *C. kefyr* (0.08%). *C. albicans* was most common in vaginal swabs. Non- *C. albicans* species were more common in the blood, respiratory tract, urine and skin.

A case of **chronic mucocutaneous candidiasis** has been reported by Noh *et.al*. with an unusual and novel immunodeficiency state. The patient had a subpopulation of CD2-/CD3+ abnormal mononuclear cells. Immunodificiency results when there is a failure of the CD2-pathway in activating T- lymphocytes. The girl subsequently developed disseminated tuberculosis and toxoplasmosis.

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CHROMOBLASTOMYCOSIS

Chromoblastomycosis or verrucous dermatitis is caused by a number of species of fungi. *Phialophora verrucosa* and some other species of that genus and *Cladosporium carionii*

are the most common. Burns-Cox reported the first case in Malaysia in 1965. It is a chronic infection of the skin and subcutaneous tissue. Although not common, when it occurs and the thought of it not entertained the diagnosis is likely to be missed and mistaken for a carcinoma. Dharan noted more than 30 cases in specimen sent to the IMR. Jayalakshmi *et.al*. collected a series of 9 case in the UH, all males. They ranged in age from 56-65 years and all had lesions in the lower limbs.

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CRYPTOCOCCOSIS

Cryptococcus neoformans was first described by Zenker in 1861. It is widely found in nature; in soil, on plants and insects and even in foodstuffs. It is yeastlike both in culture and in infected tissue. Busse first described the disease in man in 1894. In 1924 Sheppe recognised the pulmonary form of the disease. Although the main manifestation of the disease is meningitis, the route of entry is thought to be through the lungs. Besides man animals such as the horse can be affected.

Cryptococcosis, also known as torulosis, has a world wide distribution. Although not a large number of cases have been reported in Malaysia it is felt the diagnosis may have been missed often as the diagnosis which depends on cerebrospinal fluid microscopy and culture can easily overlooked by those unaware of it. The first case in Malaya was reported by the IMR in 1953. Lim and Chan collected 5 cases between 1959 and 1960 from all over the country, including a Dyak in Sarawak. Poopalasingam reported another case from Taiping in 1967. In 1969, Dutt, Krishnan and Lim described one pulmonary case at the Lady Templer Hospital. The patient, a 30 year old Chinese man made a full recovery after pulmonary lobectomy

Richardson, Mohandas and Arumugasamy noted 30 cases of cryptococcal infection in the Neurological services in GH KL in just over 11 years from 1964 noticing a rising trend in the number of cases detected over the years. 27 presented as meningitis and 3 as granuloma. A survey of hospitals in other parts of the country uncovered 25 cases of cyptococcal meningitis over the same period. Of their 30 patients 17 were male and 13 female. They ranged from 6 to 56 years with a median of 23 years. There were 20 Chinese, 6 Malays, 3 Indians and 1 Orang Asli which was similar in distribution to all admissions. The patients came from all walks of life. The only common factor was that some outdoor activity was evident in all patients. With therapy, the median time for cryptococci to disappear from the cerebrospinal fluid was three weeks. The mean hospital stay was 9 weeks. 13 (43%) patients died of the disease. Of the survivors 9 were well and 8 had moderate to severe neurological deficits.

In a review of cases seen in the UH over 6½ years from 1974, Pathmanathan and Soo-Hoo noted 85 cases, 95% diagnoses by culture, the remaining by histopathology. 72% of their patients were Chinese. Only 14% of the patients were recognised immuno-compromised hosts. In a similar series of hospital based patients diagnosed in the UKM hospital laboratory, Abdul Samad and collaegues found 31 cases between 1980 and 1986. 93% were culture positive, 90% seropositive. Males were twice as commonly affected compared to females. Again, in the UH, Doi and colleagues reviewed 27 cases at the UH in 1998, noting that it was the commonest cause of meningitis in adults without debilitating illnesses. 6 (22%) presented

primarily with pulmonary symptoms. The rest presented with CNS symptoms, mainly headaches and fever, and in a third of them chest radiographs showed pulmonary lesions.

Kong *et.al.* have reported the GH KL Nephrology Unit experience with cryptococcisis over nearly 13 years from 1976. They had 11 cases, all in patients on steroids and other immunosuppressive therapy. 8 were post-renal transplant patients, 3 had SLE. Headache, fever and mental confusion were common features but meningism was not.

In one patient cryptococcosis presented as a breast granuloma concomitantly with infection in the occipital lobe of the brain. A girl with disseminated cryptococcosis in the lungs, liver, bone and lymph nodes who had CD4 lymphopenia but was HIV negative, was encountered in Kelantan in 1998.

Majid has reported good results from resection of pulmonary cryptococcomas in 2 patients who had received antifungal therapy for cryptococcal meningitis. Chin has reported that 22% of clinical isolates of *C. neofarmans* were resistant to 5-flurocytosine and 36% indicated tolerance. All strains however were sensitive to Amphotericin B.

Since 1973 *C. albidus* has been recognised as a minor cause of cryptococcal meningitis. Two such cases has been noted locally.

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DERMATOPHYTES

The group of superficial mycoses caused by the keratinophilic fungi called dermatophytes are common in Malaysia although the actual extent is unknown due to the paucity of published works. Soo-Hoo and Adam in a study in the urban setting of Kuala Lumpur found that *Trichophyton mentagrophytes* (39%) and *T. rubrum* (46%) were the most common species isolated. There was no great difference in the distribution of the species of dermatophytes among the three main ethnic groups. Indians, though, seemed to be more commonly affected. *T. concentricum* was found to be confined to the Orang Asli, which support the findings of Marple and Smith who contend that this strain affects only those of Polynesian stock.

Ng *et.al.* have found the dermatophytes accounted for 36% of fungal nail infections.

Referance

Soo-Hoo TS and Adam BA. The isolation of dermatophytes at the University Hospital. Mal.J.Pathol. 1:85-89 1978

GEOTRICHIOSIS

Geotrichum candidum is a yeast-like saprophytic fungus widely distributed in soil, vegetable matter and is part of normal human skin flora. It is of low virulence. It caused disseminated disease in one 4-year-old girl undergoing chemotherapy for acute lymphoblastic leukemia and was successfully treated with amphotericin B.

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HISTOPLASMOSIS

Histoplasma capsulatum is a dimorphic fungus which occurs in a mycelial form in soil and decaying organic matter. Ponnampalam has isolated the fungus from soil in a cave in Malaysia but it is probably found in many other locales especially those enriched by faeces of birds and bats. It typically affects the lungs through inhalation. In 1968 Ponnampalam reviewed 8 known cases to that date including the earliest report by Kunaratnam *et. al.* in Singapore, 1960. Six were granulomatous lesions around the oral cavity, one a pulmonary infection with bronchiectasis and one patient with *H. capsulatum* seen in the adrenals at necropsy. Three more patients with oropharyngeal histoplasmosis all of whom had symptoms of systemic illness for several months were reported by Eravelly, Ramanathan and Eapen in 1975.

Cutaneous histoplasmosis was noted first locally by Dutt and Garai in 1970. Radzi and Biduwiah reported a case in 1983 which probably resulted from inoculation of the fungus onto an exfoliative erythroderma. Soo-Hoo, Adam and Yusof reported 2 more cases of disseminated cutaneous histoplasmosis. Both their patients could not identify the original focus of their infection although they had both visited limestone caves from where they might have got the fungus.

Ng and Siar have review 37 cases of oral histoplasmosis seen over 27 years at the IMR from 1967. All were males with a mean age of 57 years. 41% were Malays, 38% were Chinese, 19% were Indians and 2.7% were of other races. 5 cases presenting with mouth lesions proved to be cases of disseminated histoplasmosis. The gums, tongue and palate were involved in decreasing order of frequency. The most frequent presenting symptom was an oral mucosal ulcer. The ulcers were often suspected to be tuberculosis or squamous cell carcinoma. One case of oral and laryngeal histoplasmosis was seen in association with Addison's disease.

Jayalakshmi *et.al*. described a case of a 59 year old Chinese man in the UH who died of disseminated histoplasmosis. He presented with penile histoplasmosis ulcers mistaken at first for syphillis. Chan *et.al*. reported another case that mimicked military tuberculosis. Another case of adrenal histoplasmosis was reported in a patient with Cushing's Syndrome by Tan and colleagues at the UKM in 1990. Histioplasmosis has also caused a case of ileal perforation in a renal transplant patient 3 years after transplantation.

In 1999, Hasliza *et.al*. reported a case of a 2 year old girl with disseminated histoplasmosis, from Terengganu, whose father was a poultry farmer. She had a chronic fever, bloody diarrhoea, enlarged liver, spleen and lymph nodes. Diagnosis was obtained from a bone marrow aspirate and lymph node biopsy. She survived with amphotericin therapy. She had no underlying immune deficiency.

Not unexpectedly HIV infected patients would be more susceptible to histoplasmosis and suffer worse from it. Tan has described 3

heterosexual men who contracted HIV from sex, who developed systemic histoplasmosis. They responded to treatment but 2 subsequently died from severe opportunistic infections.

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MADURAMYCOSIS

Maduramycosis got its name from Colebrook in India who introduced the name 'Madurai foot' in 1848 after seeing cases at the Madurai Dispensary. It is a chronic mycotic infection usually affecting the extremities, characterised by swelling, deformity and the development of sinuses which pus with granules of different colours. It can be caused by a variety of fungal species from the eumycetes and the actinomycetes, such as *Madurella, Monosporium apoispermum*, *Leptoshaeria senegalensis*, *Phialophora jeanselmii* and *Cephalosporium sp*.

Early records fitting the description were seen in India as early as 1712. While this disease is common in many areas in the tropics it is rare in Malaysia. The earliest report by Ponnampalam in 1964 occurred in the foot of an Indian man from an estate in North Selangor and was due to the genus *Cephalosporium*. There have been three other reports since then; Burns-Cox in 1965 reported a case in the forearm of a Bajau in Sabah, Geh in 1969 successfully treated an Indian man in KL with a lesion in his foot due to *P. jeanselmeii* with large doses of penicillin and Kannan Kutty and Bau reported a case in the foot of a Chinese woman due probably to *M. mycetomi*. In 1992, Soo-Hoo and David noted a 64 year old woman affected in the leg by *Streptomyces somaliensis* following injuries in a road accident.

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MUCORMYCOSIS (see ZYGOMYCOSIS)

PENICILLIUM MARNEFFEI

Penicillium Marneffei infection is one of the AIDS defining events in HIV infection. It is a rare oppotunistic pathogen and infections from it hardly reported until the emergence of the HIV. It appears, to be confined peculiarly to South East Asia, and Malaysia being in the region has not been exempted.

Since gaining recognition, it has been reported in a non-immunocompromised patient. She was a 48 year old vegetable farmer and presented with pulmonary, cutaneous and lymphatic disease.

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RHINOSPORIDIOSIS

Rhinosporidiosis is a fungal infection caused by *Rhinosporidium seeberi*. It is a chronic granulomatous infection, characteristically forming soft, friable, sessile or pedunculated polypoidal masses which bleed easily. The earliest descriptions of the disease were made independently by Malbran in Argentina(1892), O'Kinealyi in India(1894) and Ellets in the United States(1897). All their patients had nasal polyps. Although it has a worldwide distribution it occurs most frequently in India. Gracia stated that up to 1953 of 510 cases of rhinosporidiosis reported in man, 233 cases occurred in India.

Fletcher in 1914 reported the first case in Malaya. It is not uncommon. Workers from the IMR reported 37 cases seen between 1955-1967. All except one occurred in males. 33 patients were Indians, seven of whom had definitely been to India. Two patients were Chinese and two Malays. 30 patients had lesions in the nose, many of whom had had multiple operations to remove the polyps. The nasopharynx, oropharynx and eye were other sites affected in decreasing order of frequency. Another report has noted oral rhinosporidiosis in Malaysia.

In other countries cattle and horses have been recorded to suffer from rhinosporidiosis.

References

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Ramanathan K, Ungku Omar A, Kutty MK et.al. Oral rhinosporidiosis in Malaysia. Dent L Mal Sing. 9:27-39 1969.

SPOROTRICHOSIS

This is a subcutaneous fungus infection first reported in 1898 by Schenck from Europe. *Sporotrichium schenckii* is a saprophyte on various plants and has been isolated from soil. Human infection is usually due to contamination of injured skin. The common lymphatic form was seen in one Chinese lady by Adams, Soo-Hoo and Rajamani. Unless it is thought of, it can easily be mistaken for pyoderma.

Reference

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TORULOPSIS

Torulopsis glabrata is a yeast which is second in importance after *Candida* in clinical isolates. In one study it accounted for 29% of the yeasts isolated in women with vaginitis. It

accounted for 10% of yeasts isolated in urine specimens in another. Ngeow et.al. in a survey of women attending a Malaysian gynaecological clinic found that the prevalence of *Torulopsis glabrata* was 6%(10/164) in women with a vaginal discharge and 5%(10/188) in women without a complaint of discharge.

References

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ZYGOMYCOSIS

The Zygomycetes are a class of fungi characterised by sexual reproduction in which two similar gametangia fuse to form a zygospore. Several species of fungi from a few genera, including *Rhiopus*, *Mucor*, *Absidia* and *Conidiobolus* in the family Mucoraceae within the class Zygometes can be parasitic on humans. The infection is called zygomycosis or, it is also often called mucormycosis. They are not common, but a nasolfacial infection with *Conidiobolus coronatus* has been reported in a 42 year old Malay man in the UH where another case of pulmonary zygomycosis was also treated by pneumonectomy. Mucormycosis has also been reported in a case with a chronic brain abscess.

Fungi are usually not destroyed by gastric juice but oesophageal mycosis normally never invade the stomach. When there is gastric ulceration however, fungi quite commonly colonize the ulcers. Ahluwalia *et.al*. have reported a case of phycomycosis involving the stomach presenting with a perforated gastric ulcer in a 41 year old Iban farmer in Sibu in 1972. The biopsied ulcer edge was a fungal granuloma but they could not be more specific as to which Phycomycete it was, as culture of the fungus was not obtained.

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CHAPTER 15

PROTOZOAL DISEASES

Protozoa are unicellular, nonphotosynthetic protists that vary from the flagellate to the amoeboid form. There are a dozen odd medically important ones that can cause a spectrum of diseases ranging from an uncommon mild illness such as *Balantidium coli* to the epidemic death rates formerly seen in malaria. Malaria dominates the protozoal diseases of man. This has been especially so in Malaysia and has been given its due prominence here.

ACANTHAMOEBA

Acanthamoeba are free living amoeba found in brackish water all over the world. They can cause keratitis and more seriously, an indolent encephalitis. A case of keratitis has been reported locally.

Reference

Kamel AG and Norazah A. First case of Acanthamoeba keratitis in Malaysia. Trans R Soc Trop. Med. Hyg. 89:652 1995.

AMOEBIASIS

Entamoeba histolytica, the causative agent of human amoebiasis can live in the large intestine of man either in the lumen or in a tissue invasive form. About a dozen studies have been reported from the 1970s on surveys of the prevalence of amoebiasis in Malaysia based on stool examinations. Those studies of children alone reported rates of 1 to 4.4%. Studies that include all ages mention rates up to 8.7%. No racial group, including the Orang Asli, have been singled out with a notably higher prevalence. The results are summarised in Table 15.1 below. It must be noted that the method of stool examination for cysts of *E. histolytica* is time-consuming, laborious and requires skill. Even with trained personnel only moderately heavy infections will be detected. People with frank watery stools may not bring such watery specimens and trophozoites may disintegrate in not well preserved specimens. Thus amoebiasis in the above surveys tend to under-report the actual prevalence.

A different approach by Che Ghani and co-workers in 1987 where stool samples were fixed in polyvinyl alcohol and stained with Trichrome stain revealed a rate of 14.4% in a population of 529. As with soil-transmitted helminths it is the urban and rural disadvantaged communities that have these order of prevalence for amoebiasis. It can be expected to be much lower among those who are socio-economically better off. A small group who may be unusually predisposed to the disease are homosexual men whom Khairul Anuar has described.

Besides *E. histolytica*, parasitic surveys in Malaysia, have commonly picked up two other benign intestinal protozoa. *Entamoeba coli* appears common. Sinniah in 1978, mentioned above found it in 11% of his subjects. It could be confused with the pathogenic *E. histolytica* under the microscope. Studies among the military community, schools and Orang Asli show that the prevalence rate of *E. coli* is from 10% up to 28%. Another benign protozoa *Endolimax nana* occurs at a rate of 1-6% in these studies.

Complications of amoebiasis include liver abscesses (see liver abscess) and bowel perforations which are not rare locally. In a 10 year review of cases admitted to the UH, Jamaiah reported in 1999 that there were 30

Table 15.1 Prevalence of amoebiasis in selected groups in Malaysia

Author	Year	Population	Sample Size	Percent Infected
Kuntz & Wells	1962	all ages, Sabah	1089	1.0
Bisseru & Aziz	1970	children, major races	678	1.5
		children, O. Asli	100	1.0
Dunn	1972	all ages, O. Asli	1273	5.1
Dissanaike *et.al.*	1977	all ages, O. Asli	126	8.7
Sinniah *et.al.*	1978	all ages, Indians	150	1.3
Nawalinski & Roundy	1978	all ages	83	1.2
Hamimah *et.al.*	1982	children, major races	305	2.3
Thomas & Sinniah	1982	all ages, O. Asli	84	8.3
		all ages, Malays	690	6.1
Sinniah	1984	children, Malays	271	4.4
Che Ghani *et.al.*	1987	all ages, major races	529	14.4
Shekhar*et.al.*	1994	children major races	7557	3.2
Rahmah *et.al*.	1996	children, O. Asli	78	9.0

cases of amoebic dysentery, 20 cases of amoebic liver abscesses and 1 case who had both. Manukaran, Haron and Ismail have reported a similar case with both these features. Males were 9 times more likely to get amoebic liver abscesses than women and 1.5 times more likely to have amoebic dysentery. Kyaw has reported a case of fulminant amoebic colitis where the colonic mucosa completely stripped off the seromuscular coat. In an unusual case reported by Othman and Ismail, an elderly woman in Kelantan with endometrial ameobiasis presented with profuse vaginal discharge that was clinically thought to be endometrial carcinoma.

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Kyaw K. Fulminant amoebic colitis causing a colonic mucosal tube. Aust N Z J Surg 64:67-69 1994.

Shekhar KC, Prathapa S and Gurpreet K. Prevalence of giadiasis among Malaysian primary school children. Med.J.Mal. 51:475-479 1996.

Jamaiah I and Shekhar KC. Amoebiasis: a 10 year retrospective study at the University Hospital, Kuala Lumpur. Med J Mal. 54:296-302 1999.

BALANTIDIASIS

Dunn and Bolton first recorded the presence of *Balantidium coli* in a Chinese patients in Singapore in 1963. Dunn reported it again among Orang Asli but it was a rare finding of less than 1% in the survey. It has been implicated as a cause of diarrhoea.

Reference

Dunn FL. Intestinal parasitism in Malayan aborigines (Orang Asli). Bull.WHO. 46:99-113 1972.

BLASTOCYSTOSIS

Blastocystis hominis, is an intestinal protozoon that has long been considered a comensal organism. Recently there have been many reports suggesting that it is some times a pathogen. There are several *Blastocystis sp*. and they inhabit the intestinal tracts of mammals, birds, reptiles and even arthropods. They are found all over the world. *Blastocystis* has been implicated in traveller's diarrhoea and other gastrointestinal symptoms in both immune competent and compromised hosts.

Sinniah and Rajeswari observed *Blastocystis* in 4.4% of children with diarrhoea in the UH, compared with 1.1% of children from a normal rural population. In a community survey Rajah Salim et.al. found *Blastocystis* in 41% of animal handlers (105) and 17% of high rise flat residents (163). *Blastocystis* infection can be eradicated by co-trimoxazole and metronidazole.

References

Sinniah B and Rajeswari B. Blastocystis hominis infection, a cause of human diarrhoea. Southeast Asian J Trop Med Pub Hlth. 25:490-493 1994.

Rajah Salim H, Suresh Kumar G, Vellayan S et.al. Blastocystis in animal handlers. Parasitol Res 85:1032-3 1999.

CRYPTOSPORIDIOSIS

Cryptosporidium is another pathogen that has been added to the growing list of infective causes of acute gastroenteritis. Che Ghani and colleagues noted the first case with the parasite in Malaysia in 1984. Mendez, M.Hamdan and Ow-Yang from the IMR have recorded a rate of 4.4% of 158 cases in paediatric diarrhoea in 1988. It was most common among the 1 to 4 year age group and also commoner among Malays and Indians. Similarly a rate of 4.3% was observed among children with diarrhoea in the Penang Hospital. Ng and Shekhar however found only 4 out of 192 (2%) children with diarrhoea in the UH had cryptosporidiosis and none among adults. Vomiting is common with the diarrhoea in cryptosporidiosis.

An interesting finding in an IMR community based study of diarrhoeal disease in Kelantan in 1990 has been that *Cryptosporidium* was isolated from 21% of hospital cases but only 3% of community cases. In a large survey of 7,557 children from poor rural, semi-urban, and estate areas between 1992-1994, Shekhar, Prathapa and Gurpreet found a similar prevalence rate of 4.1%.

Cryptosporidiosis has also been found to be common among HIV positive inmates of a drug rehabilitation centre. An asymptomatic prevalence rate of 23% was recorded in Tampin, Johore.

References

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Mat Ludin CM, Afifi SAB, Hasenan N et.al. Cryptosporidiosis among children with acute gastroenteritis in the paediatric ward in the General Hospital, Penang. Southeast Asian J.Trop. Med.Pub Hlth. 22:200-202 1991.

Ng KP and Shekhar KC. The prevalence of cryptosporiodosis in children and adults at University Hospital, Kuala Lumpur. Med.J.Mal. 48:293-296 1993.

Table 15.2 Prevalence of giardiasis in selected groups in Malaysia

Author	Year	Population	Sample Size	Percent Infected
Kuntz & Wells	1962	all ages, Sabah	1089	9.0
Bisseru & Aziz	1970	children, major races	678	5.6
		children, O. Asli	100	25.0
Dunn	1972	all ages, O. Asli	1273	10.8
Dissanaike *et.al.*	1977	all ages, O. Asli	126	4.8
Sinniah *et.al.*	1978	all ages, Indians	150	11.3
Nawalinski & Roundy	1978	all ages	83	6.0
Hamimah *et.al.*	1982	children, major races	305	2.6
Sinniah	1984	children, Malays	271	8.5
Che Ghani *et.al.*	1987	all ages, major races	529	9.5
Sinniah et.al.	1988	children Chinese	297	9.3
Sinniah et.al.	1992	children	319	9.1
Sinniah & Rajeswari	1994	children	729	8.4
Shekhar*et.al.*	1994	children major races	7557	0.21
Rahmah *et.al*.	1996	children, O. Asli	78	20.5
Norhayati et.al.	1998	all ages	917	19.2

Kamel AG, Maning N, Arulmainathan S et.al. Cryptosporidiosis among HIV positive intravenous drug users in Malaysia. Southeast Asian J.Trop. Med.Pub.Hlth. 25:650-653 1994.

Shek har KC, Prathapa S and Gurpreet K. Prevalence of giadiasis among Malaysian primary school children. Med.J.Mal. 51:475-479 1996.

CYCLOSPORIASIS

Cyclosporiasis is an opportunistic pathogen. It causes diarrhoea. In the immune competent patient the illness is self limiting. In HIV patients the diarrhoea can last for weeks and months. Two such cases have been separately reported in Malaysia.

References

Sinniah B, Rajeswari B, Johari S et.al. Cyclospora sp causing diarrhoea in man. Southeast Asian J Trop Med Publ Hlth 25:221-223 1994.

Alias A and Shukri A. Cyclosporiasis in an HIV - positive patient. Med.J.Mal. 53:311-312 1998.

GIARDIASIS

Giardia lamblia the intestinal flagellate which causes giardiasis inhabits the small intestine of man. The table 15.2 above summarises the prevalence rates found in surveys of several, mostly rural and urban disadvantaged communities. Rates are mostly in the order of 5%-10%. Children seem more prone to infection than adults. There is a suggestion that the Orang Asli have a higher prevalence, perhaps as much as 25%.

As with amoebiasis, stool examinations tend to under-report the situation. All the shortcoming related to amoebiasis apply. Furthermore, *Giardia* cysts are usually passed sporadically, and ideally stools should be collected on consecutive days. Giardiasis like amoebiasis is water borne and measures to improve the clean water supply to the poor communities will be the best health control measure.

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Shekhar KC, Prathapa S and Gurpreet K. Prevalence of giadiasis among Malaysian primary school children. Med.J.Mal. 51:475-479 1996.

Norhayati M, Penggabean M, Oothuman P and Fatmah MS. Prevalence and some risk factors of Giardia duodenalis infection in a rural community in Malaysia. Southeast Asian J Trop Med Pub Hlth. 29:735-738 1998.

ISOSPORIASIS

Isospora belli is an oppotunitic enteric pathogen, that may cause profuse diarrhoea in AIDS patients. One case of this has been reported in the UH.

References

Zaman V. Observations on human isospora. Trans R Soc Trop Med Hyg. 556-557 1968.

Shekhar KC, Ng KP and Rokiah I. Human isosporiasis in an AIDS patient - report of first case in Malaysia. Med.J.Mal. 48:355-360 1993.

LEISHMANIASIS

Malaysia does not lie in the region endemic for kala azar and there is no local transmission of the disease. Twice in the1980s cases were reported in Singapore due to international travel. In Malaysia a 35 year old Bangladeshi man was finally diagnosed with kala-azar on bone marrow aspirate at the UKM after 2 months of illness in 1995.

Reference

Hamidah NH, Cheong SK and Abu Hassan J. A case of kala-azar diagnosed by bone marrow aspiration. Mal. J Pathol 17:39-41 1995.

MALARIA

Historical Background

Malaria, it has been said, was the greatest single factor in the past two millenia which has hampered the development of the tropical regions of the earth. Malaysia was no exception. Up to the days of the Malacca Sultanate, settlements were largely restricted to river mouths and population growth curtailed.

In 1829, forty years after Penang Island was first occupied, one-third of all deaths were attributed to malaria. Conditions on the mainland at the end of the nineteenth century when economic development was attempted under the British were equally chilling. At one time the town of Jugra was abandoned while orders were actually sent by telegraph by the High Commissioner to close down Port Klang within two months of its opening, because of malaria. The old residence of the British Resident of Perak also had to be abaandoned on account of malaria. Carey recorded from the New Amherst Estate in the Federated Malay States where malaria broke out in epidemic proportions among the non-immune community

imported to work that "the estate was so riddled with malaria that the coolies were all miserably anemic and lacking in strength that the estate had eventually to be abandoned". He also noticed that between 1892 and 1898 there were on average fifty Tamil women on the rolls yet in the whole period no living child was born.

Transmission And Its Control
The Discovery of Malaria

It was extremely fortunate for the development of Malaysia that the cause of malaria was discovered at about that time. Although in antiquity a few people like the Egyptian fishermen who slept under fishing nets folded again and again until the mesh was small, may have had an inkling that malaria was mosquito borne, by and large the cause was not known. The Greeks noticed that it occurred in swampy areas and thought it was caused by drinking the water. The Italians thought it was caused by inhaling the foul air, hence the name 'mala aria' meaning bad air. Pioneers in this country who were quite aware of the high incidence of malaria and death rate connected with opening up land by felling the jungle attributed malaria to a mysterious 'miasma' set free by disturbances of the soil. Grant, a military surgeon in Penang in the early nineteenth century stated that no newly cleared hills were safe places of abode at certain seasons until after three or four years.

The role call of honour for the discovery of the cause of malaria and its eventual control begins with Alphonse Laveran, a French army surgeon who discovered the malaria parasite in the blood of patients in 1880. King, in an article in 1883 gave nineteen arguments in support of the thesis that mosquitos conveyed malaria. Manson provided a link with his discovery that mosquitos conveyed filaria. Then in 1897, Ross, following painstaking work on the suggestion of Manson discovered the malaria parasite of man in the mid-gut of the mosquito and worked out the transmission cycle.

At a time when incredulity and misgivings surrounded Ronald Ross' announcement in 1898 Malaya can be proud of being the first country in the world to have successfully applied this knowledge of malaria transmission in efforts to control it. Malcolm Watson was one of the pioneer anti-malaria workers in this country. Fresh from the London School of Tropical Medicine he was stationed at Klang, Selangor where malaria was prevalent. On his recommendation, the government approved and carried out a scheme for draining and filling the surrounding swamps with the immediate result of a reduction in the incidence of malaria. It was partly luck that this anti-larval measure worked because it was suitable for this type of terrain and the anophelines were breeding there.

The importance of this success and subsequent malaria control measures cannot be overemphasised. At that time death rates among the labour forces in the rubber estates and tin mines was over 100 per 1,000 per annum in places and admission rates to hospital numbered 300 per 1,000 per annum. With such interference to work it was evident to the British that prosperity was impossible without rendering the country reasonably safe from malaria. Drainage was one important measure. In 1901 oiling was introduced as another anti-larval tool. Great reforms in the organisation of the campaign were made following an epidemic in 1911. The Malaria Advisory Borad was inaugurated and a Health Branch was created in the Medical Department. Records from 1911 show that of 143,614 estate workers in Perak, Selangor, Negeri Sembilan and Pahang 9,040 died that year. Malaria accounted for 45% of all deaths. By 1924 the number of deaths had dropped to 1,514 from a total of 18,353 cases of malaria among a population of 144,902. The credit must go to gradual advances such as insecticide spraying, chemoprophylaxis, the use of natural enemies to the mosquito larvae like fish, and using nets and screens to prevent mosquito bites. Were it not for the success of malaria control modern Malaysia as we see it today would never have happened.

Today while all the known methods of vector control are in use the focus for the future is on biological control of mosquitos. They consist of predators such as fish, parasites such as nematodes, and pathogens such as *Bacillus thuringiensis* which show promise with bioengineering.

The Parasites And Vectors

The work of Hamilton Wright, the first Director of the IMR in Kuala Lumpur established the presence of *Plasmodium vivax, Plasmodium falciparum* and *Plasmodium malariae* in this country. It is doubtful if *Plasmodium ovale* is endemic in this country although ovale-like parasites which could have been variants of *P. vivax* have occasionally been seen.

P. malariae has a peculiar association with the aboriginal inhabitants of a number of countries and this seems true also in Peninsula Malaysia. It was probably more prevalent in the early days of Malayan history than at the present time. Figures quoted by Wright, Darling and others in the first two decades of this century give a percentage incidence of about 20 whereas current percentage incidence is less then 7. It may however be the dominant species in some isolated places. For example a recent survey found *P. malariae* in 115 of 181 infected people in some rural valleys in Negeri Sembilan.

Overall in Peninsula Malaysia today *P. falciparum* accounts for just over 50 percent of malaria and *P. vivax* accounts for just under 50 percent. In Sabah *P. falciparum* predominates, amounting to 75 percent of malaria cases. In Sarawak however *P. vivax* accounts for 67 percent of the total. Mixed infections occur in about one percent of cases.

Parasites of non-human primates have rarely been reported in man. Eyles *et al.* were the first to show that *Plasmodium cynomolgi bastianellii* of a macaque could be transmitted to man by mosquito bites in 1960. *P. malariae* has been isolated from monkeys and in places malaria may be a zoonosis although the animal reservoir is probably small.

The insect vector of malaria is the anopheles mosquito. About 60 species and sub-species are found in Peninsula Malaysia. Experimental work shows that, few if any, of the Malaysian species of Anopheles are incapable of becoming infected by local strains of *P. falciparum* and *P.vivax* under suitable conditions. Fortunately, in natural conditions however an important vector in one locality may be a non-vector in another. In each ecological zone usually only half a dozen or so species are vectors, which greatly aids malaria control work. The species which is vector for malaria changes as vegetation changes from the brackish water zone inland to the hills.

In the narrow strip of brackish water along the coast the untouched mangrove swamps have no anopheline vectors. When the mangrove is cleared *A. sundacus* breeds prolifically and becomes responsible for malaria transmission. Next from the coastal plains to the foothills the vector species of untouched jungle swamp is *A. umbrosus.* When jungle is cleared for cultivation *A. umbrosus* is replaced by *A. campestris* and *A. letifer*. In the virgin hill jungle which is sparsely populated by aboriginal tribes transmission of malaria is effected by *A. leucosphyrus* and *A. umbrosus* species. Whenever the cover of the jungle is removed from hilly areas, *A. maculatus,* numerically the most important vector in Malaysia, breeds readily and transmits malaria.

The mosquito vector in Sabah presents a different problem. About 11 species of the Anopheles have been found biting man. *A. flavirostris* and *A. balabacensis* were found to be the commonest biting mosquitos both of which harbour *P. falciparum* sporozoites. *A. balabacensis* especially has high rates of the parasites and is the most important vector for malaria. It is an outdoor biting species which

makes the control of malaria more difficult. The third important mosquito vector in Sabah is the *A. sundacus* which is found in the coastal brackish water zone.

In Sarawak there are three important vectors although several others exist. *A. leucosphyrus* is the prime vector found in densely shaded seepage water in the hilly country. *A. balabacensis* is the vector in the part of Sarawak bordering Sabah and in the coastal areas *A. sundacus* is important.

Beneficial Host Factors

Ovalocytosis which is prevalent among the Orang Asli appears to confer protection against severe malaria. Besides this, Haemoglobin E which is also widely prevalent, Glucose 6 Phosphate Dehydrogenase Deficiency and HLA-B1513 which was found to be present in 42% of Melayu Asli and 24% of Senoi are also thought to be beneficial in malaria. HLA-B1513 has a binding groove, which has amino acid sequence for the F pocket which is identical to HLA-B 5301 which is thought to confer malaria resistance on Africans.

The Malaria Eradication Programme

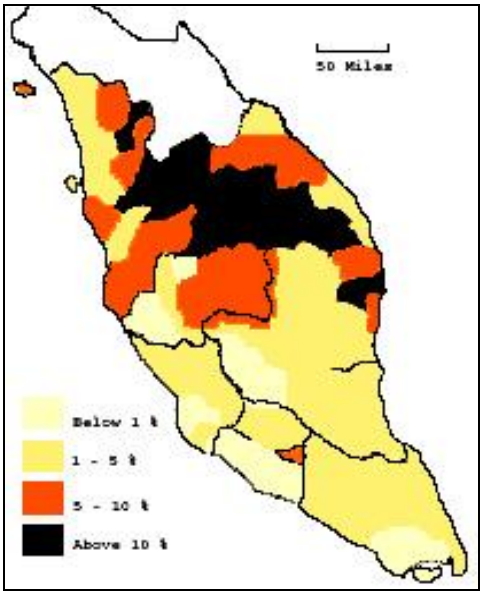
Despite the early success of malaria control in Malaysia complete eradication did not appear imminent. In fact, after, having decreased steadily from over 16,000 cases in 1951 and reaching a nadir of less than 6,000 cases of hospital admitted malaria cases in 1958, the incidence began to rise.

The idea of eradicating malaria on a world-wide scale arose following the discovery of the insecticidal action of DDT and its usefulness as a residual insecticide during the Second World War by Paul Muller of Switzerland in 1939. Greece, one of the most malarious place in Europe, was a country where the use of DDT had decreased the vector population such that malaria disappeared. The Greeks then decided to stop spraying in certain places when the cost of DDT increased as a result of American involvement in the Korean War. The authorities crossed their fingers as anopheline vectors returned in these areas in the numbers expected. But malaria did not return. What had happened was the spraying had interrupted transmission and the disease had died out. From these spectacular results the WHO accepted the feasibility of the proposition of global malaria eradication at the Eighth World Health Assembly in 1955.

Malaya however unlike some of its neighbours, did not initiate a nation-wide campaign until 1967. This delay may at first appear strange, considering that Malaya had been a pioneer country in malaria control. For one thing, Malaya was preoccupied with waging a war against Communist terrorists and it was not till 1959 that the state of emergency was lifted. For another, some Malaysian malariologists, like Sandosham were not convinced then that such a campaign would work in Malaya. Sri Lanka a country with many similarities was an example where eradication was almost achieved when there was a resurgence in 1954.

Before launching an eradication programme, between 1960 and 1964 a Malaria Eradication Pilot Project was carried out in an area measuring 501 square miles around Kuala Selangor. Transmission of malaria was arrested in the area by October 1963 even among the Orang Asli. Some believed it demonstrated a practicable and effective way of interrupting malaria transmission applicable to the whole country. However some doubts remained about the validity of these results because of the small size of the pilot area and pattern of vector distribution which was not entirely representative of the country.

Figure 15.1 Malaria prevalence rate by districts in Peninsula Malaysia 1967

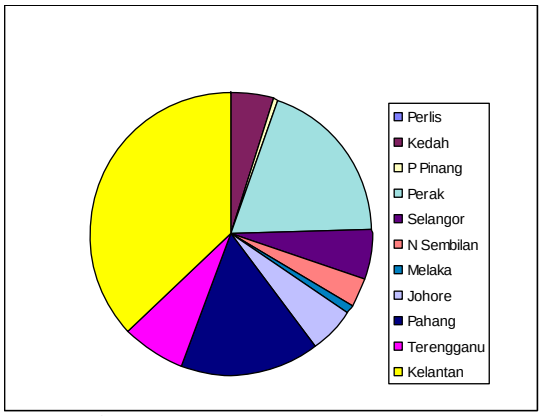


Despite misgivings Malaysia officially launched its eradication programme in 1967. The total number of malaria cases then was greater then 35,000 a year with over 150 deaths. Fifteen years later in 1982 a third of the country was still in the attack phase and more than 11,500 cases were recorded in that year. It had cost $120 million and no eradication was in sight.

Malarial Control

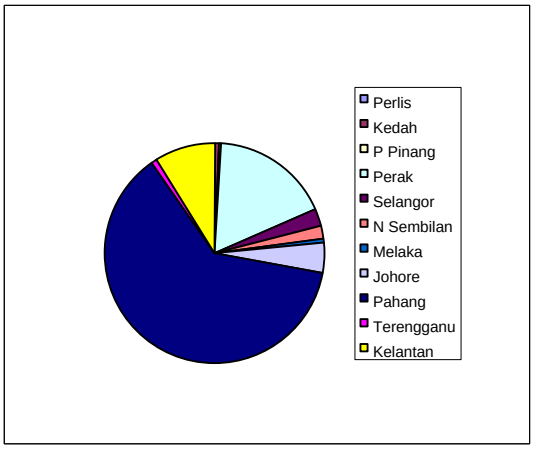
In 1981 the concept of eradication of malaria was changed to that of control. The targets set by the Vector Borne Disease Control Programme for malaria now are to bring the incidence rate below 10 per 10,000 in malarious areas and to keep it below that level in potentially malarious areas. Malaria free areas are to be kept malaria free. 77% of the population live in malaria free areas, (it is 90% in Peninsula Malaysia). About 15% live in potentially malarious areas and only about 8% live in malarious areas. Deaths due to malaria amounted to 12 in the Semenanjung, only one in Sarawak and 62 in Sabah in 1987.

Figure 15.2 Distribution of Malaria cases in Peninsula Malaysia 1981 (n=8609)



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Figure 15.3 Distribution of Malaria cases by States in Peninsula Malaysia 1997 (n=5141)



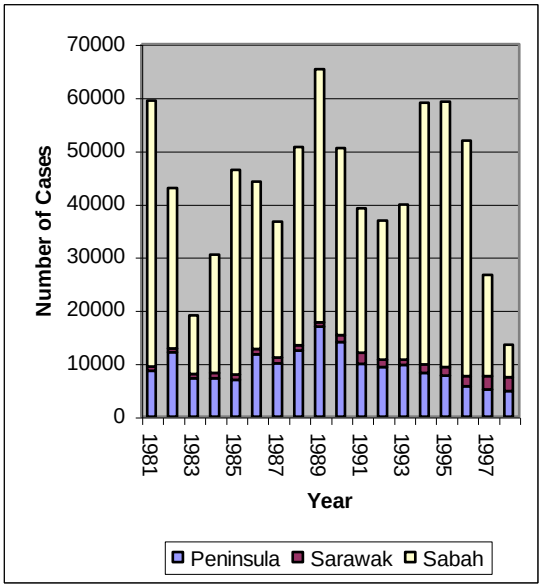
Source: Information and Documentation System Unit, Ministry of Health, Malaysia

In 1987, 30 years after independence and 20 years after the eradication programme, there was a total of 10,010 malaria cases in Peninsula Malaysia. This gave us an incidence of 7.4 per 10,000 population. Penang had the lowest rate with 0.3 per 10,000. Perlis, Kedah, Malacca, and Johore had less than 2 cases per 10,000. The highest incidences are found in Pahang (23.9), Negeri Sembilan (18.8), Kelantan (18.3) and Perak (11.8). Sarawak has an incidence of malaria similar to the Semenanjung, 7.3 per 10,000.

The malaria problem in Sabah however, is a much more serious. Back in 1956 before any organised antimalarial activities were started it was estimated that there were as many as 250,000 cases in a population of about 500,000. Following an eradication programme from 1960 the number of cases dropped to 13,000 in 1970. However, the number of cases climbed to 46,496 cases in 1975, rather strangely, only after redefining the aims of intervention as the Malaria Control Programme in 1971 when it was realised the eradication was not possible. Following that from 1978 there was a gradual decrease in the figures. In 1987 there were 25,515 cases, 70% of the national total, and its incidence was 194 per 10,000. This high incidence in Sabah can be further confined to 48% of the population who live in the areas designated malarious where 95% of the state's cases occur. These are the land schemes, the logging areas and plantations. The 11% of the population who live in 'malaria free' areas had only 91 cases, or an incidence of only 6.3 per 10,000.

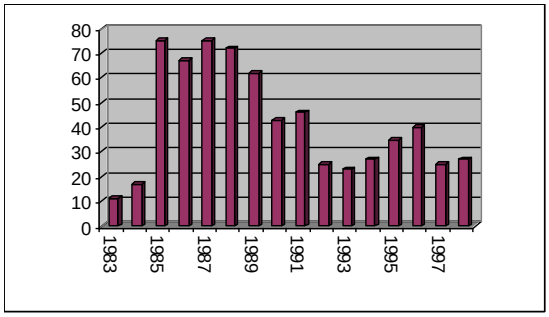
The history of malaria in Sarawak is less daunting. Following a epidemic in 1946 a WHO assisted Malaria Control Pilot Project was successfully launched in the Baram area in 1953. By 1959 it had been extended to cover the whole state. From about 40,000 cases annually in the 1950s the number dropped to 1,500 in the 1960s when the Eradication Project was launched. Despite these efforts like in Peninsula Malaysia the malaria problem remains though maintained to below 1,000 cases a year.

Figure 15.4 Malaria Cases in Malaysia (showing proportion in Sabah and Sarawak)



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Figure 15.5 Deaths from Malaria in Malaysia



Source: Information and Documentation System Unit, Ministry of Health, Malaysia

Within Peninsula Malaysia there are some special groups with a high incidence. The Orang Asli numbering less than 100,000

account for 25.6% of the malaria cases. In states like Selangor and Negeri Sembilan they make up over 60% of the state's total number, the majority occurring in technically non-malarious areas. The Orang Asli also account for large numbers in Perak and Pahang. In Pahang one particularly highly affected group seen only to a much lesser extent in Kelantan, are the land scheme settlers. They are mainly illegal Indonesian immigrants. They number over 1,000 cases forming 40% of the state's total. Because of them Pahang has now overtaken Kelantan as being the most malarious state in the Peninsula. Migrant workers also account for a significant number of malaria cases in KL.

The Malaria Status Today

The adverse factors facing the control programme now include the development of parasite resistance to antimalarials, vector mosquito resistance to insecticides, ecological changes favouring vector breeding and huge population movements from endemic areas such as from our neighbouring countries.

Chloroquine resistant parasites was first detected in the local population by Sandosham in 1963 in Perlis. It is a problem especially in the states bordering Thailand. It is also a problem in Sabah and Sarawak. In 1979 in Sabah, it was found that 87% of *P. falciparum* malaria cases in were resistant to chloroquine. Fansidar was found to be still effective. *In vitro* studies showed the chloroquine resistance rate was as high as 100% during the 1983-1986 period, but it declined to between 75%-86% in later years. This was probably due to reduce in the usage of chloroquine.

Permetrin impregnated bed nets have been evaluated in Orang Asli villages. They lower the parasite rate when introduced but it appears that the effect may not be sustained.

In Sabah, the last 10 years has shown that any apparent decline in the number of cases can be deceiving. Although the number of reported cases can drop to 26,094 in 1992, it can rise to 49,865 in 1995. Two important factors in malaria transmission a study by Asits *et.al*. in 1996 revealed were seasonal migration into the jungle and the use of bednets. Individuals who migrated into the jungle were 6 times more likely to suffer from malaria and those who used bednets reduced their risk of malaria 4 fold.

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PNEUMOCYSTIS CARINII

Pneumocystis carinii is an oppotunisitc pathogen that has become well known as a result of the AIDS pandemic. It normally inhabits the lung harmlessly but in the presence of immunodeficiency it becomes a dangerous

pathogen. It is normally classed as a protozoa although it has features that suggest it is fungal. Even in Malaysia it is the commonest AIDS defining infection in HIV patients.

Besides HIV patients pneumocystis carinii has been observed in 9 patient in UH with SLE who were on prednisolone and some also on cyclophosphamide.

Reference

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SARCOCYSTOSIS

Sarcocystis is a parasite with an obligatory two-host life cycle. It is a protozoon that inhabits the intestines of several animals, including the cat, dog and python, . The sporocysts, shed by the definitive host, probably contaminate food or drink and are ingested by man. The sarcocystis are found in skeletal muscle around the head and neck, most often the tongue, and has been found in many animals in Malaysia besides man. The first case was reported by Kutty and Dissanaike in Malay man in Seremban in 1975. In a review in 1985 Kan reported that up till then there had been 6 cases of sarcocytosis in the medical literature reported from all the ethnic groups in Peninsula Malaysia and one each from Sabah and Sarawak. In all these cases the sarcocyts were diagnosed in biopsy specimens from naso-, oro- or largngopharynx. Often in these cases a malignancy had been suspected. In 1992 Pathmanathan and Kan noted that 11 cases had been reported.

In a immunological study of sera from 243 blood donors from all ethnic groups in West Malaysia, Thomas and Dissanaike found 20% reacted positively at dilutions of 1:64 or higher to antigens from sarcocystis. Prevalence was highest in the Orang Asli (40%) and lowest in Chinese (3.6%).

Examining tongue specimens from routine autopsies in 1992, Wong and Pathmanathan found that 21% of 100 individuals were affected with sarcocystosis. The mean age of the positive cases was 38 years, ranging from 16-57 years. No particular race, sex or occupation was more commonly affected. The infections were evident clinically in most cases.

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TOXOPLASMOSIS

Toxoplasma gondii was first described by Nicolle and Manceaux in a small North African rodent *Ctenodactylus gondii* in 1908, and first recognised as a disease in man by Wolf and Cowens in 1937. Toxoplasmosis does not pose much of a health problem, except as a possible cause of congenital malformations and in the immunocompromised.

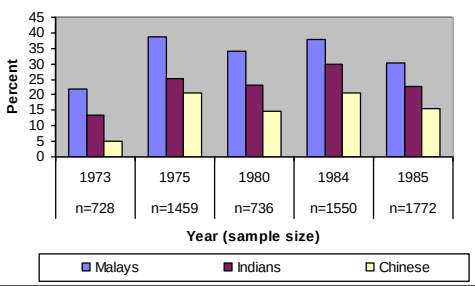
Only a single species of *Toxoplasma* has been described, but different strains of it have been reported. It has a world-wide distribution but the prevalence rate is greater in the tropics and subtropics. The endozoite parasite has little host specificity and is found in a large number of mammals and birds. In Malaysia the presence of *T. gondii* has been noted in pigs, buffaloes, goats,

cattle, stray dogs, monkeys and most importantly cats. It is an obligatory intracellular parasite of nucleated cells, especially of lymphoid macrophages, and as such can cause lymphadenopathy mimicking Infectious Mononucleosis. It is also found in muscle cells, the central nervous system and the retina. Unlike other animals domestic cats and a few other felines are special to *T. gondii*. They are the definitive host for the protozoa which undergoes a cycle schizogony, gametogony and sporogony.

Serological studies in Malaysia have shown that there is a close relationship between cats and the prevalence of toxoplasmosis. Malays who usually have closer contact with cats have the highest antibody prevalence rate among the different races. The prevalence rates using the Immunoflourescent Antibody (IFA) test in several studies is given in Figure 15.6. Among Chinese the antibody prevalence rate is higher among the younger ages and decreased among adults. This was not seen in Malays. Although toxoplasmosis can be contracted from eating meat of infected animals this is probably rare.

The prevalence among the Orang Asli does not appear to be high. In 415 serum samples, Hakim *et.al*. found a prevalence rate of 11%.

Fig 15.6 Prevalence of toxoplasma antibodies in the various races in Malaysia



Among occupational groups cattle slaughterers (55%), pig slaughterers (21%), veterinarians (20%) and padi planters (22%) have been found to have high prevalences of *Toxoplasma* antibodies. Tan and Zaman found that oil palm and rubber estate workers have a rate of 13.5% and antimalaria labourers 3.7%. Leong *et.al*. reported a high of 72% among the lower-socioeconomic group compared to 28% among the higher income group.

Clinical features

T. gondii produces a wide spectrum of responses ranging from inapparent infection to serious disease in few cases. A viral like syndrome that passes unnoticed is probably common. In Malaysia, there are no known deaths or complications due to acquired toxoplasmosis. The classical fundal lesions however, have been seen. As many as 31 cases with blurring of vision due to ocular toxoplasmosis were seen at the Opthalmology Clinic, UKM, Kuala Lumpur during a one and a half year period from 1981.

Congenital toxoplasmosis may be important in women who first contract the disease during pregnancy. The risk of congenital disease, unlike other agent, is lowest in the first trimester and higher later in pregnancy. Studies in Malaysia have shown seropositivity among a number of infants at birth but none had serious handicaps. Toxoplasmosis is thought not to be an important contributor to congenital malformations.

Erythromycin and azithromycin were the most effective antibiotics against the virulent RH strain of *T. gondii* by Tee *et.al.*

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TRICHOMONIASIS

The flagellate protozoon *Trichomonas vaginalis* causes trichomoniasis. Though it is a common genital infection it is hardly ever severe. Ngeow *et.al*. in a survey of women attending a Malaysian gynaecological clinic found that the prevalence of *Trichomonas vaginalis* was 5%(8/164) in women with a vaginal discharge and was not found in 188 controls. It is typically just an itch with a greenish discharge that is easily treated with metronidazole.

Reference

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TRYPANOSOMIASIS

The classical forms of trypanosomiasis found in Africa and South America have not been found in Malaysia, however, in 1933 Johnson did report finding a trypanosome in a child in Perak and Dissanaike, Ong and Kan have noted very scanty tyrpanosome infection in 2 asymptomatic Orang Asli, from Pos Iskandar and Kampong Guntor, in 1974 while carrying out a blood and tissue survey of parasites. Efforts, however, to culture the parasite were unsuccessful. The sera were not very reactive to antigens of *T. rhodesiense*, *T. gambiense*, *T. cruzi* and *T. lewisi.*

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TABLE 16.1 Prevalence of soil-transmitted helminthiases in the general population

AUTHOR	YEAR	PLACE	SAMPLE SIZE	%WITH WORMS			% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHRIS
				MALAY	CHINESE	INDIAN			
Russell	1934	Strait Settlements	27,396	88	39	71	63	70	70
ICNND	1964	West Malaysia	1,932				56	50	84
Kan	1982	Selangor	25,246	41	21	53	19	7	33

TABLE 16.2 Prevalence of soil-transmitted helminthiases in hospital populations

AUTHOR	YEAR	POPULATION	SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
Sandosham	1955	Singapore, Malacca and Penang GH patients	46,208			24	31	14
Kuntz & Wells	1962	QEH Sabah	200	55	25	27	41	
Lie	1964	KL GH children	2,732	43	29	8	31	51
		adults	2,054	69	27	41	43	52
Khan & Khairul	1977	Balik Pulau Hosp. patients	207	73	32	37	52	45
Itam *et.al*	1977	Penang GH children	107	41	31	3	33	61
Hamimah *et.al*	1978	KL GH child	305	35	17	3	15	
Menon *et.al.*	1999	Kelantan children receiving chemotherapy for cancer	50	42	22	2	24	

TABLE 16.3 Prevalence of soil-transmitted helminthiases rural children in Selangor

AUTHOR	YEAR	POPULATION	SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
Bisseru & Aziz	1970	Indian children	110	87	35	54	59	56
		Malay children	138	95	86	15	88	82
Lo *et.al*	1979	Children, all races	834	95	87	43	86	87
Kan	1984	Indian children	422	81	32	34	75	67

TABLE 16.4 Prevalence of soil-transmitted helminthiases in semi-rural populations in Selangor

AUTHOR	YEAR	POPULATION	SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
Bisseru & Aziz	1970	Malay children	183	90	50	34	82	61
Lie *et.al*	1971	Chinese veg. farm children	57	95	82	33	84	79
		Malay kampong children	145	51	33	24	31	45
Kan	1982	New villagers	7,627	30	9	4	25	41

TABLE 16.5 Prevalence of soil-transmitted helminthiases among urban areas and slums in KL and Selangor

AUTHOR	YEAR	POPULATION		SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
Bisseru & Aziz	1970	School children		151	36	17	1	24	17
George & Ow Yang	1982	School children		7,682	50	22	5	45	
Chia *et.al*	1978	Squatter children		253	91	64	5	84	68
Kan	1982	Flat dwellers		10,693	25	6	2	23	32
		Squatters		4,345	59	36	9	53	78
Kan	1984	Indian school children		735	94	71	3	85	76
Bundy *et.al*	1988	Slum children	Indian	245	73	9	78		
		(≤15 years)	Malays	985	60	8	76		
			Chinese	344	19	1	39		

TABLE 16.6 Prevalence of soil-transmitted helminthiases among plantation workers and families

AUTHOR	YEAR	LOCATION		SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
Sinniah *et.al*	1978	Selangor		150	83	52	28	56	46
Zahedi *et.al*	1980	Johore, Malacca and Negeri Sembilan		719	34	16	24	17	15
Kan	1982	Selangor		2,581	67	50	22	51	56
Ramalingam *et.al*	1983	Selangor		342	70	14	55	45	
Arul *et.al.*	1989	Selangor		341	77	64	12	57	62
Kan	1989	90km south of KL		819	51	34	16	36	
Kan *et.al*	1989	(Children)	Indian	1,276		23	6	30	
		≤15years	Malays	116		6	3	19	
			Chinese	107		21	8	25	

TABLE 16.7 Prevalence of soil-transmitted helminthiases in island populations

AUTHOR	YEAR	POPULATION	SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
Heyneman *et.al*	1967	P.Tioman	65	94	89	31	57	66
Balasingam *et.al*	1969	P.Pinang	119	99	97	35	98	99
		P.Perhentian	158	99	92	68	98	95
Kan *et.al*	1987	P.Ketam children	1,286	8	4	0.2	5	55

TABLE 16.8 Prevalence of soil-transmitted helminthiases among Orang Asli

AUTHOR	YEAR	SAMPLE SIZE	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS
Nevin	1938	104	70	16	14
Sandosham	1953	117	80	49	24
Polunin	1953	131	5	91	3
Bisseru & Aziz	1970	100	69	51	80
Dunn	1972	1,273	39	69	57
Dissanaike *et.al*	1977	126	48	95	81
Rahmah N *et.al*	1996	78	60	6	42
Norhayati *et.al*.	1997	205	63	29	92
Zulkifli *et.al*.	1999	259	48	6	34

TABLE 16.9 Prevalence of soil-transmitted helminthiases in various other areas

AUTHOR	YEAR	POPULATION	SAMPLE SIZE	%WITH WORMS	% WITH ASCARIS	% WITH HOOKWORMS	%WITH TRICHURIS	% WORM +VE WITH MULTIPLE INFECTION
ICNND	1964	Military men	573		25	49	74	
		Urban civilians	292		53	28	76	
		Rural civilians	1,067		72	57	92	
Kuntz & Wells	1962	Police, K Kinabalu, Sabah	189	85	35	52	63	
		School Children, Sabah	700	90	53	58	73	
Khairul A *et.al*	1977	Penang fishing villagers	433	78	67	12	55	56
Bisseru & Aziz	1970	Rural Chinese children (Pahang)	96	40	15	22	22	48
Anderson	1978	Ibans (3st Division,Sarawak)	130	65	53	15	37	
		Ibans (7th Division,Sarawak)	248	60	50	6	14	
		Malays (1st Division,Sarawak)	139	97	93	0	77	
		Penans (4th Division,Sarawak)	223	69	32	48	7	
Neo *et.al*	1987	Ibans (2nd Division, Sarawak)	142	65	5	47	43	44
Wahab	1994	Rural villages, Penang	706	41	30	33		
Lee *et.al*	1996	School Children, Serian, Sarawak	264	13	7	25	34	

CHAPTER 17

ARTHROPOD INFESTATIONS

COCKROACHES

The cockroach does not cause any human disease itself nor is it a direct vector of any specific disease. It has however, been found to be the commonest living creature lodged as a foreign body in the ear in a series in Kelantan.

There are at least 6 species of cockroaches found in Malaysia. Two studies in KL, in KL GH and in urban dwellings have found that *Periplaneta americana* and *Periplaneta brunnea* were the most abundant. 17 species of bacteria were isolated from these cockroaches and of these *E.coli* and *Klebsiella pneumoniae* were isolated in greatest numbers along with other gram negative enteric pathogens.

References

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Vythilingam I, Jeffery J, Oothuman P et.al. Cockroaches from urban human dwellings: isolation of bacterial pathogens and control. Southeast Asian J Trop Med Pub Hlth 28:218-22 1997.

Indudharan R, Ahmad M, Ho TM et al. Human otoacariasis. Ann Trop Med Parasitol 93:161-167 1999.

DEMODEX (Simon 1842)

There is one report of this very minute wormlike mite, which is a parasite of the pilosebaceous complex of a variety of mammals, in a person in Malaysia. It may be found in man on various parts of the face and be mistaken for a fungal infection.

Reference

Jeffery J, Noorhayati MI and Oothuman P. A case of human infection with Demodex folliculorum in Peninsula Malaysia. J.Perubatan UKM. 5:49-52 1983.

LICE

Pediculus humanus capitis, the common head louse may appear to be a simple problem but its eradication will not come easily. As far back as1928, Robertson recorded that 33% of Malays, 3% of Chinese and 50% of Indians in a KL study sample had head lice. He attributed the low prevalence among Chinese to keeping their hair short.

In 1949, Busvine and Reid found a prevalence rate of 55% among Malay school girls in Negeri Sembilan. In 1955, Wharton and Abu Hassan noted incidentally, as part of a filariasis control program, that dieldrin could be used to control head lice in communities. In an area in Ubai, East Pahang where houses had been sprayed with dieldrin they found that 5 months after spraying girls there had no lice. Whereas in a nearby unsprayed area 37 out of 57 (65%) of girls examined had head lice.

In a 1979 survey of 308,101 school children throughout Peninsula Malaysia, Sinniah found a lice prevalence rate of 10.7% overall. The prevalence was highest in Terengganu (34%), Kelantan (23%) and Perlis(21%). In Melaka the ethnic breakdown of the prevalence of pediculosis was 26% among Indians, 19% among Malays, 0.7% among Chinese and 6% among other races. DDT in coconut oil appeared to be rather ineffective in a small treatment sample. Malathion, gammaxene and actellic acid at 0.5% concentration, on the other hand was found to be 100% effective. Other effective

chemicals are Carbaryl, permethrin and kerosene.

In another report of 4,112 children in KL in 1983, 13% were found to have pediculosis. The racial breakdown was 28% among Indians, 19% among Malays and 5% among Chinese. Sinniah and colleagues found that the prevalence was still high in Kelang in 1984. Among 1,243 rural school children in Kelang they found rates of prevalence of 52% among Indians, 42% among Malays and 27% among Chinese. Boys (33%) had a lower prevalence of lice than girls (50%). Ayyamani also found a high prevalence in Gombak in 1986. The prevalence rates being 55% in Indians, 26% in Malays and 37% in Chinese. All studies show that girls were always more often affected than boys.

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Sinniah B, Shekar C, Ramphal L and Senan P. Pediculosis among rural school children in Kelang, Selangor, Malaysia and their susceptibility to malathion, carbaryl, Perigen and kerosene. J.Roy.Soc.Hlth. 104:114-115 1984.

MYIASIS

Infestation of organs and tissues of man and animals by the Dipteran fly larvae is known as myiasis. Neglected ulcers and wounds presenting with maggots like these are not uncommon in our hospitals even today. Reid was the first to bring medical attention and academic interest to the subject by a report from Malacca in 1953. Myiasis can take different forms.

Cutaneous myiasis

This is the commonest form. Besides Reid, Cheong *et.al*., Thomas *et.al*., Ramalingam and Edariah *et.al*. have reported on this. The flies noted include *Chrysomya bezziana*, *C. megacephala and* Sarcophaga sp. These maggots however do not cause the cutaneous ulcers they are found in and in fact they are now employed in wound management. They help debride necrotic wounds.

Urogenital myiasis

In this form maggots involve the genital region and may be excreted in the urine or found in the vagina. Ramalingam has observed this in Malaysia.

Intestinal myiasis

There are three reports of myiasis in the literature for Malaysia. Cheong *et.al*. saw maggots of the species *Clogmyia albipunctatus* in the faeces of one case. Thomas *et.al*. found large numbers of maggots of the same species in a young child who complained of severe gastro-enteritis. The fly is associated with filthy water and dirty latrines. Lee *et.al*. found maggots of *Hermetia illucens* in a 7 year old girl from K Kangsar, Perak.

References

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Lee HL, Chandrawathani P, Wong WY, et.al. A case of human enteric myiasis due to larvae of Hermetia illucens (Family:Stratiomyiadae): first report in Malaysia. Mal J Pathol 17:109-111 1995.

PAEDERUS DERMATITIS

A small rove beetle, genus paederus, causes dermatitis not by its bite but when it is crushed on the skin. UKM workers have observed the species *P. fuscipes* in several patients and medical students in Kelantan during the monsoon season from October to January. It causes a peculiar itchy erythemato-vesicular dermatitis most often in the face and neck. Treatment with topical steroids and occlusive dressings give good results.

Reference

Mokhtar N, Singh R and Ghazali W. Paederus dermatitis amongst medical students in USM, Kelantan. Med.J.Mal. 48:403-406 1993.

SCABIES

Scabies is a worldwide problem and Malaysia is as much affected as any country. The Ministry of Health records indicate that 104,233 scabies cases were treated in 1970 and about the same number, though slightly less, in 1979. Not all cases seek treatment at clinics.

In a survey to determine the prevalence of scabies in the community Gill and Kandiah studied settlers in agricultural land schemes in the Jengka Triangle in Pahang. They found 12% of the populace affected. Teenagers and children under 20 years were about twice as commonly affected as adults. Poor parental supervision of hygiene and inadequate and water supply could have been important contributing factors to the high prevalence. Males and females were found to be equally affected. In a seroprevalence study among 312 Orang Asli, using ELISA to polyvalent anti-sarcoptes, Normaznah *et.al* noted a positive rate on 24.7% (26.1% in males and 23.6% in females), although actually only 2 had clinical manifestations.

The causative agent, the mite *Sarcoptes scabiei* produced lesions in the hands in three-quarters of the cases. In about half the cases there were lesions on the arms, buttocks and legs. Treatment with Gamma Benzene Hexachloride was very effective, curing 98% with one application. But compliance to therapy especially among contacts of index cases was poor. Recurrence of the problem is to be expected in many and the problem should be checked for regularly in schools. It is not a totally harmless condition because secondary infection with streptococci among other bacteria can cause nephritis besides the morbidity of its itchiness.

The Jengka experience is probably typical for many rural communities. We do not however, know the extent of scabies in urban areas and among the higher income socio-economic groups.

A condition in which vast numbers of scabetic mite are found in encrusted skin is called Norwegian scabies. It occurs usually in patients with suppressed immunity. It has been described by Chow and Rajagopalan among 5 leprosy patients in Sungei Buloh.

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TICKS

Ticks occur widely in Malaysia and are commonly found on domestic or husbandry animals and occasionally latch on to human beings. Sometimes they enter some body orifice and present as medical problems. One notable problem is when the tick attaches itself inside the ear. The tick, *Dermacentor* sp., engorged with blood may look like a 'haemorrhagic bulla'. Indudharan *et.al*. have reported a few cases. One in a 65 year old Malay woman caused a reversible facial nerve palsy. The offending tick was removed after instilling lignocaine into the ear. Ticks accounted for 11% of all foreign bodies in the ear seen over 7 years in HUSM.

References.

Indudharan R. Dharap AS. Htun YN. An unusual differential diagnosis of myringitis bullosa haemorrhagica. Trop Geogr Med. 47:227-228 1995.

Indudharan R. Dharap AS. Ho TM. Intra-aural tick causing facial palsy. Lancet 348:613 1996.

SECTION 3: THE SYSTEMIC DISEASES

CHAPTER 19

THE EYE

NORMAL EYELID AND EYEBROW DIMENSIONS

In a study of 305 Malays, Dharap and Reddy found that eyelid crease height was lower compared to Caucasians. The upper eyelid crease represents an indentation caused by superficial insertion of the levator palpebrae superioris muscle fibres. In Orientals the muscle inserts on the levator aponeurosis at this low level, instead of higher in the skin as in Caucasians. On the other hand pretarsal skin height and eyebrow height were significantly higher compared to Caucasians. These measurements also varied with age and sex among the subject studied.

Reference

Dharap AS and Reddy SC. Upper eyelid and eyebrow dimensions in Malays. Med.J.Mal. 50:377-381 1995.

INTRAOCULAR PRESSURE

It may be of relevance to ophthalmic surgeons that a racial difference has been noted by Lee *et.al*. in the resulting rise of intraocular pressure from retrobulbar local anaesthetic infiltration. In a study where 3ml of local anaesthetic was injected, there was a mean intraocular pressure rise of 5mmHg which was not significantly different among males and females, nor young and old patients. But surprisingly Chinese had a significantly higher mean increase of intraocular pressure of 6.3mmHg compared to Malays (4.4mmHg) and Indians (3.7mmHg). Possible explanations could be smaller orbital volumes, greater intraorbital fat or a stiffer orbital septum but that could not be established.

Reference

Lee FN, Kong VY, Lee GP et.al. Intraocular pressure variation following retrobulbar anaesthesia among the different sex, age and ethnic groups in Malaysia. Med J Mal. 54:438-441 1999.

CONGENITAL PTOSIS

In a series by Fong, 19 cases of congenital ptosis formed 86%, of the total of ptosis cases seen and operated on, as compared to acquired cases of ptosis. These were consecutive cases over 3 years from 1973 to 1976 at the UH. Unilateral congenital ptosis accounted for 17 cases.

Reference

Fong ACH. The surgical management of ptosis. Med.J.Mal. 31:140-147 1976

CONGENITAL SQUINTS

Strabismus or squint is less common in Asians as compared to Caucasians. Teoh and Yow attempted to define its prevalence in a study of chlidren in the first year at primary school in PJ. Out of 650 pupils they found 14 (2.2%) which is less than the 5-6% in Caucasian series. The majority, 12 were of the divergent type. One had alternating convergent squint and one was a case of hypertropia. No amblyopia was detected in these squinters.

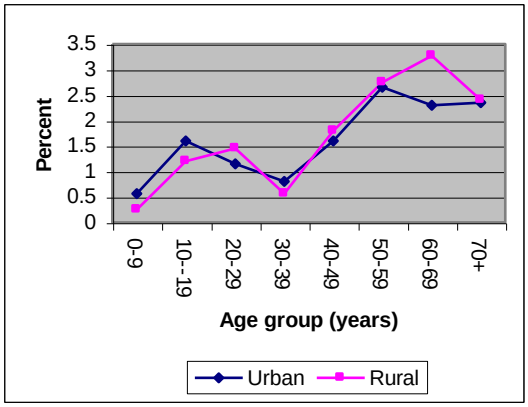
Reference

Teoh GH and Yow CS. Prevalence of squints and visual defects in Malaysian primary one school children. Med.J.Mal. 37:336-337 1982

REFRACTIVE ERRORS

In 1971 Chandran and Ooi at the UH Eye Dedpartment remarked that in their experience, myopia commences as early as 5 years and stabilises around 25years. Yeow noted that myopia in Malays stayed relatively constant from 10-50years whereas Chinese show a different natural history. Myopia in Chinese progresses rapidly from age 10-20years after which it starts to show a hyperopic shift to reach a level of myopia similar to that of Malays at around 35years. Most astigmatic errors are associated with spherical errors of a low order +0.9 to -3.0D which accounts for 77%. Direct astigmatism accounts for 50%, indirect for 35% and oblique 15%. Anisometropia was present in about 30% of their patients.

Figure 19.1 Prevalence of refractive errors in different age groups in Malaysia



In comparison to Caucasians who have a ratio of hypermetropia:myopia of 88:12, Malaysians had a reverse ratio of 28:78 in a small sample study of 1,500 eyes by Chandran. 79% of Chinese, 73% of Malays and 61% of Indians fell on the myopic side of refractive error. 40% of Chinese eyes fell between 0 to -2D compared with 39% of Malays and 37% of Indians. On the other side, 19% of Chinese eyes, 23% of Malays and 34% of Indians fell between 0 to +2D. Less than 2% of eyes had refractive errors greater than -9D.

Refractive errors were studied as part of the National Eye Survey in 1996, in a collaborative work between the MOH and universities. This was a large nationwide survey by household interview and eye examination involving 18,957 persons. The prevalence of refractive errors overall was 1.2%, higher in women (1.5%) than men (0.9%). In both urban and rural areas the prevalence showed a small peak in young adults, a dip in the 30-39 age group, then a rise among the elderly (Figure 19.1).

References

Chandran S and Ooi VES. Some aspects of refractive errors in West Malaysia. Med.J.Mal. 25:193-197 1971

Chandran S. Comparative study of refractive errors in West Malaysia. Br.J.Opthal. 56:492-495 1972.

Yeow PT. Progression of myopia in different ethnic groups in Malaysia. Med.J.Mal. 49:138-141 1994.

Zainal M, Ismail SM, Ropilah AR et.al. Estimates from the National Eye survey, 1996. Kuala Lumpur, Malaysia 2000.

OCULAR INJURY

Eye injuries alongside infections are the commonest ophthalmic conditions in clinical practice in Malaysia. Chandran and Ooi described a survey of 335 accidents involving the eye seen at the Eye Clinic at the University Hospital KL over two and a half years from 1967. This represented the urban spectrum of the population. 47% were industrial accidents, 12% home and 9% vehicular accidents. 11% were caused by sticks and stones mainly from children at play. Most cases (67%) were corneal or conjuntival cuts or foreign bodies. 4% had chemical burns from caustic soda, acid, alkali or lime and cement. 5% had flash burns from welding injuries. Intraocular foreign bodies were found in 5% mainly from industrial cases. 37 (11%) cases resulted in blindess. Another 26 resulted in slight to moderate visual loss. The

lesion causing visual loss was corneal scarring in 19 cases which, could be salvaged were corneal grafts freely available.

In 1972 Chandran highlighted badminton as a partcilarly common cause of blunt injury to the eye resulting in a hyphaema in 40 cases. From 1968 to 1971 it accounted for 56% of all hyphaemas. More than half of these cases occured around the months the Thomas Cup badminton finals were played! He found that if the level was up to 50% as a rule it cleared spontaneously provided that with rest no secondary haemorrhage occurred. Secondary haemorrhage however occurred in 10%. Permanent impairment of vision to 6/18 or worse occurred in 20%, mainly due to macular change and cataract.

Teoh and Yow from the UH studied a series of 48 cases with intraocular injuries from 1970-1979. Most of their patients were young Chinese males with accidents at work. 80% involved hand held hammers. In 9 the object was lodged in the anterior chamber. But in 39 the object was found in the posterior chamber which carried a poorer prognosis in whom 64% ended with a vision poorer than 6/60. Singh at UKM reported a similar series of 37 patients over a 5 year period and found 74% were industrial injuries, mainly hammering related. A similar number 68% had objects lodged in the posterior segment of the eye. Cataract, vitreous haemorrhage and retinal detachment were the common causes of visual loss. Visual loss to a level below 6/60 was found in 24% all patients.

In a follow up study at UH covering the period 1980-1989, Lai and Moussa, recorded 98 cases of similar intraocular injuries with penetrating foreign bodies. Again most were young Chinese males with accidents related to work.64% involved hand held hammers and 20% involved grass cutters.

Zainal and Goh review 167 perforating eye injuries, consisting of corneal and/or scleral lacerations in 159 patients between 1990 and 1992 seen at UKM. 60% of patients were between 20-39years old. Occupational injuries accounted for 35% of injuries, road accidents for 29%. Domestic accidents accounted for 23% and were mainly in children under 10years. They accounted for 17.6% of the 159 patients. At presentation 13% had normal vision, 23% had low vision and 64% had vision below 3/60. Six months after injury 42% were legally blind.

Chemical irritation causing severe conjunctivitis, chemosis, lacrimation and photophobia has been reported in one case due to contact with the sap from the decorative plant, *Pedilanthus tithymaloides*, or zigzag plant named after its branching pattern. There was complete resolution after about seven days.

References

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Lai YK and Moussa M. Perforating eye injuries due to intraocular foreign bodies. Med.J.Mal. 47:212-219 1992.

Zainal M and Goh PP. A study of perforating eye injuries at the ophthalmology department, National University of Malaysia. Med.J.Mal. 52:12-16 1997.

INFECTIVE KERATITIS AND CONJUNCTIVITIS

The healthy conjunctiva may sometime habour bacteria. Singh and Lim swabbed conjunctiva from 200 non-diabetics and 50 diabetics for culture. 30% and 62% of the groups

respectively had positive cultures. *S. epidermidis*,(53%) *Corynebacterium* sp.(32%) and *S. aureus*(6%) accounted for more than 90% of the total.

In 306 cases where bacterial culture was obtained from 527 patients with acute conjuntivitis in Kelantan, Subramania and Reddy found that the commonest isolates were *S. aureus* (27%) followed by *S. epidermidis* (11%). Among neonates *Haemophilus influenzae* (6.1%) was the commonest gram negative isolate, whereas in other cases of acute conjuntivitis it was *Pseudomonas aeruginosa* (7.4%). A combination of topical chloramphenicol and gentamicin was found to be very effective treatment.

Although some infections affect mainly the cornea while other mainly the conjunctiva, there is a spectrum where there is kerato-conjunctivitis, so that it is reasonable to put these eye infections together.

Viruses, chiefly the *adenoviruses*, *enteroviruses* and *herpes simplex* are the commonest cause of outbreaks of such infections. Bacteria may superimpose on viral infections or may occur alone.

Mycotic keratitis is probably underdiagnosed. *Fusarium solani* is one common fungal agent. *Aspergillus, Candida, Nocardia* and *Penicillium* are other causes.

References

Singh K. Epidemic kerato-conjunctivitis in Malaya. Med.J.Mal. 17:4-11 1962

Ong B and Rose L. Mycotic keratitis. Med.J.Mal. 20:84-85 1965

Tan DSK and Lee WS. An enterovirus Type 70 epidemic of acute conjunctivitis in Peninsula Malaysia. Med.J.Mal. 36:76-78 1981

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Singh M and Lim VKE. Bacteriology of healthy conjunctivae in Malaysians. Med.J.Mal. 42:50-52 1987

Subramania A and Reddy SC. Topical chloramphenicol/gentamicin in the empirical treatment of acute conjunctivitis - is it rational? Med.J.Mal. 51:490 1996.

PADI PLANTERS' KERATITIS

A form of nummular keratitis, claasically described by Dimmer, unlike epidemic kerato-conjunctivitis and punctate superficial keratitis has been seen in large numbers in Nothern West Malaysia especially among rice-field workers. Hence it has been termed `sawah keratitis' or padi planters' keratitis.

The history is usually given of padi-field water entering the eye. There is acute irritation and photophobia which subsides to be followed by varying degrees of visual impairment, due to characteristic round, discrete, coin-like scars of different sizes. The lesion persists for a long time.

The cause is unknown. Wong has studied 260 cases in Penang and been able to tell a patient his occupation by examining his eyes in many cases. He thought a virus may be responsible but was not successful in isolating any virus.

Reference

Wong PL. Keratitis nummularis (Dimmer) among rice-cultivators in North Malaya. Med.J.Mal. 22:313-322 1968

PTERYGIUM

The pterygium is essentially a triangular tongue of conjuctiva overgrowing on to the surface of the cornea of the eye. It is widely held that the prevalence of pterygium is higher in the tropics, and that solar ultraviolet rays may have a role in its aetiology, although its actual prevalence here has not been determined. Normalina and Zainal reported that 4% of 204 residents in a nursing home for the elderly had a pterygium. Leong in papers alone and with

Chong has evaluated thiotepa and mitomycin-C for preventing recurrence after surgery. It has not been noted that any particular population more at risk of being affected.

References

Leong KC and Chong YF. Pterygium and mitomycin-C therapy. Med.J.Mal. 31:69-72 1976

Normalina M and Zainal M. The dimensions of ocular morbidity amongst the nursing home geriatrics population. Med.J.Mal. 53:239-244 1998.

CATARACT

Cataract is one of the commonest ophthalmic conditions and the bread and butter of ophthalmic surgeons. McPherson reported finding 25 cases in a survey in Kelantan in 1952 and operating on all except 6 of them. He then remarked that the next year the State Surgeon operated on 380 cases, in conjunction with a case-finding welfare programme.

At the UH, Then and Chandran reported 743 cataract extraction on 671 patients from 1968 to 1972, that is about 150 cataracts a year. The peak age of patients was the seventh decade, which was about 10 years lower than in the West. Chinese made up 54% of the total extractions, and Indians contributed 39%. The low proportion of Malays (6%) was not easy to explain but probably due to a reluctance to come forward for surgery. These were all poor indicators on the prevalence of cataract disease.

In 1996, however, the National Eye Survey of 18,957 individuals finally gave us a good indication of the prevalence of cataract disease in the country. The prevalence is low up till the 40-49 year age group (<1%) after which it rises exponentially. Overall prevalence of cataract in the 50-59 year group was 6.0%, 22% in the 60-69 year group and 55% in those 70 years and above. However the prevalence of visual impairment, defined as vision of less than 6/18 in the better eye, due to cataract was 1.3% in the 6th decade, 8.2% in the 7th decade and 26% in those 70 years and above. Women had slightly higher rates than men. Indigenous races other than Malays and Indians tended to have more cataract problems than Chinese and Malays and cataracts were more common in rural than urban places.

Doing extractions in the early 1970s Then and Chandran reported vision of 6/18 or better in 84%. In the 1980s anterior implants have now replaced simple extraction offering superior results for the patients. In the National Eye Survey in 1996, 0.6% of those 50-59 years, 2.7% of those 60-69 years and 9.0% of those 70 years and above had had cataract treated. This means that only between 25-32% of those with cataracts causing visual impairment have had their cataracts treated. More men than women had treated cataract. More Chinese and Indians tended to have treated cataract than Malays and other indigenous races. The prevalence of aphakia, the old treatment for cataract, was 0.25% among the 50-59 year group, 0.67% among the 60-69 year group and 4.7% among the 70 and above group. Aphakia was most common among elderly Indians, especially in the states of Penang and Selangor. Lens implants operations, on the other hand, were done in 60% of those in the 6th decade, 75% of those in the 7th decade and in 52% of those 70 years old or more.

References

Then SM and Chandran S. Cataract extraction in West Malaysia. Med.J.Mal. 30:180-186 1975

Zainal M, Ismail SM, Ropilah AR et.al. Estimates from the National Eye survey, 1996. Kuala Lumpur, Malaysia 2000.

GLAUCOMA

Glaucoma is a disease of raised intraocular pressure. In closed-angle glaucoma the root of the iris is in apposition to the trabecular meshwork and prevents aqueous humour leaving the eye. It may present with pain as primary acute angle-closure glaucoma (PACG) or insidiously in primary chronic angle-closure

glaucoma (CACG). In primary open-angle glaucoma (POAG) the aqueous humour has free access to the trabecular meshwork, which normally drains the aqueous but for some unknown cause there is a relative obstruction to its outflow. It causes visual loss insidiously.

Selvarajah reported that over 5 years from 1986 , 1,966 patients presented with glaucoma at the KL GH eye department forming 2.9% of all their patients. 30% had PACG, 46% had POAG, 6.5% had Normal-Low Tension Glaucoma, 1.5% had infantile glaucoma and 16% had secondary glaucoma.

Among the 907 PAOG patients, 59% were males and 41% females. 41.6% were Malays, 31.9% Chinese, 24.5% Indians and 2.1% others. 95% of the patients were between 40-69 years old. Among the 590 PACG patients, again 59% were males and 41% females. 34.9% were Malays, 38.3% Chinese, 26.3% Indians and 0.5% others. 95% of these patients were also from the 40-69 years age group. 311 patients had secondary glaucoma. 26% were due to uveitis, 26% were phacogenic, 5% were due to rubeosis iridis, 23% were due to trauma and 29% were aphakic or pseudophakic. 122 patients had absolute glaucoma in one eye. 35 patients were completely blind due to glaucoma in both eyes.

Sharif and Selvarajah reviewed surgical cases for glaucoma over 4 years from1989 at the UKM. They excluded those done at the same time with other eye surgery like for cataracts. They included 61 cases. Trabeculectomy was done as primary treatment for 3 eyes. Failed medical treatment was the indication in 36 and poor compliance to treatment the reason in another 22. 24 patients operated on had POAG, 75% of them males. 50% of these patients were Malays, 25% Chinese and 25% Indians. In both types of angle-closure glaucoma, on the other hand females were the majority. In the 18 patients with PACG 78% were female. Malays accounted for 44%, Chinese 44% and Indians 11%. In the 19 patients with CACG 63% were female. 32% were Malays, 42% Chinese and 26% Indians.

At 2 years follow-up, the rate of successful trabeculectomies, defined by intraocular pressures below 20mmHg, was 62% for POAG, 48% for PACG, and 43% for CACG.

The National Eye Survey 1996 of a sample of 18027 people found chronic glaucoma, defined as the cup:disc ratio of ≥0.4 along with intraocular pressure of more than 21mmHg, prevalent in 0.05% of the population. It was detected in less than 10 people.

References

Sharif FM and Selvarajah S. The outcome of trabeculectomy for primary glaucoma in adult patients in UKM.. Med.J.Mal. 52:17-15 1997.

Selvarajah S. An analysis of glaucoma patients seen at the General Hospital Kuala Lumpur over a five year period: 1986 to 1990. Med.J.Mal. 53:42-45 1998.

Zainal M, Ismail SM, Ropilah AR et.al. Estimates from the National Eye survey, 1996. Kuala Lumpur, Malaysia 2000.

RETINAL DETACHMENT

This is not an uncommon condition. Vijendran and Fong reported 50 cases over a one year period in 1976 at the UH. The ratio of males to females was 3:1. Chinese accounted for 60% of cases. It is unclear whether this is due to a higher incidence or just that they utilised the hospital services more. As to underlying conditions, 34% of the patients were myopic (including 12% high myopia >-8D) and 28% were aphakic. Singh records that 401 patients with retinal detachment were admitted at the UKM over 5 years to 1984. 45 patients were under 20 years of age. In this young group myopia (36%) and trauma (30%) were the commonest underlying factors. He observed a similar sex and racial ratio.

In 20% of cases the detachment was total in the UH series. In 96% there was macula detachment. However, 86% of patients had

successful anatomical reapposition of the retina in both studies, mostly through the external scleral plombage surgical procedure. Vision improved in 82% of patients who had successful surgery according to Vijendran and Fong. But Singh reported that only 52% of his juvenile patients achieved a vision of 6/36 or better.

References

Vijendran M and Fong ACH. Retinal detachment. Review of 50 consecutive cases. Med.J.Mal. 31:128-132 1976

Singh M. Juvenile rhegmatogenous retinal detachment in Malaysia. Med.J.Mal. 41:156-160 1986

CENTRAL SEROUS RETINOPATHY

This is a condition first described by Von Graefe in 1866 but is uncommon in the West. Ooi reviewing 1,644 patients at the UH eye clinic, diagnosed 33 cases of central serous retinopathy in 18 months ending in 1968. The subjects usually complained of defective or distorted central vision of sudden or intermediate onset. A history of previous transient blindness may be obtained. The subject is usually an active male between 20 to 45 years. Women are 4 times less likely to be affected. The cause of the condition is not known but it runs a benign course after which good vision is restored after about one to ten months. However a relapse is not uncommon.

Reference

Ooi VES. Central serous retinopathy: a preliminary report of 33 cases. Med.J.Mal. 24:18-20 1969

RETINAL VEIN OCCLUSION

Over six years, UKM opthalmology clinic observed 95 cases of retinal vein occlusions. 55 patients had branch vein occlusions and 40 had central vein occlusions. 82% of these patients presented with visual loss but in 16% the finding was made incidentally. Pain however was infrequently experienced. 44% of patients had hypertension and 29% of patients had underlying conditions. Few had hyperlipidemia or glaucoma.

Reference

Teoh SL and Amarjeet K. A comparative study of branch retinal vein occlusion and central vein occlusion amongst Malaysia patients. Med.J.Mal. 48: 410-415 1993.

PHTHISIS BULBI

Phthisis bulbi mean the shrinkage of the eye from various causes. The affected eye is usually blind. Normalina and Zainal found that in a nursing home population in Seremban whose mean age was 71years, 3% had bilateral phthisis bulbi and another 3.4% had unilateral phthisis bulbi.

Reference

Normalina M and Zainal M. The dimensions of ocular morbidity amongst the nursing home geriatrics population. Med.J.Mal. 53:239-244 1998.

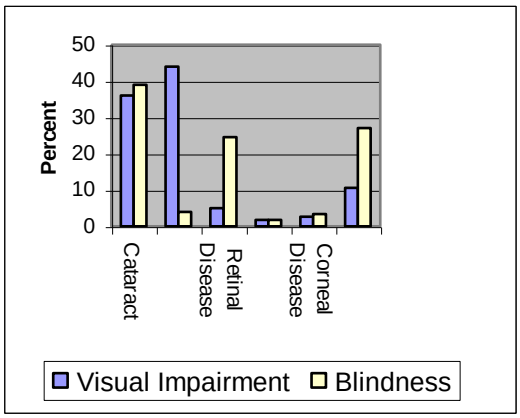
BLINDNESS AND VISUAL IMPAIRMENT

A rural survey by Osman and Rampal in Kuala Selangor found visual impairment, defined as acuity below 6/18 and/or visual field less than 10°, in 48% of those above 65 years. Among those between 40 to 65 years 11% had visual impairment and less than 2% of those younger were affected. The cause was cataract in half the total. Refractive errors and miscellaneous conditions accounted for another quarter each. Blindness as defined by WHO as vision below 3/60 was found in 1.7% overall. Another survey in 1993 in the same district found that 26% among those above 70 years had visual impairment compared to 2.1% among those ages 30-39 years. Among these 330 people

sampled the overall rate of blindness (vision below 3/60) was 0.7% and rate of visual impairment 5.6% (vision below 6/18). 79% of visual impairment was due to cataract.

In a survey of 204 elderly people (>60yrs) in a nursing home in Seremban, Normalina and Zainal found that 19% were legally blind, the commonest cause being cataract (74%). 47.5% had low vision and of these cataract accounted for 81% and glaucoma 1%.

Figure 19.2 Percentage of blindness and visual impairment due to various causes 1996



The National Eye Survey of 1996 with a sample size of 18027 individuals found a 2.7% prevalence rate of visual impairment. The prevalence of visual impairment was less than 2% among those under 40 years old but rose exponentially after that to 2.5% in the 5th decade, 5.3% in the 6th decade, 13% in the 7th decade and to 35% in those 70 years and above. The rates were slightly higher among women than men and in rural areas versus urban areas. The prevalence rate for blindness, defined as the inability to count fingers in daylight at a distance of 3 meters was 0.3% overall. This means there are over 65,000 blind people in Malaysia. The prevalence of blindness was less than 0.2% among those less than 40 years old but rose to 0.3% in the 5th decade, 0.5% in the 6th decade, 0.7% in the 7th decade and to 4.8% in those 70 years and above. As a group, the other indigenous races had a prevalence rate almost twice as high as the average with Sabah having a rate almost twice the national average. Besides that, distribution of blindness among men and women, among the 3 main races and the urban and rural were not significantly different. Figure 19.2 shows the relative importance of the different causes of blindness and visual impairment.

References

Osman A and Rampal KG. Prevalens kecacatan penglihatan di Kuala Selangor. Med.J.Mal. 43:232-236 1988

Zainal M, Masran L and Ropilah AR. Blindness and visual impairment amongst rural Malays in Kuala Selangor, Selangor. Med.J.Mal. 53:46-50 1998.

Normalina M and Zainal M. The dimensions of ocular morbidity amongst the nursing home geriatrics population. Med.J.Mal. 53:239-244 1998.

Zainal M, Ismail SM, Ropilah AR et.al. Estimates from the National Eye survey, 1996. Kuala Lumpur, Malaysia 2000.

THE LACRIMAL APPARATUS

ACUTE DACRYOADENITIS

Infection of the lacrimal gland is not common.

Reference

Mahendraraj K and Chandran S. Acute suppurative dacryoadenitis. Med.J.Mal. 42:137-138 1987

DACRYOCYSTITIS

Chronic dacryocystitis due to the obstruction of the nasolacrimal duct was described by Galen as early as the 2nd century BC. Fathilah and Chandran collected a series of 50 cases at the UH over 15 years. All ages were affected with females about 3 times more commonly than males. Simple probing was

done for children, 8 in all, with a 50% success rate. 42 patients had dacryocystorhinostomy performed with a 93% success rate.

Reference

Fathilah J and Chandran S. Chronic dacryocystitis - a review of 50 cases in the University Hospital Kuala Lumpur. Med.J.Mal. 43:229-231 1988

THE EAR

AURICULAR SINUS

An auricular sinus is usually a very small opening on the skin of the auricle or periauricular area. It is a congenital condition, common in this part of the world. It may be unilateral or bilateral. The condition is inherited in a Mendelian dominant fashion but with only 50-85% penetrance and is not sex linked. 81% of the of the sinuses open in the anterior helicine position, that is anterior to the crus of the helix. Esa and Solahuddin observed that it was twice as common in females than in males, in 56 of their patients seen over one year. Most present below 10years old because of infection.

Reference

Esa R and Solahuddin M. Auricular sinus. Med.J.Mal. 48: 286-292 1993.

CONGENITAL OSSICULAR ABNORMALITY

Deformed ossicular bones are a rare cause of congenital deafness, at least they would appear to be because they are not easy to diagnose. Khanijow, Phang and Kerr reported a 9 year old Chinese boy who had an abnormal stapes removed surgically.

Reference

Khanijow VK, Phang WK and Kerr AIG. Congenital ossicular abnormality - a case report. Med.J.Mal. 42:314-316 1987.

FOREIGN BODIES

In a retrospective survey of 348 cases of aural foreign bodies presenting to the emergency department of the HUSM, over 7 years from 1990, Indudharan *et.al* reported that 55% were arthropods. Cockroaches (31%) and ticks (21%) were commonest out of 191 arthropods, but many arthropods (23%) were unidentified. (see section on arthropods). Besides arthropods, other creatures found included a leech and a snail. Patients of all ages were affected but 70% were less than 14 years old.

Reference

Indudharan R, Ahmad M, Ho TM et.al. Human Otoacariasis. Ann Trop Med Parasitol 93:163-167 1999.

OTITIS EXTERNA

Indudharan and Subramania reported that in study where 47 bacterial culture were obtained from patients with external ear infections in Kelantan, *S. aureus* (42.5%) and *Pseudomonas aeroginosa* (19%) were the commonest pathogens isolated. Mixed flora was found in 21%.

Reference

Indudharan R and Subramania A. Is routine culture and sensitivity essential for the management of otitis externa? Med.J.Mal. 51:396 1996.

CHRONIC SUPPURATIVE OTITIS MEDIA

Chronic middle ear infection is common in children. In HUSM, Kelantan in a bacteriological study of 382 swab specimen of CSOM cases the commonest organisms cultured were

Pseudomonas aeruginosa (27.2%) and *Staph Aureus* (23.6%).

Refernece

Indudharan R, Haq JA and Aiyar S. Antibiotic in chronic suppurative otitits media: a bacteriological study. Ann Otol Rhinol Laryngol 108:440-445 1999

OTOMYCOSIS

In 130 ear swabs and ceruman of patients suspected to have otomycosis between 1969 and 1981, Chin and Jegathesan obtained isolates in 75%. 8 genera of fungi were noted. *Aspergillus* was isolated in 78% of positive specimens. *Candida* was obtained in 26%, most were not *Candida albicans*. *Cunninghamella, Epidermophyton floccosum, Penicillium, Streptomyces* and *Trichosporon* were each isolated once.

Reference

Chin CS and Jegathesan M. Fungal isolates in otomycosis. Mal J Pathol. 5:45-47 1982.

MASTOIDITIS

Mastoiditis develops as an extension of otitis media. It is becoming rare in developed countries with the advent of antibiotics. Over a period of 7 years, Elango and Than reviewed 14 patients with acute mastoiditis and 20 with chronic mastoiditis in Kelantan. 57% of those with acute mastoiditis were less than 2 years old. The age of patients with chronic mastoiditis ranged from 6-38 years. One patient had lateral sinus thrombosis, one had meningitis and four had facial nerve palsies. One boy had bilateral mastoiditis of tuberculous origin. 20 were treated with modified radical mastoidectomy and 12 with cortical mastoidectomy. Bacterial culture was obtained in 80%. *Proteus mirabilis* was the commonest organism (41%) isolated. Gram positives accounted for 33% and the other Gram negatives for 22%.

Reference

Elango S and Than T. Mastoiditis in Kelantan. Med.J.Mal. 50:233-236 1995.

MENIERE'S DISEASE

Meniere's disease may not be as common among Asians as in Caucasians. It was the diagnosis in 8% of 200 cases of vertigo and in 22% of patients presenting with giddiness in two separate studies in the UH ENT clinic.

References

Ponniah RD. A study of the aetiology of vertigo in Malaysia. Med.J.Mal. 32:41-44 1977.

Krishnan G. A review of the management of 107 dizzy patients at the University Hospital. Med.J.Mal. 49:44-48 1994.

OTOSCLEROSIS

Otosclerosis is a disease of the labyrinthine capsule in some cases involving the oval window causing fixation of the stapes. It presents as progressive hearing loss without earache or otorrhoea. Ponniah and Chin noted that there seemed to be a racial difference in the prevalence of the disease. They observed from 33 patients with the condition Indians were a majority where as they were neither the largest number of patients at the ENT clinic nor of patients with deafness. Otosclerosis formed 1:20 patients with deafness among Indians, but 1:80 among Malays and 1:100 among Chinese.

Reference

Ponniah RD and Chin YH. Incidence of otosclerosis in the three ethnic groups in Malaysia. Med.J.Mal. 31:36-37 1976.

IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

As its name describes this is an unexplained

sudden hearing loss of greater than 30db. Its occurence locally has been reported in UH. A favourable recovery occurs in 63% of patients with supportive therapy.

Reference

Amin JM. Idiopathic sudden sensorineural hearing loss. University Hospital Experience. Med.J.Mal. 48:407-409 1993.

HEARING LOSS

NOISE EXPOSURE

Maisarah and Said studied noise exposed factory workers and found that only 5% wore hearing protection devices although 80% of these workers were actually porvided with such devices. Only 35% were aware noise was hazardous to hearing. Only 17% of workers with hearing impairment realised or complained of having difficulty hearing. 30% of their sample of 442 noise exposed workers in 4 factories had hearing impairment, although 83% had some sensori-neural hearing loss. Medical practitioners ought to note that such matters come under the Noise Exposure Regulations (1989) of the Factories and Machinery Act 1967.

DIVING

Zulkaflay et.al. have studied and found an insidious development of high frequency sensorineural hearing loss among 120 divers in the Royal Malaysian Navy. Those who had been diving for more than 5 years and were above 30 years in age had thresholds of about 20 dBHL less than non-divers in the 4000-6000Hz frequency.

CHILDREN

In a survey of 1,307 school children in Kelantan, Elango *et.al*. noted that 5.8% (76 children) failed the screening audiometric test. 52 of these children had chronic suppurative otitis media (CSOM). Another 43 who had CSOM were not detected by the audiometry test. In a study of 165 deaf children, in 1993, Elango found that the cause of deafness was prenatal infection in 37%, perinatal complications in 12%, meningitis in 12% but the cause could not be determined in 20%.

RURAL

In a rural survey 241 males in Selangor, Hassim and Rampal reported a hearing loss of greater than 25dB of 45% in those 61-70years old and 70% in those above 70 years. None of those in the 15-30 year group had such a hearing loss.

References

Elango S, Purohit GN, Hashim M and Hilmi R. Hearing loss and ear disorders in Malaysian school children. Int J. Peadiatric Otorhinolaryngol 22: 75-80 1991.

Elango S. Aetiology of deafness in children from a school for the deaf in Malaysia.. Int J. Otorhinolaryngol 27:21-17 1993.

Maisarah SZ and Said H. The noise exposed factory workers: The prevalance of sensori-neural hearing loss and their use of personal hearing protection devices. Med.J.Mal. 48:280-285 1993.

Noor Hassim I and Rampal KG. Prevalens kurang pendengaran dan gangguan pendengaran penduduk lelaki luarbandar Selangor, 1993. Med.J.Mal. 49:78-85 1994.

Zulkaflay MS, Saim L, Said H et.al. Hearing loss in diving – a study amongst Navy divers. Med J Mal 51:103-108 1996.

CHAPTER 20

PSYCHIATRIC DISORDERS

INTRODUCTION

From the time of Malaysia's independence till the end of the twentieth century two large mental hospitals served as centres for most psychiatric hospital admissions; Tanjong Rambutan, which was first opened as the Central Mental Hospital in 1911, for the North, and Tampoi in Johore Bahru for the South. However, from the 1980s there has been a trend to encourage such patients to be managed in General Hospitals closer to their domiciliary origin. Tan observed from the admissions to the Tampoi Mental Hospital that for 1963 schizophrenia (90%) was the most prevalent diagnosis for admission. This is not unexpected, as inability to manage the patient at home is the main reason for psychiatric hospital admissison. Depressive illness and other psychoses formed another 3% and 2% of admissions respective. It would however be far too inaccurate to estimate incidence or prevalence of mental illnesses from these figures as such hospitalisation was not accepted by all communities.

The Gombak hospital for Orang Asli serves the majority of the approximately 50,000 Orang Asli in Peninsula Malaysia in the 1970s. Reviewing psychiatric disorders seen there, Tan and Armstrong found an average of 14 cases admitted yearly over a 5 year period. This, it is believed, gives a very rough indication of the number of serious mental illness among them. The majority of these cases (75%) were diagnosed as schizophrenia.

One method of estimating the prevalence of psychiatric disorders in a community, as Khare, Upadhyaya and Kamaruzaman have done, is to use vigetttes for a number of major mental disorders. Using 180 key informants in 3 health districts in Kelantan with a population of 26,809 in Kelantan, they identified 569 probable psychiatric cases. They found a point prevalence of 0.8%, or 215 cases of psychiatric illnesses, including epilepsy, mental retardation, schizophrenia or manic illness. 70% of the cases detected had never sought psychiatric consultation. Salleh also reported a prevalence rate of 1% for all psychoses in the general population in 1990 in a similar survey.

A total of 30,114 respondents (84% response rate) aged 16 years and above were included in a survey using a self administered General Health Questionaire (GHQ) for psychiatric morbidity in the NHMS in 1996. The prevalence of minor psychiatric morbidity by GHQ-12 was found to be 11%. The prevalence was higher among females (13%) than in males (8.5%). The prevalence was highest among Indians (18%) compared with Chinese (11%) and Malays (8%). Those widowed (29%) and divorced (21%) reported a higher rate than those single (11%) and married (9%). The states that recorded highest prevalences were Sabah (14%), Kuala Lumpur, Pahang and Terengganu (all 13%). Penang scored the lowest prevalence at 6%. Rates corresponded inversely with education status. Those with no education had the highest rates (23%) while those with tertiary education had a rate of only 3.4%.

14,550 children and adolescents aged 5-15 were surveyed in the NHMS by having their parents completing the Reporting Questionaire for Children (RQC) devised by the WHO. The overall psychiatric morbidity rate was found to be 13%. 12.5% had some learning disability. 8.7% had emotional distress, going by a positive answer whether "the child ever suffers from frequent headaches" and 5.9% by a positive response to "the child nearly never playing with other children". Speech abnormality was

reported in 3.9%.

It is relevant for primary care practitioners to be aware that some of the patients presenting to them with somatic complains come with underlying psychiatrict problems. Using a GHQ, Maniam estimated that in a Kuala Lumpur general practice 30% of patients attending clinic had psychiatric morbidity. Not surprisingly, 70% of those with non-specific aches, pains, giddyness or insomnia scored high for psychiatric morbidity.

In another survey in Kelantan from 1991 to 1993, Varma and Azhar questioned people attending a district primary health care centre for psychiatric symptoms. Out of 6,342 people, 6.1% had anxiety symptoms, 13.2% had symptoms of depression, 8.2% had 'vague somatic'/hypochondriacal symptoms, 5.1% had sleep disturbance and 21.5% of children had various psychological disturbances. 4.2% had mood swings and 3.7% some psychotic symptoms.

References

Tan EK and Armstrong HE. Mental illness in the Orang Asli (aborigines) of West Malaysia. Med.J.Mal. 31:87-92 1976.

Woon TH. A history of psychiatry in Peninsula Malaysia, 1830-1975. Med.J.Mal. 32:258263 1978.

Khare CB, Upadhyaya S and Kamaruzaman WS. Vignette method for psychiatric case detection in a rural community. Med.J.Mal. 43:100-107 1988.

Salleh MR. Psychiatric morbidity in schizophrenic relatives - use of self reporting questionaire (SRQ). Sing.Med.J. 31:457-462 1990.

Maniam T. Psychiatric morbidity in an urban general practice. Med.J.Mal. 49:242-246 1994.

Varma SL and Azhar MZ. Psychiatric symptomalogy in a primary health setting in Malaysia. Med.J.Mal. 50:11-16 1995.

Editorial Committee. Second national health and morbidity survey 1996: pschiatric morbidity in adults: in children and adolecents. Malaysia's Health. Kementerian Kesihatan Malaysia. 59-91 1998.

ATTEMPTED SUICIDE

Attempting to end one's own life may originate from a number of different motives and is not a psychiatric diagnosis in itself. Depression is a common cause, but many other factors, from psychosis to physical pain may part of the motivation. Nevertheless, attempted suicide or parasuicide is a useful handle on which psychiatric help can begin; and it deserves attention and deserved to be studied if for no other reason, it is an important cry for help from a distressed individual.

Attempted suicide can take many forms. We do not have national records for the number of suicide attempts that includes all the means a person might try. But the number of self-poisoning cases can give us a rough indication of the incidence of attempted suicide and according to surveys by Orr and Tin, and Murugesan and Yeoh, this means encompasses over 90% of all parasuicides.

Orr and Tin noted that there was a total of 577 suicide attempters admitted to GH KL in 1972. Indians stood out as the ethnic group most often involved. The racial breakdown of individuals who attempted suicide was; 50% Indians, 29% Chinese and 21% Malays. In comparison the racial composition of hospital admissions consisted of 25% Indians, 31% Chinese and 42% Malays. Murugesan and Yeoh noted 94 suicide attempts in 10 months in GH Klang in 1977, including two who made two attempts in that period. Yeoh found 74 cases in Penang over 1½ years from 1978. They consistently found Indians to be over represented. Indians were about twice as likely as the average person to commit parasuicide. Malays were half as likely as the average.

Orr and Tin studied 271 parasuicide patients who were referred for psychiatric help, noting that those excluded, *i.e*. who declined psychiatric help were more often males and Malays. In their series women outnumbered men in a ratio of 3.5:1. In the other studies

women outnumbered men in a ratio of 2 or 3:1. The peak age group involved were those from 15-35 year old. They formed more than half the total. The elderly formed less than 2% but noticeably, among them men dominated this group. All strata of society appear to be involved. There were no exceptions as regards marital status, educational attainment, occupation and home set-up. In the method employed, Chinese were seen to be more prone to use physical injury.

As to the reason for the suicide attempt, relationship problems formed two thirds of the total. 28% were due to relationship problems with their spouse, 24% were relationships with other family members and 15% problems with a fiancé, according to Orr and Tin. Conflict with elders concerning boyfriends or girlfriends was commonly noted among young Indians. Psychiatric illnesses diagnosed by Murugesan and Yeoh included depressive neurosis in 22%, personality disorder in 19%, alcohol addiction in 6.5% and psychosis in 6.5%. Orr and Tin found medical illnesses and psychiatric illnesses accounted for just under 10% each.

As to successful suicides, the data from the Department of Vital Statistics in the 1980s showed that there were 3 suicides per 100,000 population with a 2:1 male to female ratio. Indians (8.3 per 100,000) and Chinese (3.0 per 100,00) have a much higher rate than Malays (0.5 per 100,000).

The district of Cameron Highlands has one of the highest suicides rates recorded in the world. One reason why many of the attempted suicides are successful is because the means commonly chosen, namely paraquat, is highly fatal. It is specifically the Indian community, who are workers in tea estates, vegetable farms and flower nurseries who are involved. Their suicide rate may be as high as 150 per 100,000.

Maniam looked at the characteristics of families affected, considering income, overcrowding, birth order of index cases of suicides, alcohol abuse, marital disharmony, a family history of suicidal behaviour and mental illness and found that the only factor of significant difference compared to controls from an outpatient clinic was suicide cases had an increase experience of loss, such as failure in examination, failure in love, loss of health or death among relatives, in the past year. There was also more marital disharmony in index families. There were alcohol related problems in 75% of both groups and there was a surprising ignorance of almost 1 in 5 respodents regarding the harmful effects of weedicides.

References

Murugesan G and Yeoh OH. Demographic and psychiatric aspects of attempted suicides - ninety-six attempts. Med.J.Mal. 33:102-112 1978.

Yeoh OH. Attempted suicides in Penang - preliminary observations. Med.J.Mal. 36:39-46 1981.

Orr JW and Tin NP. Parasuicide in Kuala Lumpur - a descriptive study. Sing.Med.J. 26:161-170 1985.

Orr JW. Parasuicide in Kuala Lumpur - reasons for the attempt. Sing.Med.J. 26:253-258 1985.

Maniam T. Suicides and parasuicides in a hill resort in Malaysia. Br.J.Psychiatry 153:222-225 1988.

Maniam T. Family characteristics of suicides in Cameron Highlands: a controlled study. Med.J.Mal. 49:247-251 1994.

ATYPICAL PSYCHOSIS

Atypical psychosis is the term for psychotic behaviour that does not fit descriptions of schizophrenia, affective or organic mental disorders. In eastern cultures and religion, these events, such as vivid visual experiences are commonly regarded as part of the normal. There is a strong belief in the reality of supernatural beings as the cause of these experiences. Loke, Rashid and Chin describe two examples of such cases.

Reference

Loke KH, Rashid MA and Chin S. Atypical psychosis: report of two cases. Med.J.Mal. 39:151-155 1984.

DE CLERAMBAULT'S SYNDROME - 'PUKAU'

In the Malaysian culture, traditional beliefs about being charmed to fall in love is not unusual. Having a fixed erotic interest, or being love struck, would however sound unusual going by a foreign name. The Malay word for it is 'pukau' but Teoh has reviewed 4 cases that fit the description of De Clerambault's syndrome. The syndrome which De Clerambault's described in 1942 consists of a sudden onset of erotomania, that is incorrigible and persistent. Hallucination is absent, but the patient harbours a fixed delusional belief of another man or woman deeply in love with her or him. It happens in clear consciousness and with preservation of orderly thinking.

From the fairly widespread public awareness of 'pukau' it would appear that it is fairly common in Malaysia. It has, however, not been widely investigated medically.

Reference

Teoh JI. De Clerambault's syndrome: a review of 4 cases. Sing. Med. J. 13:227-234 1972.

DELIRIUM ACUTUM

Delirium acutum is an acute psychiatric crisis that produces organic physical manifestations that may be life-threatening. Chew, Leong and Yao presented a case who was comatose, with fluctuating blood pressure and temperature that was successfully treated with electroconvulsive therapy (ECT).

Reference

Chew PH, Leong LC and Yao SK. Delerium acutum - an uncommon life-threatening psychiatric emergency. Med.J.Mal. 37:370-372 1982.

DEMENTIA

Alzheimer's disease and the organic brain syndrome where there is progressive loss of most of the memory faculty is not well documented locally. It does not appear to be as common as in America and the West where it has become one of the major diseases.

Chin has reported a case where a patient treated for dementia developed the neuroleptic malignant syndrome.

Reference

Chin CN. Neuroleptic malignant syndrome: a case report. Med.J.Mal. 41:176-178 1986.

DEPRESSION

Next to schizophrenia depression is the commonest psychiatric disorder. This formed nearly 20% of outpatient psychiatric clinic diagnoses in Johore Bahru in 1963 but forms a smaller percentage of psychiatric admissions. Nair noted that depression overtakes schizophrenia as the commonest disorder in later life, that is above 50 years. Endogenous depression, reactive depression and reactive depressive psychosis was found in his group of 87 patients in the ratio of 4:2:1. We must not forget that children can be affected by depression. Woon has described 3 illustrative cases. Depression is a common condition that often presents with somatic symptoms. The clinician who forgets to consider this may search very hard yet find the diagnosis elusive.

Azhar and Varma have reported that among Malay patients with depression, psychotherapy with a religious perspective resulted in faster improvement in not only patients with depression but also patients with anxiety and in bereavement in small case-control groups. The result after 6 months however was not significantly different from those who received only supportive psychotherapy.

References

Nair V. An inpatient study of psychiatric illnesses in later life. Med.J.Mal. 35:77-85 1980.

Woon TH. Depression in children. The Famaily Practitioner. 5:53-54 1982.

Azhar MZ and Varma SL. Religious psychotherapy in depressive patients. Psychother Psychosom. 63:165-168 1995.

HYSTERIA

Hysteria or conversion disorders are probably more common than they are diagnosed. Azhar reports one case where conversion presented as hallucination. Razali reported a case of a 38 year old women with a conversion disorder who believed her problem was due to evil spirits. A Malay shamanistic healing ceremony appeared to improve her condition after previous treatments failed. The author and colleagues, found the 53% of Malay patients in Kelantan in 1996 attributed their illness to supernatural agents. These patients were less like to comply with medication and not continue psychiatric follow-up. They compared psychotherapy treatment with such religious-sociocultural components against conventional psychotherapy in patients with anxiety and depression and found that although such patients responded faster with the former, the difference was not significant at the end of 6 months.

References

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Razali SM. Conversion disorder: a case report of treatment with Main Puteri, a Malay shamanistic healing ceremony. Eur Psychaitry 14:470-472 1999.

MANIA

USM workers have reported finding low mean red-cell folate levels (193nmol/l) among 45 hospitalised patients in Kelantan with mania as compared to a control group (896nmol/l). Serum folate levels showed no significant difference.

Reference

Hasanah CI, Khan UA, Musalmah M and Razali SM. Reduced red-cell folate in mania. J Affect Disord 46:95-99 1997.

MASS HYSTERIA

Mass hysteria is a well known local condition. However, it is not exclusively a Malaysian phenomenon and there is a considerable amount of Western literature on it from the latter part of the nineteenth century. In the present day, Malaysia arguably, has one of the most instances. It has been recorded that between 1962 and 1971, 29 schools in Peninsula Malaysia had outbreaks of epidemic hysteria. It almost exclusively affected adolescent Malay school girls. It seemed that over those years, as each epidemic was highlighted by the press, more schools were affected. Only once has it been reported in an Indian family in Singapore, by Teoh and Dass, and once in a Chinese family in Kuala Lumpur, by Woon.

The duration of the outbreaks was usually from one to six months. Often, Teoh reported, it coincided with some major catastrophe or event in the life of the school or hostel. In some schools, sports practice, examinations or a natural disaster precipitated the outbreaks.

The clinical characteristics of the epidemics followed a very similar pattern. The girls screamed, hyperventilated into a state of tetanic spasms and some went into a trance-like state. One or two of the subjects then in an altered state of consciousness acted as mouthpiece for the group expressing frustrations and discontentments. Characteristically, after the

event the girls took hints from each other claiming amnesia for the episode.

References

Tan ES. Epidemic hysteria. Med.J.Mal. 18:72-76 1963.

Teoh JI. Epidemic hysteria and social change: an outbreak in a lower secondary school in Malaysia. Sing.Med.J. 16:301-306 1975.

Woon TH. Epidemic hysteria in a Malaysian Chinese extended family. Med.J.Mal. 31:108-112 1976.

NEUROSIS

Obsessive-compulsive neurosis

Obsessive-compulsive neurosis is not a common problem. Etheridge found 22 cases over 4 years from GH KL outpatient records and described one case successfully treated by behaviour therapy..

Phobic neurosis

These are thought to make up less than 5% of all neurotic cases and are uncommon. But, to the one affected it can be quite a crippling condition rendering the sufferer house-bound. Phobias can take many forms. Loke and Rashid said that in Malaysia common phobias are fear of noise, of blood and of contamination. They reported 2 cases successfully treated by behaviour therapy.

References

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Etheridge AF. Treatment of an obsessive compulsive disorder by desensitisation. Med.J.Mal. 38:137-141 1983.

SCHIZOPHRENIA

Schizophrenia is far and above others the commonest psychiatric diagnosis made and is the commonest cause for psychiatric admission. Tan reported a 1.8:1 ratio of males to females among 1,321 patients admitted to the Tampoi Mental Hospital in 1964. Buhrich and Haq found that among 1,225 schizophrenics who made up 81% of new psychiatric admissions in GH KL in 1977 and 1978 the male:female ratio was 1.9:1 among Malays, 1.4:1 among Chinese and 1.2:1 among Indians. These figures are in contrast to Western countries where usually females are in the majority. Subramaniam speculated in 1964 whether migration was a factor in schizophrenia noting that Malays who formed 43% of the population formed only 27% of schizophrenics in contrast to the immigrant Chinese and Indians who were over-represented. It could not be established whether social customs or differences in hospital utilisation was responsible or whether there was a genuine predominance of males in Malaysia.

Varma and Sharma have found that psychiatric morbidity was higher (35%) in the first degree relatives of 162 schizophrenic patients in Kelantan compared to first degree relatives of control subjects (9.2%). Psychiatric morbidity was especially high for relatives of paranoid schizophrenic patients.

The content of hallucinations experienced by Malay and Chinese schizophrenic patients in Penang and Kelantan was compared by workers at USM. They found Malays in Kelantan had more hallucinations associated with religion. Although auditory hallucinations were the commonest form experienced (80-94%) among all patient groups, significantly more Malays in Kelantan (51%) experienced visual hallucinations.

Studying patients in Kelantan who had two or more episodes of schizophrenia, Azhar and Varma remarked that that the majority of families involved (72%) had a low level of expressed emotion which was in contrast to the Western situation.

References

Subramaniam M. Migration and schizophrenia - a review and case report. Med.J.Mal. 19:134-139 1964.

Buhrich N and Haq S. Characteristics of first schizophrenic admissions to the General Hospital Kuala Lumpur. Med.J.Mal. 34:269-272 1980.

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Varma SL and Sharma I. Psychiatric morbidity in the first-degree relatives of schizophrenic patients. Br J Psychiatry 162:672-678 1993.

Azhar MZ and Varma SL. Relationship of expressed emotion with relapse of schizophrenia in patients in Kelantan. Sing Med J. 37:82-85 1996.

SEXUAL DEVIATION

The term sexual deviation covers a wide variety of conditions and must be one of the commonest psychiatric problems. Transvestites are well known in Malaysia. Teoh has described the successful treatment of one patient with aversion therapy. Homosexuality is less obvious and not as vocal in Malaysia as in the West, hence we have little clue to the prevalence. Sadism, exibitionism, and fetishism, of which Loke presented case reports, are among a long list of other disorders one might discover.

References

Teoh JI. Transvestism - treatment by aversive therapy. Med.J.Mal. 26:179-185 1972.

Loke KH. Three cases of sexual deviation seen at the University Hospital, Kuala Lumpur. Med.J.Mal. 38:339-343 1983.

SOMNAMBULATION

Sleep walking usually occurs in children and has been regarded as a benign problem. Sleep walkers are rarely reported and discussed but Chin has described 2 adult somnambulants.

Reference

Chin CN. Sleep walking in adults: two case reports. Med.J.Mal. 42:132-133 1987.

TOURETTE'S SYNDROME

Georges Gilles de la Tourette described this unusual syndrome that bears his name in 1885. It consists of a childhood onset of multiple motor tics and most strikingly, sudden outbursts of compulsive unprovoked loud utterances of obscene language. This strange disease is not unknown here and probably no less common or rare. Teoh described a series of 6 cases in 1974, aged between 16-35years. 5 were males, one female. 5 were Chinese, one Malay. Not surprisingly the patients were depressed and socially isolated.

Reference

Teoh JI. Gilles de la Tourette's Syndrome: a study of the treatment of six cases by mass negative practice and with haloperidol. Sing.Med.J. 15:139-146 1974.

CHAPTER 21

THE NERVOUS SYSTEM

CONGENITAL NEURAL TUBE DEFECTS

The commonest neurological malformation recorded by Goh and Yeo in a survey of 19,769 livebirths in Alor Star between 1984 and 1987 was anencephaly. Its incidence was 0.71 per 1,000 livebirths. Ong, Singh, Ng and Chong from the UH recorded an incidence of anencephaly of 0.55 per 1,000, being higher in Chinese (0.77) and Indians (0.53) than in Malays (0.35). All the mothers were from lower socio-economic groups but there was no pattern of age or parity.

Hydrocephalus, by Goh and Yeo, occurred at a rate of 0.45 per 1,000 and spina bifida at 0.30 per 1,000. These included a couple of cases where both these lesions co-existed. Abdullah and Naing observed 285 patients with hydrocephalus who underwent shunt operations in HUSM in Kelantan over 8 years from 1990 to 1998. Age at diagnosis, type of brain abnormality and gender, but not brain cortical thickness were found to be predictors of developmental outcome.

An anterior sacral meningocele is a rare defect of which a case was reported by Samuel and Puvaneswary in 1989.

Lissencephaly is a term meaning "smooth brain" and describes an agyric or pachygyric cortex. They are rare disorders resulting from aberrant neuronal migration within the brain. Affected children have profound mental retardation and usually die very young. The diagnosis is usually established nowadays with imaging and clinical features. UH workers have reported 2 cases, both Chinese, one with Miller-Dieker syndrome and one with isolated cerebro-cerebellar lissencephaly.

References

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Goh PP and Yeo TC. Major congenital anomalies in livebirths in Alor Star General Hospital during a three-year period. Med.J.Mal. 43:138-149 1988.

Samuel D and Puvaneswary M. Anterior sacral meningocele. Med.J.Mal. 44:243-247 1989.

Thong MK, Lim CT, Koh MT and Kumar GG. The lissencephalic syndromes. Med.J.Mal. 51:353-357 1996.

Abdullah J and Naing NN. Hydrocephalic children presenting to a Malaysian community-based university hosital over an 8-year period. Pediatr Meusurg 34:13-19 2001.

CAVUM SEPTUM PELLUCIDUM

The septum pellucidum is a midline structure that forms the medial wall of the lateral ventricles in the cerebrum. It has connections between the hippocampus and the diencephalon. An absent septum pellucidum is known to be associated with epilepsy. Gururaj *et.al*. reviewing 1,281 cranial CT scans in the USM from 1986 to 1989 found 54 patients with a cavity in the septum pellucidum, or cavum septum pellucidum (CSP). Over 50% of these patients were less than 1 year old but the oldest was 68 years. Clinical examination revealed various neurological deficits in 76% of patients. The commonest deficits were generalised hypotonia (30%), hydrocephalus (15%), coma/altered sensorium (13%), hemiplegia (9%) and spasticity (7.4%).

Reference

Gururaj AK, Pratap RC, Jayakumar R and Ariffin WA. Clinical features and associated radiological abnormalities in 54 patients with cavum septi pellucidi. Med J Mal 53:251-256 1998.

MENTAL RETARDATION

George, Yong, Lim and Lim carried out a small survey of 120 mentally subnormal children in institutions in 1975 with particular reference to the cause of their disability. Chromosomal abnormalities (24%) chiefly Down's, Perinatal causes (17%), a familial tendency (17%) and epilepsy and related conditions (18%) were the commonest aetiological factors. 3 were found to be actually autistic.

Malays (30%) were under-represented in relation to Chinese (41%) and Indians (27%). This probably reflects the cultural difference where more Malays was mentally subnormality are accepted and cared for at home. The majority of children had IQs ranging from 40-70. By anthropometric parameters 98% had small head circumferences in relation to their body weight.

Reference

George R, Yong HS, Lim G and Lim JB. A study on mental retardation in Malaysian children. Med.J.Mal. 30:83-87 1975.

DYSLEXIA

Dyslexia is a specific reading disability. When the diagnosis is missed it often leads to the individual being labelled as either mentally retarded or psychiatrically ill. Tan, Malhotra and Woon described an illustrative case in 1980.

Reference

Tan CK, Malhotra KK and Woon TH. Remedial education in specific reading retardation. Med.J.Mal. 34:273-278 1980.

HUNTINGTON'S DISEASE

This is the classical autosomal dominant inherited disorder first described by Huntington in 1872. It occurs among Caucasians in about 5-10 per 100,000 and has been located by gene studies to the short arm of chromosome 4. Spontaneous mutations are rare. There have been two affected families reported. One index patient was a 40-year old Malay man from Hutan Melintang who had two previous generations probably affected who is unlikely to have a gene from a Caucasian source. The second index patient was a 32-year old Chinese lady, who had an affected mother and brother. Her grandfather had been admitted to a mental hospital in the 1930s and may have carried the gene. He was from the Fujian Province in China and was of pure Chinese stock. The brother manifested significant psychiatric morbidity and the diagnosis of Huntington's disease might not have been detected in him if not for the sister.

References

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Chin CN, S'ng KH, Philip G and Rosdinom R. Psychiatric presentation of Huntington's disease in a Malaysian family. Med.J.Mal. 51:153-156 1996.

NEUROLEPTIC MALIGNANT SYNDROME

The neuroleptic malignant syndrome is a potentially fatal complication of antipsychotic pharmacotherapy. It is characterised by hyperthermia, muscle rigidity and other extrapyramidal dysfunction and autonomic dysfunction such as tachycardia and a labile blood pressure. The UH has reported a series of 9 cases, including one fatal case.

Another similar drug reaction, malignant hyperthermia, due to an inherited sensitivity to inhalational anaesthetics such as halothane has never been noted in Malaysia.

References

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Med.J.Mal. 41:176-178 1986.

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Lee MK, Ong SBY, Tan CT and Loh TG. Neuroleptic malignant syndrome in Malaysia: a University Hospital experience. Med.J.Mal. 47:200-207 1992.

ATAXIA TELANGECTASIA

The first description of the disease is attributed to Syllaba and Henner in 1926. Inherited as an autosomal recessive trait with progressive cerebellar ataxia from the early years, apraxia of ocular movements and choreoathetosis, it is associated with conjunctival and cutaneous telangectases and a susceptibility to sinus and pulmonary infection. An Indian boy with these features was described by Kanaganayagam.

Reference

Kanagayagam A. Ataxia telangectasia - a case report. Med.J.Mal. 35:139-143 1980.

NEUROFIBROMATOSIS

Established as a clinical entity by von Recklinghausen in 1882, it is marked by spots of increased skin pigmentation and multiple neurofibromas. The disease is Mendelian dominantly inherited. It is one of the commoner congenital medical syndromes seen in Malaysia. Though local estimates of the prevalence is 3available, it is probably not far different from about 1:3,000 estimated in the U.S. A number of case reports can be found in local literature.

References

McDougall C. A case of neurofibromatosis with elephantiasis neuromatosa, bone changes and coincidental pulmonary tuberculosis. Med.J.Mal. 9:265-275 1955.

Kader NM. Neurofibromatosis and multiple skull defects: a case report. Sing.Med.J. 27:450-452 1986.

SEGAWA'S SYNDROME

Segawa's syndrome is a childhood dystonia with two marked features - a marked diurnal fluctuation and a dramatic response with small doses of L-dopa. It is termed 'Dopa-responsive dystonia'. One case has been reported in a 10-year-old Chinese girl.

Reference

Ong LC, Tang SF and Moti Lal TR. Dopa responsive dystonia with diurnal fluctuation (Segawa's syndrome) Med.J.Mal 49:176-178 1994.

STUGE-WEBER DISEASE

This disease consists of capillary or cavernous haemangiomas, within but not always limited to the cutaneous distribution of the trigeminal nerve. Hence it is also termed 'Encephalotrigeminal angiomatosis'. Stuge is credited with being the first to describe the clinical condition in 1879 and Weber with the characteristic double curvi-linear radiographic shaddow in 1922. A fairly rare condition there has been one case report by Soo of a Cinese boy at the UH.

Reference

Soo YS. Angiographic features of Stuge-Weber disease: report of a case. Med.J.Mal. 25:288-292 1971.

TUBEROUS SCLEROSIS

This dominantly inherited syndrome classically consists of the triad of adenoma sebacum, epilepsy and mental retardation but with many other less common features. Iyngkaran, Chong and Kamath described 6 children, 5 of them 3 years and under presenting at the UH with convulsions between 1972 and

1974.

Yap, Singh and Murugasu reported a 24 year old Chinese woman with a radiological 'honeycomb' lung which biopsy showed was fibroleiomyomatous tissue and a right renal mass with angiographic appearances of angiomyolipoma in 1979 in KL. Segasothy, Yi and Sidiq have reported another 26 year old woman with angiomyolipomas involving both kidneys.

The largest collection of cases reported comes from Kelantan. Over 8.5yrs, up till 1993, Malik, Hussin, Shriwas and Kasim found 8 children with tuberous sclerosis. Seven of them presented with convulsions. There were 6 boys and 2 girls. They ranged from an age of 6 months to 9 years. A positive family history was noted in 4 cases. All patients had one or more cutaneous lesions. Fundoscopy in 6 showed bilateral harmatomas. Renal angiomyolipomas were found in 2. Four were mentally retarded. All 6 who had CT scans of the brain had multiple subependymal harmatomas. 2 of 4 patients who had echocardiography had pedunculated growths in the right ventricle. All except one patient was follow-up at the HUSM. Complete control of fits was achieved in only two, and a partial response observed in four.

References

Iyngkaran N, Chong KC and Kamath KR. Early diagnosis of tuberous sclerosis. J Sing Paediatr Soc. 18:131-135 1976.

Yap PK, Singh J and Murugasu R. Pulmonary tuberous sclerosis - a case report. Sing.Med.J. 20:402-405 1979.

Segasothy M, Yi AA and Sidiq M. Tuberous sclerosis and angiomyolipomas of the kidneys: a case report. Med.J.Mal. 38:94-97 1983

Malik AS, Hussin ZA, Shriwas SR and Kasim ZM. Tuberoous sclerosis complex: a review with a study of eight cases. Med.J.Mal. 49:375-384 1994.

MIGRAINE

Migraine is not uncommon in any clinical practice in Malaysia. Tan surveyed 50 nurses at the UH and reported that 72% had some form of chronic headache of which 33% fit the description of migraine. A further third had only some features of migraine and the remainder he labelled as tension headache. In the Peadiatric Institute in KL GH, out of 47 children with recurrent headaches 72% were classified as migraine. Alders found some form of headache present the last year in 64% of respondents in a community study. 9% had migraine (but migraine with aura only accounted for 10.6% of the migrainous population) 27% had tension headache and 28% had other types of headache. Nearly $^{2}/_{3}$ of migraine subjects graded their headache as severe while nearly $^{2}/_{3}$ of the other groups graded their headache as mild.

Investigating a small series of 17 patients with features fulfilling the diagnosis of migraine, Kam noted that both sexes were equally affected and there was no pronounced racial variation. There was a wide spread of age at presentation ranging from 10 to 60 years. A family history was obtained in 5 of the 17 patients. Three-quarters of the patients reported a triggering factor. Bilateral headache and headache localised to either side were equally common. The headache lasted from 2 to 72 hours with a median of 12 hours. Paracetamol was the most common self prescribed medication found to be of benefit.

References

Kam CS. Migraine: Epidemiological aspects of 17 Malaysian patients. Med.J.Mal. 34:221-225 1980.

Kam CS. Clinical features of migraine in Malaysians. Med.J.Mal. 37:14-17 1982.

Tan CT. Headache, a study of 50 Malaysian nurses. The Family Practitioner. 5:61-62 1982.

Hussain IHMI. Recurrent headaches in children - an analysis of 47 cases. Med.J.Mal. 50:365-369 1995.

Alders EE, Hentzen A and Tan CT. A community-based prevalence study on headache in Malaysia. Headache 36:379-384 1996.

EPILEPSY

Epilepsy is a common problem treated and encountered by all general practitioners. Generalised convulsions are commonest, but the careful clinician will detect many variants. A study at the Neurology Department of the GH KL of 2,000 cases from its opening in 1972 noted that epilepsy formed 29% of its case load. Idiopathic, postinfectious and epilepsy since infancy formed the vast majority of the group. Many were from the lower socio-economic group. In the typical history, after a high fever, the infant develops seizures and the milestones of psycho-motor development are consequently delayed. The parents however only pay attention to the child at about 3 years when speech has not appeared. Ethnically, Indians were over-represented. They numbered 39% of epileptic cases.

Between 1992 and 1994 Manonmani and Tan collected a series of 165 cases of newly diagnosed epilepsies at the UH. Excluding neonates from the series the mean age of onset of epilepsy was 19 years. Indians (35%) appeared over-represented. Location related epilepsies accounted for 58% of cases, while 42% were generalised epilepsies. The 42% generalised epilepsies were made up by 28.5% idiopathic epilepsy, 5.5% juvenile myoclonic epilepsy, 3.6% childhood absence epilepsy, 3% West syndrome, 1.2% Lennox Gastaut syndrome and 0.6% photosensitive epilepsy. 36 (22%) cases were associated with medical conditions, the commonest being cerebral palsy (13), SLE (6), meningitis/encephalitis (4) and strokes (4).

Manonmani and Tan also identified a series of 21 children with **benign epilepsy of childhood with centrotemporal spikes** (BECT) from EEG records at the UH over 3 years from 1989. BECT is an autosomal dominant, partial motor, age dependent penetration epilepsy. It was not noted in any child over 13 years old. It accounted for 4.8% of their epileptic children. There were 12 boys and 9 girls. The racial mix was 10 Chinese, 6 Malays and 5 Indians.

Reviewing infantile epilepsies in Kelantan, Gururaj, Choo and Pratap found 52 cases among 16,818 paediatric admissions. Partial seizures accounted for 67% of infantile epilepsies. The commonest form was complex partial seizures with secondary generalisation. Among the generalised seizures there were 3 (5.7%) cases of infantile spasms. There were two peaks of ages in presentation, 2 and 12 months. Significant developmental delay was seen in 64% of cases. Birth asphyxia (25%), neonatal meningitis (13%) and jaundice (10%) were the commonest identifiable aetiological factors. Win found EEG confirmation in 92% of children with epilepsy in the same hospital. However, only half of the adults clinically diagnosed with epilepsy had EEG findings to confirm the diagnosis.

Vignaendra reporting in 1976 noted that 41 cases of infantile spasms were observed in the UH over a 6 year period, giving a rate of 4.6 cases per 1,000 hospital admissions of children under 4 years. The age of onset of infantile spasms was 2 years or less in all cases, 85% began before age 1 year and 32% began before the child was 3 months old. Boys outnumbered girls 2:1. Flexor spasm was commonest (70%). 10 patients had other seizures in association with the spasms. 17 patients, especially from the lower social classes presented more than 6 months after the onset of spasms. In 23 patients the spasms were cryptogenic, 10 were due to perinatal insults, 3 to kernicterus, 2 to tuberous sclerosis, 2 followed intracranial infections and one following immunisation. 27(66%) had severe mental retardation, neurological deficits was present in 56% of which cerebral palsy and microcephaly were the commonest. 24(59%) of patients had intraictal hypsarrhythmia or modified hypsarrhythmia EEG recordings.

Inhibitory epilepsy: Inhibitory epilepsy is a

rare disorder which may present like periodic paralysis with sudden attacks of flaccid paralysis. Sinniah, Lin and Loh reported a case in a one year old Chinese boy. Therapy with primidone appeared to control the attacks.

References

Balaratnam C, Isler H and M.Aswan. Comparative analysis of 2,000 neurological cases reviewed at the Institute Kajisaraf Tunku Abdul Rahman, Malaysia. Proceedings of the 9th Malaysia-Singapore Congress of Medicine 196-202 1975.

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Sinniah D, Lin HP and Loh TG. Inhibitory epilepsy. Aust NZ J Med. 9:448-450 1979.

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Win MN. The EEG and epilepsy in Kelantan - a hospital/laboratory-based study. Med.J.Mal. 48:153-159 1993.

Manonmani V and Tan CT. Juvenile myoclonic epilepsy – a report of 11 patients at the University Hospital, Kuala Lumpur. Sing Med J. 34:378-380 1993.

Manonmani V and Tan CT. Malaysian children with: "benign epilepsy of childhood with centrotemporal spikes". Sing Med J. 35:247-249 1994.

Manonmani V and Tan CT. A study of newly diagnosed epilepsy in Malaysia. Sing Med J. 40:32-35 1999.

FEBRILE SEIZURES

A febrile fit or seizure is a symptom rather than a disease entity. There is no doubt there is an inherited component but it is associated with a fever in childhood from any cause. It is a common cause for admission to a paediatric ward in Malaysia.

117 children were admitted to the UKM paediatric ward with febrile seizures over a 9 month period from August 1990. Boys outnumbered girls by 3:2. Chinese seemed under-represented. 17% had a previous febrile seizure. 67% of the children were between 6-24months old. 76% had only one seizure although one patient had as many as nine seizures within 24 hours. None of the children suffered from any neurological deficit. 26.5% of patients had a family history of a febrile seizure. An upper respiratory tract infection was the commonest cause of the fever.

The viral cause of fever in 5 of 31 children in UH with febrile convulsions were determined to be Human Herpesviirus 6. Uvulo-palatoglossal junctional ulcers were noted to be a distinguishing feature.

References

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Chua KB, Lam SK, Abubakar S et.al. The incidence of Human Herpesvirus 6 infection in children with febrile convulsion admitted to the University Hospital, Kuala Lumpur. Med.J.Mal. 52:335-341 1997.

MENINGITIS

In a review of childhood meningitis in 5 centres Hussain *et.al* estimated the incidence to be 77 cases per 100,000 per year in the first 5 years of life. However in only 58 out of their 435 cases was the organism isolated. Of these 58 cases *H. influenzae*(48%)was the commonest organism isolated. However, the spectrum of organisms causing meningitis in one locality may not be quite like that found in another even within Malaysia.

At the UH Lee, Khoo, Puthucheary and Thong have reported their experience with purulent meningitis in children in 1977. They had 59 cases in 7 years. The commonest bacteria were *H. influenzae* and *Strep. pneumoniae* which together form 75% of the cases. *N. meningitidis* was conspicuously absent. They reported a survival rate of 50 out of 59 cases. In 1988, Parasakthi and Puthucheary reported a series of 174 cases over 10 years also from UH. *H. influenzae* and *Strep. pneumoniae* formed 45% of cases, while *F.*

meningosepticum formed another 18%. There was only one case of *N. meningitidis*.

Doi *et.al*. reported that in adults without debilitating illnesses, *Cryptococcus* was the commonest cause of meningitis seen in the UH. In another report of 40 other cases of secondary meningitis, in patients in UH with predisposing factors such as shunts, staphylococci and Gram negatives were commonest. Overlapping that period in another 10 year series from UH from 1980-1989, Tee, Puthucheary and Fatimah reported 177 cases, of not only pyogenic, but of all primary childhood meningitis. *H. influenzae*, *Strep. pneumoniae* and *F. meningosepticum* formed 46%, while viral agents formed another 20% and partially treated culture negative cases another 18%. The mortality rate was 11%. Another 28% survived with residual complications, which was more frequent in *F. meningosepticum* cases (11/17) and lowest in viral cases (0/36).

Over 25 from 1973 to 1997, Lee observed that there were 13 infants with a mean age of 4 months with *Salmonella* meningitis in the UH.

Lyn and Pan in Sandakan, reported a series of 62 cases childhood meningitis over 3½ years from 1983. The commonest organisms were *H. influenzae* (9), *Str. pneumoniae* (8), tuberculosis (8) , *L. monocytogenes* (8) and *N. meningitidis* (7). There were only 3 viral and one fungal meningitis, while in 5 the agent was unknown. Most children were infants from the urban low socioeconomic group. They had 12 (19%) deaths, in 4 of whom the organism involved was unknown.

Choo KE *et.al*. in a series reported in 1990, found 58 cases of pyogenic meningitis in children (43 infants) in Kelantan over 2½ years.The commonest organisms were *H. influenzae* (29), *Str. pneumoniae* (13) and *N. meningitidis* (3). Chloramphenicol covered all the strains of these three bacteria they encountered. Their mortality rate was also 19% overall, but was higher (21%) among infants. 19 survivors were seen in clinic on follow- up and 47% of them had neurological sequelae.

Many bacteria can cause meningitis. Case reports drawing attention to more unusual organisms include typhoid, *Plesiomonas shigelloides* and the rat lung worms, *Angiostrongylus cantonensis* which can cause an eosinophilic meningitis.

Regarding hearing loss after meningitis, Yeat *et. al*. noted that of 40 cases with bacterial meningitis 13 (32.5%) had acute hearing loss, 8 in whom it was permanent. Deterioration from mild to profound deafness occurred in 2 patients. Recovery of hearing was most likely to occur in those in whom *H. influenzae* was the infecting agent. In this series *H. influenzae* (17), *Str. pneumoniae* (4), *E coli* (3), tuberculosis (3), *N. meningitidis* (2) and *Flavobacterium* (1) were the bacteria found. No hearing loss occurred in 10 cases of viral meningitis.

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CEREBRAL ABSCESSES

Puthucheary and Parasakthi reported a 10 year series of intracranial abscesses seen in the UH in 1990.They had 31 cases. Males were more commonly affected and the peak age group affected were those from 10-29 years old. Cyanotic heart disease (32%) was the commonest predisposing factor. *Str. milleri* was the most common isolate. Except for *Corynebactrium sp*. All isolates were susceptible to penicillin or chloramphenicol.

Pit, Jamal and Cheah carried out a 4 year prospective study of cerebral abscesses from 1985 in UKM. They identified 75 patients. In 75% of these patients a predisposing cause was found, the commonest being chronic suppurative otitis media, cyanotic heart disease and meningitis. *Proteus sp, Pseudomonas sp* and *Bacteriodes sp* were the organisms found secondary to otitis media and often found in mixed cultures. *Str. milleri, Bacteriodes sp* and *Eikenella corodens* were found in pure cultures in patients with cyanotic heart disease. *Str milleri* (31% of patient) was overall the commonest organism grown. In patients with ventriculoperitoneal shunts-in-situ, *S. Aereus, S epidermidis* and *Bacteriodes sp*. were common. Based on these finding they recommended penicillin, chloramphenicol and metronidazole as the antibiotic regimen for initial therapy while waiting culture and sensitivity results.

References

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Pit S, Jamal F and Cheah FK. Microbiology of cerebral abscess: a four-year study in Malaysia. J Trop Med Hyg 96:191-196 1993.

POST-INFECTIVE POLYNEURITIS

The common feature in the conditions here are that they are said usually to follow some sort of infection, like a mild viral respiratory disease. Sometimes the infection is seen to be more closely associated with the neurological disorder and so it is also termed Infective Polyneuritis.

Encephalitis

Tan reported a couple of cases of ophthalmoplegia, ataxia and areflexia in UH which he suggests fits as a variant of the Guillain-Barre syndrome.

Myelitis

Myelitis may involve a limited number of spinal segments presenting clinically as transverse myelitis or in an ascending pattern known as the Guillain-Barre syndrome. In the first 2,000 cases at the Tunku Abdul Rahman Neurology Institues Balaratnam, Isler and M.Aswan noted 19 cases of the Guillain-Barre syndrome in 18 months, but they thought many others may have been managed in the medical wards in GH KL. In other case reports, Lim has described 5 cases of transverse myelitis that showed encouraging recovery in 1967. Koh reported three cases of Gullain-Barre, in a private centre in Ipoh in less than a year.

Peripheral neuritis

Bell's palsy is a lower motor neurone paralysis of the facial nerve of unknown cause, which is of acute onset and tends towards spontaneous recovery. Diong in Sitiawan reported a cluster of cases where an infective agent could have been the cause.

References

Lim KJ and Mahadev V. Acute transverse myelitis - a report of 5 cases with recovery. Med.J.Mal. 21:225-233 1967.

Diong KI. Bell's palsy - a retrospective study. Med.J.Mal. 27:248-250 1974.

Tan CT. Syndrome of ophthalmoplegia, ataxia and areflexia - case report. Med.J.Mal. 36:186-187 1981.

Koh CS. Gullain-Barre syndrome: three case reports. Med.J.mal. 43:84-86 1988.

VOGT-KOYANAGI-HARADA SYNDROME

This entity is a rare disease involving the uvea, retina, meninges, brain, cranial nerves, hair and skin in what is thought to be an autoimmune condition. One case has been reported from Kelantan.

Reference

Zurkurnai Y, Pratap RC, Mokhtar N and Reddy TNK. Vogt-Koyanagi-Harada syndrome - a case report. Med.J.Mal. 45:70-73 1990.

HEAD INJURY

In a 3 month series of children presenting to the A&E Unit in GH KL with a head injury, Rohana *et.al*. noted that of 388 cases 63% were due to falls, 31% due to road accidents and the remainder due to projectiles. Boy outnumbered girls 2:1. 55% of injuries occurred at home. Children involved in road accidents were generally older children, 46% of them were pedestrians. 3 children died 2 were pillion riders on motorcycles whose riders were under-aged and unlicensed. One was an infant in the front seat of the car on the mother's lap.

Chee and Ali observed a series of 100 patients with basal skull fractures admitted to the UH over 28 months from 1986. 50% of the patients were motorcyclists and 22% pedestrians. 79% were males and two-thirds were between 20-50 years old. 15 patients with severe ear and nose bleeding died within a few hours despite resuscitation probably from severe brain stem injury. 32 patients had intracranial haematomas (14 subdural, 9 extradural and 9 intracerebral). 3 patients had meningitis (2 after surgery), 6 developed epilepsy. In addition to the 15 early deaths, 3 others died. 70 patients however, made a good recovery.

References

Chee CP and Ali A. Basal skull fractures. A prospective study of 100 consecutive admissions. Aust NZ J Surg 61:597-602 1991.

Rohana J, Ong LC and Abu Hassan AA. Epidemiology of head injury in Malaysian children: a hospital based study. Med.J.Mal. 53:217-222 1998.

SPINE AND SPINAL CORD INJURY

A fractured spine is an injury to the backbone. It is a skeletal injury and should perhaps be listed with other fractures. However, it is often associated with injury to the spinal cord within it. This can cause paralysis and is the more important consideration. Since the injury to the bone and spinal cord occur together they are discussed here together.

Spine Fractures

Silva, at the UH, has reported on the experience there from 1967 to 1874. There was a total of 27 cervical fractures and 94 thoracic and lumbar injuries. There were 3.5 times more males than females involved. The peak age was the third decade. Over 60% were between 20 and 39 years old. This was more pronounced in patients with cervical injuries. 70% of cervical injuries were caused by motor accidents but in thoracic and lumbar injuries 60% were due to falls and 31% only due to motor accidents.

Razak *et. al*. at the UKM, reviewed 53 patients with cervical spine injuries requiring treatment with a Halovest from 1993 to 1996. They had 4.9 times more males than females. 40% were aged 20-30 years. 72% were from

motor accidents, mainly motorcycles. 11% were due to falls a further 8% were from falls at home. The Halovest was effective in 96%, 2 patients with non-union were surgically stabilized.

Spinal Cord Injury

A spinal cord injury is a tragedy. It happens in a split second and changes a person's life forever. Medical science is still unable to restore function to a crushed or severed spinal cord. We can only address the short and long term complications that can so quickly pile on top of the victim. It used to be all quadriplegics and paraplegics died within just a few years, from pressure sores and infection. With care they lived longer but succumbed to other things like renal failure. However, since the 1950s, in the developed world spinal injury patients now have nearly a normal life expectancy. Many are restored to return to gainful employment.

We do not have data but without doubt we are in the phase where the majority of our spinal injured victims perish after about 10 years. Most do not have a normal life expectancy and few are rehabilitated to full participation in society.

In the series by Silva, 41% of patients with cervical injuries had spinal cord damage. In 22% it was incomplete, in 19% there was tetraplegia. Among cervical injuries C2 (53%) was the commonest level of injury. Of these 4 had tetraperesis and 10 had no neurological deficit. C5 (22%) was the next common level, and two-thirds of them had complete lesions. Overall for thoraco-lumbar injuries, 30% had neurological deficits. L1 (37%) and T12 (17%) were as expected, the commonest levels involved. The chance of having neurological deficit being about the same at any level.

References

Silva JF. Review of cases of fractures of the spine at the University Hospital. Med.J.Mal. 32:268-273 1978.

Razak M, Basir T, Hyzan Y and Johari Z. Halovest treatment in traumatic cervical spine injury. Med.J.Mal. 53s:1-5. 1998.

DESSEMINATED SCLEROSIS

The most intriguing feature about the incidence of disseminated sclerosis or multiple sclerosis is that its occurrence varies with latitude. Although there are exceptions, people of European origin are generally at higher risk if they live further from the equator. The incidence in Europe and North America is greater than 30 per 100,000. More than 20 viruses have been suspected, but in no case has the association been proved. Besides climatic factors, diet, trace elements, exposure to animals and infections have been studied as possible aetiological factors.

The disease has rarely been seen among Negros, Maoris and Japanese and the existence of disseminated sclerosis in Malaysia has not been proven by autopsy. But patients that clinically fit the diagnosis have been seen. Tan estimated the prevalence rate in Malaysia to be 2 per 100,000, as in Asia, by comparison number of cases seen with cases of Amyotrophic Lateral Sclerosis which is presumed to occur in 5 per 100,000 worldwide. He noted a high female-male ratio of 5:1. Tan reported in 1989 that 54% of 52 patients presenting to the UH with idiopathic myelopathy subsequently developed clinically definite or probable disseminated sclerosis.

Tan had a series of 30 clinically definite cases of disseminated sclerosis seen at the UH over 19 years, from 1968, which he reported in 1988. 80% were Chinese. The average age of onset was 30 years with one relapse every 2 years. Optic-spinal relapse was the most common manifestation (63%). All patients had spinal involvement at some stage during the course of the illness. Mortality was 37% over the period observed with an average duration of symptoms of 7.6 years. Visual impairment was serious but it was the motor disability from

spinal cord that accounted for most of the mortality. Tan also studied high dose infusion CT in 12 of his patients. 75% showed abnormalities, with an average of 2.5 lesions a patient. 75% of the patients showed abnormalities of the cerebrum which was mostly asymptomatic. 25% had brainstem changes. No cerebellar CT changes were noted.

In a study of 26 disseminated sclerosis patients, Tan reported abnormal visual evoked potential (VEP) results in 85% of patients, abnormal brainstem evoked (BAEP) results in 31% and abnormal median nerve somatosensory evoked potential (SSEP) results in 65%. Symptomatic patients were more likely to be positive (reaching 100% for VEP). Temperature causes transient neurological deterioration in desseminated sclerosis patients. Tan reported that in Malaysians with desseminated sclerosis 5 out of 13 responded positively to the hot bath test.

Tan and Low reported 3 cases with paroxysmal tonic seizures that they felt in ways seemed close to Japanese cases of desseminated sclerosis.

References

Tan CT and Low ET. Paroxysmal tonic seizures in demyelinating disease. Sing.Med.J. 27:256-258 1986.

Muthusamy E and Tan CT. Clinically definite multiple sclerosis in a young Malay female. Med.J.Mal. 43:170-172 1988.

Tan CT. Multiple sclerosis in Malaysia. Arch Neurology 45:624-627 1988.

Tan CT. Prognosis of patients who present with an episode of myelopathy of unknown origin in Malaysia: a retrospective study of 52 patients. Aust NZ J Med 19:297-302 1989.

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Tan CT and Leong S. Evoked response study among Malaysian multiple sclerosis patients. Sing Med J. 33:575-580 1992.

Tan CT. The hot bath test among Malaysian multiple sclerosis patients. Med J Mal. 49:68-73 1994.

MOTOR NEURONE DISEASE

Amyotrophic lateral sclerosis (ALS) is reputed to have a remarkarble uniform rate of prevalence of 5 per 100,000 throughout the world. Between 1974 and 1990, 63 patients with ALS were diagnosed at the UH.

HEREDITARY ATAXIAS

These are conditions marked by a slow progressive unsteadiness in standing and walking. Pathologically they are characterised by degeneration of the cerebellum and/or its related fibre systems.

Olivopontocerebellar Atrophy

This is a rare condition which was given its name by Dejerine and Thomas in 1900. 4 cases, all Malays have been reported by A.Razif, Pratap and Gururaj from HUSM in Kelantan.

Unclassified type

Tan has described an Indian family with 4 affected members which showed autosomal dominant inheritance whose features partly resembled the spastic ataxia described by Sanger Brown and partly the spino-pontine degeneration.

References

A.Razif AR, Pratap RC and Gururaj AK. The olivopontocerebellar atrophies. Report of 4 cases. Med.J.Mal. 43:344-347 1988.
Tan CT. A family with hereditary ataxia. Med.J.Mal. 35:134-138 1980.

THE PERIPHERAL NERVES

TRIGEMINAL NEURALGIA

In a study of 44 Malaysian and Singaporean patients with trigeminal neuralgia, Loh *et.al*.

reported that the condition was more common among Chinese than Malays. Females were more often affected and the peak age at onset was between the sixth and seventh decade.

Reference

Loh HS, Ling SY, Shanmuhasuntharam P et.al. Trigeminal neuralgia. A retrospective survey of a sample of patients in Singapore and Malaysia. Aust Dent J. 43:188-191 1998.

BRACHIAL PLEXUS INJURY

In a survey of 26,176 neonates born in a year at the KL GH, Boo found 42 cases, or an incidence of 1.6 per 1,000, of parturition brachial plexus injury. The risk factors were increasing birth weight and breech deliveries.

Reference

Boo NY, Lye MS, Kanchanamala M and Ching CL. Brachial plexus injuries in Malaysian neonates: incidence and associated risk factors. J Trop Pediatr 37:327-330 1991.

JUVENILE MUSCULAR ATROPHY OF DISTAL UPPER EXTREMITES (JMADUE)

JMADUE, describes a condition first reported by Hirayama in Japan in 1959 and has been seen mainly in Japan and India. It occurs mainly in males, has an insidious onset which usually causes unilateral hand and forearm wasting with absence of sensory or pyramidal tract involvement. Electromyographic studies and muscle biopsy show neuropathic changes. Tan reported a collection of 19 cases of JMADUE from 1967 up to 1985 at the UH. The mean age of onset was 21 years but patients presented on average after 2 years. 14 patients were male, 5 female. 8 were Malays, 7 Chinese and 4 Indians. None had a family history of the illness. No clustering of cases from any state was noted. No occupational nor environmental exposure was seen as a risk factor. 14 patients had only one hand involved, 10 involving the right hand. In 5 patients who had both hand involved, the disease was asymmetrical. Overall the dominant hand was the one affected or more affected 74% of the time. The disease did not continue to progress after 2 years.

Reference

Tan CT. Juvenile muscular atrophy of distal upper extremities. J Neurol Neurosurg Psychiatry 48:285-286 1985.

NEUROGENIC MUSCULAR ATROPHY

Vigenathan and Loh described a Chinese kindred of 6 individuals with neurogenic muscular atrophy spanning 3 generations. They had a mild progressive form of muscular atrophy affecting the intrinsic hand muscles due to a neurogenic cause, probably degeneration of the anterior horn cells. The family tree suggested a dominant mode of inheritance. Symptoms of the disease appeared in the middle of second decade of life and seemed to produce greater disability in females.

Reference

Vignaendra V and Loh TG. A family with neurogenic atrophy of the distal muscles of the upper limbs. Med J Aust. 2:639-641 1976.

CHAPTER 22

THE MUSCULOSKELETAL SYSTEM

It is difficult to follow an order in discussing the diseases of the musculoskeletal system. Partly it is due to the fact not all the conditions are covered here because of the lack of relevant literature. Some relatively common disease may be omitted and some rarities found. Roughly diseases of the muscles and connective tissue are listed first here followed by those affecting joints and bones. However often some diseases affect various tissues. Some diseases are systemic some to one part of the body. By aetiology some are genetic, many are idiopathic, infections and conditions of other causes account for a few making the listing appear very arbitrary.

NORMAL HAND DIMENSIONS AT BIRTH

Often malformations of the hand and fingers are cardinal manifestations of recognisable congenital syndromes. Halder *et.al*. studied the dimensions of the hands of 509 Malay babies in Kelantan, born between 34-42 weeks gestation. There was no difference, they found, to the mean measurements of boy and girls and between those who had shorter or longer gestation. They measured the right hand. The mean total hand length was 64.4±3.4mm. The mean middle finger length was 37.1±2.9mm. The mean palmar length was 27.4±2.15mm.

Reference

Halder D, Dharap AS and Than M. Normal values for total hand length, palm length and middle finger length in Malaysian newborns from 34-42 weeks gestation. Anthropol ANZ. 57:69-75 1999.

IDIOPATHIC CONGENITAL LIMB DEFECTS

Constriction bands causing missing or shortened deformed fingers are not uncommon. Goh and Yeo estimated the incidence of these at 0.61 per 1,000 livebirths or 1:1,647 in a study in Alor Star. Polydactyly occured at 0.51 per 1,000 livebirths while syndactyly with or without polydactyly was seen in 0.10 livebirths.

Reference

Goh PP and Yeo TC. Major congenital anomalies in livebirths in Alor Star General Hospital during a three-year period. Med.J.Mal. 43:138-149 1988.

The Muscles

DUCHENNE'S MUSCULAR DYSTROPHY

This, like haemophelia is a relatively well known X-linked recessive inherited disorder. It is tragic in that the boys affected all will not survive to adulthood and it is not rare in Malaysia. Lyn highlighted the case of a Malay family in Sabah with two affected living boys, who have had 5 known affected relatives in the preceeding generation, who all died before the age of 18 years. Such a case truly examplifies the need for genetic counselling.

Lee, Manonmani and Arahata reported using the polymerase chain reaction(PCR) test to make the diagnosis of a gene defect in dystrophin in an 8 year old Chinese boy at the UH with the disease in 1993.

References

Lyn PCW. Duchenne's muscular dystrophy: socioreligious belief delays

diagnosis and genetic counselling. Sing.Med.J. 27:68-71 1986.

Lee MK, Manonmani V and Arahata K. Detection of gene deletions by PCR analysis in a Malaysian patient with Duchenne Muscular Dystrophy. Med.J.Mal. 48:46-50 1993.

BECKER'S MUSCULAR DYSTROPHY

This also is a sex-linked recessive disease similar to Duchenne dystrophy but pursuing a milder course with some patients living to the fifth and sixth deacde. Delikan has written of a 22 year old Chinese patient whose macroglossia posed an anaesthetic problem. The patient had 2 affected nephews and an elder brother who died at 19 years of age.

Reference

Delikan AE. Anaesthetic problems in a case of pseudo-hypertrophic muscular dystrophy presenting with macroglossia. Med.J.Mal. 23:253-255 1969.

MYASTHENIA GRAVIS

Myasthenia is not common but on the other hand not rare. Local literature has mainly been froom the UH. Tan and Loh collected 62 cases from 1968 to 1969 giving a rate of 2.6 per 10,000 admissions. Adjusting for the racial difference in admissions the relative risks of Chinese, Malays and Indians was 3.4 : 1.5 : 1.

The two sexes were about equally represented. The mean age was 30 years but ranged from 1 to 72 years.

In this series 31 were treated with anticholiesterases alone. 10 patients had steroids as part of their treatment. 27 patients had thymectomy. Among these patients 5(19%) died. Of the thymectomy specimens the were 8 thymomas, of which one was malignant. 16(59%) patients apparently benefitted from the thymectomy.

Reference

Tan CT and Loh TG. Myasthenia gravis - a clinical survey in Malaysia. Med.J.Mal. 35:144-149 1980.

POLYMYALGIA RHEUMATICA

Ramanathan and Hwang mention that polymyalgia rheumatica is thought to be rare in non-Caucasians but suggest that it is actually probably not uncommon here with 4 case reports.

Reference

Ramanathan M and Hwang SL. Polymyalgia rheumatica: are we missing them? Med.J.Mal. 42:196-198 1987.

POLYMYOSITIS

Polymyositis is an autoimmune disorder in which skeletal muscle is destroyed by an inflamatory process. The term dermatomyositis is used when polymyositis is associated with the typical skin rash. Tong recorded 8 cases of dermatomyositis in HBKL over 5 years. All but one were Chinese, 75% were female. 2 patients had nasopharyngeal carcinomas, one of which was discovered on screening these patients. One died of metastases from an occult primary 3 years after diagnosis of dermatomyositis.

Goh, Wong and Tan have reported a patient with polymyositis of the neck extensor muscles causing head drop which was responsive to steroids. At the same time they had a patient with similar symptoms but with muscle biopsy revealing a necrotising myopathy without inflammation.

References

Zulkifli A. Calcinosis of hand and axilla in polymyositis/dermatomyositis. Med J Mal. 33:362-364 1979.

Tong M. A review of dermatomyositis cases at Hospital Besar Kuala Lumpur 1989-1993. Med J Mal. 50:32-36 1995.

Goh KJ, Wong KT and Tan CT. Myophatic dropped head syndrome: a

syndrome of mixed aetiology. J Clin Neurosci 7:334-336 2000.

MUSCLE ABSCESSES

TROPICAL MYOSITIS

Tropical myositis is a condition characterised by the presence of suppurative lesions within skeletal muscles in patients who seem otherwise well. It has been given various other names including tropical pyomyositis, tropical skeletal muscle abscess, spontaneous bacterial myositis or epidemic abscess. It has been described worldwide but as its name suggests, principally in the tropics, with a high incidence in New Guinea and Uganda. Patients are often young and fairly healthy and do not succumb to the disease.

G S Robin described 12 cases from Peninsula Malaysia in 1961 although only one was in a local Malay man. In 1963, Ashken and Cotton recorded 32 cases among expatriate Gurkha military personnel. There have been little documentation since then except for a report of four cases seen over four months in the Penang General Hospital in 1984. An average general hospital probably sees about five cases a year. Kong and other at the UKM have observed a case caused by *Staph. aureus* that was methicillin resistant.

One unusual case of anaerobic Strepococcal myositis and abscess in the anterior compartment of the leg was reported in a 22 year old primigravid following an induced abortion which led to septic shock.

PSOAS ABSCESS

Historically psoas abscesses are associated with tuberculosis. They become more uncommon with better living standards. In Sabah, Bajaj and Choong described a series of 9 cases in 1998, 7 males and 2 females. They ranged from 27 to 63 years old. 4 had a history of illness of about 1 week, 4 had symptoms for more than a month. 3 patients died, one before surgery, one with *Pseudomonas* perinephric abscess also died, and in the last fatal case no organism was identified. Tuberculosis was diagnosed from the abscess wall in two other cases, and in one case from the radiograph of the spine. The six survivors were all put on anti-tuberculous therapy and recovered health.

References

Chan WF, Ong HC and Wong WP. Acute bacterial myositis following septic abortion. An unusual complication. Int Gynaecol Obstet 13:6-8 1975.

Shepherd JJ. Tropical myositis: Is it an entity and what is its cause? Lancet ii; 1240 1983.

Menon SP, Subramaniam P and Lim KG. Tropical myositis: An underdiagnosed entity? Med.J.Mal. 39: 297-299 1984.

Kong NC, Asmah J, Lim VK et.al. Pyomyositis revisited. Ann Acad Med Sing. 25:609-611 1996.

Bajaj HN and Choong LT. The management of psoas abscess. Med.J.Mal. 53s:95-98 1998.

The Connective Tissues

ARTHROGRYPOSIS MULTIPLEX CONGENITA

Haridas in 1947 reported a one year old Chinese child with deformities he termed myodystrophies, which he considered fit the diagnosis of arthrogryposis multiplex congenita. He saw a second case the next year. Goh and Yeo noted 7 cases in 19,769 livebirths in Alor Star GH, giving an incidence of 1:2,824.

References

Haridas G. A rare case of congenital myodystrophy. Med.J.Mal. 1:185-188 1947.

Goh PP and Yeo TC. Major congenital anomalies in livebirths in Alor Star General Hospital during a three-year period. Med.J.Mal. 43:138-149 1988.

MARFAN'S SYNDROME

It is believed that Marfan's Syndrome is an inborn error of protein metabolism, particularly in collagen or elastin. The syndrome was reported first in 1896 and is autosomal dominant in transmission with variable penetration. Sufferers characteristically have long and thin limbs. They usually have mitral or tricuspid valve prolapse and can get aortic aneurysms and dissection of the aorta. Another feature is dislocation of the ocular lens. A number of cases have been observed and reported. Some cases border with Elher-Danlos syndrome and have been called Marfanoid.

References

Ong S and Ng WH. Marfan's syndrome. Med.J.Mal. 34:86-88 1979.

Goh KL, Zaed H and Tan CT. Infective endocarditis in Marfan's syndrome - a case report. Sing.Med.J. 27:446-449 1986.

Tai YS. Marfan or Marfanoid: a case study. Med.J.Mal. 41:233-235 1986.

STENOSING TENOVAGINITIS

More familiar as trigger finger, this is not an uncommon condition. Huang review a personal series of 29 patients. He noted that 93% were females. 79% of his patients were above the age of 50 years. Most (72%) had only one finger affected and that was most often the middle finger or the thumb. 52% of patients had complains of other rheumatic conditions. In his experience a steroid injection cured most.

Reference

Huang KA. Trigger finger, a report on a series of cases. Med.J.Mal. 33:7-9 1978.

The Joints

CONGENITAL ATLANTO-AXIAL DISLOCATION

Wadia drew attention in 1960 that such a condition was not uncommon where he was in India. Tan, Loh and Balasubramaniam have noted 3 cases at the UH, 2 in young adult Indians and the third in an elderly Chinese woman.

Reference

Tan CT, Loh TG and Balasubramaniam P. Congenital atlanto-axial dislocation. Med.J.Mal. 36:230-233 1981.

OSSIFIED POSTERIOR LONGITUDINAL LIGAMENT

Ossification of the posterior longitudinal ligament has been reported quite frequently in Japan but does not appear to be as common in non-Japanese Orientals. This ossification can cause spinal cord compression. Zulkurnai and Pratap have reported a 28 year old Malay woman affected with this together with having diffuse idiopathic skeletal hyperostosis.

Reference

Zulkurnai BY. Pratap RC. Cervical cord compression due to ossified posterior longitudinal ligament associated with diffuse idiopathic skeletal hyperostosis. Aust NZ J Med. 20:697-700 1990.

CONGENITAL DISLOCATION OF HIP

There is a great variation in the reported incidence of congenital dislocation of the hip (CDH)in different countries. It appears to be extremely rare in negros and Australian aborigines. Caucasians have incidences ranging from 1.0 to 19.0 per 1,000 livebirths. The incidence is very high among Lapps and certain American Indians.

Boo and Rajaram studied babies born at the MH KL prospectively over 2 years from 1986 for CDH and found 36 neonates positive by both Otolani's and Barlow's manoeuvre, out of 52,379 deliveries. The rate is 0.7 per 1,000 births. CDH was commoner among females (female:male ratio 2.3:1), first borns (50% of the affected) and babies who had breech delivery (10.7 per 1,000). 58% of neonates affected had bilateral CDH. According to the classification by Finlay *et.al.* 89% had unstable hips while 8% had pathological hips. 5% of patient had a family history of CDH. 22% of the neonates had other congenital abnormalities.

Reviewing 22 cases seen at the Institute of Orthopaedics from 1975-1988, Ang and Sivananthan also noted a female preponderance of 3.4:1. On follow up 88% were found to have good or excellent clinical results. The occurrence of avascular necrosis was 16%.

Neonatal proximal femoral epiphysiolysis, a much rarer disease due to birth trauma can be mistaken for CDH.

References

Dhillon KS. Neonatal proximal femoral epiphysiolysis - a case report. Med.J.Mal. 40:41-43 1985.

Boo NY and Rajaram T. Congenital dislocation of hips in Malaysian neonates. Sing.Med.J. 30:368-371 1989.

Ang LC and Sivanantham. Congenital dislocation of hip in children: a review of patients treated in the Institute of Orthopaedics and Traumatology, General Hospital, Kuala Lumpur. Med.J.Mal. 45:159-168 1990.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is probably not as common in Malaysia as in temperate countries. The number of patients with rheumatoid arthritis was just a bit more than those with SLE in the UH clinic between 1967-1970 Rheumatoid arthritis was however still the commonest condition at the Rheumatology clinic at the UKM, according to Chin and Shukor.

Lim and Leong at the IMR evaluated the rheumatoid factor, which use the Sheep Cell Agglutination Test in Malaysian subjects in 1967. They tested random blood samples from apparently normal adults. The positive rate was 2.3% overall. 36% of the seropositive indivuduals had clinical evidence of arthritis.

Toh *et.al.* found 57 patients satisfying the American Rheumatism Association criteria for rheumatoid arthritis in the Uh over 4 years from 1967. The ratio of females to males was 4.2:1. Most has suffered the disease for years and had onset of their disease between the age of 26 to 65 years. There was no significant racial predilection for rheumatoid arthritis but it appeared less common in Chinese than Malays and Indians. Only 19% of patients were serological positive (≥1:32) to the Waaler-Rose, 33% to the latex-fixation test (≥1:160) and 14% had LE cells. Among clinical manifestations subcutaneous rheumatoid nodules were significantly absent.

Veerapen *et.al.* compared the clinical manifestations of 70 consecutive patients with classical rheumatoid arthritis in the UH with patients matched for age, sex and disease duration seen in a British University. They found no difference in measures of disease activity, overall functional status or serology in the two groups. However Malaysian patients had less severe disease in the feet and a lower prevalence of nodules, vasculitis and pulmonary fibrosis. The Malaysian patients had fewer erosions, more frequent involvement of the wrists and cervical spine and a much higher incidence of the secondary sicca syndrome.

References

Lim TW and Leong WW. A survey of the Rheumatoid Factor using the Sheep Cell Agglutination Test. Med.J.Mal. 22:110-114 1967.

Toh BH, Sengupta S, Ang AH et.al. Pattern of rheumatoid arthritis in West Malaysia. Ann Rheum Dis. 32:151-155 1973.

Veerapen K, Mangat G, Watt I and Dieppe P. The expression of rheumatoid arthritis in Malaysian and British patients: a comparative study. Br J Rheumatol. 32:541-545 1993.

STILL'S DISEASE

Still's disease is juvenile rheumatoid arthritis. Still's original description of the disease in children was in 1897. It is not uncommon in Malaysia but we have no documented indication of its frequency. Lyn has reported two cases to highlight the possibility of growth suppression of such patients put on corticosteroids too long.

Bywaters in 1971 recognised Still's disease in adults. It has also been recognised here. Ramanathan reported 2 cases in Malacca in seen in 1986. One case with cerebral infarction secondary to vasculitis in a child has also been reported.

References

Lyn PCW. Corticosteroids causing severe growth suppression in juvenile rheumatoid arthritis. Med.J.Mal. 39:300-305 1984.

Ramanathan M. Adult Still's disease: a missed diagnosis. Sing.Med.J. 30:223-225 1989.

Gururaj AK, Chand RP and Chuah SP. Cerebral infarction in juvenile rheumatoid arthritis. Clin Neurol Neurosurg 90:261-253 1988.

SEPTIC ARTHRITIS

Razak and Nasiruddin have reviewed a series of 41 patients with septic arthritis seen in KL GH for 5 years from 1989. One patient had 2 hip joints involved. Children under 15 years were the commonest age group (37%) but there was a fairly even spread among adults. Closed trauma (13patients and open trauma (7patients) were common predisposing factors. However besides these there were 21 cases with a wide assortment of other predisposing factors including, diabetes (5), intravenous drug use (5), distant primary sepsis (3), adjacent osteomyelitis (3) and arthroscopy (2). The commonest joint involved were knees (32) followed by hips (7), elbows (2) and the shoulder (1). Synovial fluid culture was obtained in 62%. *Staph aureus* account for 77% of these. The remainder were *Salmonella* (12%), *Proteus, Enterobacter* and *Pseudomonas* (4%)(one case each). The outcome was poorer in patients with *Staph aureus* septic arthritis compared to others.

Septic arthritis in neonates differs from that in older children in that systemic manifestations are usually absent. Affected neonates usually survive but with permanent skeletal deformity. Halder et.al. reviewed 10 cases in HUSM between 1989 and 1993. All except one was a premature baby. The mean age at presentation was 15.6days. The commonest joint affected was the knee (60%), followed by the hip and the ankle. The organism cultured was MRSA in 90%

References

Razak M and Nasiruddin J. An epidemiological study of septic arthritis in Kuala Lumpur Hospital. Med.J.Mal. 53s:86-94 1998.

Halder D, Quah BS, Alam SM and Choo KE. Neonatal septic arthritis. Southeast Asian J.Trop.Med.Pub.Hlth. 27:600-605 1996.

IDIOPATHIC CHONDROLYSIS OF THE HIP

Idiopathic chondrolysis of the hip is a diagnosis of exclusion, when slipped upper femoral epiphysis, septic arthritis, tuberculous arthritis and juvenile monoarticular rheumatoid arthritis have been eliminated. It presents with pain and joint destruction, with the cartilage showing degeneration and bone showing avascular necrosis, vascular invasion and other features. It is a rare condition and there has been only one case reported locally.

Reference

Sivanantham M and Kutty MK. Idiopathic chondrolysis of the hip: report with a review of the literature. Aust NZ J Surg. 47:229-231 1977.

The Skeletal System

CROUZON'S SYNDROME

Crouzon's disease or craniofacial dysostosis, is usually autosomally dominantly inherited. Its prominent features are shallow orbits and protruding eyes, premature closure of the cranial sutures and a hypoplastic maxilla. Cases have been seen locally and reported.

Reference

Majid ZA. Crouzon syndrome. A review of literature and case report. Sing Dent J. 13:33-35 1988.

ACHONDROGENESIS

This is an autosomal recessive disease in which is lethal. The affected neonates are usually delivered prematurely, and are stillborn or die soon after birth. There is chrondrodysplasia with extreme micromelia and marked discrepancy between the relatively large head and decreased trunk length. Masood and Choo reported one case born to a Malay woman in Seremban.

Reference

Masood KA and Choo KE. Lethal neonatal dwarfism: a case of achondrogenesis. Med.J.Mal. 35:64-67 1980.

OSTEOGENESIS IMPERFECTA

Characterised by easily fractured bones osteogenesis imperfecta is a group of heterogeneically inherited genetic disorders. There appears to be two `congenita' varieties, where features are present at birth, distinguishable on radiography as `thin bone' and `thick bone' types which are recessively inherited. The type where fractures occur after birth, called osteogenesis imperfecta `tarda' is commoner and appears autosomal dominantly inherited.

Chew reported a Chinese family with two affected members already adults in 1969. Kassim, Cheah and Sameon reported an affected child with a family history from the father in 1995. Jeyamalar *et.al*. reported a 19 year old male who presented with a rare complication of infective endocarditis and heart failure.

References

Chew KK. Osteogenesis imperfecta: report of two adult cases with severe deformity. Med.J.Mal. 24:62-70 1969.

Jeyamalar R, Hashim R and Kannan P. Aortic valve replacement in osteogenesis imperfecta tarda - a case report. Sing.Med.J. 30:316-317 1989.

Kassim MS, Cheah I and Sameon H. Osteogenesis imperfecta and non-accidental injury: problems in diagnosis and management. Med.J.Mal. 50:170-175 1995.

OSTEOPOIKILOSIS

Osteopoikilosis is a rare, inheritable, sclerosisng bone dysplasia, sometimes mistaken for bone metastases. Pan and Ibrahim have reported one case.

Reference

Pan KL and Ibrahim S. Osteopoikilosis – a case report. Med J Mal. 55sC:107-108 2000.

ACHONDROPLASIA

Achondroplasia is not uncommon in Malaysia but we do not have any estimate of its frequency. Having the condition does not usually constitute a medical complaint per se. Sivanesaratnam has reported pregnancy followed by elective Caesarean section in one patient.

Reference

Sivanesaratnam V. Pregnancy in the achondroplastic patient: a case report. Med.J.Mal. 26:285-287 1972.

CONGENITAL COXA VARA

This is a rare disorder where the angle of the femoral neck is less than 120 degrees. Dhillon reported 3 cases in the UH over 10 years.

Reference

Dhillon KS. Infantile coxa vara. Med.J.Mal. 41:273-277 1986.

CONGENITAL TALIPES

Club feet or congenital talipes equino varus (CTEV) and calcaneo valgus (CTCV) are common birth anomalies with reported incidences ranging from 0.39 to 7.0 per 1000 livebirths from different parts of the world. In Malaysia, Goh and Yeo reported an incidence of 1.26 per 1,000 among 19,769 livebirths at the Alor Star GH over a 3 year period from 1984. Boo and Ong however, reported an incidence of 5.6 per 1,000 among 8,369 neonates at the MH in KL over 4 months in 1988. The latter noted that CTEV accounted for 4.5 per 1,000 livebirths. The sexes were equally involved and though the Chinese had a higher rate, it was not significantly different. Only 32% of CTEV was unilateral. For both types of club feet, low birth weight babies were more commonly affected.

Reference

Boo NY and Ong LC. Congenital talipes in Malaysian neonates: Incidence, pattern and associated factors. Sing.Med.J. 31:539-542 1990.

PATELLA CUBITI

Having a sesamoid bone in the elbow similar to the patella in the knee is a rarity. Gunn reported a man who had associated bilateral ulnar nerve palsy.

Reference

Gunn DR. Patella cubiti. Med.J.Mal. 19:314-317 1965.

KLIPPEL-FEIL SYNDROME

The Klippel-Feil syndrome is characterised by complete fusion of the cervical spine, giving the patient a short neck, a low hair line and limited movement. It is a rather rare condition. A case with concurrent schizophrenia and chronic renal failure due to pyelonephritis has been reported.

Reference

Krishnaswamy S and Masture M. A case of schizophrenia with the Klippel-Feil syndrome. Med.J.Mal. 40:330-332 1985.

IDIOPATHIC SCOLIOSIS

Scoliosis of the spine affects children in their growing years and for yet to be determined causes results in a crooked spine. Because it can range from being mild to severe its prevalence can only be obtained from population screening studies and to date none have been done in Malaysia. However in a series of cases subjected to surgery with a Cobb's angle of greater than 40 degrees (and <90 degrees), UKM workers reported 22 adolescent patients with a mean age of 16 years over 5½ years from 1992. 19 were females and only 3 males. Using a spinal fusion technique they achieved a mean correction angle of 54% but the average loss of correction at final follow up was 17%.

In a series of younger patients, with a mean age of 11 years, UH workers operated on a 31 children (29 females and 2 males) with King II scoliosis over 5 years and 10 months from 1989. The Cobb's angle for thoracic curves was

improved by an average of 45% and lumbar curves by 36% but with an average of loss 22% and 59% respectively at final follow up.

Considering both series there does not appear to be and racial predisposition for this condition in Malaysia.

References

Razak MA, Fazir M and Ibrahim S. HUKM instrumentation system in surgical treatment of adolescent idiopathic scoliosis – an early experience. Med J Mal. 55sC:2-8 2000.

Lim HH and Choon DS. Selective thoracic fusion of King II scoliosis with segmental spinal instrumentation. Med J Mal. 55sC:29-34 2000.

SPINAL STENOSIS

Lumbar spinal stenosis is defined as a narrowing of the osteoligamentous vertebral canal and/or the intervertabral foramina causing compression of the spinal cord withing the theca or the nerve roots. It is a degenerative disease. With sophisticated imaging technology the diagnosis can more frequently be made nowadays. Untreated it has been observed that 70% remain unchanged, and the remainder equally divided into a group that improve and a group that become worse. Non-operative treatment with physiotherapy, physical support, anti-inflamatory medication and corticosteroid injections. Razak et.al. report a series of 25 patients who were operated on at the UKM. They ranged in age from 33 - 64 years with a mean age of 51 years. 7 were males and 18 females. All had claudication pain, 92% had low back pain, 72% had nerve root pain, none had bladder or bowel dysfunction. Surgery produced an excellent result in 16%, a good result in 44%, a fair result in 32% and 8% judged the surgery of no use to them.

Reference

Razak MA, Ong KP and Hyzan Y. The surgical outcome of degenerative lumbar spinal stenosis. Med.J.Mal. 53s:12-21 1998.

OSTEOMYELITIS

The occurrence of acute haematogenous osteomyelitis in Malaysia does not appear to show any unusual features. Razak et.al. review a series of 81 of their cases in UKM from 1983 to 1990. Children between 2-6 years were the most commonly, boys outnumbering girls 5:2. 70% presented within a week of symptoms and in about 50% a history of a recent infection that may have provided a bacteraemia episode was obtained. Lower extremity bones was more commonly affected. Where bacteria was isolated, the most commonly cultured organism was *Staphyllococcus* (85%, of which 30% were penicillin resistant) followed by group A *Streptococcus* (10%). 44 patients were surgically treated. 6 patients had long-term problems, 4 had chronic osetomyelitis, one an infected pseudoarthritis of the tibia and one a pathological fracture.

Reference

Razak M, Ismail MM and Omar A. A review of haematogenous osteomyelitis in children in Kuala Lumpur Hospital. Med.J.Mal. 53s:83-85 1998.

LONG BONE FRACTURES

If listed as one entity, skeletal fractures is by far the commonest disease of the locomotor system. They have a common aetiology in trauma. But so many different bones can be fractured in so many ways that a brief description of each would be very lengthy. However, an overview of fractures at the UH is provided by Iqbal covering 1,564 patients over the years 1967-1971. He noted that most of the fractures (67%) occurred in those under 30 years old. 75% occurred in males. The right and left sides were about equally affected and a small minority had bilateral fractures as might be expected. 63% of the fractures involved the upper body. Falls accounted for 40% of fractures, road accidents for 39%, sports for 10% and the rest were made up of home and

industrial accidents and other causes. The radius and ulna (36%) were the commonests fractures in the UH, followed by the femur (20%), tibia and fibula (17%), the humerus (14%) and the clavicle (13%).

Again from the UH Sengupta reported that between 1983 and 1987 there were 1,836 fractures seen in children under the age of 12 in the UH. 45% were fractures of the radius and ulna (29% were fractures of the distal radius and 16% fractures of both forearm bones). Next commonest were supracondylar fractures of the humerus (14%).

Over 17 months from 1997 Chai and Saw collected 132 cases of supracondylar fractures of the humerus in the UH prospectively. Boys were 2½ times more often affected than girls and patients ranged in age from 1 to 14 years. 53% of the injuries occurred at home, a further 23% in the playground and 14% in school. 50% of the accidents occurred between 4 and 10 pm. By Gartland's classification 33% were Type I, 30% Type II and 37% Type III. Reporting their experience with a technique of arm traction for supracondylar fractures of the humerus in children, Harwant and Borhan noted that there were 156 such cases in the Ipoh GH over 2 years from 1990-1991.

There have been no large series illustrating completely what the commonest fractures are although a glimpse of the numbers can be seen from various reports on selected orthopaedic problems a few of which are perhaps worth mentioning in brief notes here. Between 1985 and 1991, Baba and Razak reported that there were 218 cases of humeral shaft fractures were seen at the UKM. 23(11%) resulted in non-union (failure to unite after 8 months). UKM workers also reported that, 61 cases of elbow dislocation with or without fractures were noted over 6 years and 5 months from 1988, 80% were posterior dislocations. Falls (64%) were more often the cause of injury than road accidents in these cases. Over 18 months from 1996 14 patients with acromio-clavicular joint

References

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Ibrahim MM, Mohd R and Ruslan R. Closed tibia fracture. Med J Mal 53s:27-33 1998.

Baba R and Razak M. Contributing factors in non-union of the humeral shaft fracture and the results of treatment. Med J Mal 53s:42-51 1998.

Azmi I, Razak M and Hyzan Y. The results of treatment of dislocation and fracture-dislocation of the elbow – a review of 41 cases. Med J Mal 53s:59-70 1998.

Harwant S, Borhan TA. The efficacy of side arm traction in the reduction of supracondylar fracture humerus in children. Med J Mal. 55:311-317 2000.

Sengupta S. Supracondylar fractures of the humerus in children. Med J Mal. 55sC:1 2000.

Chai KK and Saw A. Supracondylar fractures of the humerus in children – anepidemiological study of 132 consecutive cases. Med J Mal. 55sC:39-43 2000

PAGET'S DISEASE

Paget's disease of the bone or osteitis deformans is commonly seen in the West but a rare condition in the East. Khoo has reported a case but the diagnosis made radiologically is doubtful in a 57 year old patient who had moderately advanced tuberculosis. Soo and Singh reported 3 cases at the UH, 2 in Indians and 1 a Chinese, aged between 57-68 years at presentation.

References

Khoo FY. Paget's disease in the Chinese. Med.J.Mal. 9: 1955.

Paget's disease of bone (osteitis deformans) amongst the West Malaysians. Austras Radiol 16:152-154 1972.

CHAPTER 23

THE ENDOCRINE SYSTEM

THE PITUITARY

GIANTISM AND ACROMEGALY

The features of hypersecretion of growth hormore are usually well remembered. The visually enlargement of jaw, hands and extremities made Pierre Marie coin the word acromegaly in 1886 even before growth hormone had been assayed. Those affected young are striking in their height. The occasional case is observed in Malaysia and it is probably not any rarer here than elsewhere. But there have not been many case reports.

References

Monteiro ES. Acromegalic giant. Med.J.Mal. 7:244-246 1953.

Teo SK and Cheah JS. Hypersecretion of growth hormone in an acromegalic of 25 years duration. Med.J.Mal. 27:220-222 1973.

HYPERPROLACTINAEMIA

From serum sample from hospitals all over the country sent to the IMR over 2 years, hyperprolactinaemia was found in 20% of all infertile women. If mildly elevated values on single estimates are included, the rate rises to 38% in amenorrhoeic women and 51% in non-amenorrhoeic women.

Reference

Kamariah K and Satgunasingam N. A reference range for serum prolactin in women with observations in menstrual disorders and infertility. Proc. XV Mal.-Sing.Cong.Med. 1980

THE THYROID

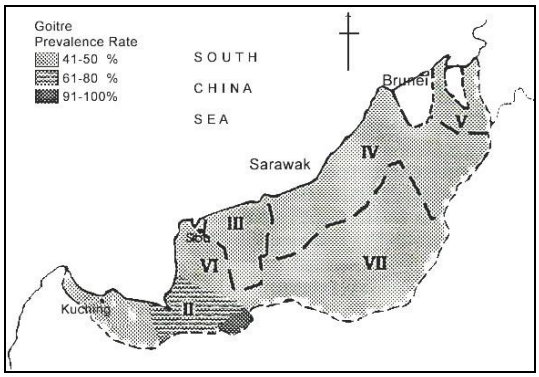
ENDEMIC GOITRE

The inland areas of Sarawak have been established as highly endemic for goitres through many studies. Examining 692 girls between the ages of 10-14 years and 1,058 women from all the different divisions in Sarawak, Polunin was the first to give a measure of the prevalence. He found the prevalence of goitres ranging from 45% to 80% among women and between 35% to 50% among girls aged 10-14 years. Maberly and Eastman in 1974 recorded the highest prevalence of 99.5% in the district of Lubok Antu in the second division. It is possible this is one of the highest prevalence anywhere in the world. Alexander recorded a rate almost as high (93.3%) in Lemanak but in a study only of women. The gravity of the condition is brought home clearly by Maberly and Eastman who estimated the prevalence of neurological cretinism in Lubok Antu to be 3.6%.

Iodine deficiency is the main cause of goitre in Sarawak. Iodine present in soil is continually being leached out by rain and Sarawak which is mainly mountainous with fast flowing rivers and a heavy annual rainfall has soil which contains very little of the original iodine. Ogihara *et. al.* reported in 1972 that the mean iodine content of six rivers and streams in the Rajang basin of Sarawak was 0.3μg/l as compared with a control of 3.4μg/l found in the tap water of the Honshin district in Japan. Goitrogens in tapioca, cabbage and groundnuts have been implicated as a contributory factor of endemic goitre but in most parts of Sarawak they only play a minor role. But in Lubok Antu where rice is sufficient for only 3 to 4 months of the year, and where tapioca is consumed in very large quantities, iodine deficiency and the presence of

goitrogens combine to create situations where goitres are almost universal.

Figure 23.1 The prevalence rate of endemic goitre in the seven division of Sarawak 1974



The problem of endemic goitres has received less attention in Sabah but Chen has found some places with incidences as high in the Keningau Division. Muruts were the predominant ethnic group in the area. The overall prevalence rate was 77% for females aged 15 years and above. Remoteness of the area correlated with a higher incidence. It ranged from 83% in Dalit, the most remote, to 63% in Keningau town.

In Peninsula Malaysia, Polunin in 1951 surveyed the upper reaches of the Perak, Kelantan, Terengganu and Pahang rivers. He found endemic goitres in about 40% of Malays and Orang Asli. Studies by IMR workers in rural areas in Sik and Baling in Kedah in the late 1980s revealed a high prevalence of 49%. The more remote villages were worse affected. Women and pubertal children were more often affected. Comparing Malays and Orang Asli in the coastal area of Selangor and remote inland area of Baling in Kedah, Ali *et.al*. noted a 6.3% prevalence of goitre in the coastal area versus a 30.7% prevalence in the inland area. The levels of iodine in drinking water was not lower in inland areas, although urine levels of iodine in the inland areas were lower. The difference could be explained perhaps by the intake of more sea food in the coastal area.

A recent study in Kelantan of 2,450 subjects sampled from 31 localities found an overall prevalence rate of goitres of 39%. The prevalence was 23% in the coastal area, 36% in the most inland area and highest (45%) in the area in between the coast and interior. However only only 2-3% were large goitres (class II and III). Levels of urinary iodine excretion (56.2-57.1µgI/gCr) were below WHO recommendation.

Ali has also compared urine iodine levels of Malays and Orang Asli in rural villages in central Pahang (Post Betau and Lanai) in 1994 and found that they were lower (2-5µg/l) than those of Malays in KL (5-10µg/l). No severe endemic goitre existed but goitre could be detected in 20-70% of the females and this increased with remoteness of the areas. 10-30% of Malay women in KL had detectable goitre. Apart from drinking water, consumption of tapioca or cassava root and leaves contributed to endemic goitres.

In KL, Sakinah noted that among 203 pregnant women in the third trimester 61% of Indians, 28% of Malays and 29% of Chinese had detectable goitres. The prevalence of thyroid antibodies (15% overall) was not different among the races. TSH was higher and serum albumin was lower among Indians and the investigators attributed these findings to protein malnutrition among Indians.

Salt iodization

Salt iodization has been shown to be an effective means of preventing endemic goitres as early as 1920 and been put to good effect in Switzerland, Columbia and other countries. In Sarawak a voluntary salt iodization programme has been in existence since 1957. But the inland areas where 10-15% of Sarawak's population

live is a poorly developed area. Poor commercial distribution meant that those who need the iodised salt most in the inland regions did not receive it. In 1979 the government began distributing iodized salt free of charge at medical and health facilities and in 1981 the state government passed legislation requiring that fine table salt be iodised.

In some remote place such as Entabai in the sixth division, Yap in 1985 found 43% of households consumed iodised salt. However other recent studies by Chen and Yap have shown that in less accessible places in the Tinjar and Baram areas as few as 10% of households used iodised salt. Most households use coarse rock salt. Here women had a goitre prevalence rate of over 60-70% and even those aged 5-14 years in the Tinjar area had a prevalence of over 70%. A study of salt iodine content in Sarawak in 1995 showed that of the two salt iodisation plants in the state the Kuching plant was quiet inefficient as less than half of the samples distributed to medical facilities contained iodine. The Sibu plant fared much better.

Despite the ongoing distribution of iodizied salt a survey by IMR worker is 1993 found that only 23% of salt sample were iodized in Lubok Antu. They found a goitre prevalence of 32% overall, which although high is lower than earlier surveys. Women above 15 years had prevalence rates of goitre of 74% and 49% in the more interior Ai river and the Lemanak river areas respectively.

In the Keningau Division of Sabah, Chen found only 3% or less used iodinised salt. The is no legislation for salt iodisation in Sabah.

Water iodization

Another measure to provide iodine in Sarawak that has been successful is a simple device to iodinize water supply in rural villages. It has been done in Lubok Antu in Sarawak.

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Mafauzy M, Wan Mohd WB, Yasmin Anum MY, et.al.. The prevalence of endemic goitre in Kelantan, Malaysia. Med.J.Mal. 48:64-70 1993.

Sakinah SO, Khalid BA and Aishah AB. Racial disparity in the prevalence of thyroid disorder during pregnancy. Ann Acad Med Sing. 22:563-566 1993.

Foo LC, Zainab T, Letchumanan GR et.al. Endemic goitre in the Lemanak and Ai river villages of Sarawak. Southeast Asian J Trop.Med.Pub.Hlth. 25:575-578 1994.

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HYPERTHYROIDISM

Although there have recently been a few clinical series of this common condition, we have no community based surveys on the local incidence of the disease. The largest reported series consists of 180 cases seen between 1983-1987 at the UKM Endocrine Clinic. Females outnumbered males in a ratio of 2.8:1, similar to findings by Ramanathan in Malacca. 83% of patients were between 20 to 40 years of age, the youngest being 7 the oldest 58. Chinese had 1.5 times more, and Indians 0.2 times only of the number affected with Graves' disease than expected from the ethnic composition of patients seen at the UKM medical clinic.

A group from the UH reported a series in 1989 of expectant mothers who developed hyperthyroidism. They had 28 cases which constituted 0.9 per 1000 births, a rate similar with series from elsewhere. Carbimazole was the mainstay of treatment and they had no case of foetal goitre.

Hypokalaemic periodic paralysis is a relatively common complication of thyrotoxicosis in Asians. It was noted in 5% of the patients in the UKM series. 7 were males, 2 females. Hypercalcaemia was seen in 1.7% of patients. Pretibial myxoedema was extremely rare (one patient only). The presence of antibodies was detected in 62% for thyrotropin-binding immunoglobulins, 26% for anti-thyroglobulin and 42% for anti-microsome antibodies. Ramanathan, Muhamad and Muthukumarappan studied the prevalence of skin manifestations in 236 patients in Malacca. They found itching (6.4%) and alopecia (2.6%) to be notewothy complaints. Palmar erythema (4.7%) was not an uncommon sign but not a complaint. Other manifestations were uncommon.

In the UKM series, euthyroid status was achieved in 91% of patients with anti-thyroid drugs. Remission was obtained in 59%, but long term remission of more than one year only in 27%. Subtotal thyroidectomy or radioiodine were needed in 31%.

Thyrotoxicosis was reported in association with psychoses in 20 cases by Tan. But in only 6 was a parallel relationship in the course of their thyroid and psychotic illness to suggest a causal relationship. Ramanathan has reported two unusual features. In one patient thyrotoxicosis mimicked a lymphoma. Another was a patient who was euthyroid with an elevated serum thyroxine in whom there may have been a peripheral resistance to thyroid hormone.

T3-toxicosis can occur and has been documented.

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HYPOTHYROIDISM

Between 1991 and 1997, 5 studies on congenital hypothyroid screening were completed in Malaysia after proposals were made by the Malaysian Paediatric Association.

In a study of 9,402 cord blood samples from the MH in KL in 1992-1993, for congenital hypothyroidism, 96 (1.02%) newborns were found to have a TSH level above 35mIU/l. 50 babies responded to a recall but none of them showed any features on congenital hypothyroidism. Over 8 months in 1995 another study of 11,000 newborns in MH KL was done to estimate the incidence of congenital hypothyroidism. 250 (2.27%) had a cord TSH level >20mIU/l and were recalled for evaluation. 48% however did not respond to the recall. Of those who did 4 had a level >100mIU/l. One had transient hyperthyrotropinaemia and 3 were confirmed to have congenital hypothyroidism, giving an estimated incidence of 1:3,666 live births. All three had prolonged neonatal jaundice, dry skin and widely opened posterior fontanelles.

In 1998 the Ministry of Health began screening for congenital hypothyroidism in 3 regional hospitals and one district hospital. The next year after evaluating the programme it was extended to 2 more hospitals and plans were made for the programme to be nationwide by 2001. The strategy employed by the MOH is to use cord blood and measure TSH as the primary index, supplemented by T4 determination in borderline samples.

Among the rare causes a hypothyroidism a lingual thyroid has once been reported and among the uncommon clinical features, a case with a combination of massive pericardial effusion, hypertension and galactorrhoea has also been described in Malaysia.

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THYROIDITIS

Autoantibodies to thyroglobulin and microsomal antigen are found in nearly all patients with Hashimoto's thyroiditis, and 50-80% of patients with Grave's and primary hypothyroidism. These antibodies though could be present in the healthy population. Pang, Yap, Ngan and Bosco noted that these antibodies were present in 8.1% of a study sample of 468 adults in Malaysia which is within the range observed in Caucasian populations.

One case of thyroiditis associated with portal hypertension has been reported locally. The patient was hypothyroid and had elevated antimicrosomal and antithyroglobulin antibodies.

Pregnancy thyroiditis is usually considered a form of Hashimoto's thyroiditis but Sakinah, Sharifah and Yusof have reported a case of painful post-partum thyroiditis without antibodies to microsomal and thyroglobulin antigens to highlight its occurrence. The patient was normal at 36 weeks postpartum.

Subacute thyroiditis (Dequervain's)

Mahadev *et.al* observed 7 cases of subacute thyroiditis among 1,500 patients with miscellaneous thyroid conditions in the KL referal centre. Features common to all were a febrile illness, thyroid pain, swelling and tenderness, an elevated ESR and depressed Iodine 131 uptake. In 4 patients seen within one year viral studies were done and all had high titres to influenza antibodies.

All patients had complete recovery. Subsequent test demonstrated an exaggerated HTSH response to TRH in 6 cases, indicating

some persisting marginal degree of thyroid insufficiency.

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THE PARATHYROIDS

HYPERPARATHYROIDISM

Primary hyperparathyroidism is a condition with protean manifestations. It must be considered in hypercalcaemia, polydipsia, polyuria, abnormal behaviour, recurrent kidney stones, diffuse osteoporosis and peptic ulcer disease. Classically it is called the disease of "moans, stones, bones and groans". Previously considered rare it is increasingly being detected in the West since routine serum calcium measurements became more widely used in clinical practice. Malaysia has not seen such a similar impact.

Goh and Wang collected a series of only 15 cases over14 years at the UH. 7 presented with predominantly bone disease, 5 with urolithiasis and 3 were asymptomatic. Other complications included acute psychosis, pancreatitis, myopathy and renal tubular acidosis. One patient had the multiple endocrine adenomatosis (MEA) Type 1 syndrome. All their patients were below 60 years old and the mean age was 36 years. Males and females were equally represented. There were 5 Indians in the group but the number is too small to really comment on. At diagnosis patients usually had a history exceeding a year.

Deshmukn *et.al*. reported 3 cases presenting with pathological fractures. Shanmugham and Alhady noted a patients with osteitis fibrosa cystica in the maxilla. These make the point that we have patients presenting in the advanced stage of the disease and probably not diagnosing of them biochemically while they are yet asymptomatic.

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PSEUDOHYPOPARATHYROIDISM

Albright first described this syndrome in 1942 where the characteristic features of hypoparathyroidism are manifested. Injection of parathyroid extract failed however, in this cases, to evoke the expected phosphaturic response. It is a genetic disease where inheritance is thought to be due to a dominant X-linked gene. Wong in 1973 reported the first local case in a boy and found a female sibling who had the somatic features without the biochemical features that would fit with the less severe form termed **pseudo-pseudo-hypoparathyroidism**. Chang reported another case of the latter in a girl, from Penang in 1975. The main somatic features are a short stocky stature, short metacarpals and tetany or convulsions that should not be mistaken for epilepsy.

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THE PANCREAS

DIABETES MELITUS

An estimated 150 million people are currently affected by diabetes mellitus world-wide and the number is rising rapidly. In Malaysia there may be up to 800,000 diabetics. Not surprisingly, management of diabetes forms a big proportion of any primary medical care practice in Malaysia.

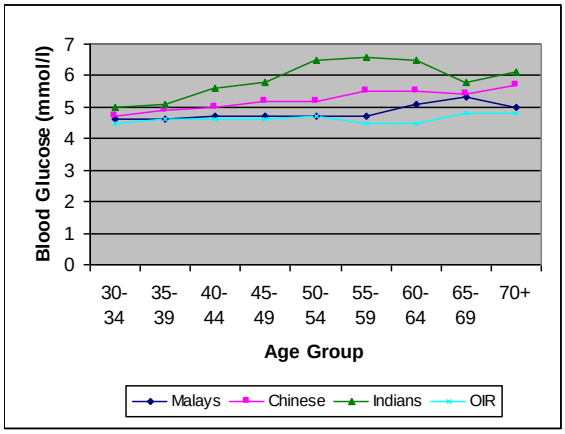
The incidence of diabetes is also definitely increasing in Malaysia. Pillay and Lim found a prevalence of 0.65% in 1960, but they excluded known diabetics from their survey. The U.S. ICNND study in 1962 recorded a rate of 3%. In a 5 year study of his general practice in Klang from 1972, Balasundaram found that 1.6% of his patients were diabetic.

In a community survey of 515 people above 15 years of age in Kuala Selangor in 1984, Osman and Rampal, found 4% to be diabetic. 60% of them were diagnosed for the first time at the survey. Of those surveyed 9.7% had glycosuria. A study in the same area in 1993 of 360 randomly chosen subjects found 14.6% diabetic; a huge increase. Again 60% of them were newly diagnosed at the survey. Physical inactivity and obesity were associated with diabetes. The greatest increase in prevalence was seen in the 40-60 year age group.

A survey of 1986 subjects among railway workers in Sentul KL in 1989 by Khalid *et. al* found an even higher rate of 6.6% of whom 17% were not previously known to be diabetic. These have however not been large studies representative of the population of the whole country but the MOH has conducted 2 such surveys lately.

The National Morbidity Survey of 1986 took a random sample of 10,854 adults nationwide above 35 years old. On the basis of a 2 hour post-prandial blood glucose level after a 50gm glucose load 1.8% were found to be diabetic. However, 4.5% reported that they were already diabetics, giving a total prevalence of 6.3%. The prevalence of diabetes increased with age with the big majority being over 40 years old. There was little difference among sex. However, twice as many urban dwellers compared to rural folk reported being diabetic.

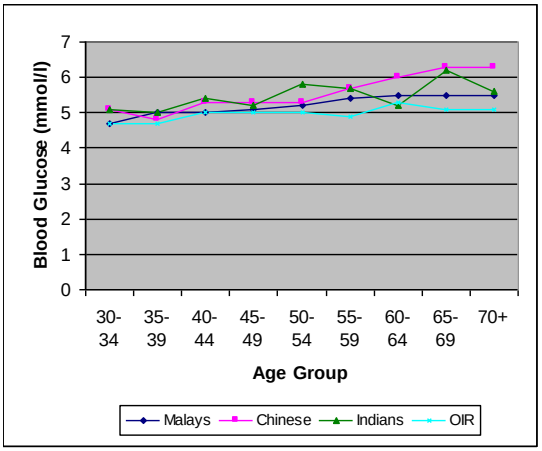
Figure 23.2 Median blood glucose in non-diabetic males in Malaysia 1996



In the National Health and Morbidity Survey of 1996, 20,041 adults 30 years and above who were not diabetic were studied for the normal distribution of 2 hour post-prandial blood glucose after a 75gm glucose load (Figures 23.2 and 3). Indians had the highest mean blood glucose values, followed by Chinese, Malays then other indigenous races. Women had higher blood glucose than men except among Indians. The survey found that by WHO classification, overall 7% were diabetic. By ethnic groups, 3.5% of indigenous ethnic groups, 6.4% of Malays, 7.1% of Chinese and 14.3% of Indians were diabetic. In addition, another 5% overall had impaired glucose tolerance.(the lower levels seen in the elderly in some of the groups may not be a true decline of blood glucose with age but rather the result of selective survival and that diabetics are excluded, and at that age those liable to diabetes have already become diabetics

and been excluded).

Figure 23.3 Median blood glucose in non-diabetic females in Malaysia 1996



(OIR=other indigenous races)

Khoo *et.al*. in reporting the results of surveys done by the Heart Foundation of Malaysia on volunteers in health awareness campaigns between 1992-1994 and 1995 –1997 noted similar mean blood glucose levels in the different age groups and different races as the NHMS and finding diabetes surprising in only 3.3% in the first period and 2% overall based on random blood glucose samples.

Risk Factors

In a 1993 report, Ali *et.al*. studied 706 Malay and Orang Asli adults. Among Malays the prevalence of diabetes was 2.8% in traditional villages, 6.7% in land schemes and 8.2% in urban areas. Among Orang Asli the prevalence of diabetes was only 0.3% and impaired glucose tolerance 4.4%. A higher income, obesity, less daily activity were associated with a higher prevalence of diabetes. Obviously diabetes increase with a modern urban lifestyle.

Mustaffa noted in 1980 that nearly 70% of Malay and Indian diabetic patients were obese.
In a community study of 2,284 subjects above 20years old chosen by cluster sampling in 9 districts reported in 1996 in Kelantan, Wan Mohamed *et.al*. noted that 7.9% of the lean, 10.5% of the overweight (BMI above 25kg/m^2), and 6.7% of the obese (BMI above 30kg/m^2) were diabetic. They reported in another paper that these diabetics had a higher prevalence of cardiovascular risk factors, such as, obesity (38%), hypertension (13%) and hypercholesterolaemia (72%) compared to normal subjects.

Males and females are about equally affected. Indians have the highest prevalence among the ethnic groups in Malaysia. West and Kalbfleisch quoted a prevalence of 4.2% for Indians, 4.7% for Chinese and 1.8% for Malays in 1966. Khalid *et.al.* found the prevalence 16% among Indians, 5% among Chinese and 3% among Malays among adult railway workers. Increasing age increased the risk of diabetes. 9.2% of those above 55 years were diabetic according to Osman and Rampal while it was only 1% for those under 35 years. 10.8% of those who were overweight were diabetic compared with only 1% of those who were not overweight. Diabetics also had a higher rate of hypertension according to Kandiah *et. al*(21%), and Balasundaram(23%), compared to the general population (14%). An even higher rate of hypertension among diabetics of 37% was found in the survey of railway workers.

Non insulin dependent diabetes mellitus (NIDDM) forms the vast majority of our diabetics but the more severe insulin dependent diabetes mellitus (IDDM) is also increasing in number. From a cross-sectional study of medical records of 2 health districts in Pahang, in a 1991 report, Lim estimated the prevalence of IDDM among those under 40 years old to be 7 per 100,000 inhabitants while the prevalence of NIDDM was 30 per 100,000. Even in patients below the age of 20 years at diagnosis 56% had NIDDM. Mention should also be made of the

idiopathic malnutrition related type of diabetes (MRDM) which may be seen in rural areas. This type also affects the younger ages around 20 to 30 years and possibly the ingestion of food toxins such as cassava may be involved.

Autoimmune Markers

Wan Nazaimoon *et.al*. studied the prevalence of autoantibodies to glutamic acid decarboxylase (GAD65), insulin, tyrosine-like phosphatase and islet cell in a group of 213 young Malaysians with IDDM (according to WHO recommendations) recruited from all over peninsula Malaysia in 2000. Insulin autoantibody was detected in 47%, GAD65 antibody in 34%, tyrosine-like phosphatase antibody in 9% and islet cell antibody in 1.4%. 32% of patients were seronegative although they showed near or total β-cell destruction in the glucagons test suggesting a difference in aetiology of our type1 diabetics from their Caucasian counterparts. Antibodies were detectable however in 73% of those with poor or no β-cell function. By C-peptide response to glucagon stimulation actually only 81% of the 213 had poor β-cell function of type 1 diabetes. 19 of the 41with autoantibodies could belong to the subset of 'latent autoimmune diabetes in adults' (LADA) among type 2 diabetics.

In another report on 926 young Malaysian diabetics (<40 years) the same group found that 36% of patients with IDDM had GAD65 antibodies compared with 7.5% of NIDDM patients. There was no racial differences in the prevalence of GAD65 antibodies.

Control

Based on drug prescriptions less than 250,000 diabetics on treatment could be accounted for in 1982. In addition, many on treatment receive less than adequate care because of poor compliance and understanding of their condition. Mustaffa observed that more than 50% of NIDDM patients were overweight and may have been controlled by diet alone. Among railway workers Khalid *et.al.* found that diabetic control was poor in 71% using HbA1c measurements. 30% of these diabetics had renal impairment. Inadequate training and care of patients may be more so in the rural setting. Lim in Mentakab, felt that only 9% of the patients at the district hospital surveyed achieved good glycaemic control. 12% had evidence of retinopathy although the average duration of diabetes in these young patients who were under 40 years old was only 4.5 years. 61% had at least one episode of hypoglycaemia a week, and most did not understand its nature.

Lim *et.al*. compared the reliability of fasting blood glucose as a measure of control comparing it with serum fructosamine among 228 diabetic patients in Mentakab in a 1992 report. 162 (71%) had poor diabetic control indicated by their serum fructosamine concentration (>320μmol/l). Fasting blood glucose, they found, was not a reliable predictor of good control but was useful in predicting poor control.

Studying the glycosylated haemoglobin HbA1c in 926 diabetics from 7 different large hospitals throughout the country in 1999, Ismail *et.al*. found that glycaemic control was poor overall with the HbA1c mean level of 8.6%, and 61% of patients having a level >8%. Chinese patients and patients with access to nurse educators were significantly better controlled. For type 1 diabetes, a high household income was a predictor of good control. For type 2 diabetes use of insulin was a significant predictor. Education status surprisingly was not an indicator of glycaemic control.

Complications

In a survey at the UH eye clinic it was found that 44% of diabetics had retinopathy, albeit 33% had only background retinopathy. Among 90 patients presenting with diabetic retinopathy of the UH eye clinic from 1989 to

1991, 87.7% had NIDDM. 59% had severe eye disease at presentation. The mean duration of diabetes to presentation was 12.3 years and duration correlated with severity of retinopathy. The overall mean age of these patients was 54 years. Besides duration of diabetes USM ophthalmologists found that diabetic retinopathy was correlated with high serum creatinine and proteinuria among 140 of their patients in a diabetic clinic between 1992-1994. They did not find a correlation with glycaemic control, as measured by HbA1, nor cholesterol or C-peptide. They found retinopathy in 49% of their patients and a similarly high proportion of NIDDM like the UH series.

Diabetic ulcers and limb gangrene leading to amputations and carbuncles are common occurrences seen in most Malaysian hospitals. In GH KL diabetics account for 43% of major lower limb amputations which is high in comparison to Europe and North America. Khalid has noted that diabetic foot complication accounted for 12% of hospital admissions among diabetics in KL GH. Among 60 consecutive patients with diabetic foot infections admitted to GH KL, Harwant *et.al*. found 53 had NIDDM, and their mean age was 59 years, while 7 had IDDM, and their mean age was 48 years. 68% were males, 62% were manual workers and 82% of patients had 82% had only primary school education or less. 6 patients had had prior amputations. 20% of these 60 patients required major limb amputations while foot sparing surgery such as toe disarticulation and ray amputation was performed in 32% and debridement alone was required in 48%.

Pregnancy

In a prospective study throughout 1989, Boo found 54 (2.2 per 1000 livebirths) neonates born to diabetic mothers in Hospital KL. The incidence was highest among Indians (3.9 per 1,000 livebirths), was 2.2 per 1,000 among Malays and lowest (1.8 per 1,000) among Chinese. 37% of these neonates were large-for-gestational age and 30% of them had a birthweight above 4kg. Shoulder dystocia occurred in 7, hypoglycaemia occurred in 9, respiratory distress in 7 and congenital abnormalities in 4. Three neonates died.

We do not know accurately the rates of cardiovascular and renal disease among diabetics. Nevertheless, it is clear that with its high prevalence rate, lifelong progressive course and its many complications we can safely conclude that diabetes ranks high among the diseases causing the heaviest economic burden on the country. Poor management will only increase the burden. The primary medical practitioner stands at the critical point in care for diabetes and should constantly seek room for improvement. More studies auditing the care of diabetes in Malaysia should be revealing and will probably help point the way forward.

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HYPERINSULINISM

Nesidioblastosis refers to the diffuse proliferation of pancreatic islet cells which causes hyperinsulinism and hypoglycaemia in the neonatal period. Jayalakshmi and colleagues reported a neonate with the disease treated by subtotal pancreatectomy unsuccessfully but the parents refused total pancreatectomy when it was advised. Over a period of 3 years from 1992, Rahmah *et.al*. identified 10 cases in HUKM. 7 were symptomatic by day 2 of life. Near total pancreatectomy was performed in 9 patients. 2 early cases had recurrent hypoglycaemia, one needed insulin therapy still at 5 months after surgery.

15 cases of insulinomas were managed at HUKM over 20 years from 1979. There were 8 males and 7 females and their mean age was 43 years. There were 8 Chinese and 7 Malays. 12 patients had benign adenomas including 1 with MEN-1 syndrome. 2 patients had malignant insulinomas and 1 refused surgery. Delay in diagnosis ranged from 2 to 10 years. Of those with benign adenomas, 11 survived and remained well following enucleation (n=5), distal pancreatectomy (n=5) or Whipple's procedure (n=1). One died following Whipple's procedure. Of the 2 with malignant disease 1 with metastatic disease died after 3 years but one remained well at the time of reporting 6 years later.

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THE ADRENALS

THE ADRENOGENITAL SYNDROME

What is termed here as the adrenogenital syndrome is actually not just one disease but a number of enzymatic deficiencies in steroidogenesis. There are at least 5 different enzyme deficiencies that have been identified. Any enzymatic block along the biochemical pathway results in a feedback that increases ACTH output that produces compensatory hypertrophy of the adrenal gland. They variously produce features such as, Addisonian crises, hypertension, salt wasting, hypoglycaemia or feminization, due to insufficiency of the glucocorticoids, mineralocorticoids or androgens and features of virilization in cases that result in excess androgens. It is said that some Eskimos have a high incidence but Malaysia like the rest of the world has only the occasional rare case.

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CUSHING'S SYNDROME

Cushing's syndrome consists of hypersecretion of glucocorticoids by the adrenal. In the experience of Meah and Haron at the UKM, there were 20 cases of Cushing's between 1978 and 1982, including 4 children. In adults women outnumbered men in a ratio of 7:1 but boys and girls were equally represented. There were 11 Chinese, 6 Malays and 2 Indians. In a report extending to 1993, they had another 20 cases. The cause of Cushing's syndrome was adenomas in 32.5%, diffuse bilateral hyperplasia in 40%. Pigmented macronodular hyperplasia in 20% and carcinomas in 7.5%.

CONN'S SYNDROME

Conn's syndrome is the hypersecretion of mineralocorticoids. Meah and Haron had only one case in their series from 1978 to 1982, but a total of 57 more cases by 1993. The commonest cause of Conn's syndrome was an adenoma (96.5%) which affected the left gland 4 times more often than the right.

PHAEOCHROMOCYTOMA

Over 5 years from 1978 Meah and Haron treated 2 patients, both Indians, with phaeochromocytoma. Both remained well with normal blood pressures after surgery. In a continuation of the series, by 1993, 20 cases of phaeochromocytoma had been treated surgically. 25% of phaeochromocytomas were extra-adrenal.

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CHAPTER 24

METABOLIC DISORDERS

The diseases listed here are nearly all inherited conditions and mostly single defects although the mode of inheritance of some are uncertain. They can be traced down usually to biochemical problems that involve the handling of nutritional products in the body, usually an enzyme deficiency. To roughly organise them, defects in carbohydrate, lipid, amino acid and nucleotide metabolism are discussed first, followed by minerals and other co-factors. Finally there are other enzyme deficiency problems.

GLUCOSE 6 PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

Erythrocyte G6PD deficiency was first recognised in Malays by Weatherall in 1960. He found the disease in Singapore, in 3 neonates with kernicterus. The most important advance in being able to screen the population for G6PD deficiency was made between 1966 and 1968 by Beutler who devised a fluorescent screening spot test. Being a common condition in Malaysia, all newborns are now routinely screened for this condition. The incidence has been found to be in the range of 3.1-4.5% in Chinese, 1.4-3.5% in Malays and 0.2-1.5% in Indians. The overall rate for Malaysia in 1993 and 1998 is 2.4%. The incidence is highest, however, among the Orang Asli (16%). In Sarawak, Ganesan has found G6PD deficiency in 5.3% of Bidayuh and 5% of Ibans. IMR workers have found evidence that G6PD deficieny has malaria resistant effects in a study of Orang Asli (Temuans).

It is an X-linked recessive condition so females make up only about 1 to 5% of those affected in view of the fact that the gene frequency is about 1 to 5%. Newer screening methods now allow less severe variant G6PD deficiency to be detected so that the prevalence is relative and depends on what level of enzyme activity is considered a deficiency.

Boo *et.al*. determined the G6PD activity in the cord blood of 262 normal term neonates in KL. Malays, they found had a significantly higher mean G6PD enzyme activity level compared to Chinese. Indian babies had a mean level between that of Malays and Chinese which was not significantly different from either race. The difference could be due to different G6PD variants. There was no difference in enzyme activity between the sexes in each ethnic group. In a study of 51 G6PD deficient males of all 3 races they found a mean enzyme activity level of 0.47iu/gHb. They had one female neonate with G6PD deficiency who had an enzyme activity level of 1.1iu/gHb. Workers in Kelantan have assayed the activity of the G6PD enzyme in Malays. The mean enzyme activity of normal males was 12.1iu/gHb and was 0.74 iu/gHb in deficient males. Female heterozygotes had a mean enzyme activity of 6.5iu/gHb but had a wide scatter (SD 3.2iu/gHb). A cut off level of 9.0iu/gHb gave a sensitivity of 87% and a specificity of 84% in detecting heterozygote females. This group could be more accurately defined by combining quantitative assays with family studies.

Advances in genetic technology studies have shown that there are over 200 mutant alleles of the G6PD gene in man. Most of these are point mutations suggesting that larger mutations such as long deletions are probably incompatible with life. UKM workers have screened 38 G6PD-deficient Chinese male neonates for known mutations and found that 50% were due to a 1376G→T (termed the Canton mutant) substitution, 34% were 1388G→A, 5.2% were

95A→G, 2.2% were 1024C→T and 7% remained uncharacterised. The pattern of distribution is similar to those found among Chinese in Taiwan and southern China. The neonates with the 1388G→A mutation had the highest rates of moderate to severe hyperbilirubinemia. Malays have also been studied and showed a wider range of mutants. A sample of 90 children revealed that 32% had a 871 G→A mutation (given the name Viangchan mutant), 19% the 563 C→T mutant (Mediterranean), 11% the 487G→A mutant (Mahidol), 4.4% the 1376C→T mutant (Canton), another 4.4% other mutants leaving 28% uncharacterised.

Of the G6PD deficient babies observed in the nursery in Johore Bahru, Tang Balakrishnan and Zamri noted that the serum bilirubin peaked at 96 hours to a mean value of 12mg%. None recorded a level above 15mg%. However, neonates admitted with jaundice and were G6PD deficient sometimes required exchanged transfusion. It had been noted in Singapore in 1964, that 44% of kernicterus was caused by this deficiency. In a study in 1977 of 178 babies with severe neonatal jaundice requiring exchange blood transfusion, admitted to GH KL, G6PD deficiency was found in 21% of the Chinese, 17% of the Malays and 11% of the Indians. In addition to G6PD deficiency abnormal haemoglobins, most noticeably Hb Bart's, contributed to the high incidence of severe neonatal jaundice.

Lie-injo, Pillay and Virik described 45 patients with haemolysis due to G6PD deficiency seen in GH KL over a 2 year period in 1966. 42 were males and 3 females. 36 were Chinese, 6 Malays and 3 Indians. They were aged between 3 days old to 57 years. The cause of haemolysis was antipyretics in 9 cases, Chinese drugs in 7 and a medicine that was not known because it was not brought by the patient in 17 cases. In 2 Chinese patients the precipitant was the Chinese broad bean *Vicia faba*. In 2 cases infectious hepatitis was determined to be the cause as they were admitted with infectious hepatitis without any haemolysis, had not received any drugs before or after admission and developed anemia after several days. The severity of anemia was variable, but most of these documented were severe and there was one patient who died of uremia.

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Boo NY, Ainoon BO, Ooi LH et.al. Glucose-6-phosphate dehydrogenase enzyme activity of normal term Malaysian neonates of different ethnic origins. J Paediatr Child Hlth 30:273-274 1994.

Boo NY, Ainoon BO, Arif ZA et.al. Enzyme activity of glucose-6-phosphate dehydrogenase deficient Malaysian neonates during the first 10 days of life. J Paediatr Child Hlth 31:44-46 1995.

Ainoon O, Joyce J, Boo NY et.al Glucose-6-phospahte dehydrogenase (G6PD) variants in Malaysian Chinese. Hum Mutat 14:352 1999.

GENERALISED LIPODYSTROPHY

Generalised lipodystrophy occurs in a congenital autosomal recessive form and an acquired form. It was first described by

Lawrence in 1946 in a syndrome characterised by complete absence of body adipose tissue, hepatomegaly, hyperlipaemia, insulin-resistance diabetes without ketoacidosis and other features. It is rare. The aetiology is obscure. Choo *et.al*. reported one case from Kota Bharu in 1990. Lim and Chong encountered a patient with lipodystrophy and scoliosis at the UH in 1999.

References

Choo KE, Sharifah A, Ariffin WA and Mafauzy M. Generalised lipodystrophy. Sing.Med.J. 31:289-292 1990.

Lim HH and Chong CS. Scoliosis in a patient with lipodystrophy – treatment difficulties and literature review. Med J Mal. 54:368-370 1999.

HYPERCHOLESTEROLAEMIA

The mean value of serum cholesterol in our local population appears from several small surveys to have slowly increased over the years due to better nutrition.

In 1961 Lloyd Davies and Willsher showed that there was a small but progressive increase of the serum cholesterol level from first generation to third generation male immigrants in a small sample of Singapore dockyard workers. The cholesterol level among men who were born in China or India who had emigrated to Singapore, (by a modified King-Wootton method) was 131 mg/dl among Chinese and 135 mg/dl among Indians. The mean total cholesterol for the next generation was 130 mg/dl for Chinese and 139 mg/dl for Indians. In men who were third generation Singaporeans the mean was 143 mg/dl in Chinese and 172 mg/dl in Indians. A lower mean was observed among the poorer daily paid workers. The trend however clearly shows that in all comparable groups Indians have higher cholesterol levels than Chinese.

Reviewing cholesterol levels in 84 young male blood donors using the Abell *et.al.* method, in KL in 1961, Chong found a mean value of 161 mg/dl in 20-24 year olds, rising in a significant trend to 223 mg/dl in 35-39 year olds. There was no racial difference among Malays, Chinese and Indians. Lau, Lopez and Gan studying a larger sample of 512 similar subjects, reported similar findings, noting that the rise of mean serum cholesterol with age plateaus and in facts declines a little from the 30-39 year group to the 60-69 year group. The mean value of all adults together was 171 mg/dl.

A study among the armed forces published in 1982 noted a mean cholesterol level of 199 mg/dl. The non-fasting level of triglycerides was 168 mg/dl, the mean HDL cholesterol was 45 mg/dl and the β-lipoprotein level was 523 mg/dl These values are similar to other series for healthy Malaysian males for this period.

Teo, Chong and Zaini surveyed urban male executives for coronary risk factors between 1982 and 1985. 406 subjects were recruited on a voluntary basis. 31% of the sample had hypercholesterolemia, taken as a level above 250 mg/dl. Malays had a higher prevalence of hypercholesterolemia, obesity, low HDL cholesterol, hypertriglyceridemia and hyperuricaemia when compared to Chinese. Indians though small in number had a cholesterol level as high, if not higher than the Malays.

Studying men aged 18-60yrs (mean 36yrs) in and around Kuala Lumpur matched for body mass, smoking and age in 1992, Zaraihan, Azman and Tariq found that Indian men had significantly higher LDL-HDL cholesterol and total cholesterol-HDL indices than Malays and Chinese, although the lower mean absolute values of HDL (Indians 1.2mmol/l, Malays and Chinese 1.3mmol/l) and higher total cholesterol (Indians 5.7mmol/l, Malays 5.5mmol/l and Chinese 5.4mmol/l) were not statistically different. Indian women who do not have a much higher risk of coronary heart disease compared to Malay and Chinese women did not have any significantly different

cholesterol indices.

Cholesterol levels in voluntary participants in Heart Week Exhibitions in KL, Penang, Seremban and Kuantan have been measured in 2,670 people between 1992-94. Males (5.32mmol/l) had a higher mean total cholesterol value compares to females (5.18mmol/l). Chinese (5.20mmol/l) had lower mean values than Malays (5.42mmol/l) and Indians (5.37mmol/l). There was an increase of cholesterol with age (Figure 24.1). Values for 6,858 volunteers in similar Heart Weeks between 1995-1997 in 10 urban areas produced similar results. Khoo, Tan and Liew also reported similar results in a general practice survey in KL from 1989 to 1991 involving 1,116 subjects. They recorded a mean fasting triglyceride level of 1.58mmol/l in males and 1.09mmol/l in females.

Banerjee and Saha have shown that there was no significant difference in the mean serum cholesterol between vegetarians and non-vegetarians, athletes and non-athletes and among the different ABO blood group.

The Orang Asli in peninsula Malaysia, number only about 100,000 and form a small group even when included among other indigenous races (OIR) in national surveys. Studying the Semai, Gajra *et.al*. have noted that they appear to have the lowest mean cholesterol level ever recorded of 1.6mmol/l for males and 1.9 mmol/l for females. They had a high frequency of the e2 and e4 alleles of apolipoprotein E.

In notable contrast to the studies above are the results of the National Health and Morbidity Survey of 1996. This study had a design sample drawn from across the country who were contacted at their residence. 20,041 individuals had evaluable blood samples. What was notable and unexpected was the mean serum cholesterol was low at 4.5mmol/l and prevailed among all ethnic groups and did not rise significantly with increasing age (Figure 24.2 and 3). The contrast of these results with those of volunteer participants can be seen best in the figures.

Figure 24.1 Mean cholesterol level in different age groups of volunteer participants from urban areas in National Heart Weeks

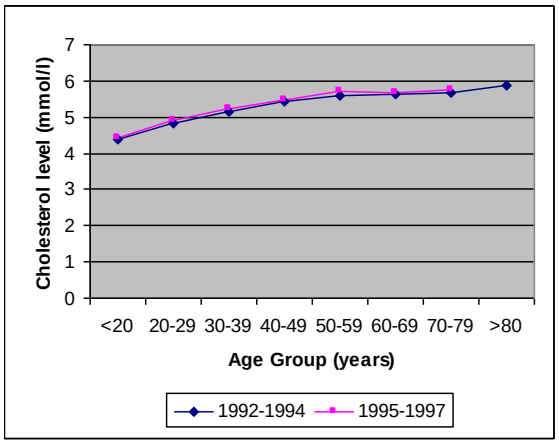
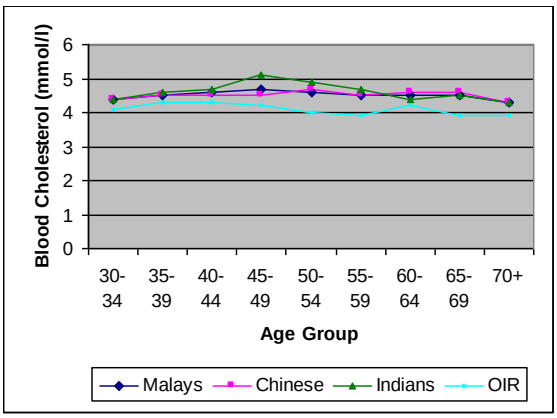


Figure 24.2 Median cholesterol level in males in Malaysia 1996



(OIR=other indigenous races)
NB. 1mmol/l of cholesterol = 40.3mg/dl)

(refer also to section on coronary artery disease)

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Chong YH and Khoo KL. Serum lipid levels and prevalence of hyperlipidaemia in Malaysia. Clin.Chim.Acta. 65:143-148 1975.

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Teo PH, Chong YH and M.ZAini AR. Coronary risk factors among Malaysian male executives in two urban areas. Med.J.Mal. 43:125-133 1988.

Gajra B, Candlish JK, Saha N et.al. Effect of apolipoprotein E variants on plasma lipids and apolipoproteins in the Orang Asli ('aborigines') of Malaysia. Hum Hered 44:209-213 1994.

Khoo KL, Tan H, Sambhi JS and Aljafri AM. Screening for blood pressure, cholesterol and glucose during National Heart Weeks 1992-1994. Med.J.Mal 51:307-316 1996.

Lim TO, Ding LM, Zaki M et.al. Distribution of blood total cholesterol in a national sample of Malaysia adults. Med J Mal. 55:78-89 2000.

Khoo KL, Tan H, Liew YM et.al. Blood pressure, body mass index, heart rate and levels of blood cholesterol and glucose of volunteers during National Heart Weeks, 1995-1997. Med J Mal. 55:439-450 2000.

FAMILIAL HYPERLIPIDAEMIA

Some genetically inherited hyperlipidemia have been linked to a high incidence of coronary artery disease and Khoo has described a number of families in 1980.There are several gene defects, each now known to have a range of defective mutations, that cause pronounced alteration of serum lipids from a young age. Among those that have been described in Malaysia are:

Familial Hypercholesterolemia.

Khoo, Chong and Pillay reported a Chinese family, in 1973, with 7 of 14 siblings affected with Fredrickson's type II lipoproteinaemia, now believed to be due to a deficiency of LDL receptors, demonstrating a dominant mode of inheritance. Khoo has also described an 11 year old Chinese boy presenting in 1973 who was homozygous for the autosomal dominant hypercholesterolemia gene who had a blood cholesterol level of 19.4mmol/l. He died at the age of 15 years of his third myocardial infarction. His parents were non-consanguineous but had high cholesterol as did 3 of his 5 siblings. Studying 86 unrelated Malaysians with familial hypercholesterolaemia in the year 2000 Khoo *et.al*. found 23 with LDL receptor gene mutations, but none with the Apoliprotein B-3500 mutation. Mutations were found on 11 of the 18 exons in the LDL receptor gene. All races were represented. Chinese formed the great majority but that might merely reflect the population sample from which the patients were drawn. Males and females were evenly represented. Patients with LDL receptor gene defects had a mean total cholesterol level of 9.3mmol/l and an LDL cholesterol of 7.2mmol/l. These patients had a mean age of 53 years. 65% had xanthomas, 61% had a positive stress test and 39% had a previous myocardial infarction. Hypertension (26%) and diabetes (9%) were not correlated.

Familial Hypertriglyceridaemia

Chong and Alhady described a case believed to be Fredirickson's type V lipoprotein pattern lipoproteinaemia in a Chinese woman in 1969. Khoo also described a Chinese family with type V lipoproteinaemia. A 2 year old girl presented in 1997 having triglyceride levels ranging from 14.5-19.5 mmol/l whose parents and other sibling also had raised triglycerides. The girl has the Apo CII and Apo E2/E3 phenotype which might mean she has a collection of genetic defects.

References

Chong YH and Alhady SMA. Hyperlipoproteinaemia in a Malaysian family. Far East Med.J. 5:156-159 1969.

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hyperlipoprotienaemia in a Chinese family. Med.J.Aust. 1:1048-1050 1973.

Khoo KL. A study of certain lipid abnormalities in Peninsula Malaysia. MD thesis. University of Singapore, 1980.

Khoo KL, Tan H and Liew YM. Familial hyperlipidaemia in Malaysian children. Med J Mal.55:249-258 2000.

Khoo KL, Acker PV, Tan H and Deslypere JP. Genetic causes of familial hypercholesterolaemia in a Malaysian population. Med J Mal. 55:409-418 2000.

CEREBROTENDINOUS XANTHOMATOSIS

Cerebrotendinous xanthomatosis is a rare lipid storage disease due to a defect in bile acid metabolism. It is an autosomal recessive disorder. Patients show raised cholestanol and tendinous and tuberous xanthomas, cataracts and cerebral impairment. Nor Hayati and Sabariah have described a Malay family with 5 affected members in Kelantan.

Reference

Nor Hayati O and Sabariah AR. Cerebrotendinous xanthomatosis with cholestanolaemia - involvement of five individuals in a Malay family. Med.J.Mal. 45:275-280 1990.

GAUCHER'S DISEASE

Gaucher's disease is a group of recessively inherited inborn errors of glucosphingololipid metabolism, characterised by accumulation of glucosylceramide in the reticuloendothelial system. One variant presents with principally massive hepatosplenomagaly. Nunis recorded one case in Chinese boy whose parents were first cousins. A second variant presents with mainly neurological features.

Reference

Nunis GV. Gaucher's disease type 1A: a case report. Med.J.Mal. 40:257-259 1985.

NIEMANN-PICK DISEASE

The disease is named after the German paediatrician Niemann who first described the clinical features in 1914, and Pick who defined it as a distinct entity in 1927. The cause is sphingomyelinase deficiency of which there are a few variants. Affected children are marked by failure to thrive, very noticible hepatosplenomegaly, vomiting, progressive loss of motor and intellectual functions, generalised hypotonia and finally respiratory deterioration which leads to infection and death. Haridas described one local case in Singapore in 1950.

Reference

Haridas G. A case of Niemann-Pick disease Med.J.MAl. 4:285-287 1950.

HURLER'S DISEASE

Hurler's disease is an autosomal recessive mucopolysaccharidosis. Gunn reported one 12 year old mentally retarded Chinese girl with the condition in 1954.

Reference

Gunn DR. A brief report of two cases of chondro-osteo-dystrophy. Med.J.Mal. 9:84-90 1954.

ALKAPTONURIA

Alkaptonuria was the first human disease to be shown to be inherited as an autosomal recessive trait. It is a disorder of catabolism of tyrosine in which deficiency of homogentisic acid oxidase leads to the excretion of large amounts of homogentisic acid and its accumulation in connective tissue (ochronosis). In early life alkaptonuria may go unrecognised if not for the urine that darkens to blackness on standing. After many years ochronosis gives rise to degenerative arthritis. Accumulation of the bluish black pigment in intervertebral discs can

produce disc prolapse and as reported by Koh KB *et.al.*, root canal stenosis as well.

Reference

Koh KB, Low EH, Ch'ng SL and Zakiah I. A case of alkaptonuria with root canal stenosis. Sing Med J 35:106-107 1994.

HOMOCYSTINURIA

Carson and Neil first described this disorder in 1962 as a cause of mental retardation among institutionalized children. The defect lies in the conversion of the amino acid homocysteine to cystathionine. The accumulated homocysteine overflows into the urine. A Marfanoid habitus and 'dislocated lenses' are the signs that give away the diagnosis. Mental retardation is also characteristic. Lin and Perumal described the first local case in a Chinese boy in KL in 1976.

Reference

Lin HP and Perumal R. Homocystinuria - a case report. Med.J.Mal. 30:213-219 1976

PHENYLKETONURIA

Phenylketonuria is an autosomal recessive condition that untreated causes mental retardation. Folling first found excess phenylpyruvic acid in the urine of such patients in 1934. Jervis in 1953 identified the metabolic error to be an inborn error in aromatic amino-acid metabolism and Bickel *et.al.* reported success of low phenylalanine diet therapy. The incidence in Europe has been reported at between 15-20 per 100,000 live births. Japan and the USA have an incidence of about 5-9 per 100,000. It is thought to be rare in Asia but there are a few case reports from Singapore and Thailand. Only one case has been reported in a Malay boy in Malaysia.

Reference

Karnaneedi S, Choo KE, Ariffin WA and Norimi M. Phenylketonuria in a six year old Malay boy - a case report. Med.J.Mal. 44:248-251 1989

MAPLE SYRUP URINE DISEASE (MSUD)

MSUD is the commonest inborn error of metabolism reported in Western neonatal screening programmes. The unusual urine odour has been described as that of "boiled Chinese herbs", which may be more meaningful in our local context. The disease is usually lethal to the neonate unless intake of dietary branched chain amino acids is restricted. Affected individuals lack an enzyme in the oxidative decarboxylation of the branched chain amino acids that allow these amino acids and their products to accumulate in the urine serum and cerebrospinal fluid.

In 1993, IMR workers examined specimens from 404 children using high performance liquid chromatography in order to screen for MSUD. These were received from all over the country and were children in which MSUD was considered possible. MSUD was found in 4.2% (17). Malay males were most commonly affected.

As we have no screening programme for MSUD, pediatricians need to be alert for the possibility of this disease in neonates that are born well but become lethargic, feed poorly and vomit at the end of the first week.

References

Zakiah I, Ashikin YN Aishah SM and Ismail HI. Inborn errors of metabolic disease in Malaysia: a preliminary report of maple syrup urine disease for 1993. Southeast Asian J Trop Med Pub Hlth 26:134-136 1995.

Ong LC, Khoo TB, Zulfiqar A et.al. Computed tomography findings in maple syrup urine disease. Sing Med J 39:370-372 1998.

ORNITHINE TRANSCABAMYLASE DEFICIENCY

Ornithine transcabamylase (OTC) is a mitochondrial enzyme that is involved in urea biosynthesis. OTC deficiency results in hyperammonemia and an aversion to high protein foods. There is an elevation of glutamine in blood and other tissue fluids. Because mitochondria originate from the ovum in human development, the OTC enzyme is transmitted through maternal non-mendelian inheritance. A novel mutation of the OTC gene has been found in a Malaysian family.

Reference

Khoo AS, Balraj P, Rachedi A et.al. A novel complex mutation of the OTC (ornithine transcarbamylase) gene in a Malaysian pedigree. Hum Mutat 14:448 1999.

HYPERURICAEMIA

Urate is the end product of purine metabolism in man and primates. Illness arises because of the low solubility of uric acid. Other mammals seem more fortunate in having an enzyme that converts urate to allantoin which is about 100 times more soluble. Urate is formed from xanthine by the enzyme xanthine oxidase which generates undesirable free radicals (hydrogen peroxide) in the process. Man like sheep, cats, pigs and goats has low activity of xanthine oxidase in serum. Xanthine oxidase is the rate limiting enzyme in purine degradation and is inhibited by the drug allopurinol.

The activity of xanthine oxidase can be measured by its generation of oxygen. Newaz and Adeeb report measuring this in a sample of 46 Malaysians. Males had a higher activity of xanthine oxidase (2.71 nmol/O_2/ml plasma/min) compared to females (2.35nmol/O_2/ml plasma/min). There was a strong correlation of the enzyme activity with age and with weight. Malays had higher xanthine oxidase activity compared to Indians and Chinese. We can therefore expect uric acid levels to be higher in Malay males.

The normal range of serum uric acid appears to vary considerably in different human populations. Europeans, Americans and Asians have mean values for males of between 4.5 to 6.0 mg/dl. Values reported however, sometimes vary from study to study in the same region perhaps due to differences in the method of measuring the serum uric acid. Women usually have mean values 1 mg/dl lower than men. One race that appears to have a much higher mean serum uric acid are the Polynesians and other Pacific Islanders. Males there have mean values of about 7.0 mg/dl. It also appears that Africans have low mean values of about 4.0 mg/dl.

Gout

Gout is the classic disease of hyperuricaemia. Hyperuricaemia usually occurs not because of enzyme defects in the degradation of purines but because of enzyme defects that result in the increased synthesis of purines. Not all hyperuricaemics have gout, only about 15% do. Khaira reported in 1969, that in a series of 130 gout patients, Malays and North Indians appeared to be at greater likelihood of suffering from gout. As expected, males greatly outnumbered females. The ratio was 7:1. Only adults were involved but there was a wide spread of ages. He found no association with the higher income group nor comsumption of alcohol. All sorts of joints were involved in the arthropathy. 21% of the patients had gouty tophi which was seen more commonly among Chinese. 8% of patients had renal colic or stones.

From Sabah, there is a report by Burns-Cox in 1964, that gout was the commonest form of acute arthritis seen in Kota Kinabalu, contrary to what was then thought that it was uncommon in the tropics.

References

Burns-Cox CJ. Thrity-three cases of acute arthritis in Sabah. Med.J.Mal. 19:25-29 1964.

Khaira BS. Gout in Asians. Proceedings of the third Malaysia Singapore congress of medicine. 259-264 1969.

Newaz MA and Adeeb NNN. Detection of xanthine oxidase in human plasma. Med.J.Mal. 53:70-75 1998.

WILSON'S DISEASE

Wilson described the disease that bears his name in 1912 as a neurological disorder with associated liver problems. It has also been called hepato-lenticular degeneration. It is an autosomal recessive abnormality characteristically associated with a deficiency of caeruloplasmin, that results in toxic accumulations of copper in the liver brain and other organs. Because it is uncommon, the diagnosis of Wilson's disease is often not made until often over a year after the patient has had symptoms of the disease.

Haq and Smyth were probably the first to report case in Malaysia in a Chinese patient from Perak in 1956. Lim and Choo reported it in a 2 year old child in 1979. Mohamed, Tan and Wong reviewed a series on 18 cases over 11 years from 1981, diagnosed at the UH. 3 patients were found as a result of screening relatives of patients. The mean age of patients at diagnosis was 15.5 years. There were 10 Chinese, 7 Indians and only 1 Malay patient. There were 13 males and 5 females. There were seven families where more than one member was affected and in five of these there were consanguineous marriages. Their patients were treated with penicillamine but compliance was poor in nine. Two patients were lost to follow-up. Seven died ranging from three months to six years after diagnosis, five survive with troublesome neurological manifestations and only four remained well.

References

Haq SM and Smyth VOG. A case of hepatolenticular degeneration. Med.J.Mal. 11:134-138 1956.

Lim CT and Choo KE. Wilson's disease - in a 2 year old child J Sing Paediatr Soc 21:99-102 1979.

Mohamed R, Tan CT and Wong NW. Wilson's disease - a review of cases at University Hospital, Kuala Lumpur. Med.J.Mal. 49:49-52 1994.

HAEMOCHROMATOSIS

Haemachromatosis is an autosomal dominantly inherited disorder of excessive iron absorption. The end result is cirrhosis. It is uncommon but it does occur in Malaysia.

Reference

Oram TFD. A case of haemochromatosis in a male Chinese. Med.J.Mal. 8:337-342 1954.

THE PORPHYRIAS

These are collectively disorders of haem metabolism.

ACUTE INTERMITTENT PORPHYRIA

A rare condition, this was first documented in Malaysia by Chong, Omar and Rejab in a 23 year old woman in KL who had one affected parent and one affected sibling in 1978. Jeyamalar and Ch'ng reported another case in a 28 year old Malay woman from Rawang in 1986.

References

Chong KF, Omar AR and Rejab S. Acute intermittent porphyria - a case report. Sing.Med.J. 19:61-63 1978.

Jeyamalar R and Ch'ng SL. Acute intermittent porphyria: the first case report in Malaysia. Sing.Med.J. 27:548-552 1986

ERYTHROPOIETIC PROTOPORPHYRIA

This is also rare. The first reported case in Malaysia was noted in a Malay man seen by Ch'ng *et.al.*.

Reference

Ch'ng SL, Gangaram HB, Suriaya HH and Rajagopalan K. A case of erythropoietic protoporphyria. Med.J.Mal. 43:243-245 1988

DRUG RESPONSE AND METABOLIC INJURY

SILENT PLASMA CHOLINESTERASE

Abnormal variants of plasma cholinesterase are a rarity but they can give rise to prolonged apnoea after administration of suxamethonium in general anaesthesia. It is a recessively inherited condition. Ganendran and Ogle failed to detect any such individuals in a multiracial study in 1975. However within a year two cases were reported in Johore Bharu. One Indian patient had 8 other heterozygotes in his family tree. Another Chinese patient had only one heterozygote in his family.

References

Ganendran A and Ogle CW. Absence of abnormal variants of cholinesterase (E.C. 3.1.1.8) in a Malaysian population with three major racial groups. Sing.Med.J. 16:256-258 1975.

Mohandas K and Sivaneswaran N. Prolonged apnoea after suxamethonium in a Malaysian patient due to silent plasma cholinesterase - first case report. Med.J.Mal. 37:158-159 1982.

Sivaneswaran N and Inbasegaran K. Suxamethonium sensitivity - yet another case. Med.J.Mal. 37:298-299 1982.

BETA-BLOCKERS

Rasool AH *et.al*. investigated the ethnic differences in response to propanolol in 35 healthy male volunteers. Six hours after 80mg of propanolol given 12 hourly, there was no significant difference in plasma propanolol. Chinese were however, least sensitive to the bradycardic and hypotensive effects of propanolol at rest and exercise. Percentage reduction of systolic blood pressure and heart rate while supine, sitting and at exercise was significantly higher in Malays compared to Chinese. The average increase in potassium concentration at peak exercise and recovery was significantly greater in Indians compared to Chinese. There was however no significant interethnic difference seen in the reduction of glucose levels at rest, peak exercise or recovery. Similarly, there was no interethnic difference in the reduction of Forced Expiratory Volume in 1 second (FEV1) values.

Reference

Rasool AH, Rahman AR, Ismail R et.al. Ethnic differences in response to non-selective beta-blockade among racial groups in Malaysia. Int J Clin Phamacol Ther 38:260-260 2000.

REYE'S SYNDROME

Reye's syndrome is an acute illness, predominantly in children. It is characterised by vomiting, encephalopathy, signs of hepatic injury and hypoglycaemia. The liver shows microvesicular fatty changes and widespread mitochondrial injury. Recognition of the condition dates from 1963 when Reye and others first described it. Often Reye's syndrome follows a few days after influenza A or B or chicken pox illness, especially if aspirin has been administered. Its pathophysiology has not been clearly established but studies with margosa oil in rats suggest that uncoupling of the mitochondrial respiration could be the cause.

Leong recorded 3 fatal cases in 1976 at the UH, in children between 8-30 months old with no noticeable aetiological features in particular.

Sinniah *et.al*. undertook a one year study of 8 major hospitals in Malaysia in 1986 into definitve Reye's and Reye-like disease. They

found that less than 50% fulfilled the full criteria for Reye's syndrome and it was not possible to differentiate Reye's from other encephalopathies either by clinical features or biochemical parameters. They concluded that liver biopsy was necessary to diagnose Reye's syndrome in Malaysia because of the high prevalence of Reye-like diseases.

All over the world a marked decrease in the incidence of Reye's has been observed with the avoidance of aspirin in viral illnesses. In Malaysia the possibility of Reye's in patients that have used margosa oil must be borne in mind.

References

Leong AS. Reye's syndrome in Malaysian children. J Sing Paediatr Soc. 18:38-42 1976.

Sinniah D, Sinniah R, Yap YF et.al. Reye and Reye-like syndromes: results of a pilot study in Peninsula Malaya, 1986. Acta Paediatr Jpn 32:385-390 1990.

OTHER ENZYME DEFICIENCIES

ALPHA-1-ANTITRYPSIN DEFICIENCY

$Alpha_1$ antitrypsin (α1AT) deficiency is a disorder where there is reduced serum levels of α1AT, an antiprotease that protects the lower respiratory tract against the ravages of neutrophil elastase. The loss of this protection results in emphysema. α1AT is produced in the hepatocyte and in the severe deficiency state it also causes neonatal hepatitis and progressive cirrhosis.

The α1AT gene has seven exons and is located on chromosome 14. There are at least 75 alleles of the gene known and at least 20 that cause a deficiency state. The two most common deficiency mutations of the α1AT gene are, the S mutation (exonIII, $Glu^{264} \rightarrow$ Val) which is carried by up to 1 in 25 Caucasians, and the Z mutation (exonV, $Glu^{342} \rightarrow$ Lys) which is carried by about 1 in 50 Caucasians. It is the Z mutation that causes the severe form of the disease. The S mutation causes a less severe deficiency of α1AT and even homozygotes are not at risk for emphysema. SZ heterozygotes are at mild risk. Hence the minimal protective level of α1AT is between that of the S and Z homozygotes. This has led to therapy of administering intravenous α1AT weekly at a dose of 60mg/kg to provide sufficient antielastase protection to the alveoli.

Lie-Injo *et.al*. examined the sera of 908 Malays, 371 Chinese and 231 Indians in Malaysia for the different variant M, S and X types of antiprotease or protease inhibitor (Pi) in 1978. Their findings are put in Table 24.1. Besides these 3 types they noted 2 variants they could not identify. They did not report the presence of the Z mutation.

Table 24.1 Frequency of 3 different protease inhibitor types in Malaysian races

	Malays	Chinese	Indians
PiM	0.979	0.981	0.976
PiS	0.015	0.019	0.24
PiX	0.007	0	0

In 1979, Menon, Vaterlaws and Cheok performed serum electrophoresis studies on 85 patients with emphysema seen over 5 years looking for α1AT deficiency. They did not detect any. In 1992 Zakiah *et.al* studied 310 babies with prolonged jaundice admitted to GH KL over a 3 year period to determine the role of α1AT deficiency as a cause of the jaundice. 92 (30%) were found to be α1AT deficient. The percentage was found to be highest among Indians (33%), followed by Malays (32%) and least in Chinese (27%). Males outnumbered females in a ratio of 1.6:1. Most of these babies presented between 2 to 4 weeks of life.

The Z mutation however does occur in Malaysia. In a study of 950 samples from suspected patients reported in 1995, Desa found that 10 were homozygous PiZZ in phenotype.

References

Lie-Injo LE, Ganesan J, Herrera A and Lopez CG. Alpha-1 antitrypsin variants in different racial groups in Malaysia. Hum Hered 28:37-40 1978.

Menon MA, Vaterlaws AL and Cheok T. EmphysemaII. The role of alpha-1 antitrypsin deficiency in Malaysian patients. Med J Mal. 33:304-306 1979.

Zakiah I, Zaini AR, Jamilah B and Zawiah A. Alpha-1-antitrypsin deficiency in babies with prolonged jaundice. Mal J Pathol 15:91-94 1992.

Desa NM, Ismail Z, Beran Z and Musa SH. The Malaysian experience in the typing of genetic variants of alpha-1-antitrypsin. Southeast Asian J Trop Med Pub Hlth. 26s1:311-414 1995.

CHAPTER 25

THE BLOOD AND IMMUNE SYSTEM

NORMAL BLOOD PARAMETERS

Blood Groups

The most important blood group system remains the earliest one discovered, that is, the ABO system that Landsteiner found in 1901. Early studies on the distribution of ABO blood groups in Malaysia were done in the early 1950s by Green, Simmons *et.al.*, Schebesta and others on usually only a few hundred subjects. Larger studies for West Malaysia were later reported by Poon and Amarasingham, from blood samples sent to the Chemistry Department and by Duraisamy and Amarasingham from blood donors in KL. These large samples should closely resemble the distribution in the general population. Below is a table of the distribution of blood groups from the different studies (Table 25.1).

TABLE 25.1 ABO Blood groups among different races in Malaysia

Author	Sample Size	BLOOD GROUP O	A	B	AB
Malays					
Schebesta	44	30%	20%	43%	2.3%
Poon & Amara.	616	37%	25%	32%	6.0%
Durai. & Amara.	14,556	44%	24%	25%	6.2%
Chinese					
Simmons et.al.	250	46%	25%	21%	7.6%
Poon & Amara.	940	46%	23%	26%	5.3%
Durai. & Amara.	7,586	48%	25%	23%	4.3%
Indians					
Poon & Amara.	826	35%	22%	36%	7.3%
Durai. & Amara.	6,898	43%	21%	29%	6.4%
Orang Asli					
Simmons et.al.	165	54%	10%	31%	4.8%
Polunin & Sneath	269(Negrito)	59%	25%	14%	1.8%
	340(Senoi)	49%	6%	42%	2.6%

Chinese have a relatively higher proportion of Group O. Indians have relatively more Group B. The numbers are small in the studies of Orang Asli but Group O seems quite common and among the Senoi, Group A was relatively infrequent.

Of next importance to the ABO is the Rhesus (Rh) system discovered by Landsteiner and Wiener in 1940. It was determined a few months later that humans could develop antibodies to these antigens as a result of pregnancies or blood transfusions. This became the most important cause of haemilytic disease of the newborn. Unpublished records of all Malaysian hospital blood banks confirm that Rhesus negative individuals are rare locally. Duraisamy, for example, quoted finding only 16(0.3%) Rhesus negative individuals among 5,282 Malay transfusion recipients. Among Indians Rh negative individuals may be commoner. Ng *et.al.* reported 3 such cases of Rhesus isoimmunisation who had bad obstetric histories but were successfully treated with intrauterine blood transfusions at the UH.

Other blood groups which are less important have been reviewed in an article by Hawkins in 1974. However, he confined himself to only the Malay population. In the MNS system, historically the second to be discovered, he commented that the S gene appears somewhat higher than other mongoloid populations. The Kell gene appears to be rare and is a characteristic of mongoloid populations. The Duffy gene appears to be common.

There are 2 equally common types of Duffy antigens, Fy^a and Fy^b. The Duffy blood group antigens function as receptor sites for at least one species of malarial parasite, *Plasmodium vivax*. More than 70% of West Africans lack these red

cell antigens suggesting malaria induces a selective pressure on the population. One wonders if this effect might be evident in the Orang Asli who have been native here in a malaria endemic area for a long time. However, in a study of 314 Orang Asli, 313 were found to be Fy^a in genotype and none were Duffy negative.

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Lewis GE Jr, Miller LK, Ibrahim L et.al. Duffy phenotypes in Malaysian populations: correction of previous unusual findings. Trans R Soc Trop Med Hyg. 82:509-510 1988.

Lymphocytes

Pang, Parasakthi and Yap reported a small local study of the percentages of T and B lymphocytes in 33 healthy adults in 1979. The values obtained were 71% T cells and 9% B cells. There were no significant difference between sexes or races. In 1980 Gan and Yeoh found on a larger sample results that were generally in agreement but noted that there was a decline with age. Neonates had a mean of 80% T cells and 15% B cells that dropped to 55% T cells and 9% B cells in the over 55 years age group.

Dhaliwal *et.al.* studied the monoclonal antibody detected cell-surface markers of lymphocytes in a sample of 152 normal individuals (56% Malays, 26% Chinese 18% Indians) in a report in 1995. They found no significant differences in the distribution among the races. However the absolute number of CD4 and CD19 cells in Chinese was significantly lower compared to the Indians and Malays. As a group the lymphocyte subset distribution among Malaysians was different from Caucasians but similar to Japanese. Their results are given in Table 25.2 below. UKM workers have also done a similar series given in the same table. In a sample of 212 adults they also found CD19 counts (B cells) lower in Chinese. The CD4/CD8 ratio was significantly higher in Chinese females than males and was found to increase with age among Chinese. Indians had higher numbers of CD3 (T cells) and CD4 (helper/inducer cells) cells but lower CD56+CD16 (natural killer) cells than the Malays and Indians.

Table 25.2 Lymphocyte subsets in the peripheral blood of healthy Malaysian adults

. count Surface Antigen cells/L)	Chin *et.al.* 1993 Percentage	Dhaliwal *et.al.* 1995 Percentage (mean ± SD)	Absolute (mean No.
CD3	70.9	66.5 ±8.6	2,066 $x10^6$
CD4	38.2	33.2 ±8.5	1,028 $x10^6$
CD8	37.8	31.6 ±8.9	982 $x10^6$
CD19	11.4	12.0 ±5.0	374 $x10^6$
CD56+CD16	17.5	20.9 ±9.1	638 $x10^6$

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Dhaliwal JS, Balasubramaniam T, Quek CK et.al. Refernece ranges for lymphocyte subsets in a defined Malaysian population. Sing.Med. J. 36:288-291 1995.

Choong ML, Ton SH and Cheong SK. Influence of race, age and sex on the lymphocyte subsets in peripheral blood of healthy Malaysian adults. Ann Clin Biochem 32:532-539 1995.

Immonuglobulins

Yadav and Shah wrote a number of reports on the normal levels of immunoglobulins in healthy subjects in the 1970s. Their results of a sample of 635 Malays, 445 Chinese, 409 Indians and 217 Orang Asli adults are summarised in the table below (Table 25.3).

Table 25.3 Mean immunoglobulin levels among different races in Malaysia

	Serum concentration in mg/100ml.		
	IgG	IgA	IgM
Malays	1331±280	188±77	157±62
Chinese	1281±443	191±72	152±57
Indians	1284±316	222±78	152±55
Orang Asli	1809±662	394±107	246±77

In general the serum immunoglobulins of the three major races are comparable to levels reported for Caucasians in temperate regions. The Orang Asli however, have significantly higher levels of all these immunoglobulins than the other three races. This must be a result from their more primitive lifestyle that exposes them to more infections. Among Malays, Chinese and Indians, the serum IgM levels were comparable, but IgG was higher significantly among Malays and IgA significantly higher among Indians.

Females had higher IgM levels than males in Malays, Chinese and Indians but not among the Orang Asli. Females also had higher levels of IgA among Malays and Chinese but there was no sex difference for IgG in any race. Teenagers (11-20 years) in general tended to have a higher level of IgM and IgA than adults but a slightly lower level of IgG.

In a study of newborns, the level of IgG ranged from 1092±270 mg/100ml. among Chinese to 1254±441 mg/100ml. among the Orang Asli. Indians and Malays had values closer to the Orang Asli. In Malaysians, as in Taiwanese and Africans, the (cord)foetal IgG level was generally slightly lower than maternal IgG unlike Caucasians among whom foetal IgG is generally slightly higher. Mean foetal IgM ranged from 10.9 to 16.7 among the four races. IgA was detectable in about a third of the cord serum of the three urban races but nearly in two-thirds of the Orang Asli. Cord serum immunoglobulins showed no correlation to birthweight or gestation age. Of these three immunoglobulins only the IgG shows a correlation between foetal and maternal levels.

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Yadav M and Shah FH. Variation in serum immunoglobulin G, A and M levels in Malaysian blood donors. Med.J.Mal. 33:57-71 1978.

Yadav M and Shah FH. Normal serum immunoglobulin G, A and M levels in full term Malaysian newborn. Med.J.Mal. 33:247-251 1979.

Blood volume

Sharifah reported some results of normal vascular volumes from a small sample of ten male students. Their mean height was 1.66m and mean weight was 57kg. The mean whole blood volume was 4.33 lit., and mean plasma volume was 2.49lit.

Reference

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STEM CELL DISORDERS

APLASTIC ANAEMIA

Aplastic anaemia is a disease of bone marrow failure in which there is, on histology, hypoplasia of the bone marrow without either fibrosis or infiltration by malignant cells. The survival outlook for patients is usually poor. Lie-injo *et.al* in 1967 reported favourable results in a trial of treatment with testosterone. All their 5 patients were under 35 years in age and Malays and Chinese were represented. Leong *et.al* reported a response in 4 of 6 patients given anti-lymphocyte globulin therapy in UH in 1993. 3 had sustained remissions and were transfusion free after follow up of over a year.

Yong *et.al*. noted that aplastic anemia was unusually common in Sabah. In a review of 39 months from 1993 to 1996 they found 31 cases confirmed by a bone marrow trephine biopsy, although a further 16 with clinical features did not have bone marrow biopsy and another 15 had inconclusive bone marrow trephine biopsies due to inadequate sampling. There were 3.4 times more males than females and 77% of the patients were from the Kadazan-Dusun ethnic group which form 18% of the population. Although the median age of the patients was 23 years, the calculated incidence for the whole population was highest among those above 60 years (8.6 per 1,000,000) and those between 15-24 years (7.9 per 1,000,000). The ratio of aplastic anaemia to acute myeloid leukaemia was 0.91 and to total acute leukaemia was 0.37. In contrast, it has been noted that in Western countries acute leukaemia is 5-10 times more common than aplastic anaemia (ie a ratio of 0.1-0.2).

References

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Yong ASM, Goh AS, Rahman M et.al. Epidemiology of aplastic anaemia in the state of Sabah, Malaysia. Med.J.Mal. 53:59-62 1998.

POLYCYTHAEMIA RUBRA VERA

Polycythaemia rubra vera results from an abnormal proliferation of the blood elements. It is not common but we have little indication of it incidence. It ought to be diagnosed though, because untreated, the prognosis is bad. Nuclear medicine offers good prospects for remission. Zulkifli, Chelvam, Ng and Dharmalingam have reported on 8 cases, about one a year, seen at the Institue of Radiotherapy KL. They ranged from 42 to 64 years of age.

Reference

Zulkifli A, Chelvam P, Ng WH and Dharmalingam SK. Response to radioactive phosphorus treatment of polycythaemia rubra vera in Malaysians: analysis of 8 cases. Med.J.Mal. 33:346-348 1979

PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA

Commonly regarded as a type of haemolytic anaemia, paroxysmal nocturnal haemoglobinuria (PNH), in reality a stem cell disorder characterised by the formation of defective platelets and granulocytes as well as abnormal erythrocytes. It is an acquired membrane defect that causes a chronic haemolytic disorder. A positive Ham's test is specific for the disorder. A number of cases have been found in Malaysia and a few reported. Though not a common disease it occurs more frequently in this region than in other parts of the world.

References

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Koh CS. A case of paroxysmal nocturnal haemoglobinuria (PNH). Med.J.Mal. 42:122-123 1987

RED CELL DISORDERS

HAEMOGLOBINOPATHIES

The abnormal haemoglobins were at first identified on the basis of their electrophoretic mobility. Normal Haemoglobin (Hb) has been named A and all the various alphabets have been used till they have been exhausted. Following that proper names have been used, such as Hb Bart's and the catalogue stands at over 400 today. However these include 2 groups of diseases; namely the Haemoglobinopathies, which are mutations of either the α or ß globin chains and the Thallasaemias, which are deletions of either the α or ß globin chains. The following are the haemoglobinopathies of local importance.

Hb Constant Spring Disease

Hb Constant Spring (HbCS) was discovered in 1971 in a large Chinese family living in Constant Spring, Jamaica. It has an α chain elongated at the C- terminal by 31 amino acid residues. Lie-injo and Duraisamy showed that it occurred in 2.2% of Malays, <1% of Chinese and rarely among Indians in Malaysia. 2.4% of Malays of Minangkabau descent in Ulu Jempol were found by Ganesan, George and Lie-Injo to have HbCS. Among the Orang Asli the prevalence of HbCS was 4.2% among the Temuan and 2.6% among the Jakun, but it was not detected among over 300 Senois (Semai and Temiar). The significance of HbCS is that in combination with α thalassaemia it causes a severe form of Hb H disease (see below). In Sarawak, Ganesan *et.al*. found that HBCS was the only abnormal hemoglobin detected in a survey of over 500 Bidayuh and Ibans. It occurred in 0.8% of Ibans and 0.4% of the Bidayuh.

A 12 year old Malay boy homozygyous for HbCS has been described. He only had mild microcytic, hypochromic anemia, splenomegaly and a liver that was just palpable. His parents and 6 other siblings were heterozygotes. He had normal HbA and HbA_2 as there is duplication of the gene for α–chain production.

References

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Lie-injo LE, Baer A, Lewis AN and Welch QB. Hemoglobin Constant Spring (slow moving Hemoglobin X components) and Hemoglobin E in Malayan aborigines. Am J Hum Genet 25:382-387 1973.

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Ganesan J, Lie-injo LE and Ong BP. Abnormal hemoglobins, glucose-6-phosphate dehydrogenase deficiency and hereditary ovalocytosis in the Dayaks of Sarawak. Hum Hered 25:258-262 1975.

Hb E Disease

Hb E was discovered by Vella and Field in soldiers in Malaya and Singapore in 1958. It can be described as ß26 (B8)Glu→Lys, a lysine substitution for glutamine on the ß globin due to a G→A substitution on codon 26. It has been sometimes said that Hb E is the hallmark of the Southeast Asian populations. There have been reports that in certain parts of Thailand and Burma the prevalence is above 30%. In West Malaysia the prevalence has been found to be between 3-12% probably higher among Malays than Chinese and Indians. Lie-injo, McKay and Govindasamy, for example, found rates of 8% and 11% in children and adults respectively in Hulu Terengganu. Ganesan, George and Lie-Injo found that 5.3% of Malays of Minangkabau descent in Ulu Jempol had the gene. Among the Senois Lie-injo has reported a prevalence of 40% but among other Orang Asli like the Jakun the prevalence was only 4%. The prevalence rate drops the further one goes outwards towards the Indonesian islands.

The homozygous condition causes only a mild anaemia. When present with elliptocytosis, another common condition among Malays and Orang Asli, the anaemia is a bit more noticeable

but may still be asymptomatic. The trait, or the heterozygous form, produces only a mild microcytosis which is compensated by erythrocytosis so that these individuals have a normal haemoglobin content. There has been speculation that Hb E, like elliptocytosis, may be a beneficial factor in malaria infection. The only real importance of Hb E is its interaction with the heterozygous form of β thallasaemia described below.

Ong studied the obstetric outcome of 20 patients with Hb E trait and 8 patients with Hb E disease found among 126 pregnant Orang Asli women. He noted an increased frequency of abruptio placenta, but there was no increase in fetal wastage or stillbirths. The mean birthweight in these pregnancies was significantly lower but the incidence of prematurity not increased. Blood loss at delivery, postpartum haemorrhage, preeclampsia and malaria were not increased in Hb E patients. No maternal deaths or congenital fetal abnormalities were observed.

References

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Lie-injo LE, McKay DA and Govindasamy S. Genetic red cell abnormalities in Trengganu and Perlis. Southeast Asian J.Trop.Med.Pub.Hlth. 2:133-139 1971.

Ong HC. Maternal and fetal outcome associated with hemoglobin E trait and hemoglobin E disease. Obstet Gynecol 45:672-674 1975.

George E and Sivagengei K. Haemoglobin E trait: microcytosis and erythrocytosis. Med.J.Mal. 37:102-103 1982.

George E and Kudva MV. Homozygous haemoglobin E in association with hereditary ovalocytosis. Med.J.Mal. 44:255-258 1989.

Hb A2 Indonesia Disease

Hb A2 Indonesia ($\alpha_2\delta_2$ 69(E13)Gly→Arg) is a fast moving Hb between Hb A and Bart's on electrophoresis. It is symptomatic. It has been found to occur in 0.8% of 629 Malays of Minangkabau descent in Negeri Sembilan. Ganesan and Lie-injo have noted that individuals doubly heterozygote for Hb A2 Indonesia and either Hb E or β thalassaemia had essentially normal haematological findings.

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Ganesan J and Lie-injo LE. Interaction of Hb A2 Indonesia trait with beta-thalassaemia trait and with Hb E trait. Acta Haematol 59:341-347 1978.

Hb Koln Disease

Hb Koln ($\alpha_2\beta_2$ 98 Val→Met), produces a thermolabile haemoglobin that leads to the formation of Heinz bodies in red cells, more prominently seen after splenectomy. It is more often seen in non-Asians but Lie-injo has noted a Malay family with 3 siblings having mild haemolytic anaemia.

Reference

Lie-injo LE, Lopez CG, Eapen JS et.al. Unstable haemoglobin Koln disease in members of a Malay family. J Med Gene. 9:340-343 1972.

Hb Leiden Disease

Hb Leiden ($\alpha_2\beta_2$ 6or7 Glu→O) was found to cause severe haemolytic anaemia, in combination with β thalassaemia which improved after splenectomy in a Chinese boy. His father and brother who also had the trait had 23% and 19% of the unstable Hb Leiden respectively. His mother was heterozygous for β thalassaemia.

Reference

Lie-injo LE, Ganesan J, Randhawa ZI et.al. Hb Leiden-beta (0) thalassaemia in a Chinese with severe haemolytic anemia. Am J Hematol 2:335-342 1977.

Hb Malay Disease

This abnormal Hb ($\alpha_2\beta_2$ 26 (B1) Asn → Ser), was first described in 1988 in a patient homozygous for the condition who suffered a microcytic anaemia. The father and a sibling with the trait had microcytosis but no aneamia. The mother had the Hb E gene with this Hb Malay and was anaemic.

Reference

George E et.al. First observation of haemoglobin Malay $\alpha_2\beta_2$ 26 (B1) Asn → Ser - A case report. Med.J.Mal. 44:259-262 1988

Hb Q

Hb Q was first discovered by Vella *et.al.* in 1958 in a Chinese patient who also incidentally had Hb H. It is a substitution which can be described as α74 (EF3) Asp→His. It has been seen in a only handful of Chinese patients, symptomless in the heterozygote. Less than 0.2% of Malays in Negeri Sembilan were found to have the gene in a survey of 629 people. It is only symptomatic when associated with α thalassaemia where it causes a total absence of Hb A . Lie-injo *et.al*. showed that this was because the α globin gene adjacent to the HbQ mutant gene was deleted.

References

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Hb S Disease

This is the classical sickle-cell disease common among Africans first described in 1910 in a 20 year old Negro by Herrick. It is a substitution on the β globin chain where valine occurs instead of glutamic acid (Glu→Val) at codon 6. Besides Negroes, the condition also occurs in those of Mediterranean and Indian stock. It was first described in Malaysia by Vella and Hart in 1959 in an Indian family who ancestors had originated from Orissa in India. The gene occurs in a high frequency among rubber estate workers in Negeri Sembilan who originated from Orissa. But unlike the African form, it is milder and many with the condition have reached old age. Chew and Durham reported another family with sickle cell disease in 1965, of Indians whose ancestors came from Tamilnadu.

Rachagan, Raman and Cherian have reported a patient who successfully went through a pregnancy. Joishy, Hassan, Lopes and Lie-injo have found no reduced number of children nor excessive pregnancy problems in Indian families with the Hb S gene. They also found that falciparum occurred less frequently in carriers of the Hb S gene but that individuals had a high association of the α^+ thalassaemia gene. In fact 12 patients homozygous for Hb S, were all either homozygous or heterozygous for the α^+ thalassaemia gene while 24 of 30 Hb S trait carriers also had the α^+ thalassaemia gene. No α^o thalassaemia gene was found. This association explains the less severe form of the disease seen and appears to be protective, resulting in higher levels of HbF and relatively low levels of Hb S. As a side note two other Hb gene abnormalities were found among the Indians Hb S population, an Eco RI fragment in 5 and unindentified one in another 2 people. The sickle-cell trait is not found in Malays, Chinese or the Orang asli.

References

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Joishy SK, Hassan K, Lopes M, and Lie-injo LE. Clinical, genetic and fertility studies of Indians with the beta S-globin gene and the influence of Hb S on Plasmodium falciparum malaria infection. Trans R Soc Trop Med Hyg 82:515-519 1988.

Hb Tak

Hb Tak is an abnormal β globin chain elongated at the C end by 11 residues. It has been found in 2 Thai families and noted in a Malay mother and her child who were heterozygote for the gene. The 4-day old newborn child suffered severe neonatal jaundice but recovered, and did not show any clinical or haematological symptoms at age 4 years.

Reference

Lie-Injo LE, Randhawa ZI, Ganesan J et.al. Hemoglobin Tak in a newborn Malay. Hemoglobin 1:747-757 1977.

THALASSAEMIA

First recognised by Cooley in Detriot in 1925, thalassaemia takes its name from the Greek word `thalassa' meaning the sea. This was largely on account that many of the patients first diagnosed originated from the Mediterranean region. The thalassaemias are the commonest of the inherited haemoglobin disorders, and are probably among the commonest gene disorders in the whole world. Molecular studies of the genes have shown though that they are in fact not just a single type of mutation but many different forms that only have in common the end result of defective globin synthesis.

The haemoglobin molecule consists of 2 α globin chains combined with either 2 β, δ or γ chains. Most important are the deficiencies in the α and β chains.

α Thalassaemia

Although the α thalassaemias are commoner than the ß thalassaemias they pose less of a public health problem. This is because the severe homozygous α° form causes death in utero or in the neonatal period and the milder forms do not produce major disability. Humans carry two copies of the α globin gene on each chromosome 16. There are actually two types of α thalassaemia genes that occur about equally frequently in our region. The severe α° gene results in absolutely no synthesis of a globin. The majority of cases have an 18.1kb deletion, known as the Southeast Asia (SEA)gene, causing this that deletes both copies of the α globin gene but spares the ζ (embryonal) globin gene (the globin gene that is used even before the foetal globin gene is activated) adjacent to it. A small number have a non-deletional defect while another few have a deletion that includes the ζ globin gene. The milder α^+ is able to produce half the normal amount of α globin. At least two types α^+ genes have been observed, one involving a 4.2kb deletion another involving a 3.7kb deletion. Together the prevalence of these genes in Thailand is as high as 20% and in parts of Northern Thailand up to 30%. In Malaysia it is estimated to be about 20-27%. The α° gene is less common with a frequency of at least 2%. A survey by George and Khuziah in 1983 found the α^+ trait in 26% of Malay males.

Homozygous Disease

Hb Bart's: Lie-injo was the first to describe homozygous α° thalassaemia presenting as hydrops foetalis with Hb Bart's, which consists of 4γ chains, in Indonesian Chinese in 1960. Although the α thalassaemia gene occurs widely from the Mediterranean to Southeast Asia, hydrops foetalis occurs almost exclusively in Southeast Asia. Rare cases have been seen in Greeks and Cyproits. From a study of records of

the Maternal Hospital in KL, Lie-injo found the condition to be as frequent as 1.6 per 1,000 newborns in Chinese in Malaysia in 1964. Malays and Indians were not found to be affected. However in a survey of healthy newborns Lie-injo found Hb Bart's in 5% of Chinese, 3% of Malays and 1% of Indians indicating that the prevalence of the trait is quite high. Newborns who are heterozygous for α thalasaemia have Hb Bart's in their cord blood.

In the second α thalassaemia gene named the α^+, the homozygous form is no more disabling than the heterozygous α°, which is clinically not very significant. However, in the double heterozygote, where the α° and the α^+ genes are both present, Hb H disease is produced.

Double Heterozygous Disease

Hb H disease: Hb H consists of 4 ß chains due to the surplus production of ß chains when α chain production is sufficiently impaired. This condition was first found in Malaysia in 1956 by Lehmann and Singh. By 1966 over 50 cases had been found indicating that it is not that uncommon. Hb H occurs in two important ways.

It occurs in the α thalassaemia double heterozygous, where 3 of the 4α-globin gene are deleted.The clinical picture of these patients is about the same as ß thalassaemia major but milder. These patients often present later in life. Such individuals carry a high risk of having babies with hydrops foetalis. Chinese are more usually affected but Malays and Indians also suffer from it.

Hb H occurs with varying clinical severity and a more severe form occurs in the α thalassaemia heterozygote with the combination of the non-deletional Hb Constant Spring. Hb Constant Spring causes a remarkable reduction in the α gene product.

Hb E, Constant Spring - α Thalassaemia: In view of the fairly high frequency of all these genes, a combination of all 3 in one patient might reasonably be expected to occur and one case of a 20 year old girl has been reported.

Hb Q Thalassaemia: Vella first reported this condition in Singapore in 1958. In 1973 Lie-injo reported 5 cases of this disease, which is also called the Hb Q-H disease, all in adult Chinese in Malaysia. It is a combination of the gene for Hb Q and the gene for α thalassaemia.

ß Thalassaemia

The distribution of ß thalassaemias, like the α thalassaemias, occur widely in a broad belt ranging from the Mediterranean and parts of north and west Africa through the Middle East and Indian subcontinent to Southeast Asia. There are over 180 different mutations found to cause ß thalassaemia occurring in different parts of the world. It is estimated that the prevalence of ß thalassaemia in Malaysia is about 5% but we do not actually have large surveys to show this. In 1983 George and Khuziah found a prevalence of 2.2% among Malay males. Thalassaemia major, the homozygous form was the original form described by Cooley. It is characterised by a severe anaemia that appears within the first two years of life, associated with hepatosplenomegaly and bone changes. It is usually fatal in childhood.

The cause of death is often related to iron overload in the liver, endocrine organs and heart. Siderosis of the heart and chronic hypoxia leads arrhythmias and congestive heart failure. Among other causes Lee reported two children who died of intra-cranial heamorrhage.

In Malaysia the Chinese are the ethnic group most frequently affected by ß thalassaemia. From 1961 to 1968 Lopez and Lie-injo at the IMR collected 58 cases of the homozygous disease, slightly fewer than the cases of Hb E thalassaemia. No cases among Indians were found and Chinese outnumbered Malays 6.25:1.

A mild form of the homozygous disease can occur as reported by Ganeson, Gill and Lie-injo where the patient presented only at 22 years of age.

Lyn, Teh and Mulvey in Sandakan have observed ß thalassaemia in Sandakan to be about equally prevalent in all the local tribes. They urged that at district hospitals blood donor recruitment programmes be set up to enable such patients to be put on a hyper-transfusion regime. They noted the need for genetic counselling.

The β globin is located on the short arm of chromosome 11. The nature of the mutations involved in ß thalassaemia in Malaysia has been characterised in a number of small studies reported in the last few years. There are at least 7 different mutations seen among Malays, 9 among Chinese and 10 among Indians. In all races though, about 5 mutations account for more than 90% of the cases. The commonest thalassaemia mutation among Chinese is the FSC 41-42 that accounts for about 50%. Among Malays, the IVS 1-5(G-C) ß+ gene is commonest, also accounting for about 50% and is frequently present with the HbE gene (about 20%). However Wan Ariffin et.al. have noted that Kelantan Malays have mutations different from the Johore-Singapore Malays and more akin to Thai-Malays, where HbE (39.3%) is the commonest mutation followed by IVS 1-5 (17.9%).

Among the Dusun in Sabah, a single mutation, a deletion from a 5'breakpoint at position 4279, was found to be responsible for 20 children with ß thalassaemia major. All were homozygous for the gene which was similar to one described among Filipinos.

It is now clear that the many different thalassaemia mutations that occur in Malaysia bring about varying degrees of severity of the disease. George has formulated a scoring system to predict the clinical severity of each mutation.

Hb E Thalassaemia: In the presence of the ß thalassaemia gene haemoglobin E is inefficiently synthesized. Hence when both the genes are inherited, there is a marked deficiency of ß chain production resulting in a clinical picture closely resembling homozygous ß thalassaemia, but usually presenting later in life. Lehmann and Singh were the first to describe the disease in Malaysia in 1956. By 1968, 74 cases had been diagnosed at the IMR. Reports have shown a remarkable variability in the severity in the expression of HbE thalassaemia, which can now be explained by the different mutations known to cause ß thalassaemia. Like a thalassaemia these can be designated as ß° and $ß^+$ genes. George, Farida and Sivagengei in a study of 83 cases found that ß° was the predominant gene.

Malays form the majority of patients with Hb E thalassaemia, outnumbering Chinese 3.6:1. Again cases among Indians were not found. It is interesting to note that among Malays, Hb E thalassaemia is more than 4 times commoner than homozygous ß thalassaemia, whereas in Chinese the reverse is true. This underlines the fact that prevalence of the Hb E gene is higher among the Malays and Orang Asli while the ß thalassaemia gene is higher in the Chinese. Bolton and Lie-injo had documented an interesting Orang Asli family with 7 living cases of Hb E thalassaemia. A Chinese grandfather introduced the ß thalassaemia gene into family, in whom Hb E was prevalent.

In reviewing 4 cases of pregnancy among Orang Asli with Hb E thalassaemia, Ong noted that in all cases there were premature deliveries. Maternal blood transfusion was required in one case. Pregnancy can aggravate the anemic state or even provoke severe haemolysis as seen in 2 cases, but improved during the post-partum period.

Homozygous β thalassaemia can be ameliorated by the co-inheritance of certain genes. Lie-injo, Duraisamy and Vasudevan described a case where the α^o thalassaemia gene

favourably influenced the clinical condition in a Chinese woman.

δß Thalassaemia

These are a rare group of thalassaemias where there are large deletions of ß and δ globin genes that fail to retard the switch from Hb F to Hb A production. They are actually quite heterogenous at the molecular level. The homozygous form of a newly found type of gene defect has been reported locally in a young Malay male. His red blood cells contained 100% foetal haemoglobin.

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SPHEROCYTOSIS

Apart from the haemoglobinopathies, thalassaemias and their combinations, congenital spherocytosis is another important but rather uncommon cause of congenital haemolytic anaemia locally. It is a defect in the red-cell membrane that allows an abnormal influx of sodium to distend the cell. As a result the spleen destroys the red-cells prematurely. In 17 cases seen at the IMR from 1961 to 1968, 10 were Chinese, 5 Malays and 2 Indians. Koh and Ng at the UH reported that over 13 years, from 1974 to 1986, only 16 patients were detected in

that hospital. Interestingly, ethnically these patients consisted of 10 Chinese and 6 Malays. Splenectomy results in complete remission of the anaemia.

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OVALOCYTOSIS

Dresbach first described elliptocytosis in 1904 in a patient who was a mulatto (mixed Caucasian and Negro in South America). Bishop made the observation in 1941 that it was hereditary. It is autosomal dominantly inherited and due to deficiency of a membrane protein, called protein 4.1. In Southeast Asia although the term elliptocytosis is used, the finding of elliptical or oval red corpuscles is often called ovalocytosis. Lie- Injo reported it in 1965 in 54 of 440 Orang Asli giving a prevalence rate of 12.3%. Southeast Asian ovalocytosis results from deletion of residues 400-408 in the red-cell anion exchanger band 3. Among Malays also the prevalence is high, measured by George *et.al.* in 1988 to be 5% from babies born at the KL GH. Ganesan, George and Lie-injo found that 13% of Malays of Minangkabau descent in Ulu Jempol had ovalocytosis. In Sarawak it has been found in 13% of Bidayuh and 9% of Iban subjects in one survey. Those with the gene do not suffer from frank haemolytic anaemia. In fact Mohandas *et.al.* have findings to suggest that they may be more resistent to malaria. Foo *et.al* have confirmed this in 1992. They found that among Orang Asli, those with ovalocytosis had a malaria infection rate of 9.7 per 100 person-months compared with 15.2 per 100 person-months among similar normocytic individuals. Those with ovalocytosis were also protected from heavy infections.

In one girl who had significant anaemia it was found she had a combination with ß thallasaemia. Ti reported the case of a Chinese boy with ellipticytosis who had concurrent acute lymphoblastic leukaemia. Whether the two conditions could be linked was questioned. Thong reported 3 children in one family with co-existent distal renal tubular acidosis. The possibility of linkage of the genes was also raised.

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CONGENITAL DYSERYTHROPOIETIC ANEMIA

The congenital dyserythropoietic anemias (CDAs) are a group of relatively rare disorders that share in common ineffective erythropoiesis and morphological abnormalities of mature red

blood cells and their precursors. Three major types of CDAs and a few types of variants have been described. Diagnosis is facilitated by microscopic examination of the blood and bone marrow and by serology. Management of patients currently consists of observation and supportive care. They are at risk of secondary haemochromatosis. Splenectomy may be of benefit in cases of severe anaemia. Ariffin WA *et.al*. has reported 3 cases, two of them siblings, who became transfusion dependent before the age of 4 months seen between 1985 and 1992 in HUSM. One of them had a successful bone marrow transplant.

Reference

Ariffin WA, Karnaneedi S, Choo KE, Normah J. Congenital dyserythropoietic anaemia: report of three cases. J Peadiatr Child Health 32:191-193 1996.

IRON DEFICIENCY ANAEMIA

As a cause of mild anaemia this is probably the most prevalent form of anaemia in Malaysia. There have been many papers written about its prevalence in the colonial days when anaemia was very common and often very severe. The three important contributing factors were poor nutrition, parasitaemia and blood loss especially through menstruation and multiple pregnancies in women.

Poor Nutrition

Immediately after the Second World War, Bourne in 1949 completed one of the earliest large scale nutrition survey in this country. Among 730 children in welfare centres, 224 orphans and 287 children in refugee camps, he found anaemia of below 70% (10.2g/dl) in 71%, 41% and 90% among the 3 different groups respectively. Even in school children in Selangor, considered fairly well-to-do, he found anaemia in 40% of boys and 63% of girls.

In 1962, the United States ICNND study of civilians and military dependents, using a cut-off of 12 g/dl, reported that 36% of children less than 5 years and 13% of the age group 5-14 years were anaemic. In 1966, in a study of 2,025 children in GH KL, Lie-injo and Virik reported that (258)13% had a haemoglobin below 8 g/dl. Indian children were the worst off. Of 179 with very severe anaemia, 60% were found to be suffering from iron-deficiency anaemia, the most important cause.

Over the late 1960s and 1970s, on a broad scale, nutritional anaemia, mainly from iron-deficiency, dropped to tolerably low levels in the economically developed West coast towns of Malaysia. However, in rural areas, studies like Chappel and Janowitz (1965) of a Felda scheme in Pahang and Chong, McKay and Lim (1970) of Hulu Terengganu showed that the prevalence was above 30%. Likewise Kandiah and Lim reported rates of 37% in school children and 47% in preschool children in rubber estates in Selangor.

In Sarawak, Anderson surveyed a number of Ibans, Malays and Penans from various divisions between 1976 and 1978. He found the prevalence of anaemia of haemoglobin below 12 g/dl. to be between about 20% to 35%. From Sabah, Chen reported in 1981 that the prevalence of anaemia in the Interior, West Coast and Kudat divisions was about 26% overall.

Toward the end of the twentieth century nutritional anaemia is no doubt declining but it has been shown that in some places the problem is still with us. In a study of nutritional status in Endau, Johore, a rural area, in 1981, iron deficiency was considered to occur in up to 13% of the community, although adult males appear not to be affected. Another study of poverty stricken kampongs along the West bank of the Perak river in the Perak Tengah district in 1983 revealed that 25% of the populace had low haemoglobin levels. Worms were thought to be the major cause and was found in 75% of

the people, which is higher than most communities.

Parasitaemia

In the late 1950s, Tasker at the IMR showed, from patients at the KL GH, that the prevalence of hookworms correlated with lower haemoglobin levels. Using a radioactive tracer technique, he estimated that daily blood loss increases from about 2 ml with a light infestation of about 20 hookworms to about 90 ml. with a heavy infestation of greater than 1,500 hookworms.

In contrast to this, Tasker found that the degree of anaemia was unrelated to the proportion of stools containing *ascaris* ova. The prevalence of worm infestation is presented in its own section in this book.

Menorrhagia and Multiple Pregnancies

Lourdenadin wrote in 1964 that "anaemia in pregnancy is still the nightmare of practising obstetricians in this country". Interest in this matter goes many years back. Corke and Bush in 1930 and Pallister in 1934 had emphasised in the Malaysan Medical Journal that this was one of the greatest causes death among Indian estate workers.

Lourdenadin in collaboration with Tasker and others found that between 1957 and 1961 the incidence of severe anaemia of below 6.5 g/dl. at the Maternity Hospital KL was 2.3%. 76% of these were due to iron deficiency, the remainder mainly due to folate defiencies. Studying expectant mothers in 1964 he found 69% had haemoglobin estimations of below 11 g/dl. All races were equally affected. From the 1970s onwards the incidence of mild anaemia reported has shown an improvement. It has ranged between about 15% to 30% in several studies. Measurements of iron, folate and vitamin B12 show that iron is the most important factor but folate deficiency is also common.

A study of blood samples in women attending ante-natal clinic by Tee *et.al.* in the Maternity Hospital KL reported in 1984, revealed that iron deficiency was present in 48% of women, on the basis of low transferrin saturation. 41% of women were anaemic based on a haemoglobin value below 11g/dl. Most women from this study, however, were from the lower socio-economic group and were in their third trimester and not truly representative of the KL population. In the UH which serves an urban population, the rates of anemia in pregnancy (Hb<10gm/dl) declined from above 8% in 1970 to less than 2% in 1984.

The Orang Asli, many of whom dwell deep in the jungles, might be expected to have significant problems of anemia in pregnancy. Ong found an overall incidence of anemia (Hb<10gm/dl) of 26% in 1974, with 1.4% having severe anemia. Malnutrition he remarked was holoendemic and parasitic infestation present in 70% of anemic Orang Asli mothers.

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FOLATE AND B12 DEFICIENCY ANAEMIA

These causes of megaloblastic anaemias are said to be generally uncommon in the tropics. It is hard to say what the prevalence of megaloblastic anaemia is. The Malaysian diet is one of great variety, but mainly of plant origin, and many foods contain the minor nutrients such that most people receive a sufficient amounts of them. But this is probably just sufficient, and in many during pregnancy where there is a greater demand, megaloblastic anaemia is not rare.

Tasker remarked in the pre-independence days where for practical purposes "all anaemias can be considered iron deficient, the peripheral film may hide a concomittant megaloblastic anaemia" and it was important to study the bone marrow. One indication is given by a study in 1966 by Lie-Injo and Virik who put it at 11% of children in GH KL with severe anaemia below 8 g/dl. Others had put the percentage of megaloblastic anaemia as much as 20%.

Between the two vitamins, folate has usually been found to be more important. Jaffar, Khalid and Hamid found that 59% of women had low serum folate and 32% had low RBC folate at parturition. Babies however appear to be protected and cord blood had higher folate levels than maternal blood. Lourdenadin noted that in severe anaemia in pregnancy where the haemoglobin was lower than 6.5gm% next to iron deficiency, 22% were macrocytic and mainly folate deficient. In yet another study Tee *et.al.* detected low serum folate levels in 61% of pregnant women. But they were all from the lower socio-economic class.

In these studies vitamin B12 deficiency was absent. Nevertheless, one group that is susceptible to this are vegetarians of South Indian origin. It has been shown that South Indian vegetarian diets provide only 0.3 to 0.5 µg of vitamin B12 per day.

In a report from UH in 1988, in a 5 year study, 28 adults with megaloblastic anaemia were treated. 71% were Indians. Though in most the cause was nutritional deficiency, 3 patients had pernicious anaemia and 2 had myelodysplastic syndrome. Ishak and Hassan looked at folate and B12 status in over 9,000 patients in 1987 to 1988 at the UH. They found folate deficiency in 31% and B12 deficiency in 2.6%. In another series of over 9,000 patients in1992 to 1993, however, they found a folate deficiency rate of 7.6% but a higher B12 deficiency rate of 8.2%.

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AUTOIMMUNE HAEMOLYTIC ANAEMIA

The autoimmune haemolytic anaemias were first distinguished from the congenital haemolytic anaemias when auto-agglutination was noted. Coombs in 1945 discovered the antiglobulin serum and the test for the presence of the antiglobulin that causes haemolysis still bears his name. Although cases are seen in Malaysia we do not have large series to tell us the patterm the disease has here.

Reference

Chan KE and Thuraisingham V. Autoimmune haemolytic anaemia. Med.J.Mal. 17:163-169 1963

SIDEROBLASTIC ANAEMIA

Sideroblastic anaemia encompasses anaemia due to various causes that results in ringed erythroblasts with ferritin granules in the bone marrow. In addition the bone marrow shows erythroid hyperplasia with decreased red cell production indicating ineffective erythropoiesis. Siderablastic anaemia can be an inherited condition or an acquired one.

Jackson and Hamizah reported an unusual female patient in Kelantan who developed sideroblastic anaemia in her first and third pregnancies which resolved spontaneously. Pyridoxine deficiency was postulated as the possible cause.

Reference

Jackson N and Hamizah I. Sideroblastic anemia recurring during two pregnancies. Int J Hematol 65:85-88 1996.

WHITE CELL and IMMUNE SYSTEM DISORDERS

Immunoglobulin Disorders

PANHYPO-GAMMA-GLOBULINEMIA

A rare disorder, Lokman, George Sukumaran and Nasuruddin reported an Indian family of consanguineous parents with two affected children in 1988. B cell numbers were low (5%) but not absent. One of the affected was a girl, hence this was thought not to be the X-linked Bruton's disease but and autosomal recessive one.

Reference

Lokman MN, George R, Sukumaran S and Nasuruddin BA. Common variable immunodeficiency (hypogammaglobulinemia) with an autosomal recessive pattern of inheritance. Med.J.Mal. 43:237-242 1988

(BRUTON'S) X-LINKED AGAMMAGLOBULINEMIA

Bruton's agammaglobulinemia affects boys almost exclusively as it is inherited on an X-linked gene and is recessive. It is a B cell deficiency. Patients usually have recurrent eye, throat, skin, ear and respiratory infections and begin presenting at about eight months old when maternal immunoglobulins have disappeared. The most common organisms are pyogenic (eg. *S. aureus*). Noh *et.al*. noted that although cases among Malays and Indians were found they had not seen a Chinese child affected.

Wahab, Hanifah and Choo have reported a case of an affected child with cryptococcal empyema thoracis and preauricular abscesses.

References

Wahab JA, Hanifah MJ and Choo KE. Bruton's agammaglobulinaemia in a child presenting with cryptoccocal empyema thoracis and preauricular pyogenic abscess. Sing. Med.J. 36:686-689 1995

Noh LM, Ismail Z, Zainudin BM et.al. Clinical patterns of X-linked

agammaglobulinaemia in Malaysian children. Acta Peaditr. Jpn.37:331-335 1995.

HYPER IgM IMMUNODEFICIENCY

As the name of this disorder indicates, this is a disease in which IgM levels are raised but IgA and IgG levels are low. It is a rare disorder due to defective isotype switching of B cells into IgA and IgG producing cells that may be inherited autosomal dominantly or arise as new mutations. An associated reduction numbers of T helper cells has been noted in some patients as well. There has been one case report from UKM, in Malaysia of a 20 month old Indian boy who succumbed to Pseudomonas septicaemia and meningitis.

Reference

Noh LM, Low SM, Lajin I and Abdullah N. Antibody deficiency with hyper IgM - a case report. Mal.J.Pathol. 14:121-123 1992.

HYPER IgE SYNDROME

In the hyperimmunoglobulin E - recurrent infection - syndrome, also called Job's syndrome, patients suffer from, eczema, intense pruritus, skin abscesses, recurrent pneumonias with *Staph. aureus*, mucocutaneous candidiasis and other infective complications. Serum IgE levels are markedly elevated and there is defective neutrophil chemotaxis. Lee, Boey and Goh reported one child with this condition in UH who died of pulmonary nocardiosis.

Reference

Lee WS, Boey CC and Goh AY. Pulmonary nocaridosis in a child with hyperimmunoglobulin E syndrome. Sing Med J 40:278-280 1999.

IgA DEFICIENCY

Selective IgA deficiency is the commonest primary immunodeficiency disease in the temperate regions. Reported incidences range from about 1:500 to 1:700. The condition is characterised by serum IgA levels less than 5mg/100 ml. Affected individuals may suffer from recurrent sinopulmonary infections, gastrointestinal disorders or about 10% remain asymptomatic. Teh and Bosco detected a young patient with selective IgA deficiency who presented with hypersplenism and spenomegaly who reverted to having normal blood counts with splenectomy. An important aspect is the fact some affected individuals have the potential of forming anti-IgA antibodies that may result in fatal anaphylactoid reactions on transfusion with IgA containing plasma.

Yadav, Thong and Sinniah reported a 10 year old Punjabi girl with IgA deficiency with chronic diarrhoea, otitis media and bronchiectasis in 1977. However, Yadav and Iyngkaran sought to detect the condition in a survey of 2,025 sera from healthy people from a wide variety of sources. They did not detect a single case and suggest that the incidence in the tropics is low.

References

Yadav, Thong YH and Sinniah D. Decreased serum immunoglobulin A level in a patient with bronchiectasis. Med.J.Mal. 31:292-295 1977.

Yadav M and Iyngkaran N. Low incidence of selective IgA deficiency in normal Malaysians. Med.J.Mal. 34:145-148 1979.

Teh A and Bosco JJ. Selective IgA deficiency presenting with hypersplenism. Br J Clin Pract 48:276-277 1994.

Cellular Immunity Disorders

SEVERE COMBINED IMMUNODEFICIENCY

One Malay boy of consanguineous parents, with candidiasis, cytomegalovirus and *Pseudomonas aeruginosa* infection at 3 months was diagnosed with this rare condition in KLGH in 1993. He had lymphopaenia affecting both T and B cells, and was HIV antibody negative. He

succumbed at 7 months waiting for bone marrow transplantation.

Reference

Noh IM, Amir HL and Hung LC. Severe combined immunodeficiency in a Malaysia child. Med.J.Mal. 52:88-91 1997.

WISKOTT-ALDRICH SYNDROME

This is a recessive sex-linked disorder, characterised by low isohaemagglutinins and low IgM, which is rarely reported in the East. Nevertheless Tong *et.al.* have reported 2 Malaysian Chinese boys with the condition.

Reference

Tong YH, Sinniah D, Murugasu R and White JC. Two Malaysian Chinese male children with the Wiskott-Aldrich syndrome. Sing.Med.J. 20:355-357 1979.

CHRONIC GRANULOMATOUS DISEASE (CGD)

CGD is a rare inherited disorder, either autosomal recessive or X-linked, of granulocyte function caused by failure of intracellular superoxide production. It usually presents in the first years of life with severe recurrent bacterial and fungal infections manifesting as abscesses, lymphadenitis and granuloma formation. Two infant Malay boys have been diagnosed with the condition by Mohd Noh *et.al*.

Reference

Mohd Noh L, Noah RM, Wu LL et.al. Chronic granulomatous disease - a report in two Malay families. Sing Med J. 35:505-508 1994.

HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

Haemophagocytic lymphohistiocytosis (HLH) comprises two forms, a familial form described by Farquhar and Claireaux in 1952 and a non-familial form described by Risdall *et.al*. in 1979. It is characterised by recurrent fever, hepatosplenomegaly, cytopenia, hypertriglycaemia and evidence of haemophagocytosis in the bone marrow. Its cause is unknown but a viral trigger is suspected in the non-familial form. 5 cases of non-familial childhood HLH have been reported from UH over a 3 year period. 2 patients died of *cytomegalovirus* pneumonitis.

Reference

Hoh MC and Lin HP. Non-falimial haemophagocytic lymphohistiocytosis in children. Med.J.Mal. 52:146-150 1997.

MYELODYSPLASTIC SYNDROME

This term is now widely accepted for a preleukaemic state, where the blood film may show pancytopenia or macrocytic anaemia while the bone marrow aspirate shows certain features of ineffective haemopoiesis. Cheong and Ainoon at UKM managed 5 cases over 5 years. They ranged from 33 to 76 years in age. 3 died of unknown causes, one died after transformation to AML. Over a 5 year period from 1981, 20 such patients were diagnosed in the UH. 90% were more than 40 years old. Despite poor follow-up only 4 patients were noted to undergo leukaemic transformation.

References

Cheong SK and Ainoon O. Experience with primary myelodysplastic syndromes in a university haematology unit: report of five cases. Med.J.Mal. 42:272-275 1987.

Ng SC, Kuperan P, Bosco J and Menaka N. Myelodysplastic syndrome: a review from University Hospital, Kuala Lumpur. Sing.Med.J. 31:153-158 1990.

SEA-BLUE HISTIOCYTE SYNDROME

The Sea-blue histiocyte syndrome is a rare disorder first described in 1970, which consists

of splenomegaly and where there are numerous histiocytes which are stained sea-blue with Romanowsky's stain. Most case reports have been from the West. Fadilah *et.al*. have however found an Indian family in Malaysia of consanguineous parents in which a girl and her brother were found to have this condition at age 13 and 11 respectively, when they each presented with empyema of the lung. 3 other siblings were not affected. This girl presented again at 27 years of age 23 weeks pregnant with decompensated liver cirrhosis, coagulopathy and restrictive lung disease. Her condition worsened as her pregnancy progressed but she was delivered of a normal healthy baby at 30 weeks gestation by Ceasarian section. She had a splenectomy 6 months after that for a painful spleen and had no progression of the disease the following months.

Reference

Fadilah SA, Mazeni NR and Cheong SK. Successful pregnancy in a patient with familial Sea-blue histiocyte syndrome. Med J Mal. 55:510-512 2000.

Complement Disorders

HEREDITARY ANGIOEDEMA

An autosomal dominant defect resulting in C1 esterase inhibitor (C1 INH) deficiency results in this rare disorder. Antihistamines and corticosteriods give no benefit hence it is easily mismanaged. Relief is obtained with fresh frozen plasma to replace the deficient C1 INH and tranexamic acid that prevents activation of plasmin. Leong and Bosco described a Chinese family with one man and two of his sons affected.

Reference

Leong KW and Bosco JJ. Hereditary angioedema: Report of a family in Malaysia. Med.J.Mal. 50:197-198 1995.

PLATELET DISORDERS

Roshidah and Khalid suggested that platelet disorders were in general not common in children in a screening study of 1,299 ten to twelve year olds.

Reference

Roshidah I and Khalid H. Screening for platelet abnormalities in normal school children in Kuala Lumpur. Med.J.Mal. 42:36-39 1987

ESSENTIAL THROMBOCYTHAEMIA

Essential thrombocythaemia or thrombocytosis (ET) is a clonal stem cell disorder that manifests itself with an elevated platelet count. It is diagnosed by exclusion of other myeloproliferative disorders and reactive thrombocytosis. Patients are at risk of clotting diseases.

One case with complications in pregnancy resulting in postpartum haemorrhage and disseminated intravascular coagulation has been reported.

Reference

Rashid Z, Hamidah NH, Othman A et.al. Primary thrombocythaemia presenting as postpartum haemorrhage: a case report. J Obstet Gynaecol 21: 221-225 1995.

ACQUIRED PLATELET DYSFUNCTION WITH EOSINPHILIA (APDE)

APDE appears to be a syndrome confined to children in Southeast Asia. The hallmark of this disorder is recurrent spontaneous bruising with eosinophilia, prolonged bleeding time, abnormal platelet adhesiveness and associated parasitic infection. The haematocrit, platelet count and coagulation profile are normal. The importance of recognising this benign condition, which usually does not need any specific therapy, is to avoid the pitfall of diagnosing

more serious bleeding disorders instead in children presenting with ecchymosis. The platelet aggregation with ADP which is abnormal returns to normal usually within six months to a year. Ramanathan and Duraisamy reported three cases in 1987.

Among 13 children investigated for easy bruising in the UH between 1987 and 1999, Ng and Koong remarked that APDE (54%) was the commonest cause noted.

References

Ramanathan M and Duraisamy G. Acquired platelet dysfunction with eosinophilia (APDE): an underdiagnosed condition. Med.J.Mal. 42:53-55 1987

Ng SC and Koong PL. A study of 31 patients with easy bruising from University Hospital, Kuala Lumpur. Med.J.Mal. 45:325-328 1990.

THROMBASTHENIA

Also known as Glanzmann's disease, this is a rare platelet dysfunction due to deficient ADP induced platelet aggregation and clot retraction. It is an autosomal recessive inherited disease. There has been one local case report by Zulkifli at the UKM. The clinical picture of spontaneous bleeding, bruising and prolonged bleeding after trivial injury and prolonged partial thromboplastin time may mislead one to diagnose haemophilia.

Reference

Zulkifli A. Glanzmann disease (Thrombasthenia) - a case report. Med.J.Mal. 34:174-175 1979

INHERITED THROMBOCYTOPENIA

A number of rare genetic syndromes produce thrombocytopenia. Jackson *et.al*. described a Malay family with 7 affected members showing an autosomal dominant inheritance in Kelantan. It needs to be recognised as steroids are of no benefit to such patients.

Reference

Autosomal dominant thrombocytopenia with microthrombocytes: a family study. Med.J.Mal. 50:421-424 1995.

IDIOPATHIC THROMBOCYTOPENIC PURPURA

Adult Idiopathic Thrombocytopenic purpura (ITP), usually the chronic form, is caused by autoimmune antibodies directed againts glocoprotein IIb-IIIa or glycoprotein Ib-IX complexes. The antibodies act as opsonins and accelerate platelet clearance by phagocytic cells. Jackson, Mustafa and Baba reviewed 32 cases in Kelantan over 16 months from 1993, with a female to male ratio of 3.6:1. Their mean age was 31.6yrs but 62.5% were under 30yrs. One had Evan's syndrome one developed systemic lupus erythematosus. 7 were lost to follow-up before therapy evaluation. 8 achieved prolonged complete remission with prednisolone. 12 (48%) were offered splenectomy after failure to respond or relapse requiring prolonged steroid therapy. All refuse surgery. Of these one died and the rest show significant morbidity.

Reference

Jackson N, Mustafa M and Baba AA. Adult idiopathic thrombocytopenic purpura without the option of splenectomy. Med.J.Mal. 50: 250-255 1995.

THROMBOTIC THROMBOCYTOPENIC PURPURA

Thrombotic Thrombocytopenic Purpura (TTP) is a fulminant haemolytic condition that may be initiated by endothelial injury or be cyrptogenic. The LDH level is elevated intravascular haemolysis but tests of coagulation like prothrombin time and partial thromboplastin time remain normal. It can lead to lethal

neurologic and renal dysfunction. Ng and Adam reported a case of a 27 year old woman in the 12th week of her pregnancy who developed TTP and died from this condition.

Reference

Ng SC and Adam BA. Thrombotic thrombocytopenic purpura with terminal pancytopenia. Postgrad Med J. 66:955-957 1990.

CLOTTING DISORDERS

FACTOR VII DEFICIENCY

Congenital factor VII deficiency was first described in 1951 by Alexander. It is autosomally inherited, the gene being located on the long arm of chromosome 13. Heterozygotes have a partial deficiency and homozygotes have more severe deficiency. Manifestations commonly noted are epistaxis and haemarthrosis. But of particular note is menorrhagia that masquerades as iron deficiency anaemia of which an example has been reported locally.

Ariffin and Lin described two siblings in 1997 who both died in the neonatal period of sepsis, who both had intracerebral bleeds, and were homozygous or compound heterozygous. They had factor VII assays of 5% and less.

References

Zulkifli A. Congenital factor VII deficiency presenting as iron deficiency anaemia - case report. Med.J.Mal. 33:360-361 1979

Ariffin H and Lim HP. Neonatal intracranial hemorrhage secondary to congenitl factor VII deficiency: two case reports. Am J Hematol. 54:263 1997.

HAEMOPHILIA (FACTOR VIII)

An X-linked recessive disorder of Factor VIII deficiency, haemophilia was well known in Europe for its presence in a number of royal families. Before 1964 haemophilia was thought to be uncommon in Asian countries. Today we know it is not the case. A hospital serving a population of a quarter of a million can expect to have one to five patients with haemophilia on follow-up. The first Malaysian case to be reported was by Lie-injo and Pillay in 1964. The patient was an Indian boy. The next year they found another two cases in Chinese.

Acquired haemophilia may occur due to spontaneous development of antibodies inhibiting factor VIII. Two cases have been reported from UH and one from HUSM.

References

Lie-injo LE, Loncin M and Pillay RP. Haemophilia due to factor VIII deficiency in an Indian boy. Med.J.Mal. 18:219-222 1964.

Teh A, Leong KW, Bosco JJ et.al. Acquired haemophilia - a therapeutic challenge. Med.J.Mal. 50:166-170 1995.

Jackson N, Hashim ZA, Zainal NA and Jamaluddin N. Puerperal acquired factor VIII inhibitor causing a von Willebrand-like syndrome in a patient with anti-DNA antibodies. Sing Med J 36:230-231 1995.

FACTOR XIII DEFICIENCY

Factor XIII deficiency is a very rare autosomally inherited recessive trait with only a few hundred documented cases. Factor XIII is a transglutaminase which stabilises fibrin. Deficiency does not cause severe problems but patients can be prone to bleed and have wounds that heal poorly. Deshmukh and Bosco detected one case, who was a child from a consanguineous marriage locally.

Reference

Deshmukh RG and Bosco J. Claw toes correction and factor XIII deficiency - a case report. Med.J.Mal. 50:417-419 1995.

VITAMIN K DEFICIENCY

The most well known vitamin K deficiency is

the neonatal condition called the haemorrhagic disease of the newborn. Routine vitamin K prophylaxis has greatly reduced its occurrence and eradicated it in some areas. However, over a 2 year period (1987-8), Choo reported that 42 infants were admitted to the HUSM with this disease. 81% of these were babies born at home. The case fatality rate was 14%. Subdural haemorrhage was a very significant contributing factor. There has been a case report of the disease presenting as a haemothorax in a 3 day old child and another case of adrenal haemorrhage.

References

Choo KE, Tan KK, Chuah SP et.al. Haemorrhagic disease in newborn and older infants: a study in hospitalised children in Kelantan, Malaysia. Ann. Trop. Peadiatr 14:321- 327 1994.

Kaur P and Tan KK. Hemothorax due to hemorrhagic disease of the newborn. Acta Paediatr Jpn 36:95-96 1994.

Ram SP, Kassim Z, Haeque E and Noor AR. Adrenal haemorrhage in a newborn - a case report. Sing Med J. 35:532-534 1994.

THROMOBOTIC DISORDERS

ANTIPHOSPHOLIPID ANTIBODIES

Antiphospholipid antibodies is one of a few conditions that carry a predisposition to thrombosis. Lee, Cheng and Ng *et.al*. report 3 such cases in a prospective study of under 50year old stroke patients.

Reference

Lee MK, Cheng HM, Ng SC et.al Antiphospholipid antibodies and stroke in the young - a study of three cases. Med.J.Mal. 48:330-335 1993.

ANTITHROMBIN III DEFICEINCY

Antithrombin III deficiency is a rare autosomal dominant trait. Overt thrombosis occurs at antithrombin III levels below 60% of normal. Thrombotic episodes from this condition have mainly been reported in children. Lee and Ng reported a case antithrombin III deficiency causing cerebral venous thrombosis and deep vein thrombosis of the left leg in a 31 year old Chinese woman after she developed a spontaneous abortion.

Reference

Lee MK and Ng SC. Cerebral venous thrombosis associated with antithrombin III deficiency. Aust NZ J Med. 21:772-773 1991.

BONE MARROW TRANSPLANTATION

The first bone marrow transplant service in Malaysia was set up in 1987 in the UH and catered first only for children. In 1994 the unit reported having done 89 transplants with an overall survival rate of 73%. The immediate mortality rate was <10%, and the early and late infection rates were 46% and 13% respectively.

Umbilical Cord Blood Transplantation

Chan and Lin reported a case of successful transplant of umbilical cord blood for a 25-month boy with β–thalassaemia major, from an unborn sibling who was only a carrier, in 1999.

References

Lin HP, Chan LL, Tan A et.al.. Bone marrow transplantation in Malaysia. Bone Marrow Transplant 13:725-729 1994.

Chan LL and Lin HP. Cure of beta-thalassaemia major by umbilical cord blood transplantation – a case report of Malaysia's first cord blood transplantation. J Trop Pediatr 45:243-254 1999.

THE THYMUS

MASSIVE THYMIC HYPERPLASIA

Lee *et.al*. described 2 infants with febrile illness and respiratory symptoms who had large masses in the left hemithorax encountered in 1993 and 1994. One had 0.5kg of tumour removed, which was 4% of patient's weight.

Reference

Lee YM, Koh MT, Omar A and Majid A. Hyperplasia of thymic gland. Sing Med J. 37:288-290 1996.

THYMOLIPOMA

Thymolipomas are benign tumours consisting of encapsulated thymic and fat tissue in the anterior mediastinum. There have been 2 case reports from the UH. The first in a 22 year old girl, was a tumour that weighed 3.7kg. The second was a tumour that weighed 1.06kg in a 19 year old Chinese girl. Both large tumours did not produce much symptoms.

References

Nuruddin R and Daud A. CT and sonographic diagnosis of thymolipoma. A case report. Australas Radiol 32:497-499 1988.
Majid AA. Thylipoma. Aust NZ J Surg. 62:74-76 1992.

THE SPLEEN

SPLENIC ABSCESSES

Abscesses are uncommon in the spleen. Two case with obscure aetiology, diagnosed ultrasonically were reported in Ipoh. Melioidosis has been known as a possibility in some cases.

Reference

Sivalingam S. Ultrasound in the diagnosis of splenic abscess: case report. Med.J.Mal. 43:338-339 1988.

OTHER MISCELLANEOUS GRANULOMATOUS AND IMMUNE DISEASES AFFECTING MULTIPLE ORGAN SYSTEMS

AMYLOIDOSIS

Amyloid is a pathologic proteinaceous material deposited between cells in various tissues and organs of the body in a variety of disease conditions. Virchow, designated it 'amyloid' or starchlike as it is turns iodine painted onto the cut surface of affected organs into a blue or violet stain when dilute sulphuric acid is applied. Nowadays, Congo red is the most widely used stain to study amyloid. Amyloid is a fibrillary protein deposit characterised by an antiparallel, beta-pleated configuration which imparts to it an apple-green birefringence after Congo red staining. The chemical composition of amyloid fibrils is very diverse including AA(amyloid associated – synthesized by the liver) protein, AL(amyloid light chain – contains immunoglobulin derived from plasma cells) fragments, transthyretin, procalcitonin, islet amyloid polypeptide, atrial natriuretic peptides, beta-amyloid protein and several other proteinaceous material. Different amyloid fibril proteins relate to different amyloidosis syndromes and histological patterns.

In a 5½ year review of 27,052 routine biopsy specimens, from 22,827 patients in the UH, published in 1991, Looi detected 186 (0.8%) cases of amyloidosis. 5.9% were systemic AL amyloidosis, 3.2% were systemic AA amyloidosis, 58% were localized amyloid in tumours, 14% were isolated atrial amyloid, 7.5% were primary localized cutaneous amyloid, 3.2% were other localized deposits and 8.6% were dystrophic amyloid.

From 334 consecutive autopsies on Orang Asli subjects from 1967 to 1978 in the UH, 9(2.7%) cases of amyloidosis was found. In 6 cases amyloidosis was probably secondary to tuberculosis. The remaining 3 exhibited a pericollagenous distribution characteristic of primary amyloidosis.. Though involvement of

the heart and lungs were most prominent, the renal involvement was the one that most often gave rise to clinical symptoms.

Leprosy is the commonest cause for systemic AA amyloidosis . In 37 consecutive autopsies on leprosy patients Looi found a 19% (7) prevalence rate of systemic amyloidosis, all of these AA amyloidosis. There were 5 males and 2 females. All were Chinese and their ages ranged from 52 to 85 years. 6 had lepromatous leprosy while the remaining one had tuberculoid leprosy. 3 died of chronic renal failure and 2 of congestive cardiac failure attributable to renal and cardiac amyloidosis respectively. One patient died of septicaemia and the remaining one died of an acute myocardial infarction.

Looi has found isolated atrial amyloidosis (IAA) in 3% of 247 healthy adults who were autopsied after traumatic deaths. She also found IAA in 26(16%) of cardiac biopsy specimen obtained during cardiac surgery from 167 patients. These patients were between 25 to 52 years old. 23 of these were from patients with chronic rheumatic heart disease while 3 were from patients with atrial septal defects. The prevalence of IAA in chronic rheumatic heart disease was 23% and in patients with atrial septal defects it was 15%.

In 1969 Dutt noted that amyloid in subcutaneous tissue was interestingly found in 4 cases in Chinese women. Rajagopalan and Tay reported familial lichen amyloidosis in 1972 in a Chinese family with 19 people in 4 generations affected. In a review of 85 patients with primary localized cutaneous amyloidosis Looi noted that 63 had papular amyloidosis and 22 macular amyloidosis. Chinese were more frequently affected overall, but macular amyloidosis was more common among Indians. Papular amyloidosis was associated with connective tissue disease in 3 cases but macular amyloidosis was not found to be associated with any other disease.

In a study of renal amyloidosis from renal biopsies, Looi and Cheah found that the commoner glomerular pattern seen in 14 of 18 cases tended to present with nephritic syndrome and chronic renal failure.The 4 remaining which had a vascular pattern tended to present with non-renal manifestations. The pattern of amyloidosis did not help differentiate AA from AL amyloidosis.

In a review of 15 cases of amyloidosis in the lung in 1999, Looi found 2 cases of localized depositions limited to the lung. They presented with symptomatic lung/bronchial masses clinically diagnosed as a tumour. In both these cases amyloid deposits were immunopositive for lambda light chains and negative for kappa chains and AA protein. One patient was a known systemic lupus erythematosus patient, the other was found to have plasma cell dyscrasia with monoclonal IgG lambda gammopathy. In contrast the remaining 13 cases, lung involvement was part of the picture of systemic amyloidosis. In cases of systemic AA amyloidosis, amyloid was evident histologically on autopsy but was not obvious clinically or macroscopically. In one case of systemic amyloidosis associated with multiple myeloma, an 'amyloidoma' occurred in the subpleural region. Another case of pulmonary amyloidosis was reported by Srinivas in the year 2000 in a 52 year old woman who had primary Sjogrens syndrome the past 25 years.

In screening tumour material at the UH, Looi reported that amyloid was found in 100% of medullary carcinomas of the thyroid, 66% of basal cell carcinomas, 56% of islet cell tumours of the pancreas, 12% of nasopharyngeal carcinomas, 6% of carcinoids and 1% of thyroid adenomas. All these deposits showed variable amounts of AL amyloid and amyloid P component but did not contain AA protein.

References

Dutt AK. Lichen amyloidosis. Med J Mal. 24:164-165 1969.

Rajagopalan K and Tay CH. Familial lichen amyloidosis. Report of 19 cases in 4 generations of a Chinese family in Malaysia. Br J Dermatol

87:123-129 1972.

Looi LM and Prathap K. Amyloidosis in Malaysian aborigines (Orang Asli). Pathology 11:575-582 1979.

Looi LM. Intratumour amyloidosis in Malaysians: an immunohistochemical study. Ann Acad Sing. 15:52-56 1986.

Looi LM, Jayalakshmi P, Lim KJ and Rajagopalan K. An immunohistochemical and morphological study of amyloidosis complicating leprosy in Malaysian patients. Ann Acad Med Sing 17:573-578 1988.

Looi LM. Histomorphological variations in systemic AA amyloidosis: clues of AA protein polymorphism. Histopathology 14:111-120 1989.

Jeyamalar R, Pathmanathan R, Yap SF and Kanan P. Primary cardiac amyloidosis. Ann Acad Med Sing. 20:795-797 1991.

Looi LM. The pattern of amyloidosis in a Malaysian patient population. Histopathology 18:133-141 1991.

Looi LM. Primary localized cutaneous amyloidosis in Malaysians. Australas J Derm 32:39-44 1991.

Looi LM. Isolated atrial amyloidosis: a clinicopathologic study indicating increased prevalence in chronic heart disease. Hum Pathol 24:602-607 1993.

Looi LM. Fibrillary deposits: amyloids and tactoids. Mal J Pathol 17:1-10 1995.

Looi LM and Cheah PL. Histomorphological patterns of renal amyloidosis: a correlation between histology and chemical type of amyloidosis. Hum Pathol 28:847-849 1997.

Looi LM. The pattern of amyloid deposition in the lung. Mal J Pathol 21:29-35 1999.

Srinivas P, Liam CK and Jayaram G. Localised nodular pulmonary amyloidosis in patient with sicca syndrome. Med J Mal. 55: 385-387 2000.

KIMURA'S DISEASE

The disease that goes by Kimura's name, which he described in 1948, is granulation characterised by hyperplasia of subcutaneous angiolymphoid tissue with eosinophilic infiltration. It seems similar cases were previously reported as **angiolymphoid hyperplasia with eosinophilia** and **eosinophilic hyperplastic lymphogranuloma**. Yasmin reviewed a small collection of 6 cases of specimens excised from the head and neck region between 1983 and 1985. Two were from West Malaysia and four from Sarawak. They ranged in ages from 15 to 50 years and included 2 men and 4 women. They appeared not to be serious conditions and came to surgical excision on account of a long standing mass needing diagnosis. Jayaram and Peh have demonstrated that the diagnosis can be made from a fine needle aspirate.

References

Yasmin A. Kimura's disease. Mal J Pathol. 8:57-64 1986.

Ng KH, Siar CH and Loh HT. Kimura's disease: a case report. Ann Dent 50:26-27 1991.

Jayaram G and Peh KB. Fine-needle aspiration cytology in Kimura's disease. Diagn Cytopathol. 13:295-299 1995.

KIKUCHI'S DISEASE

Kikuchi's disease is a histiocytic necrotizing inflamation of lymph nodes, originally described in Japan in 1972. It occurs in Malaysia probably more frequently than Kimura's disease although there have been no published studies of its occurrence.

POEMS SYNDROME

POEMS syndrome is an acronym for polyneuropathy, organomegaly, endocrinopathy, M proteins and skin changes. This syndrome appears more prevalent in Japan and is also labelled the 'Takatsuki syndrome' or 'Crow-Fukasa syndrome'. The underlying pathophysiology of the disease is unknown but there is an abnormality of lambda light chains and localized collections of plasma cells causing sclerotic bone lesions. Bosco and Pathmanathan have reported one case in a 40 year old Indian woman whose lymph node biopsy showed features of the hyaline vascular type of Castleman's disease.

Reference

Bosco J and Pathmanathan R. POEMS syndrome, osteosclerotic myeloma and Castleman's disease: a case report. Aust NZ J Med. 21:454-456 1991.

SARCOIDOSIS

Sarcoidosis is a multisystem granulomatous disorder commonly affecting young adults. It usually affects the lung, hilar lymph nodes, skin and eye. It is considered rare in Southeast Asia. Dutt was the first to report 10 cases in Malaysia in 1970. All races were affected. 3 were Malays, 3 Chinese and 4 Indians. Murugasu recorded only 2 cases in the UH between 1967 and 1977. Reviewing the literature prior to 1977, he remarked that only a total of 5 cases, interestingly all Indians, had been reported in Malaysia. However, there was one case in a Malay in Brunei and a Chinese patient in Singapore. Teoh, Yow and Gong reported a case of ocular sarcoidosis in 1982. From 1972 to 1990 Liam and Menon noted 14 cases of sarcoidosis in UH. There were equal numbers of males and females. Their mean age was 42.4 years. 10 were Indians, 2 Malays and 2 Chinese which bears out earlier observations that it is more common among Indians.

References

Dutt AK. Sarcoidosis among Chinese in Malaysia – with a report of 10 cases. Med J Mal. 24:234-237 1970.

Murugasu R. Sarcoidosis: a report of two cases. Sing Med J 18:205-207 1977.

Teoh GH, Yow CS and Gong NC. Ocular sarcoidosis – a case report. Sing Med J. 23:181-183 1982.

Liam CK and Menon A. Sarcoidosis: a review of cases seen at the University Hospital, Kuala Lumpur. Sing Med J 34:153-156 1993.

SCLERODERMA

Scleroderma or systemic sclerosis is uncommon and as an example it formed only about 1% of cases at the Rheumatology clinic at UKM. Anuar and Singham have reported two cases of interest with associated complete heart blocks. Anandan has reported a case of a 51 year of Chinese patient with scleroderma and pulmonary silicosis after 8 years of exposure to silica.

References

Anuar M and Singham KT. Systemic scleroderma with complete heart block. Med.J.Mal. 38:65-67 1983.

Anandan S, Othman M, Cheong I and Chin GL. Scleroderma secondary to silica exposure – a case report. Sing Med J. 36:559-561 1995.

SYSTEMIC LUPUS ERYTHREMATOSIS

Often considered a connective tissue disease, systemic lupus erythrematosis (SLE) actually affects all the systems in the body, especially the kidneys, lung and nervous systems. Hobson said in 1954 "whereas in the standard textbook in the United Kingdom it is considered that SLE is a rare condition, the writer has gained the impression whilst serving in the Far East during the past few years that the condition is relatively common amongst young Chinese females". He recounted seeing 4 cases in a year besides which there were a number of case reports in the local medical literature in the 1950s.

Race and Age

Comparative racial differences in prevalence were first seen from hospital based studies. Frank reported from a fairly large series of 175 cases over 9 year from 1967, that of patients seen at the UH, Chinese who formed 81% of SLE patients were about 4 times more likely to suffer from it than other ethnic groups. There was no difference in the rates seen between Malays and Indians.

In a series of 539 patients that follows on from 1974 to 1990, Wang *et.al*, noted that Chinese continued to have the highest prevalence

of the disease. By comparing the rate of SLE with the frequency of Amyotrophic Lateral Sclerosis (which has a remarkable uniform rate of 5 per 100,000 throughout the world), they estimated the prevalence of SLE to be 46 per 100,000 in Chinese, 26 per 100,000 among Malays and 12 per 100,000 among Indians. The overall female to male ratio was 12:1 and was seen in all the three racial groups. The mean age of onset of SLE was 25 years (SD 10yrs) and was the same for all the races and between the sexes.

Patient who develop SLE after the age of 50yrs formed only 4% of SLE patients in a UH in a report in 1995. They had an insidious onset and a benign course of disease with a favourable response to steroids. All were women and 16 out of 17 were Chinese. Renal and neurological manifestations were less common but lung manifestations more common.

Risk Factors and Serological Features

Kong *et al*. have examined the HLA markers among Malay SLE patients and found that the strong association with the DR marker seen among Chinese was also evident. Moderate to strong association to the B-7, and Cw-7 markers was also found.

The large UH series from 1974 to 1990 found that Malay SLE patients had a lower prevalence of anti-DNA antibodies (57%) compared with Chinese (70%) and Indians (73%).

Teh *et.al*. noted a higher prevalence of antiribosomal P protein antibodies in Malaysian Chinese patients (38%) compared to Caucasian (13%) and Afro-Caribbean patients (20%). However anti-dsDNA and anti-SSA antibodies were found in comparable frequencies while anti-Sm and anti-SSB antibodies were rarely found in Malaysian Chinese patients.

An association between idiopathic SLE with genetically determined slow N-acetylation has been suspected from studies in Caucasians. Ong *et.al*. investigated this in our local population but found the frequency of slow acetylators in idiopathic SLE patients did not differ in Chinese (13%) and Malays (38%) significantly from the respective healthy Chinese (20%) and Malays (29%). The small number of Indians did not allow a valid comparison.

Fc-gammaRIIIB is a low affinity receptor that removes immune complexes from the circulation. UH workers studied that distribution of two allelic forms of the antigens. Fc-gammaRIIIB-NA1 and Fc-gammaRIII-NA2 occurred in 0.62-0.68 and 0.32-0.38 in Chinese and Malay patients and controls with no significant differences.

Anticardiolipin antibodies (ACA) occur in a subset of SLE patients manifesting as recurrent arterial or venous thrombosis, thrombocytopenia and recurrent abortions and has been termed the antiphospholipid syndrome. Jones *et.al*. reported that 16.5% of their patients in the UH had ACA, with 13% having raised IgG ACA and 2.5% having raised IgM ACA. Among patients with relatively active lupus nephritis in the Institute of Nephrology, Azizah *et.al*. reported that 56% of their patients had ACA, IgG ACA was raised in 56% and IgM ACA was raised in 5.6%.

Clinical Features

Renal Involvement

In their series from 1974 to 1990 Wang *et al*. found that 74% of SLE patients had significant proteinuria, half of these constituting the nephrotic syndrome

In a study of the renal involvement of SLE, Kong and co-workers at the KL GH found that, in 219 cases over 7 years from 1970, the ethnic composition resembled that of the general population which is in contrast to the UH study of all SLE cases. Females accounted for 79% of patients with lupus nephritis and the peak age was the third decade of life (41%). 62% of

patients had the nephrotic syndrome, 21% had proteinuria and 5% had oliguric renal failure. Histologically, the diffuse proliferative form (48-68%) and the membranous form (11-29%) were the commonest in both the KL GH and UH experience.

Suleiman *et.al*. reviewed 112 patients with SLE nephritis treated between 1976 and 1982 in GH KL. 92% were women. Their mean are was 26 years. 31(28%) were known to have died. 12% died within one year of known renal involvement, 10% died 1-4 years and 6% died more than 4 years after known renal involvement. Renal failure was the main cause of death in 10(32%) patients. Gastrointestinal haemorrhage (16%) septicaemia (13%) and sudden deaths (13%) were the other major causes of death. Renal biopsies in 15 of 16 of those who died showed diffuse proliferative glomerulonephritis.

Chan and Hooi examined the outcome of 85 lupus nephritis patients in Johore Bahru in the year 2000 who were put on cyclophosphamide therepy. 89% of there patients were WHO class IV on initial renal biopsy. 20% did not complete treatment because of death, default, reaching ESRD or due to complications. Overall survival was 75% at 5 years and 64% at 10 years. Of those the 19 who died, the mean duration from biopsy to death was 2.7 years.

Wang and Looi divided a group of 31 SLE patients with membranous lupus nephropathy (MNL) into 13 patients in Group 1 with purely MLN and 18 in Group 2 with MNL and segmental proliferation in up to 35% of glomeruli. The extrarenal manifestations of SLE in both groups were severe but both groups responded to initial treatment. Relapses however were frequent. The 6 year survival in Group 1 was 62% and in Group 2 was 50%.

Adam *et.al*. noted in 1981 that patients who had a positive lupus band test were 2.5 times more likely to have renal involvement of lupus, and more likely to have diffuse proliferative glomerulonephritis.

Neurological Involvement

In a series of 24 children with SLE with a mean age of 11 years, Hussain *et.al.* noted that 75% had CNS involvement. 11had seizures, 5 manifested psychosis, 5 showed signs of encephalopathy, 5 had headache, 4 had personality changes, 3 had strokes, 3 had movement disorders and one had myelitis. In 4 of these children cerebral lupus was the presenting manifestation. 16 (75%) of these children also had renal involvement. 8 children made a full recovery, one child died of cerebral haemorrhage during a hypertensive crisis. 6 children had learning disabilities at one-year follow-up, 4 had epilepsy and 2 had motor deficits.

Chin *et.al*. surveyed all 79 SLE patients attending their clinic for psychiatric disorders in 1979. 51% were found to have some disorder. 26 had depressive neurosis, 6 anxiety neurosis, 5 endogenous depression and 3 dementia.

Reviewing CT scan findings on 27 consecutive adults patients with SLE and neurologic symptoms, Raymond *et.al*. in 1996, found some abnormality in 59%. The lesions noted were cerebral atrophy, calcification and/or infarcts. 10 patients had only one type of lesion, 8 had a combination of 2 or all 3 lesions. Altogether 8 patients had brain calcifications but no relationship was found between the degree of calcification to the age of the patient nor duration or type of neurological presentation.

Cardiac Involvement

Cardiovascular examination was carried out in a series of 40 consecutive SLE patient admitted to the UH by Ong *et.al*.80% had active disease at the first examination while only 41% remained with active disease in a follow up visit 6-12 months later. During the first visit 73% had

an abnormal echocardiogram. Valvular disease was observed in 38%, most commonly affecting the mitral valve. A pericardial effusion was seen in 36%, most associated with hypoalbuminaemia. Libman-Sacks endocarditis was rare (2.5%). 52% had some abnormal echocardiographic finding still on the follow up examination.

Other Manifestations

From a study of SLE from 1974 at the UH, Menon, Wang and Ng, found 5 patients who developed primary pulmonary hypertension out of 300 SLE patients over 10 years. All were young women and all died after 7 to 87 months from the onset of pulmonary hypertension. Wang, Chua and Bosco have also noted that herpes zoster is more common among SLE patients, seen in 24 out of 184 patients on follow up (11%), than in the general population (said to be 0.25%).

Unusual associations with SLE that have been written about locally include separate cases with cheimosis, hyperphagia and myocardial infarction. Gout is infrequently associated with SLE. Veerapen has reported 3 instances.

Outcome

UKM clinicians reported a survival rate among102 patients to be 93%, 86% and 70% at 1, 5 and 10 years respectively. There were two peak periods for the occurrence of death. These were the first 2 years and the 6^{th} and 7^{th} year. Infection was the direct cause of death in 52% and a contributing factor in further 19% of deaths. Methylprednisolone therapy was associated with a 6.24 relative risk of death. It may be a reflection of this therapy being used as a final manoeuvre in the very ill, but caution ought to be taken regarding its use in view of the high rate of fatal infections. Paton *et.al*. reported that in the month following pulse methylprednisolone therapy the risk of major infection was 20 times higher and the risk of minor infection was 10 times higher that at other times. However disease flare itself carried a 10 and 6 times higher risk for major and minor infection respectively. Lupus nephritis carried a relative risk of death of 4.34 and cerebral lupus that of 3.08.

At the UH Wang *et.al*. noted survival up to 5 and 10 years to be 82% and 70% respectively from a series of patients from 1974 to 1990. Chinese and Malay patients had similar survival rates but Indian patients had the poorest survival rates being 70% at 5 years and 65% at 10 years.

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WEGENER'S GRANULOMATOSIS

Wegener's granulomatosis is one rare entity that every physician should be aware of. It can be very rewarding to diagnose because even though its cause is not known, treatment with cyclophosphamide gives an excellent prognosis. If it is not recognised and untreated it is universally fatal within a few months. Wegener's granulomatosis is characterised by necrotizing vasculitis of small arteries and veins with granuloma formation typically involving the upper and lower respiratory tract. In addition, the kidney, the eye, skin, heart and other organs may be affected.

It seems rare in Malaysia. Liam reported a man presenting with hyperplastic gingivitis, though the diagnosis was established through an antral biopsy. Loke and Tan reported, a 35year old Malay man in Terengganu, who first had uveitis but 2 years later had a cavitating lung lesion and an inflamed area in a perforated nasal septum from which a biopsy established the diagnosis.

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CHAPTER 26

THE CARDIOVASCULAR SYSTEM

INTRODUCTION

Cardiovascular diseases have greatly increased in frequency over the last few decades to become the most significant health problem in our population today. They ranked third among the causes of death in Malaysia in 1950. By 1970 however, they had risen to become the leading cause of death. The cardiovascular diseases are a group dominated by 3 major diseases. Coronary artery disease account for slightly more than 1/3 of the group. Cerebrovascular disease accounts for another 1/3 while hypertension and heart failure from various causes account for the remaining 1/3. In all these diseases atherosclerosis constitutes a major underlying pathology. Besides these two other important cardiovascular diseases are the rheumatic heart diseases and congenital heart diseases. But together they account for only about 3% of cardiovascular deaths. In 1998, cardiovascular diseases accounted for nearly 30% of the medically inspected deaths.

NORMAL HEART FUNCTION

Because of the need for quantitative measurements to accurately manage patients in cardiology, normal values for the local population are important.

Asma, Omar and Singham reported their finding on 87 normal subjects studied at the UH over 16 years with regards right heart pressures and gas saturations. The right heart pressure measurements were comparable to values in Caucasians. However, the calculated total pulmonary vascular resistance and systemic vascular resistance was significantly lower than those obtained in Caucasians. They attributed this to the higher cardiac output in their subjects.

Exercise tolerance

As regards cardiorespiratory fitness in exercise, in a sample of 26 youths between 12-18 years it was found in 1974 that Malay boys had a mean maximal oxygen uptake of 49.5 ml/min/kg compared to 43.6 ml/min/kg in Chinese and 47.2 ml/min/kg among Indians which, in view of the small sample, was not statistically significant. The maximal oxygen uptake for Temiar youths was 45.9 ml/min/kg and that of Temiar men aged 19-40 years was 53.2 ml/min/kg. There has been another study in 1981 that does not appear quite comparable. Adult men with ages between 40-45 years seemed to have a much lower maximal mean oxygen uptake. These were volunteers from the Malaysian Police Force. The men who had physically active work had maximum oxygen uptake of 35.0 ml/min/kg while their sedentary colleagues had a mean value of 29.8 ml/min/kg.

The maximum heart rate recorded in exercise for the sample of Malay, Chinese and Indian boys was 193/min, 196/min and 198/min respectively. The mean serum lactate achieved was 78 mg/dl, 85 mg/dl and 69 mg/dl for the races respectively while the mean pH was 7.24, 7.23 and 7.27. While these figures do not reach significant values their trend would suggest that this is the basis for the commonly held belief that Indians for example, tolerate long distance running better as they accumulate less lactate. Temiar boys had maximum heart rates of 194/min. and a mean lactate level of 75 mg/dl. The Temiar men had maximum heart rates of 187/min with a lactate level of 94 mg/dl.

Chan *et.al*. have recorded the normal values of blood pressure in children aged from 6 to 12 years.

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CONGENITAL HEART DISEASE

In a survey of 19,769 livebirths in Alor Star GH, Goh and Yeo estimated the incidence of acyanotic congenital heart disease at 1.21 per 1,000 livebirths and cyanotic congenital heart disease at 0.56 per 1,000 livebirths.

In the 1970s, the UH started the first Cardiac Surgery service. Being a referral centre a total of 1,037 patients with congenital heart disease were seen in just 2½ years starting from 1975. The commonest defects were simple ventricular septal defects (40%), patent ductus arteriosus (15%) and Fallot's tetralogy (14%). These figures did not include lesions seen in combinations which were separately listed in a total of 31 entities.

Reviewing all congenital heart disease children referred to 4 major hospitals (in Ipoh, Teluk Intan, Kuching and Kota Kinabalu) prospectively in 1995, Hung *et.al*. also noted that ventricular septal defects (37%) was the commonest lesion, followed by patent ductus arteriosus (19%), atrial septal defects (10%) and Fallot's tetralogy (9%) among 250 new patients. They noted that there were 204 surgical procedures done for congenital heart cases that year, including 13 done outside the country. All the cases operated on locally were done at the National Heart Institute in KL. Since then such services have been extended to Penang and Johore Bharu.

Reviewing all open-heart operations done at the KL GH in 1987 from the start of the Cardiothoracic Department in 1982, Yahya, Abdullah and Ahmad noted that congenital heart disease constituted 52% of the 1110 operations done. There was a operative mortality of 3%. The four most common conditions were, atrial septal defect, ventricular septal defect, Fallot's tetralogy and pulmonary stenosis.

Down's Syndrome children are well known to be at higher risk of having congenital heart lesions. In a prospective study, of all 34 babies born with Down's at the MH KL over 18 months, Hoe, Chan and Boo found that 17 (50%) had demonstrable heart lesions, which is comparable with findings overseas. 41% had ventricular septal defects, 18% had patent ductus arteriosus, 12% had a combination of both these, 12% had A-V canal defects and other heart lesions made up the rest.

Patent Ductus Arteriosus

Singham and Wong reviewed 181 patients with patent ductus arteriosus in the UH detected over 9 years from 1967. More than 50% of their patients were over 10 years old, the eldest being 54 years of age. The male to female ratio was 1:3. 32% of their patients had significant dyspnoea or were in heart failure. The complications they had included elevated pulmonary vascular resistance, Eisenmenger syndrome, bacterial endocarditis and cardiac failure. Patent ductus arteriosus was first successfully treated by ligation by Gross in 1938. A review by Tan in 1987 showed that 645 patients had had such operations in KL and Klang between 1982 and 1987. Being the national referral centre this probably represent

nearly all the cases done in Malaysia. There were patients from every state, and surprisingly most came from Sarawak. Females were three times as often seen as males as in the UH experience. They ranged in age from under a year to over 30 years but most were treated between 1 to 5 years of age. The races seemed equally represented. There were 15 cases with associated congenital rubella and a few other miscellaneous conditions. There was no mortality in the series but there was some post-operative morbidity.

Transposition of the Great Vessels

Transposition of the Great Vessels was first described by Ballie in 1797 and was long considered lethal and not amenable to surgery. Today with balloon atrial septostomy at birth and elective reconstruction several months later some babies can be saved. In the UH review in 1978, it constituted 1.6% of the 1,037 cases. In the KL GH experience described by Chan and Mazeni in 1987 the first 11 cases of balloon atrial septostomy done achieved some clinical improvement in the neonates. In the 1995 review by Hung *et.al*. it formed 2% of 250 cases.

Ebstein's anomaly

This consists of a tricuspid valve which is displaced into the right ventricle greatly reducing its size. Ebstein noted this in 1866 at post-mortem. It causes effort dyspnoea. Rarely it can be diagnosed clinically by auscultation, but it can be seen on echocardiography. Anuar and Singham reported a series of 10 cases from the UH over the period from 1967 to 1979.

Right coronary artery to atrium fistula

This is a rare condition, of which Singham, Saw, Johnson and Ganendran reported one case. The child required surgery when 4 years old, due to chronic circulatory overload from a large left to right shunt, which he survived.

Pulmonary Artery Sling

This is another rare condition. It has been reported is an infant with bronchiolitis-like respiratory failure. The child had a corrective procedure to relieve compression for a left pulmonary artery sling but died of bronchospasm.

Absent Pulmonary Valve

`There has been one case of this reported in a girl.

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ACUTE RHEUMATIC FEVER & RHEUMATIC HEART DISEASE

Acute rheumatic fever is actually a multisystem disease, a delayed sequel to group A streptococci throat infection. But because the main cause of morbidity and sequelae are cardiac it is treated here as a cardiac problem. It has probably a history going into antiquity but 'rheumatic fever', the name we know it by was given by de Baillon, a court physician to Henri IV of France. Rheumatic fever was a great problem in the West in the previous century and thought erroneously to be rare in the tropics. Today rheumatic fever is fading out in the West but it probably will still be a major problem with us for yet a while.

It is important to realise that underpriviledged children are most affected because it tends to receive much less attention than ischaemic heart disease. Probably one of the earliest observations of the pattern of rheumatic heart disease in Malaysia was reported by Balasundaram at the Assunta Hospital PJ in 1967. In a collection of 74 cases he noted no racial, sex, nor urban-rural predeliction for the disease. 7 patients had rheumatic fever, 2 had bacterial endocarditis, the rest had rheumatic valvular heart disease. As such all ages were seen. Of the valvular lesions 85% had only mitral involvement, the rest had mitral and aortic valve disease.

Gururaj, Choo, Ariffin and Sharifah reported a series of 42 children admitted with rheumatic fever under 12 years old in Kelantan seen over 4 years from the hospital's inception in 1985. Boys and girls were equally represented and ranged from 5 years 9 months upwards in age. 11 had a prior admission for rheumatic heart disease. Ther was a seasonal low noted in the months of May and June. Carditis was present in 67%, Arthritis in 57%, Chorea in 7%, Subcutaneous nodules and Erythema marginatum in 4% each. The outcome reported was complete recovery in 11, residual valvular heart disease in 20, death in 2 of intractable heart failure and 9 were lost to follow-up.

Between 1981 and 1990, 134 children were diagnosed to have acute rheumatic fever in the UH. 34 of these were recurrent attacks occurring in 20 patients. Boys outnumbered girls by 1.4:1. The children ranged from the age of 4 years to 18 years, but 85% were below 12 years. Indians had a relative risk of 2.4 times that of Malays and were more likely to get recurrent attacks. Chinese were 1.4 times as likely as Malays to be affected. 73% of patients came from families with a low monthly income of less than RM500 a month. Over the 10 years studied there appeared to be a declining trend in the number of cases.

Ong and Ramanathan have reported transient complete heart block as a rare complication of acute rheumatic fever.

Chronic Rheumatic Valvular Heart Disease

As a cause of death, rheumatic heart disease in Malaysia showed a rise from 0.41% of medically inspected deaths in 1965 to 0.91% in 1980. Since then there has been a decline to 0.50% in 1989 which will hopefully continue. In its relative importance among cardiovascular diseases however it has slipped only because of the rise in coronary artery disease. There are twice as many deaths from rheumatic heart disease among women as there are among men.

Rheumatic valvular heart disease is however still a major clinical problem in our population, with thousands needing treatment. In the review of the first thousand odd cases seen at the Department of Cardiothoracic Surgery from 1982 to 1987, it was noted that rheumatic heart disease accounted for almost all the valvular heart lesions seen. Most patients (more than

80%) were under 30 years old and more than 75% were functionally in class III and IV of cardiac failure. Valve replacements formed 27% of open heart surgeries and valvotomy formed 9%. Mortality was 3% for the former and 1% for the latter.

Screening 46,986 primary school children in Kelantan between 1988-1990, Ibrahim *et.al* reported a rheumatic heart disease prevalence rate of 11 per 100,000 which is comparatively low. The reason perhaps is children above 12years were excluded.

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HEART TRAUMA

Stab wounds to the heart undoubtedly have an element of drama about them. Saving such a patient is a feat worthy perhaps of a medal or at least a case report – and so we have a few. Singh noted two cases treated by Frazer in KL in 1961 and Menon in Ipoh in 1962. Cheong and Fong reported one case in Taiping in 1984. Aung reported another from Tawau in 1996.

Wong reported a case of a patient in Johore Bahru who had a pericardial rupture and herniation of the heart into the right hemithorax following a blunt injury to the chest in 1999.

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ENDOCARDITIS

Singham *et.al*. review the UH experience of 101 patients over 10 years from 1977. The majority of patients were between 10-40 years old and males outnumbered females in a ratio of 3:2. 69% had underlying rheumatic valve disease especially with aortic and mitral disease co-existed. Other patients had congenital heart disease, most commonly patent ductus arteriosus and one had a prosthetic valve. Micro-organisms were identified in 77 patients. *Streptococcus sp*. Were the commonest. The hospital mortality rate was 23%.

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CORONARY ARTERY DISEASE

Myocardial infarction and other forms of coronary artery disease have risen from being 3.0% of medically-certified deaths in Malaysia in 1965 to 11.3% in 1989. Though we cannot be certain what proportion of total deaths it accounts for as about 60% of deaths are not medically inspected, coronary artery death has almost surely become the chief cause of death in Malaysia.

All the races are similarly affected by the rising trend. Coronary heart disease has increased from 3.7% of death in 1970 to 10.5% in 1989 for Malays. Among Chinese it rose from 3.9% in 1970 to 10.4% in 1989 and for Indians it climbed from 7.0% in 1970 to 15.4% in 1989. The rate does not appear to have kept rising since then but stabilised at about that level in the 1990s and may have declined a little. This may perhaps be the result of awareness and intervention.

Historically, the first attempt at a population based study of coronary artery disease in Malaysia was made by the American Interdepartmental Committee on nutrition for national defence study in 1962. A very high percentage of females (60%) and males (32%) appeared to have chest pain resembling angina. But when only subjects with electrocardiographic changes commonly seen in ischaemic heart disease are counted 9% of females and 5% of males fitted the criteria. These findings contradict hospital experience where other studies show males are more often affected than females. Also unlike hospital experience Malay males had the highest prevalence of electrocardiographic evidence of myocardial infarction.

One of the early epidemiological features about coronary artery disease to be noted locally was the higher incidence among Indians. Danaraj *et.al.* in a series covering 1950 to 1954 and Muir in a series covering 1948 to 1957, both showed in autopsy studies in Singapore that there was a marked increased number of Indians, among whom Indian Muslims were even more at risk of deaths from myocardial infarction. Pallister in Penang also observed that among 89 cases of hospital admissions for myocardial infarction between 1952 and 1955, that it was more common among Indians. Indians seemed to have about 1.5-1.8 times the risk greater than Chinese or Malays. In Singapore a corresponding higher incidence had also been noted, estimated at as much as 3 times that of the other races. Table 26.1 shows the mortality rate from coronary artery disease in Malaysia between 1968-71 calculated by Safiah and Margetts. This concurs with the relative risk of Indians seen in the Singapore figures. However they made some assumptions. They assumed most deaths in urban areas are medically certified and the ethnic distribution of the urban population is the same as in the overall population which may not be true.

In contrast Burns-Cox *et.al*.and others have noted an absence of coronary heart disease among the Orang Asli which they attribute their low levels of serum cholesterol. Their mean serum cholesterol level was only 143 mg/dl. Prathap and Montgomery confirmed the absence of atherosclerotic disease in the Orang Asli in a post-mortem series.

Table 26.1 Mortality Rate (per 100,000) due to arteriosclerotic and degenerative heart disease, in the urban population in Malaysia 1968-1971 aged 30-69years

Race	Mortality Rate	
	Male	Female
Chinese	105.6	31.2
Malay	142.3	33.0
Indian	367.2	74.4

Quek and colleagues studying myocardial infarct patients admitted in GH KL over 6 months in 1986 also noted the over-representation of Indians. They observed it again in among women subsequently. Eurasians and Sikhs who account for other races also had a high risk. The peak age was between 50-60 years for men but above 60 years for women.

Some other data that Khoo, Tan and Khoo presented in 1991 are males are 1.5 times more often affected than females. Although in men myocardial infarction is the leading cause of death, among women it ranks behind strokes. The age mode for coronary mortality was 55-

59 years for men but has shifted up lately to the 60-64 years bracket. For women the age mode has shifted the other way from 70-74 years to the 65-69 year group.

***Risk Factors**:*

Beside increasing age and being male, which cannot be changed, classically the risk factors of coronary artery disease recognised are hyperlipidemia, obesity, hypertension, diabetes mellitus and smoking. Each of these factors are diseases in their own right and besides their prevalence in patients with coronary disease they are discussed separately in this book (NB hyperlipidemia is discussed under hypercholesterolaemia).

In a descriptive study, Ridzwan *et.al*. noted that among Malays with myocardial infarction in GH KL in 1982, 44% were hypertensive, 20% were diabetic, but only 23% of their patients had hypercholesterolemia.

Although each independently poses a risk, in practical terms they tend to occur in the same subjects. In a general practice survey of 1,116 subjects between 1989 and 1991 in KL, Khoo, Tan and Liew report a correlation between high cholesterol with obesity and hypertension. High triglycerides correlated with glucose intolerance, smoking and alcohol consumption. It stands to reason that an affluent lifestyle promotes these factors together.

From the analysis of the results of the National Health and Morbidity Survey of 1996, Lim *et.al*. also observed that there was clustering of the 4 major coronary risk factors in the Malaysian population. When hypertension was taken to be a blood pressure level above 140/90 mm/Hg, abnormal glucose tolerance (by WHO criteria), hypercholesterolaemia (a level above 5.2mmol/l) and obesity, a body mass index above 25kg/m2, they found that 39% of the adult population had no risk factors, 34% had 1 risk factor, 19% had 2 risk factors, 7% had 3 risk factors and 1% had all 4 risk factors. The number of patients having 4 risk factors, "the deadly quartet", was 6 times higher than expected by chance. Individuals with 1 risk factor had a 1.5 to3 times higher prevalence of other risk factors. Indian and Malay women had at particularly high risk for clustering of risk factors. One explanation for clustering is that the factors have a common antecedent, such as insulin resistance or hyperinsulinaemia.

Race

One might presume that the higher prevalence of coronary disease among Indians is due to their higher rates of the known risk factors. It is possible however that might not entirely explain it. In a retrospective study of young patients (under 40years) with coronary artery disease who had angiograms done in the UH, Rajadurai *et.al* had 103 patients over 6 years and found Indians (56%) more often affected than Malays (31%) and Chinese(12%) and found the racial differences could not be explained by the commonly known risk factors – smoking, hypertension, diabetes and hypercholesterolaemia. They also found men more often affected than women in a ratio of 16:1.

Smoking

Quek *et.al* in 1987, looked at smoking among patients admitted to the coronary care unit in GH KL, and compared those with myocardial infarction with those with non-coronary events. Among these patients they believed smoking was the single most prominent factor, outweighing hypertension and diabetes. 65% of their myocardial infarct patients were smokers. This risk was true for men as well as for women, they showed in a later study. The relative risk was about 2.4 times higher in women overall but was more marked in those under 40 years whose relative risk was over 10 times higher. Smoking and coronary events also

showed a dose-related relationship. In an earlier study of Malays with myocaridal infarction in GH KL in 1982, Ridzwan *et.al.* had noted a higher percentage (82%) of their patients were smokers.

Outcome

Ng noted in 1982 that in a 3 year review of 304 patients admitted to the Coronary Care Unit in KL, 62% had come within 5 hours of the onset of symptoms. However, another sizeable groups (20%) came more than 24 hours after their symptoms began. There was a 13% early fatality rate of which 80% occurred within 24 hours of admission. 50% of deaths were due to arrhythmias and 45% due to myocardial pump failure.

Quek, Ong and Lim observed that there was a circadian pattern in myocardial infarctions admitted to the GH KL. There were two peak hours for the onset of pain, 8-9.00am. and 8-9.00pm. The part of the day most common for infarcts was the morning hours from 6am. till noon. The time of arrival at hospital conveniently peaked between 10.00am to 4.00pm. which happen to be working hours. They also noted that 71% had come to hospital by six hour after onset of symptoms. Similarly Loke in Kuala Terengganu also noted that 70% of the patients there arrived in the hospital within 6 hours of the onset of symptoms.

It has been observed in a series between 1977 and 1979 of patient from UKM, that in 164 cases with 24 hour electrocardiographic monitoring, 80% developed some arrthythmia (which is not unlike worldwide experience) and 27% developed cardiac failure (including 5% who had cardiogenic shock). Between 1980 and 1985, Chin and Khalid from the UKM, collected a series of 68 patients with complete heart block following myocardial infarction who required temporary pacing. The overall mortality was 44%.

Quek and colleagues noted in 1987 an early hospital fatality rate of 68 out of 311 myocardial infarct patients (22%) which was not significantly different between smokers and non-smokers.

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with other coronary risk factors in healthy subjects in a city clinic. Med.J.Mal. 52:38-52 1997.

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SICK SINUS SYNDROME

This is a diagnosis describing electrocardiographic and clinical evidence of sinus node dysfunction. Chin, Singham and Anuar collected 49 cases over 9 years at the UH. Just more than half were idiopathic, one quarter were ischaemic in origin. 23 of their patients required permanent pacing.

Reference

Chin K, Singham KT and Anuar M. Sick sinus syndrome in Malaysians. Med.J.Mal. 38:108-111 1983.

SUPRAVENTRICULAR TACHYCARDIA

One case of a baby diagnosed and managed from just before delivery till three months of life was reported by Soh *et.al.*

Reference

Soh EBS, Raman S and Chia PMK. Fetal supraventricular tachycardia - a case report. Med.J.Mal. 53:280-283 1998.

COMPLETE HEART BLOCK

In 100 patients with complete heart block, Chin, Singham and Masduki noted that myocardial infarction (31%) and angina pectoris (9%) were the commonest identifiable causes. A further 38% were idiopathic and the remainder made up of myocarditis, myocardiopathy and 5% congenital cases. There were 19 deaths and 61 patients with irreversible blocks. 74 required temporary pacing,45 going on to permanent pacing. 13 were put on long term medical therapy.

References

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SINUS OF VALSALVAR ANEURYSM

This condition, said to be rare in the West, was first operatively corrected successfully in 1957 independently by two groups, one led by Lillehei the other by Morrow. Reports from China and Japan suggest that the incidence is much higher in Asia. Yap and Jeyamalar support this claim in describing 18 cases seen over 9 years at the UH from 1976. All cases were symptomatic. Most were males and the mean age was 27 years. All aneurysms ruptured into the right ventricle. 7 of these patients were surgically treated for closure of the fistula.

Reference

Yap S and Jeyamalar R. The surgical repair of ruptured sinus of Valsavar aneurysms. Med.J.Mal. 42:182-185 1987.

HYPERTROPHIC CARDIOMYOPATHY

Hyperthrophic cardiomyopathy is uncommon and of uncertain aetiology. It usually affects young adults. Chin reported one case with coexisting hypertension.

Reference

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ATRIAL MYXOMA

Atrial myxomas are uncommon but can be a cause of a picture suggestive of mitral stenosis or insufficiency. Cases have been reported by Singham and Anuar, Segasothy, Tai and Robaayah, Ram and Malik. Yahya and Ahmad collected a series of the KL GH experience of 12 cases over 5 years from 1984. 2 patients had right heart myxomas compared to 10 left ones. There were 9 women and 3 men ranging in age from 16-60 years. They had one peri-operative death. One patient developed a recurrent myxoma but the rest were well on follow-up ranging from 1 to 44 months.

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Ram SP and Malik AS. Cardiac tumours in children. Med.J.Mal. 49:96-99 1994.

PERICARDITIS

12 cases of purulent pericarditis were seen over 6 years in the UH. *Staph. aureus* was the causative organism in 50% of the cases. A respiratory illness was the most common precedeing illness. One death occurred in a patient who was seen late in the illness.

Reference

Majid AA and Omar A. Diagnosis and management of purulent pericarditis. Experience with pericardiectomy. J Thorac Cardiovasc surg 102:413-417 1991.

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HYPERTENSION

Raised peripheral arterial blood pressure is not a disease entity like a gallstone or malaria, which is either present or absent. What is considered abnormally high actually depends on how one chooses to define it. Therefore how prevalent it is, or more important to an individual, whether you have it or not, depends just on a definition. Furthermore in the majority of 'patients' it is symptomless, although many lay people locally associate it as a cause of headache. It is clear however that, essential hypertension, which is what the vast majority of hypertensive people have and what one may call just the upper spectrum of the normal range of blood pressure in the population, carries a very significant risk for serious complications like myocardial infarction, strokes, renal disease and hypertensive heart disease. This involves such a lot of mortality and morbidity that hypertension itself is universally considered a disease.

The WHO defines hypertension as a pressure above 160/95mm.Hg., but in studies various other criteria are often used, such as a level above 140/90 being considered mild hypertension. The ICNND in 1962 was one of the earliest community surveys in Peninsula Malaysia. It involved 834 subjects. They noted an increasing prevalence of hypertension with age in all races and both sexes which has been consistently seen in all other later studies. The mean blood pressure rose from 123/75 and 120/76 for men and women aged 25-34 years to 143/80 and 157/82 for both males and females respectively in the over 65 years age group.

In 1980, Kandiah, Rampal, Paranjothy and

Table 26.2 Crude percentage distribution of blood pressure of Malaysians according to JNC classification 1996

	Normotensive			Hypertensive		
	% Optimal (SE)	% Normal (SE)	% High normal (SE)	%Stage I (SE)	%Stage 2 (SE)	%Stage 3 - 4 (SE)
Systolic BP	<120	120-29	130-39	140-59	160-79	>=180
Diastolic BP	<80	80-84	85-89	90-99	100-109	>=110
All	32 (0.5)	20 (0.3)	17(0.3)	20(0.3)	8 (0.2)	4(0.2)
Men	29 (0.5)	23 (0.5)	19 (0.5)	20(0.5)	7(0.3)	3(0.2)
Women	35 (0.6)	18 (0.4)	15 (0.4)	20(0.4)	8 (0.3)	4(0.2)
Malay	31 (0.6)	21 (0.5)	17(0.4)	20 (0.5)	8 (0.3)	4(0.2)
Men	30(0.8)	23 (0.7)	18 (0.7)	1910.6)	7 (0.4)	3(0.3)
Women	31 (0.8)	18 (0.6)	15 (0.6)	21 (0.6)	9 (0.4)	5(0.3)
Chinese	34(0.8)	19 (0.6)	16 (0.5)	20(0.6)	7(0.4)	3 (0.3)
Men	28 (1.0)	21 (0.9)	18 (0 8)	22 (1.0)	7(0.5)	4(0.4)
Women	40(1.1)	18 (0.7)	14 (0.7)	18 (0.7)	7(0.5)	3 (0.4)
Indian	37(1.4)	20 (1.0)	15(1.0)	18(1.1)	7(0.8)	3(0.5)
Men	29 (1.8)	22 (1.6)	17(1.5)	20 (1.6)	8 (1.1)	4(0.8)
Women	45 (1.9)	18 (1.3)	13(1.3)	16 (1.4)	6 (1.0)	3 (0.6)
Other indigenous	28 I0.9)	20 (0.8)!	21(0.8)	19 (0.8)	8 (0.5)	4 (0.4)
Men	26 (1.2)	22 (1.2)	23(1.2)	19 (1.1)	7(0.7)	4(0.5)
Women	30 (1.2)	18 (1.0)	19(1.1)	20(1.0)	9 (0.8)	5(0.5)

***Joint National Committee on Detection, Evaluation and Treatment on High Blood Pressure**

Gill reported a survey of 1,030 persons sampled throughout Selangor. They found no urban-rural, male-female nor racial differences in prevalence. Only smokers had a higher prevalence. Using 140/90 arbitrarily as the mark of hypertension they found a rate of 7.4% among 25-34 year age group rising to 37.5% in the 55-64 year age group. However, only about 5% overall had a pressure above either 160mm.Hg. systolic or 95mm.Hg. diastolic. 67% of the hypertensives were aware of their illness but only 36% of them were under treatment.

In a rural survey of Malays in 1984, Osman, Rampal and Syarif noted, that among a total of 359 subjects the prevalence of hypertension was 9% among the 25-34 year age group and rose to 42% in 55-64 year age group. In the group above 65 years it rose to 56%. They took a blood pressure of above 140/90 to be hypertensive. They also noted that smokers were more often hypertensive. In a community study of 2,284 subjects above 20years old chosen by cluster sampling in 9 districts reported in 1996 in Kelantan, Wan Mohamed *et.al*. noted that 10% of the lean, 13.2% of the overweight (BMI above 25kg/m^2), and 23.3% of the obese (BMI above 30kg/m^2) were hypertensive.

The National Morbidity Survey of 1986 - 1987 was a large study involving a random sample of 26,005 respondents that defined hypertension as a blood pressure above 160/95mmHg. The prevalence of hypertension was 2% in the 25-34 year age group and rose to 14.5% in the 65+ age group. Only 38% were aware of their condition. Of these 78% were on medication or dietary therapy, of whom only 30% were under control. The overall prevalence rate in the study was 7.3%, and it estimated that 360,000 persons in Malaysia above the age of 25 years had hypertension.

The National Health and Morbidity Survey

of 1996, described the distribution of blood pressure in 21,391 individuals chosen as a representative sample of the whole Malaysian population. It showed no significant difference in race or gender but systolic and diastolic blood pressure did rise with age. The mean blood pressure rose from 123/78 and 118/75 for men and women aged 30-39 years to 144/78 and 152/80 for both the sexes respectively in the over 70 years group, which is quite comparable to the ICNND study in 1962. As expected the distribution has a right skew but the magnitude of the skew decreased with age. While younger and middle age men in all ethnic groups had higher systolic blood pressures than women the centile curves of the 2 sexes cross at age 40-65 years so that in the elderly, systolic blood pressure of women exceeded that of men. Diastolic blood pressure increased with age in early adulthood but beyond the sixth decade it declined, especially in men. The percentage of blood pressure according to the classification of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC) is given in Table 26.1. Overall 12% of the population have stage 2 hypertension (which is nearly equivalent to the WHO classification) and 32% have a blood pressure above 140/90mmHg.

Khoo *et.al*. reported the blood pressure of volunteers at health screening campaigns in 4 urban areas between 1992-1994 and in 10 urban areas between 1995-1997 and found the prevalence of hypertension similar to the NHMS.

Management and Compliance with treatment

In 1982, Supramaniam noted that there were 347 hypertensives in the entire Malaysian Armed Forces giving the prevalence rate of 4.03%. He found that patient eduaction was unsatisfactory in 53%, and adherence to drug intake poor in 59%, to weight reduction poor in 96% and cessation of smoking poor in 70%. These figure probably apply to the general population as much. Lim, studying 60 hypertensives in Mentakab who had dropped out of treatment (accounting for 56% of patients admitted to hospital for complicated hypertension) found that lack of motivation (85%) was the chief reason for defaulting and that economic reasons were unimportant. 95% were unaware that the condition and the treatment was lifelong, 60% were unaware of the consequences, 52% believed long term consumption of western medicine harmful, 78% believed relief of symptoms like headache and dizziness was successful treatment and 72% complained of a long waiting time at clinics.

Lim *et.al*. studied 168 patients in the Mentakab Hypertension Study Project and found by the pill counting method that 26% were not compliant to medication. As might be expected the patient's self-reporting was a poor predictor of non-compliance (sensitivity 71%, specificity 50%). Assessing adequacy of hypertension control among drug compliant patients followed up for at least one year in the outpatient department at the Mentakab Hospital the study found only 18% of 55 such patients achieved adequate blood pressure control. The audit also revealed other deficiencies in care that would be instructive to similar clinics.

Disease burden

Lim found that hypertension accounted for 9% of all visits to the outpatient department in the Mentakab Hypertension Study Project. Complicated hypertension was seen in10% of 1,066 medical admissions over 4 months in 1989. All had uncontrolled hypertension, 85% had hypertensive heart disease, 33% had cerebrovascular disease, 30% had ischaemic heart disease and 2% had malignant hypertension.

Hypertensive Heart Disease

Hypertensive heart disease is usually defined as electrocardiographic evidence of left

ventricular hypertrophy or its other clinical manifestations. In his review of cardiovascular diseases in Penang GH in 1960, Khaira noted that this was the commonest disease, ahead of coronary artery disease accounting for 39% of heart disease in the hospital population. Indians recorded the highest rate. In the ICNND study the overall prevalence of hypertensive heart disease was found to be about 1%, being highest also in Indian males (4.6%) while lowest in Malays (1.1%). Lim also found this to be the commonest complication (85%) in hypertensives admitted to hospital in Mentakab.

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Khoo KL, Tan H, Liew YM et.al. Blood pressure, body mass index, heart rate and levels of blood cholesterol and glucose of volunteers during National Heart Weeks, 1995-1997. Med J Mal. 55:439-450 2000.

CONGENITAL AORTIC DEFECTS

Malformations of the aorta are not very often diagnosed. Coarctation the most well known was described first by Morgagni in the 18th century and successfully treated by Gross in 1945. In Malaysia, Saw, Grieve, Singham and Delikan reported a neonate successfully operated on in 1977.

Saw, Lim, Singh and Singham described three cases with aberrant arteries causing oesophageal constriction successfully treated surgically in 1979. Hoe, Chan and Robaayah described a patient with an aortic arch high in the neck associated with coarctation and Fallot's tetralogy in 1987.

References

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Hoe TS, Chan KC and Robaayah Z. The cervical aortic arch. Med.J.Mal. 42:90-92 1987.

AORTIC ANEURYSMS

Abdominal Aortic Aneurysms

Like other Asian countries, abdominal aortic aneurysms did not appear to be very common in Malaysia 30 to40 years ago, but collected series show an increasing number of cases. In 13 years from 1967 to 1980 only 53 patients were diagnosed to have aortic aneurysms in the University Hospital, KL. However, the availability of specialist surgical services probably did influences the detection rate of the disease. In a prospective review of 22 months from 1985 at University Kebangsaan Malaysia, Leong detected 55 patients. The same author reported a further 67 patients over 36 months from 1991 when in private practice. In GH KL,

over a 30 month period beginning 1993, Zainal and Yusha reported a prospective series of 124 cases. As the Vascular Surgical Unit became more established it collected more surgical experience. By the year 2000 over 200 abdominal aortic aneurysms had been surgically repaired at GH KL.

In the series reported in 1998 from GH KL, the median age of patients was 69 years and 85% were males. Malays formed 60% of patients. 27% of these patients were from the Klang valley, the rest came from other parts of Malaysia, including 13% from Sabah and Sarawak. Following Malays, Chinese formed 25% of patients and Ibans formed 7.3%. 34% of patients had associated hypertension and 18% had ischaemic heart disease, which is lower than what might be expected and diabetes melitus was present in less the 5% of patients. 47% of patients were admitted as emergency cases. Surgery was performed in 45% of all these patients. The mean diameter of the aneurysms operated on was 7cm. In 34 patients (61%) the operation was done electively and in the other 21 emergency surgery was performed. The operative mortality was 8.8% in elective surgery and 59% in emergency surgery.

Thoracic Aortic Aneurysms

Anuar and Singham have reported two patients with ascending aortic aneurysms due to cystic medial necrosis both of whom died. This is often the case with such patients and as such not much is reported. Thoracoabdominal aortic aneurysms accounted for just about 3% (7cases) in the surgical experience in GH KL between 1993 and 2000.

Pseudoaneurysms

A pseudoaneurysm or mycotic pseudoaneurysm, is a rupture of an artery, usually of a traumatic or infective origin which is contained within a haematoma and give the appearance of an aneurysm. Adeeb, Yusha and Samad reported an aortic pseudoaneurysm due to Salmonella in a 52 year old man with diabetes.

References

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Leong YP. Results of 50 consecutive aneurysmectomies for abdominal aortic aneurysms at a private specialist centre. Med.J.Mal. 50:330-333 1995.

Adeeb SJSM, Yusha AW and Samad SA. Primary repair with in-situ interposition graft for infrarenal mycotic aortic pseudoaneurysm. Med.J.Mal. 52:178-180 1997.

Zainal AA and Yusha AW. Profile of patients with abdominal aortic aneurysm referred to the Vascular Unit, Hospital Kuala Lumpur. Med.J.Mal. 53:423-427 1998.

ACUTE AORTIC OCCLUSION

Most commonly it is an embolus from the heart that causes an acute occlusion of the aorta, but in a few cases thrombosis or aortic dissection is the cause. Patients present gravely ill with painful paraperesis. In a 1 year series from GH KL in 1997 where 11 patients were seen, most had emboli but 2 had thrombosis of a small aortic aneurysm and 1 an aortic dissection. Their mean age was 58 years and 10 were male. 7 patients had underlying hypertension, 5 each had diabetes and ischaemic heart disease. 9 patients died, 6 after attempted balloon embolectomy. The 2 survivors had vascular reconstructive surgery.

Reference

Zainal AA, Oomen G, Chew LG and Yusha AW. Acute aortic occlusion: the need to be aware. Med J Mal. 55:29-32 2000.

The Cerebral Circulation

INTRACRANIAL VASCULAR MALFORMATIONS

Chee and Loh described a series of intracranial arterio-venous malformations (AVM) at the UH which included 16 cases in about 7 years before CT-scans became available and 18 cases in about 8 years after having CT-scans. This gave a hospital admission rate of AVMs of 11 and 8 per 100,000 admissions respectively. Consistent with reports elsewhere young (mean age 24 years) males (74%) were preponderant. Chinese seem to be commoner. 56% of the lesions seen were parietal and occipital which was unlike a report from Singapore. 21 patients presented with intracranial haemorrhages and 9 with epilepsy, the leading two symptoms.

Intracranial Aneurysms

It has been mentioned by some that in this region AVMs are a 4 to 10 times commoner as a cause of subarachnoid haemorrhage than aneurysms. Chee and Loh however disputed that in a series from the UH. They noted that of 84 cases with subarachnoid haemorrhages from 1979 to 1987, 20 were shown to have aneurysms while 7 only had AVMs. 36 patients did not have angiograms for diagnosis. Nevertheless, 80% of these were above 40 years old which would favour under reporting of aneurysms as none of their AVM patients were more than 41 years old.

Of 21 patients with aneurysms, 14 (67%) were female. The mean age was 45 years but ranged from 15 to 65 years. There were 3 giant aneurysms, all at the internal carotid artery. 14 patients had surgery among whom there were 6 deaths.

Mycotic aneurysms, meaning blood borne infective emboli, originally fungal, but now taken to mean bacterial emboli also that causes an aneurysm following focal arteritis from a very small percentage of intracranial vascular malformations. Cheah has described treating one case.

Moyamoya Disease

Moyamoya, a Japanese word meaning "puff of smoke" describes an abnormal network of collateral blood vessels in the region of the basal ganglia seen with stenosis or occlusion of the internal carotid bifrucation which gives a distinctive angiographic image. It was first described by Takenchi and Shimazu in Japan in 1957 but has since then been reported throughout East Asia. Ng WK *et.al.* documented 2 cases, in young Chinese males, in Malaysia and were aware of 2 more.

Spinal Arteriovenous Malformations

These are malformations also within the central nervous system but involving the spinal cord. 2 men presenting with transient paraperesis have been reported.

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Ng WK, Tan CT, George J, Lee MK and Loh TG. Moyamoya disease in Malaysia: two documented cases. Med.J.Mal. 50:186-188 1995.

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STROKES and T.I.A.

Strokes are sudden focal and at times global loss of brain function due to infarction of the

area of brain as a result of a haemorrhage, thrombus or embolus. When these vascular insults cause a loss that resolves completely without infarction within 24 hours the incident is called a transient ischaemic attack (TIA).

Second to coronary artery disease, strokes or cerebrovascular disease are the commonest cardiovascular cause of death. It rose from being 6.6% of all medically inspected death in 1975 to 8.9% in 1989. However like coronary artery disease the percentage of deaths from cerebrovascular disease did not continue to rise further in the 1990s and may have decreased a little. Women outnumber men by a ratio of 1.2 in respect to cerebrovascular deaths. In fact, the number of women dying of strokes outnumber the number of dying of coronary deaths.

Relatively little has been written about strokes in Malaysia considering the fact it is such a common disease. , Lim observed 131 cases, in a study of female stroke patients over a year at the Penang GH in 1983. The mean age of the women was 62 years and similar in all races. Chinese seemed to have the highest incidence, as seen in Singapore. They had a relative risk more than 2 times higher than Malays and 3 times higher than Indians. There were more hypertensives among Chinese.

The case fatality rate was 34% but of the fatal cases 60% of Malays and 40% of Chinese requested AOR discharge for the patients to die at home. This occurrence was not seen among Indians. Case fatality rose with age from 50 years upwards but young stroke patients, under 50 years had a mortality as high as those in the 70s.

Pratap and Mafauzy found that 73% of 100 patients with strokes and TIA in Kelantan had extracranial vascular abnormalities using continuous wave doppler ultrasound. 33% had evidence of obstruction of cerebral vessels below the neck. In 62% the carotid vessels were affected and in 35% the vertebro-basilar teritory was affected. 48% had multiple vessels involved. There were 65 males and 35 females in this series of consecutive patients. The common predisposing factors to cerebrovascular disease were hypertension (60%), smoking (39%) obesity (19%) and ischaemic heart disease (13%).

Risk Factors

In a series of 13 young patients (under 40 years in age) who had cerebral infarction, Vignaendra *et.al*. found that 2 had features of Moyamoya disease. Among 80 patients under the age of 50 years with strokes at the UH between 1982-1992, Lee *et.al*. found that 3 with anti-phospholipid antibodies, a recognised cause of ischaemic strokes. Only one of the 3 had active SLE.

References

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Pratap RC and Mafauzy M. Profile of extracranial cerebrovascular disease in Kelantan: a study by continuous wave Doppler ultrasonography. Med.J.Mal. 48:51-55 1993.

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SUBARACHNOID HAEMORRHAGE

A subarachnoid haemorrhage is similar to a haemorrhagic stroke but the bleeding occurs not into the brain substance but in the subarachnoid space. It is detected by finding uniformly blood stained fluid on lumbar puncture or nowadays by imaging blood in the subarachnoid space. Aneurysms and arteriovenous malformations are two important causes of subarachnoid haemorrhages. Besides these subarachnoid haemorrhage is labelled as of unknown origin.

Chee reported that 22(47%) of 47 patients with subarachnoid heamorrhage in UH between 1979 and 1987 who had angiography done had subarachnoid haemorrhage of unknown aetiology. There was however signs of vasospasm in 12 of these cases. Besides these 47 cases there were 41other patients suspected to have subarachnoid haemorrhage on clinical findings, in the hospital in that period excluded from that series. They did not have angiography as only those who were judged likely to need neurosurgery were subjected to the investigation.

Reference

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SUBDURAL HAEMATOMA

Chronic subdural haematomas usually present a few weeks or months after a head injury which may have been forgotten. Many will probably go undiagnosed. Any clinical series therefore will not reflect the true spectrum of its occurrence. Nevertheless Cheah and M Amin reported that in the experience at GH KL 50 cases were observed over 6 years from 1979. The peak age group was the fifth decade and 90% were males. Headache (69%) and a change in level of consciousness (50%) were the commonest presenting features. All their patients had the haematomas successfully evacuated through burr holes, most through just one. Most had good recovery but 4 were left severely disabled.

Reference

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The Limb Circulation

KASABACH-MERRIT SYNDROME

The Kasabach-Merrit syndrome includes a triad of vascular tumours, thrombocytopenia and haemorrhagic diasthesis. The vascular tumours are usually benign, but the coagulopathy may be life threatening. Ram has observed a case in a neonate with Down' syndrome in HUSM.

Reference

Ram SP. The Kasabach-Merrit syndrome and Down' syndrome. J R Soc Med. 90:159-160 1997.

OCCLUSIVE PERIPHERAL ARTERIAL DISEASE

Arterial disease was generally regarded as less common in Asia. For example, in 1988 the orthopaedic unit records in GH KL showed that vascular diseases accounted for only 10% of major lower limb amputations where as in the West they form the majority. The first vascular surgical unit in Malaysia, in KL GH received only about 150 cases in 2 years in the 1980s which represented only 0.8% of all general surgical cases in the period. However the prevalence of a problem often only becomes more apparent when a service to manage it becomes available. It remains to be seen how great is the need for vascular surgery.

Embolism

Leong and Sahabudin reported on a prospective of study of 40 cases of acute limb ischaemia due to embolism seen over 3½ years from 1986. Many patients presented or were referred late and the over all mortality (50%) was high. 25 embolectomies were performed but only 10 patients were discharged well with their limbs intact. 50% of their patients were smokers. Ischaemic heart disease (43%), diabetes (28%) and other associated disease were common. The source of the embolus was

not known in about half the cases. In one quarter there was atrial fibrillation and in another quarter there was mural thrombus from a myocardial infarction or rheumatic heart disease.

Atherosclerotic

Leong noted that the vascular surgery unit in GH KL in 1989, saw about 3 times as many chronic limb ischaemias compared to acute ones. The small number of such cases may only reflect the pattern of disease presentation and referral. Many patients with chronic limb ischaemias present at peripheral hospitals only when gangrene has set in and receive an amputation there. Such cases are common although their incidence not known.

Arteritis

Leong mentioned that about 10% (5) of patients with chronic limb ischaemias in his series had Buergers' thromboangiitis obliterans. They ranged from 25 to 44 years and were all males and heavy smokers. He made a diagnosis of Takayasu's disease in a similar number of cases. One woman had chronic peripheral limb ischaemia. 4 others showed aortitis and renal artery involvement on angiography for investigation of hypertension. They had no limb ischaemia. Giant cell arteritis is not uncommon in Malaysia and has been reported.

References

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PSEUDOANEURYSMS

Intravenous drug users often cause themselves infected pseudoaneurysms from inadvertent injection of an artery with contaminated needles and adulterated drugs and failure to apply direct pressure on the artery after that. In 3 years from 1993, Zainal and Yusha surgically managed 54 such patients, 53 of them males, in the KL GH. 82% of them were between 25-44 years old. 57% of them were Chinese. 39% of them were infected with HIV. The femoral/iliac artery at the groin was most commonly affected (93%). The remainder were affected in the brachial. In one-third of patients, culture grew *Staphylococcus aureus*, in another one-third Gram negative organism or mixed growth was obtained, and in the remainder microbial culture of the clot was not done. All patients underwent artery ligation and debridement. Four patients required amputations, two of whom already had non-viable limbs on admission.

Reference

Zainal AA and Yusha AW. A 3-year audit of infected pseudoaneurysms in intravenous drug users managed surgically in the Vascular Unit, Hospital Kuala Lumpur. Med.J.Mal. 53:372-375 1998.

DEEP VEIN THROMBOSIS

Deep vein thrombosis (DVT) following surgery is very common in Western countries and been reported to occur in 20-40% in most studies. It has been uncommon in Malaysia as in other parts of Asia. Cunningham and Yong, in a study of 68 patients in the University Hospital KL using 125 I-labelled fibrinogen in post-operative surgical patients found deep vein thrombosis in 8 (12%). Indirect evidence that it was uncommon comes also from the fact that death from massive pulmonary embolism was thought to be rare. Hwang found only 29 cases of pulmonary embolism in over 36,000 consecutive necropsies in Singapore from 1952-1966. He noted that out of 52,861 major operations in

the Singapore GH over 5 years there were only 5 cases of pulmonary embolism.

In a retrospective survey of 10 years, from 1977, at the UH, Liam and Ng found 81 cases with DVT. The incidence of clinically apparent DVT following surgery was 2.1%. Symptomatic pulmonary embolism occurred in 13.6% of the cases of DVT.

In 1996, Dhillon et.al. reported rather different result in 88 post-operative patients who had no prophylaxis against DVT. They found 62.5% of their patients showed venographic evidence of DVT. Their patient however, had all undergone orthopaedic surgery. They found the highest rates in patients after total knee replacement (76.5%) followed by total hip replacement (64.3%) and the fracture group (50%).

Deep vein thrombosis in the puerperium has been quoted to occur in 0.09 to 0.27 percent of all deliveries in the USA. Maternal death due to pulmonary embolism occurred in 1 per 28,000 deliveries in England and Wales between 1958 to 1966. Wong and Teoh reported 4 cases of deep vein thrombosis in pregnancy from the UH over a 2 year period during which there were 8,000 deliveries giving an incidence of 1 in 2,000 (0.05%). Liam and Ng reported a pregnancy related incidence of DVT of 0.39% over 10 years from 1977 at the UH noting that it was 3 times more frequent in the puerperium than in the antenatal period.

Ramanathan, Yong, Wang and Loh have reported 3 cases of deep vein thrombosis which happened `out of the blue' among adults.

Other Phelobothromboses

Occlusion of the hepatic vein (Budd-Chiari syndrome) and portal vein are rare entities worldwide. Lee *et.al.* have diagnosed portal vein thrombosis in one 27 year old Indian woman initially thought to have tropical splenomegaly. Tay and Leong have reported a case of mesenteric venous thrombosis in a diabetic.

Segasothy has described a case of sagital sinus and inferior vena cava thrombophlebitis in a young woman with Behcet's syndrome.

References

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Tay SKS and Leong YP. Primary mesenteric venous thrombosis - a case report. Med.J.Mal. 44:171-173 1989.

Lee SM, Wong NW and Rathakrishnan V. Are we missing portal vein thrombosis? Sing.Med.J. 30:388-389 1989.

Liam CK and Ng SC. A review of patients with deep vein thrombosis diagnosed at University Hospital, Kuala Lumpur. Ann Acad Med Sing 19:837-840 1990.

Dhillon KS, Askander A and Doraisamy S. Postoperative deep-vein thrombosis in Asian patients is not a rarity: a prospective study of 88 patients with no prophylaxis. J Bone Joint Surg 78:427-430 1996.

PRIMARY LYMPHANGIOMYOMATOSIS

This rare disease, also termed lymphangioleiomyomatosis, has been reported twice from UKM close together in time. Raymond *et.al*. reported the case of a 41 year old Malay woman in 1993. Diagnosis was established at laparotomy and she was subsequently managed with dietary fat restriction and medium chain triglycerides. Abdul-Rahman and colleagues reported another case in a 36-year-old Indian lady in 1994. It is postulated that these benign cystic tumours of lymph channels are harmartomatous proliferations of atypical

smooth muscles. It seems to occur exclusively in women. The second case had a cystic hygroma removed at 9 years and further lymphangiomatous left supraclavicular cyst in adulthood. She also had abdominal pain, chylous ascites, numerous mesenteric, liver and splenic cysts and underwent laparotomy 4 times at different hospitals, including operations to insert and remove peritoeovenous and pleuroperitoneal shunts.

References

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Abdul-Rahman I, Tay SKS, Meah FE and Abdullah T. Primary lymphangiomyomatosis with chylous ascites. Med.J.Mal. 49:179-181 1994.

Zulfiqar MA, Zaleha AM, Zakaria Z and Amin T. The treatment of neck lymphangioma with intralesional injection of bleomycin. Med J Mal. 54:478-481 1999.

OTHER VISCERAL LYMPHATIC DISORDERS

Intestinal lymphangiectasia: Paediatricians at UH have reported 3 Chinese children with intestinal lymphangiectasia. 2 children responded to low fat diet and medium-chain triglyceride supplement, one had recurrent chylous ascites.

Neonatal chylous ascites: or Congenital Chylous Ascites. Again 3 cases of this detected as fetal ascites by antenatal ultrasonography in the UH have been reported. They were managed by dietary measures as before. 2 infants were well when reviewed more than a year later. One child had gut malrotation and a pyloric septum. He died from complications after a laparotomy.

References

Chye JK, Lim CT and Van der Heuvel M. Neonatal chylous ascites - report of three cases and review of the literature. Pediatr Surg Int 12:296-298 1997.

Lee WS, Boey CC, Goh AY et.al. Intestinal lymphangiectasia - report of three Chinese children in Malaysia. Sing Med J 39:418-421 1998.

IDIOPATHIC OEDEMA

Ramanathan has written one case report of this condition, marked by a large diurnal alteration of weight (1.8kg) as a result of orthostatic retention of sodium and water.

Reference

Ramanathan M. Idiopathic oedema: a lesson in differential diagnosis. Med.J.Mal. 49:285-288 1994.

CHAPTER 27

THE RESPIRATORY SYSTEM

Respiratory diseases are one of the leading causes of attendance at a medical clinics in Malaysia. They account for about 25% of all new attendances at government medical facilities. Respiratory diseases account for just over 5% of admissions of MOH hospital and of all medically certified deaths. The main respiratory diseases are infections, which include tuberculosis.

NORMAL LUNG FUNCTION

Surveying 103 healthy working males and 34 females, who were mostly student nurses in 1968, Chan and Raman found that in Malaysia lung vital capacity was correlated to height, weight and age, but best correlated with body surface area. The mean vital capacity was smaller than Western values but did not differ when the smaller body size is accounted for. There was no difference between Malays, Chinese and Indians. There was also no difference between Malaysian males and females when body size is accounted for.

Predicted normal value equations for Forced Vital Capacity (FVC) among Malaysian adults was calculated from 2,000 healthy subjects by USM workers in Kelantan. They are given in Table 27.1 below. Ismail and Zurkurnian however recorded lower spirometry values for Malay subjects between 15-75 years even when height was accounted for. It should be appreciated that these predictive values and those below have not been extensively validated and are the results of single studies.

Duncan *et.al.* studied lung function in a small sample of 13 young Malay male adults during Ramadan, the fasting month, and found that water deprivation did not cause significant changes to ventilatory function.

Table 27.1 Predicted Normal Forced Vital Capacity among Malaysian Adults

Males: FVC (lits) = 0.0407Ht - 0.0296Age - 2.343
Females: FVC (lits) = 0.031Ht - 0.022Age - 1.64
in this and all equations below Height(Ht) = in cm and Age = in years

Children

Measuring peak expiratory flow rate (PEFR) in 1,020 recordings of children to establish normal standards, Azizi and Henry found that slightly lower values for local children than Caucasian counterparts. Malaysian girls had a 10-20% lower value than white Americans while boys up to a height of 115 cm had similar values to white Americans but had an increasingly prominent lower value as height increased. Malaysian boys had higher PEFR value than girls. They reported in 1994 that Chinese children had generally higher forced expiratory volume in 1 sec (FEV1), FVC and forced expiration flow between 25-75% of vital capacity (FEF 25-75) values than Malay and Indian children. Indian children consistently had the lowest lung function values.

Ismail, Azmi and Zurkurnain reported lower PERF, FVC and FEV1 in Malay children compared to Caucasian or Chinese counterparts. The predicted indices for these parameters they formulated are given in Table 27.2 below. Dugdale similarly found lower lung function indices in Orang Asli children.

Azizi and Henry have noted that children sharing the same room with adult smokers had a significantly lower than normal FEF 25-75. Exposure to kerosene stoves was associated with

a significantly lower FVC and FEV1.

Table 27.2 Predicted Lung Function Indices for Malaysian Children

	Index	Prediction Formula	R
Boys:	PEFR =	15.14Age + 1.5Ht - 88.54	0.71
	FVC =	0.021Ht - 1.503	0.66
	FEV1 =	0.02Ht - 1.67	0.52
Girls:	PEFR =	4.34Age + 3.31Ht - 226.71	0.74
	FVC =	0.02Ht - 1.45	0.63
	FEV1 =	0.23Ht - 2.021	0.71

R=correlation

The Elderly

UH workers have surveyed 1,414 healthy ambulatory elderly persons aged 55 years and above from Kuala Langat, Selangor. The PEFR was lower in women compared to men of similar ages. The PEFR declined with age for both men and women. Men who had smoked had a significantly lower PEFR compared to men who had not. Respiratory symptoms like cough, wheeze and phlegm were related to lower PEFR values. They produced a predictive PEFR equation given in Table 27.3

Table 27.3 Predicted PEFR for Elderly Malaysians

Men:	PERF = 345 – 3.9Age + 59(COPD) +1.56Ht – 14(smoking)	multiple $r^2 = 0.22$
Women:	PEFR = 264.6 – 3.9Age + 59(COPD) + 1.56Ht – 14 (smoking)	

Chronic Obstructive Pulmonary Disease (COPD) present = 0, absent =1
Smoking never = 0, ever = 1

OBSTRUCTIVE SLEEP APNOEA

Snoring was for many years, never considered a serious pathological problem. The hazards of obstructive sleep apnoea was only recently recognised with the advent of pulse oximeters that documented the reduction of oxygen saturation during poor sleep. On hind sight, the link between excessive daytime drowsiness and snoring could have been made by any keen observer.

Liam, How and Tan reported 3 cases of drivers involved in accidents who had the problem and benefited from treatment with CPAP (continuous positive airway pressure). It is obvious the condition is under-recognised. Awareness of its presence ought to be heightened in view of the potential treating it has on accident prevention and possibly reducing cardiovascular deaths.

Reference

Liam CK, How LG and Tan CT. Road traffic accidents in patients with obstructive sleep apnoea. Med.J.Mal. 51:143-145 1996.

PERENNIAL RHINITIS

Perennial or chronic rhinitis is a common problem accounting for about a third of patients at Ear, Nose and Throat clinics and perhaps 1 in 20-30 patients seen in general practice. Some times, in our context it is labelled as tropical rhinitis. In Kelantan, using the international study of asthma and allergies in childhood (ISAAC) questionnaire on 7,055 children, Quah found a prevalence of rhinits to be 18% in 5-7 year olds and 38% in 12-14 year olds in 1995.

In reports from UH, Gnanapragasam and Werner did not separate allergic and non-allergic (vasomotor) cases. They reported that males were twice as often affected than females and Chinese were predominant, although this may be due to the population the hospital serves. Most patients were young adults, the peak being the 21-30 years age group. Among 774 patients with perennial rhinitis seen at the UKM, Imran and Hamimah reported in 1983 that the commonest allergens were the house dust mite, *D. pteronyssinus* (52%), house dust (43%) and shrimp (24%). Moderately common were egg (18%), crab (16%), cat fur (13%) and dog fur (11%).

In Kelantan, Elango *et.al.*. found, that most people were sensitive to more than 2 allergens and the commonest allergens were cat fur (77%), poultry feathers (77%), house dust mite *D. pteronyssinus* (75%) and crabs (60%). Grass pollen a common allergen in the West featured in only 18% of their cases. Less than 5% of their cases with perennial rhinitis had vasomotor rhinitis.

Ho *et.al.* in a series of 314 patients from KL GH reported in 1995 found that 68% were allergic to 4 or more allergens by a prick test. The commonest allergens were cat fur (73%), dog hair (41%), mixed mould (26%) and mixed grass pollen (24%).

Studies on the distribution of house dust mites which are important not only in rhinitis but also in bronchial asthma show that they are universally present in Malaysia. Even in new land schemes within a few years nearly all households have the mite and they are no less present in the highlands. *D. pteronyssinus* is the commonest mite but over 30 species were found.

References

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Elango S, Purohit GN, Gan SC, Zahara M and Hilmi R. A study on perennial rhinitis in Kelantan. Med.J.Mal. 44:231-235 1989.

Duncan MT, Husain R Raman A et.al. Ventilatory function in Malay Muslims during normal activity and the Ramadan fast. Sing.Med.J. 31:543-547 1990.

Ho TM, Shahnaz M, Radha K, Singaram SP. Prevalence of alley to some inhalents among rhinitis patients in Malaysia. As. Pacific J. Allergy and Immunology. 13:11-16 1995.

Quah BS, Razak AR and Hassan MH. Prevalence of asthma, rhinitis and eczema among schoolchildren in Kelantan, Malaysia. Acta Paediatr Jpn 39:329-335 1997.

BRANCHIAL POUCH CYSTS

Sharma *et.al*. have reported a neonate presenting on the third day of life with a rare fourth branchial pouch cyst causing respiratory obstruction and stridor that required surgical excision.

Reference

Sharma HS, Razif A, Hamzah M et.al. Fourth branchial pouch cyst: an unusual cause of neonatal stridor. Int J Pediatr Otorhinolarnygol 38:155-161 1996.

LARYNGEAL CYSTS

Benign retention cysts in the larynx are very infrequent medical problems and are not dangerous. Over 8 years Singh and Prasad treated 8 cases surgically.

Reference

Singh AP and Prasad U. Clinical study of larnygeal cysts. Med.J.Mal. 37:223-226 1982.

LARYNGEAL INTUBATION TRAUMA

There have been two reports in 1976 of iatrogenic laryngeal problems due to intubation probably with the old red-rubber tubes where the balloon cuffs were not of a fixed volume. Liew reported a case of stenosis while Chin and Khanna had two cases with laryngeal granulomas.

References

Liew PC. Glottic and subglottic stenosis following intubation during surgery. Med.J.Mal. 30:241-242 1976.

Chin YH and Khanna DK. Granuloma of the larynx following intubation. Med.J.Mal. 30:319-320 1976.

RESPIRATORY INFECTIONS

Respiratory infections are the commonest infections acquired. It is estimated that about 37% of patients seen in general practice in Malaysia are on account of respiratory infections. They can usually be clinically divided into upper respiratory tract (URTI), tracheitis down to bronchiolitis and pneumonias. For practical purposes they are also divided into community acquired ones, recurrent ones, debilitated host infections, and hospital acquired ones. This classification helps guide the choice of antibiotic therapy. In a large community based survey of acute childhood respiratory infections (ARI) Lye *et.al*. reported that 30% of children below 7 years experienced an episode of ARI in the preceding 2 weeks. 5% of the infections were judged severe. They noted, however, a lack of concurrence of the perception of severity of the illness between the mother and the investigators.

In a general practice setting in KL, Ong, Thong and Tay attempted to diagnose the aetiologic agent in 65 children with URTI to bronchiolitis during a 10 month period in 1974. Viruses were isolated in 40%, bacteria in 15% and both together in 8%. The screening they did for infective agents however did not include mycoplasma, cytomegalovirus and picornavirus among others. The influenza and parainfluenza viruses were the commonest and the commonest bacteria were *Haemophilus* and *Strep. pneumoniae*. From paediatric in-patients in the UH Ong found that 29% of children with respiratory infections had viruses.

In one report of childhood pneumonias, Kumaradeva observed in 1967 that children under one year were prone to right upper lobe pneumonia and felt that inhalation of matter in the supine position was the cause. Azizi and Henry have reported that kerosene and wood stoves, mosquito coils and vapour mats and aerosol insecticides were not associated with an increased rate of childhood respiratory infections, but sharing a bedroom with an adult smoker and bedroom crowding (more than 3 people) were. Breast feeding was found to be a protective factor.

References

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Azizi BH and Henry RL. The effect of indoor environmental factors on respiratory illness in primary school children in Kuala Lumpur. Int J. Epidemiol 20:144-150 1991.

Lye MS, Deavi U, Lai KP et.al. Acute respiratory infection in Malaysian children. J Trop Pediatr 40:334-340 1994.

Azizi BH, Zulkifli HI and Kasim MS. Protective and risk factors for acute respiratory infection in hospitalised urban Malaysian children: a case control study. Southeast Asian J Trop.Med.Pub.Hlth. 26:280-285 1995

LUNG ABSCESS

Yaacob and Ariffin observed 13 cases of lung abscesses in HUSM over a 5 year period from

1984 to 1989. Patients ranged in age from 16-68 years and males and females were almost equally affected. 8 patients had underlying predisposing factors such as pneumonia, chronic obstructive airway disease, bronchiectasis, lung cancer, diabetes and nephritic syndrome. Sputum bacteriology was obtained in 4 cases. *Staphylococcus aureus* was grown in 2 cases and *Haemophilus influenzae* and *Klebsiella pneumonia* in one each. Prior antibiotic therapy, poor specimen collection and culture, especially for anaerobes probably accounted for the low rate of positive cultures. 12 patients were treated only with antibacterials, and one had therapeutic aspiration of the pus. There was only one fatality in the series.

Reference

Ismail Y and Ariffin Z. Empyema thoracis and lung abscess. Sing Med J. 32:63-66 1991.

INHALED FOREIGN BODIES

Shanmugham at the UH found 22 cases, all children, admitted for the removal of inhaled solid matter from 1970 to 1980. Their ages ranged from 7 months to 5 years, but 74% were between 1 and 2 years old. There were 16 boy and 6 girls. Most belonged to low income families. 81% had stridor. 3 did not actually give a history of having inhaled the object. A peanut was the offending object in 10 cases, and a watermelon seed in 4. In 19 children the foreign body was retrieved at bronchoscopy. 9 were from the right main bronchus, 8 from the trachea and 2 from the left main bronchus. One required a right thoracotomy, one coughed up the object after a tracheostomy and in one it was not found. 8 children had post-operative complications and one died of bronchopneumonia.

Yip, Wong and Somamsundram reported an overlapping series of 40 cases from the UH covering the years 1973 to 1982. Their findings were similar.

Razi Hadi, Said and Kartini at the UKM reported 16 cases between 1983 and 1987. Again children, mainly toddlers were the patients, and peanuts were the commonest objects. Like the UH experience just over half the foreign bodies were retrieved from the right main bronchus. One boy needed a thoracotomy but the rest were successfully saved with bronchoscopy.

Indudharan has also reported 3 cases, under 2 years old, from HUSM Kelantan with food particles in the tracheobronchial tree requiring bronchoscopy. Sharma reported 2 children under 2 years old seen at HUSM with subglottic laryngeal impaction of a foreign body which resulted from attempts to remove the foreign body by blind finger sweeping.

A. Rahim reported an unusual case of a 1.5 cm. metal nut removed from an adult in Seremban.

References

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Razi Hadi A, Said H and Kartini A. Foreign bodies in the laryngotracheobronchial tree. Med.J.Mal. 43:74-83 1988.

Yip CH, Wong TJ and Somasundaram K. Foreign bodies in the larynx and tracheo-bronchial tree. Med.J.Mal. 43:150-154 1988.

Indudharan R, Ram SP and Sidek DS. Tracheobronchial foreign bodies in relation to feeding practices in young children. J Accide Emerg Med. 14: 341-345 1997

Sharma HS and Sharma S. Management of laryngeal foreign bodies in children. J Accid Emerg Med 16:150-153 1999.

BRONCHOPULMONARY DYSPLASIA

Bronchopulmonary dysplasia or hyaline membrane disease has become the most common cause of death among preterm infants in Malaysia. It can be a very challenging battle for

paediatricians trying to save very premature babies. Its incidence is a function of the number of premature deliveries and we can only guess at the number in Malaysia. As reiterated in a case report by Sivarajah *et.al.*, the only hope of success in managing such babies is in patient long-term ventilatory support where necessary.

An observational study of 209 infant born after less than 34 weeks of gestation over 8 months from December 1994, in the KL Maternity Hospital showed that those mother who received a course of antenatal steroids had babies who were less likely to develop the respiratory distress syndrome.

References

Sivarajah RS, Koh MT, Tan P, Ooi SE and Ong G. Long-term ventilatory support in an infant with broncho-pulmonary dysplasia. A case report. Med.J.Mal. 39:88-91 1984.

Boo NY. Outcome of very low birthweight neonates in a developing country: experience from a large Malaysian materinty hospital. Sing.Med.J. 33:33-37 1992.

Umathevi P, Boo NY and Lim NL. Antenatal steroids reduced the risk of respiratory distress syndrome in Malaysian preterm infants of gestation less than 34 weeks. Med.J.Mal. 53:144-152 1998.

CYSTIC FIBROSIS

Cystic fibrosis is an autosomal recessive disease due to a gene located on chromosome 7. The defective gene causes a defect in the cystic fibrosis transmembrane regulator (CFTR) protein. It produces an abnormal chloride ion membrane transport especially in the airway epithelial membrane. This predisposes the individual to chronic airway infection by certain bacteria. Cystic fibrosis is detected in approximately 1 in 2,500 livebirths among Caucasians, but 30-40 times less frequently among Asians. Norzila and Azizi have reported the disease occurring in 3 Malay children.

Reference

Norzila MZ and Azizi BH. Cystic fibrosis in Malay children - a report of 3 cases. Sing Med.J. 37:273-274 1996..

BRONCHIAL ASTHMA

Bronchial asthma is one if the commonest respiratory disabilities in Malaysia as it is in many countries. A few studies from the UKM from 1976 using the American Thoracic Society criteria found males slightly outnumbering females. Chinese were slightly under-represented. In 38% the illness started before the age of 10 years and in 89% before the age of 40 years. A family history was obtained in half the patients. A history of allergy was noted in 81% and rhinitis in 52%. Hooi also noted that asthma was more common among Malays than other races in the Balik Pulau area in Penang.

In a survey of primary school children in KL, Omar noted that the prevalence of persistent wheeze and doctor-diagnosed asthma was 8% and 8.7% respectively. The prevalence of asthma (defined as persistent wheeze and/or doctor diagnosed asthma) was 14%. A study in a rural padi farming area in Selangor in 1991 recorded a prevalence rate of bronchial asthma of 6.2% among children under 12 years. As reported earlier boys had a higher prevalence rate and it was more common among the older children. They found no relationship between asthma and chronic respiratory disease, exposure to cigarette smoke, wood stoves or mosquito coils. Azizi *et.al*. reported however in 1995 that sharing a bedroom with an adult smoker and exposure to mosquito coils at least 3 night a week were risk factors. They found that wood and kerosene stoves and aerosol mosquito repellents were not risk factors.

In Kelantan using the international study of asthma and allergies in childhood (ISAAC) questionnaire on 7,055 children, Quah found a prevalence of 'ever diagnosed with asthma' of 9.4% in 1995. Ismail and Elangi noted that 65% of adult asthmatics had associated rhinitis that usually started within 2 years of one another.

Allergens

In the earlier studies, besides allergens and rhinitis which acted as triggering factors for bronchial asthma, other triggers were infection (50%), the weather (42%), exercise (41%) and emotions (20%). Studying patients in Kuantan, Lim *et.al.* found that the ambient temperature was associated with attacks of asthma, the lower the temperature the more the cases seen in hospital. However there was no association with other factors such as rainfall, humidity and daily drop in temperature. Allergens found on skin testing by Zulkifli and Chen in 74 patients at the UKM were, house dust (81%), the house dust mite, *D. pteronyssinus* (75%), cat fur (35%), grass pollen (32%) and shrimp (19%). Sam *et.al*. in the UH also reported that 80% of asthmatics reacted to house dust mites, 43.5% to cockroach and 21.5% to grass pollen. In USM Kelantan, Ismail reported that the commonest allergens found on skin testing asthmatics were the house dust mite (70%), cotton (67%), kapok (60%), aspergillus (54%) and shellfish (46%).

Management Audit

Patients with asthma are frequently put on inhalers which they need to know how to use properly. Unfortunately, incorrect usage is common. In one survey, Zainudin and Sufarlan found that as many as 62% of patients at a clinic were not able to use the inhaler properly. 43% made more than one error.

In an audit of 70 asthmatic patients seen in 2 district hospital in Pahang recruited in a 3 month period from December 1990, Lim *et.al*. noted that patients were prescribed an average of 2 items of drugs, most of which comprised an oral beta agonist and a theophylline. Only 43% received inhaler therapy. 77% took daily medication regularly. However 86% had sleep disturbed by asthma, 63% felt their activities restricted by asthma, 40% had a PEFR below 50% predicted (but only 8.5% of the patients ever had their PEFR recorded).

Hooi and Yew reported an audit of 62 patients seen in an Asthma clinic in the Balik Pulau District Hospital. These were patients who had been seen for more the 6 months over 6 years up to 1994. When first seen most patients were on oral beta2 agonists or oral theophylline. 17.7% were on inhaled steroids. 84% had severe asthma. At last follow up all but one were on inhaled beta2agoints, and all but one on inhaled corticosteroids. In addition 65% were on oral theophylline. Their average PEFR improved from 67% when first seen to 78% recorded in the last 3 months of follow-up. The proportion of patients requiring hospital admission in one year dropped from 49% to 7.3%. Emergency use of nebulised bronchodilators and time of work also decreased.

Looking at management of acute asthma in the hospital emergency room in HUSM in Kelantan, Yaacob noted that there were two peak periods during a day, which was between 8 pm till midnight and between 6 to 10am. This may however be affected by not only by the time of onset of an attack but by at what hour patients feel it appropriate to go to hospital. In a 3 month period 271 visits were made by 212 patients. 11% of patients were admitted to hospital. However 5% (13/240)of those discharged from the emergency room relapsed within 24 hours.

In a 1993 study of 75 adult asthmatic in remission Yaacob and Mohammad found that 92% did not achieve normal values in spirometric tests. In reviewing a series of radiographs of asthmatics, Zulkifli and Kamal found that 67% were normal, 20% showed overinflation and 8% had 'tramline' shadows.

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Sam CK, Soon SC, Liam CK et.al. An investigation of aeroallergens affecting urban Malaysian asthmatics. Asian Pac J Allergy Immunol 16:17-20 1998.

DIFFUSE PANBRONCHIOLITIS

Diffuse panbronchiolitis was first described by Yamanaka in Japan in 1969. It is characterised by chronic small airway obstruction due to inflamation of the terminal and respiratory bronchioles. It occurs in the Orient but is rare in America and Europe. Zainudin *et.al*. reported 3 cases locally, one of whom was confirmed histologically by transbronchial lung biopsy. The other two were diagnosed on the bases of radiological features. Two patients were Chinese, one Malay.

Reference

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BRONCHIOLITIS OBLITERANS

Bronchiolitis obliterans is an uncommon sequelae of acute bronchiolitis which is characterised by chronic respiratory obstruction not responsive to bronchodilator therapy. Failure to thrive is common in such children. The adenovirus is most often the organism incriminated instead of the respiratory syncytial virus the more common respiratory pathogen. Azizi and Akashah at the UKM have reported a small series of 6 such children seen over 8 years. Only in one child was an infective agent found, which was the adenovirus. Although the illnesses were prolonged, the long term prognosis was satisfactory in the majority of cases. Lung function and general health improved over four to eight years. In another report, Chan *et.al*. found that there was a viral aetiology in 6/14(43%) of their cases and mycoplasma was the cause in a further 3/14(21%).

The **Swyer-James-MacCleod syndrome** is a rare sequelae of respiratory infection occurring in early childhood which is considered to be similar to bronchiolitis obliterans but it happens unilaterally. There is unilateral loss in lung volume, lung vascularity and lung perfusion. Chan *et.al*. reported 2 cases from the UH in 1999.

References

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Chan PW, DeBruyne JA, Goh AY and Muridan R. Swyer-James-MacCleod syndrome. Med J Mal. 54:520-522 1999.

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EMPHYSEMA

Menon, Vaterlaws and Cheok noted that in a chest clinic at the UH, over 5 years, 85 patients satisfied clinical, radiological and lung function criteria for diagnosis of emphysema. Most of the patients (63%) were between 50 and 69 years and 87% were male. There were 3.5 times as many Chinese as the other races. 94% admitted to smoking.

The disease appeared diffuse radiologically in 42% and signs of old tuberculosis were seen in 22%. Only 19% presented solely with emphysema, while 81% had chronic bronchitis. None of the patients had evidence of severe α1-antitrypsin deficiency, and only one presented with lower zone emphysema of early onset.

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PNEUMOCONIOSIS - ENVIRONMENTAL LUNG DISEASES

It should not be forgotten that industrial disease such as the pneumoconioses are notifiable diseases under the Factories and Machinery Act of 1967.

Asbestosis

Asbestos has been fairly widely used in construction in Malaysia for its heat resistance and insulation properties as in many countries. Asbestos is a generic term for naturally occurring fibrous mineral substances which include two main groups, serpentine (eg. Chrysotiles) and amphiboles (eg. Crocidolite). Having searched the medical literature and SOCSO records and found no previous cases, Lim *et.al*. reported what they believed were the first 2 cases of asbestosis in 1999. Both were Malay men, one 54 years and one 55 years old. Both had worked from the mid 1960s in a factory manufacturing asbestos cement pipes and building materials.

Rice Millers' syndrome

In 1984, Lim and colleagues did a case control study on 122 male rice mill workers and 42 controls. They documented findings that suggest a distinct syndrome associated to exposure to rice husk dust. This included allergic responses such as nasal catarrh, chest tightness, asthma and eosinophilia, with radiological opacities in the chest, probably representing early silicosis or extrinsic alveolitis. In addition subjects had chronic irritant effects affecting the eyes and skin. USM workers in Kelantan documented similar problems in 69 rice mill workers. Their lung function tests reveal some impairment and 35% complained of chest tightness.

Portland cement

UPM workers have investigated the lung function of workers in a Portland cement factory in Rawang. They noted dust levels exceeding $3000\mu g/m^3$ for fine dust and $5000\mu g/m^3$ for total dust in the environment. They recorded lower spirometric values for workers exposed to the dust but did not correlate the duration they have worked there with lung function.

Siderosis

Welder's pulmonary siderosis was first described by Doig and McLaughlin in 1936. It results from inhaled iron oxide and is a benign condition not associated with respiratory symptoms and does not lead to fibrosis. Lim and Liam reported a case in a 33 year old man on routine chest radiograph who had been an arc welder for 14 years. His Xray had diffuse ill defined small nodules in both lower lobes but he was asymptomatic and had no respiratory disfunction.

Silicosis

Malaysia may not be noted for its quarrying industry but silicosis is probably the most important occupational lung disease in Malaysia. In 1977 Singh showed in a study of 226 workers in 7 government granite quarries that the prevalence of silicosis was 33%. The prevalence of tuberculosis and silicotubeculosis was 11% which was more than twice the national prevalence. 96% of silicosis occurred in workers with more than 10 years exposure.

Among tombstone makers, Singh and Jorgensen found a slightly higher prevalence of 36%. 80% of the workers with more than 15 years exposure were affected while only 11% with less than 5 years exposure were affected. 17% suffered from tuberculosis. Anandan has reported a case of a 51 year of Chinese patient with scleroderma and pulmonary silicosis after 8 years of exposure to silica.

Stannosis

One would expect with Malaysia's tin industry that there might be a considerable amount of lung disease from stannosis. But stannosis appears to be a rather benign condition. Dicken and Scott surveyed workers in a tin smelting plant found 12 cases of stannosis by means of chest radiographs. 8 of these were among the 120 workers still employed in tin smelting. They suffered no disability despite having stannosis radiologically. It was established that cassiterite dust (particles >5 μm) was not the cause but it was 'tin fumes' (particle mainly <5 μm) that produced the stannosis.

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PULMONARY EOSINOPHILIA

Pulmonary eosinophilia is a syndrome that develops in certain individuals infected with lymphatic filarial species. It has chiefly been reported from India where it was first described in 1940 by Frimodt-Moller and Barton. In Malaysia, Danaraj described 8 illustrative cases in 1947. Cases have also been reported from Sabah by Barclay in 1966. In our local context, worms such as filariasis and ascaris have been highlighted as the cause of tropical pulmonary eosinophilia, but like others, Schacher and Danaraj failed to show any

association between intestinal helminthiases and pulmonary eosinophilia in 1960. Other cases may also be due to fungi such as *Aspergilus*, or to various drugs or may be idiopathic.

Tropical pulmonary eosinophilia may present late with cor pulmonale (central cyanosis, finger clubbing, tachypnoea, elevated jugular venous pressure, hepatosplenomegaly, cardiomegaly, right pleural effusion) as illustrated in the case of a 9 year old Malay girl by Quah *et.al*. She had antibodies to filarial and responded promptly to treatment with diethylcarbamazine. Late stage pulmonary eosinophilia results in interstitial pulmonary fibrosis probably led to right heart failure.

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FIBROSING ALVEOLITIS

Cryptogenic fibrosing alveolitis is an uncommon progressive inflamation of the alveolar wall leading to fibrosis. Liaw described a case involving a 20 year old Kadazan in Kota Kinabalu who had a fatal outcome.

Reference

Liaw KF. A case of cryptogenic fibrosing alveolitis. The Family Practitioner. 8:71-73 1985.

IDIOPATHIC INTERSTITIAL LUNG DISEASE

Interstitial lung diseases are conditions where the alveolar walls and perialveolar tissue are involved with chronic inflammation which eventually result in interstitial fibrosis. Paediatricians in UKM reported their experience with four cases of this rare disease who presented in early infancy with failure to thrive, cough, cyanosis and respiratory distress.

Reference

Norzila MZ, Azizi BO, Deng CT and Zulfiqar A. Interstitial lung disease in children - a report of four cases. Med.J.Mal. 52:429-432 1997.

IDIOPATHIC PULMONARY HAEMOSIDEROSIS (IPH)

IPH is a rare clinical entity often presenting with haemoptysis due to recurrent episodes of diffuse alveolar haemorrhage that results from deposition of haemosiderin iron in the alveoli. It leads to pulmonary fibrosis. Patients also have iron deficiency anaemia. The aetiology could be toxic or immunological but is still obscure. It has been reported in one young East Malaysian female.

Reference

Hanip MR, Isa MR, Zainudin BM. Idiopathic pulmonary fibrosis occurring in a Malaysian patient. Sing.Med.J. 35:353-357 1994.

PULMONARY LYMPHANGIETASIS

Congenital pulmonary lymphangiectasis is a rare condition that is fatal in the neonatal life. Liew reported one case in 1974 who also had a diaphragmatic hernia.

Reference

Liew SH. A case of congenital pulmonary lymphangiectasis. Med.J.Mal. 28:293-295 1974.

CHEST TRAUMA

Blunt injuries to the chest are common in motor vehicle accidents. Fractured ribs and flail chest are frequently managed in our hospitals. Among the more unusual injuries that have been reported, are rupture of a main bronchus, by Selvarajah and Radha Krishna and traumatic chylothorax by Krishnan and Jeyaratnam.

References

Selvarajah N and Radha Krishna S. A case of rupture of a main bronchus from a closed chest injury and its management in a child. Med.J.Mal. 28:276-278 1974.

Krishnan MMS and Jeyaratnam K. Traumatic chylothorax following a closed chest injury. Med.J.Mal. 37:270-272 1982.

SPONTANEOUS PNEUMOTHORAX

Spontaneous pneumothorax presents with a sudden sharp chest pain and some breathlessness due to escape of air from the lung into the pleural space. Reviewing 29 patients admitted to HUSM over 7 years from 1984 Harun, Yaacob and Mohd Kassim found 10 patients less than 10 years old, of whom 9 were girls and 19 other above the age of 10 years. The majority were males and with a peak in the third decade of life. 61% of patients had associated lung disease. The commonest associated disease was pneumonia (7 patients), followed by chronic obstructive airway disease (4), old tuberculosis with emphysema (3) and active tuberculosis (2). 70%(20) of patient required a chest tube and 3 patients required pleurodesis for either persistent leak of recurrent pneumothoraces. 4 patients developed surgical emphysema as a result of chest tube insertion and one developed a haemothorax. 8 patients died, all of whom had underlying lung disorders.

Reference

Harun MH, Yaacob I and Mohd Kassim Z. Spontaneous pneumothorax: a review of 29 admissions into Hospital Universiti Sains Malaysia 1984-90. Sing Med J. 34:150-152 1993.

EMPYEMA THORACIS

In a review of 29 adults with culture positive thoracic empyema, seen in 5 years between 1984 and 1988, a UH team noted that 16 occurred following bronchopulmonary infections, 9 followed thoracentesis and a few followed surgery and trauma. A wide spectrum of organisms were found, but the commonest were *Strep. milleri* (20%), *Pseudomonas aeruginosa* (15%) and *Klebsiella pneumonia* (13%).

In Kelantan, over 5 years between 1984 and 1989, Yaacob and Ariffin reported 9 cases of empyema thoracis in patients aged between 25 to 67 years admitted to HUSM. An underlying cause was found in only 3 patients, 2 had pneumonia and one chest trauma. Despite efforts bacteriological culture was successful in only one patient who grew *Strep. viridans* and another who grew anaerobic Streptococcus. All 9 patients had some drainage procedure. 2 patients developed a bronchopleural fistula, 1 a persistent pneumothorax, 1 was given presumptive antituberculous therapy and 1 died. The rest recovered without sequelae. In the same period the authors observed 13 cases of lung abscesses. In children, in a study over a 4½ year period reported in 1995, 31 children were admitted with empyema thoracis in HUSM. Their mean age was 1.9 years. The commonest bacteria grown were *S. aureus* (48%) and *Strep. Pneumoniae* (7%), but no growth was seen in 13 patients. Blood cultures were negative in 81%. These children stayed an average of 21 days in hospital. There was no mortality.

References

Liam CK, Rokiah P, Parasakthi N, Hamimah H, Puthucheary SD, Aljafri AM and Samani AG. Culture-positive thoracic empyema in adults. Med.J.Mal. 45:169-176 1990.

Yaacob I and Ariffin Z. Empyema thoracis and lung abscess. Sing Med.J. 32:63-66 1991.

Maziah W, Choo KE, Ray JG, Ariffin WA. Empyema thoracis in hospitalised children in Kelantan. J Trop Peadiatr 41:185-188 1995

MEDIASTINAL MASSES

There are a wide variety of non-malignant tumours that can occur in the chest. In a local survey of the spectrum seen, Manavalan at the Lady Temple Hospital found that 24 were various types of cysts, 13 were neurogenic tumours (mainly neurofibroma), 13 others were connective tissue tumours (such as chondromyxomas, fibromas, lipomas etc.) 12 were teratodermoids, 5 were retrosternal goitres and 2 were thymic tumours.

Reference

Manavalan AS. Anaesthetic problems of space-occupying lesions of the chest. Med.J.Mal. 24:124-127 1969.

CHAPTER 28

THE ALIMENTARY SYSTEM

CLEFT LIP AND CLEFT PALATE

Cleft lips and cleft palates occur as a result of the elements that form the face failing to fuse properly during intrauterine development. Cleft lips are obvious and do not usually miss medical attention but cleft palates occurring alone may be neglected unless looked for. Cleft lips and palates however, commonly occur together as a result of a similar defect in the developmental process. Although an inherited disorder, the inheritance is multifactorial and little is known currently about how it can be prevented.

Its local incidence has been studied in a number of epidemiological surveys. Boo and Arshad found that out of 52,379 babies delivered in the Maternity Hospital KL, over a 2-year period ending 1987, 64 were born with cleft lip and/or palates. The rate of occurrence of cleft was 1.24 per 1,000 livebirths. Chinese babies had the highest incidence (1.9 per 1,000) while Malays had the lowest (0.98 per 1,000). The rate among Indians was 1.1 per 1,000. The most common type was a complete unilateral cleft of the primary and secondary palates. Among the Indian babies, cleft of the secondary palate was the most common. 19% of all the affected babies had a positive family history of cleft. 11% of the mothers of affected babies had positive history of drug ingestion especially Chinese herbs during pregnancy. Associated congenital abnormalities occurred in 15.6% of the babies with cleft lip and/or palate.

The dental surveys of the Ministry of health have also noted the presence of cleft lips and palates. Table 28.1 summarises the prevalence found.

Table 28.1 Prevalence of cleft lip and palate in Malaysia

Region	Year	Incidence of	
		Cleft lip	Cleft Palate
Peninsula Malaysia	1970	1:700	1:600
	1988	1:738	1:1230
Sarawak	1980	1:1800	1:1310
Sabah	1985	1:700	1:600

Cleft palates have the potential to predispose children to middle ear effusions that can cause hearing loss. In a study of 66 patients with repaired and unrepaired cleft palates, Lokman *et.al*. found that 58% had middle ear effusions. Repair of the palate did not reduce middle ear effusion. Only 12% of the patients complained of hearing loss, and not all the patients were subjected to audiometry for objective measurement of hearing loss.

A cleft of the lower lip is a very rare condition. One case in a girl has been reported locally.

References

Boo NY and Arshad AR. A study of cleft lip and palate in neonates born in a large Malaysian Maternity Hospital over a 2-year period. Sing.Med.J. 31:59-62 1990

Lokman S, Loh T, Said H and Omar I. Incidence and management of middle ear effusion in cleft palate patients. Med.J.Mal. 47:51-55 1992.

Arshad AR. Incomplete midline cleft of lower lip. Cleft Palate Craniofac J. 32:167-169 1995.

DENTAL HEALTH

The Dental Division of the Ministry of Health has undertaken several extensive surveys on the state of the national dental health. Beginning in 1970, school children in Peninsula Malaysia were studied, followed by

adults in 1974. Surveys in Sarawak in 1980 and Sabah in 1985 followed, revealing similar results. Repeat surveys of children and adults in Peninsula Malaysia were carried out in 1988 and 1990. In 1997 school children all over Malaysia were studied in the First National Oral Health Survey of School Children.

Tooth decay

The 1970 survey covered 15,197 children from 6 to 18 years. The results were sobering. 95% of all school entrants, aged 6 years, suffered from caries in the deciduous dentition. 92% of all school leavers, aged 18 years, were similarly affected in their permanent dentition. Had root fragments been included the percentage would have been higher. 59% of the 6 year olds had root fragments as did 12% of the 18 year olds. The 1988 study covered 11,070 children, and found there was a slight improvement. 89% of 6 year olds had dental caries, and the mean 'dfx'(decayed, filled, indicated for extraction) index which was 6.3 in 1970 dropped a little to 5.67 in 1988. 86% of 16 year olds had caries and their mean 'DMFX'(decayed, missing, filled or indicated for extraction index) was 4.35 compared to 4.8 in 1970.

The 1997 survey found that 81% of 6 year olds had caries in their deciduous teeth, while 76% of 16 year olds had caries in their permanent teeth. The 'dfx' index of 6 year olds was 3.8 while the 'DMFX' index of 16 years was 2.8. 6 year old children in Perlis, Perak and Pahang had significant poor 'dfx' scores that were in range between 5.9 to 6.2. The results show an encouraging improvement over time overall. 12 year old were included in the survey and overall their 'DMFX' index for the whole country of 1.9 was below the WHO target of less than 3 by the year 2000. 12 year olds in Sabah, however, had a score of 3.3.

14,090 children were surveyed in Sarawak in 1980. 92% of 6 year olds and 70% of 16 year olds had caries. The 'dfx' index for 6 year olds was 5.81 and 'DMFX' index for 16 year olds was 6.34. The children in Sabah seem to be poorer off in dental health. Of 14,519 children surveyed in 1985, 97% of 6 year olds and 82% of 16 year olds had caries. Correspondingly, the 'dfx' index for 6 year olds (7.39) and 'DMFX' index for 16 year olds (7.92) were worse. In 1997 Sarawak children aged 6 years had a 'dfx' index of 3.9 while in Sabah they still lagged behind with an index of 6.3. The 'DMFX' index for 16 year olds was 3.7 in Sarawak and 6.7 in Sabah. It is obvious Sabah is in need of special attention.

The level of unmet treatment in 1970 need was alarming. Only 5% of carious deciduous teeth were filled. At the other end, premature loss of permanent teeth meant 1 in 5 children required dentures. Among these 16% of 13-18 year olds who needed dentures only 3% had them. In 1988 only 1.4% of 12 year olds and 4.6% of 16 year olds required dentures. In 1997 only 2.6% of children were found in need or were wearing dentures.

As a group the Chinese require some special mention. They had a higher prevalence of dental caries, earlier loss of deciduous and permanent teeth and lower number of permanent teeth in the mouth at examination compared to the Malays and Indians. A pilot study has shown that their preference for sweets is probably the crucial factor.

In the 1974 survey of 9,061 adults all over Peninsula Malaysia, 95% were found to have caries. 24% of the sample were wearing dentures but actually 55% required them, the Chinese forming the largest group.

The dental health status of children with heart defects were examined by Johnson and Grieve in 1978. The prevalence of dental caries was found to be comparable to children with non-cardiac diseases.

Periodontal Disease

In 1970, more than 50% of children between the ages of 7 and 13 years showed materia alba accumulations. After 13 years there is a gradual decline. There was no appreciable difference among the races. The number of children with calculus, or tartar increased with age from 32% in those at the age 6 years. Chinese children (37%) had considerably less calculus than Malays (59%) and Indians (56%). About 60% of all children suffered from inflamation of the gingiva. The mean number of inflamed gingival units was 2.8. The peak aged seemed to be the 11 year olds of whom 67% were affected. Chinese showed a higher prevalence (64%) compared to Malays (55%) and Indians (53%).

In the adult survey, 72% had some form of periodontal disease, with 29% having periodontal pockets greater than 3mm.

In the 1988 survey, it was found that 93% and 90% of 6 year olds and 16 year olds respectively, had healthy periodontal tissue. Bleeding was found in only about 5% of all children, calculus in .2% of 6 years olds and 4% of 16 year olds. Almost no shallow pockets or deep pockets were detected. In 1997 only 4.4% of children had bleeding gums and 1.2% had calculus.

Abdul Razak, Jaafar and Mat Nor reported that periodontal disease was the cause of tooth extraction in 20% of their patients at the UH. It was the major factor for tooth extraction in the population above 50 years old.

Dental Hygiene

Tooth brushing is widely practised in Malaysia. Overall 81% of adults surveyed in 1974 brushed their teeth. But age was a factor. 90% of those under 35 years brushed their teeth while over 60% of those above 65 years did not.

Water Fluoridation

In the two surveys in 1970 and 1974, it was found that 76% and 60% of the people, respectively, received a town supply of water. The content of natural fluoride in drinking water in Malaysia is low, between 0.05 and 0.4 ppm. which is below the recommended level of 1 ppm. to prevent dental caries. As a large majority of the population would benefit, a fluoridation programme was adopted by the Ministry of Health, especially after dental surveys in the towns of Johore Bahru and Kluang before and after 7 years of fluoridation indicated a 60% and 75% reduction in dental caries respectively. This had begun in Johore in the 1960s. Today there are over 250 water treatment plants with fluoride feeders. The output from these plants forms 79% of the total water capacity and it is estimated fluoridated water supplies, benefit about 67% of the population.

Tetracycline-stained teeth

After the tetracycline antibiotics came into use in the 1950s it soon became apparent that it could stain the undeveloped teeth in the unborn child of pregnant mothers and young children taking them. Because the tetracyclines have been widely used locally and this rather occult and latent side effect not appreciated well enough, a large number of children from that time on have been affected.

Hashim, M.Ali and Jasmah at the UH found in a survey of 4,500 that 2% of those between the ages of 4 and 30 years were affected. The majority (59%) had yellowish-brown stains. 38% had greyish-brown stains and 3.4% had black stains.

Dental Abrasions

A small number of older people clean their teeth using salt and charcoal applied to a Melastoma brush or their forefinger. Yaacob and

Park reported that 9% of 350 inhabitant of two villages surveyed had a distinct form of abrasion cavity on the labial surface of their teeth from this habit. The habit is injurious to both the soft and hard oral tissue and is to be discouraged.

Ectopic teeth

Rare cases of a tooth growing in the nose and into the maxillary sinus has been reported locally.

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ORAL APHTHOUS ULCERS

Aphthous mouth ulcers are a painful nuisance and tend to affect some people recurrently. Zain reported that a survey of 11,697 randomly selected Malaysians found that the prevalence of oral recurrent aphthous stomatitis among adults was 5 per 1,000. The prevalence was highest among the indigenous people of Sabah and Sarawak (1.2%), followed by Chinese (0.7%), then Malays (0.5%) and was lowest among Indians (0.1%). This racial difference might lead to clues about its aetiology.

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ODONTOGENIC TUMOURS

Records of amelioblastomas and other odontogenic tumours and keratocysts have been collected at the Division of Stomatology at the IMR since 1967. In numerous reports since then till the present, Siar and Ng have published data about the spectrum of tumours seen.

Up to 1991, covering 25 years, they found 401 cases of **ameloblastomas**. Males outnumbered females in a ratio of 1.14. 50% were Malays, 35% Chinese, 8% Indians and 7% were other races. 72% of patients were between 10-39 years old (mean age 31 years). 93% of tumours occurred on the mandible, 6.3% in the maxilla. 84% were conventional ameloblastomas, 12% were the unicystic variant,

and 1% were peripheral ameloblastomas. Histologically 34% were plexiform, 17% follicular and 18% a mixture of these. 59 cases had recurrences after enucleation. They have reported 45 cases of **adenoameloblastomas** or **adenomatoid odontogenic tumours** over 18 years.The mean age of these patients was 16 years and 66% were females. 57% were Malays, 23% Chinese 18% Indians and there was 1 Kadazan. In a report on 17 cases of the **desmoplastic variant** in 1993 they found that these were 2.4 times more common in females. They reported cases of **calcifying and keratinising ameloblastomas** in 1991 and 1993, and one case with a **clear cell component** and a case of granular cell ameloblastoma in combination with a plexiform granular cell odontogenic tumour in1990. Khoo, High and Awang reported a unicystic ameloblastoma with a late recurrence after excision in 1995.

In 1986 Siar and Ng reported a series of 53 cases of **odontogenic keratocysts** seen over 20 years. The mean age of patients was 33 years and 60% were males. 57% were Chinese, 26% Malays and 17% Indians. 6 cases recurred after surgical enucleation. They also reported 30 cases of **calcifying odontogenic cysts** seen over 16 years. These patients had a mean age of 38 years but the youngest patient was just 5 years old. Females formed 60% of these patients. They did not find any recurrent cases. In 1988 they reported 9 cases of **orthokeratinised odontogenic keratocysts** seen over 20 years from 1967. These occurred equally on the maxilla and mandible. Chinese were especially affected.

In 1997 they reported 104 cases of **odontomas** seen over 29 years, from 1967 to 1995. Males and females were equally affected. 45% were Malay patients, 40% Chinese, 11% Indians and 3.8% other races. The mean age at presentation was 25 years. Histologically, 43% were compound and 36% were complex. Over the same period they reported 13 cases of **calcifying epithelial odontogenic tumour (Pindborg tumour)** in 1996. In these tumours females outnumbered males in a ratio of 8:5. 61% were Malays, 23% Chinese, 8% Indian and 8% other races (Melanau). The mean age was 31 years. The maxilla was the commoner site. In another report in 2000, also covering the same period they recorded 46 cases of **peripheral odontogenic fibromas**. The mean age at onset was 32 years with a slight female preponderance (M:F ratio 1:1.3). There was no racial predilection and just more than half (52%) were located in the mandible.

From the UH Dental faculty, Ngeow *et.al*. found 61 cases of **odontogenic keratocysts** from patients in Malaysia and Singapore between 1981 and 1992. They also found slightly more males (57%) than females. The mean age of patients was 27 years. 75% of patients were Chinese, 7% were Malays, 10% were Indians and 8% were other races. 66% of the lesions were in the mandible especially the posterior mandible. 7 cases occurred at the site of the dentigerous cyst.

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EPULIS

An epulis is a localised swelling of the gum, which may be fibrous, granulomatous or sometimes associated with pregnancy.

In a study of 204 fibrous lesions of the gum, Zain and Fei found that 46% contained calcification. Half had collagenous connective tissue, slightly less than half had cellular and collagenous connective tissue. 36% of the lesions were ulcerated, 80% of these were the type with cellular connective tissue. An attempt was made to subcategorise these lesions as fibrous epulis and peripheral fibromas with and without ossification.

Zain, Khoo and Yeo also analysed 304 cases of oral pyogenic granuloma seen at the UH. They excluded pregnancy tumours but still found females more affected than males. Chinese were the ethnic group mainly affected. The mean age of the patients was 29 years. The majority of lesions were ulcerated and pedunculated. The lesions had a mean diameter of 10.8mm and a mean duration of 6 months at presentation. The maxilla side was more often affected than the mandible. After excision there was a recurrence rate of 14%.

Epulis may also be congenital. Congenital epulis are uncommon, but has been reported at least twice locally.

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SALIVARY MUCOCELES

Salivary mucoceles or rentention cysts are fairly common complaints presenting to the surgical clinic or general practitioner. In reviewing 250 cases, Ramanathan, Ganesan and Raghavan found a wide distribution among all races and in both sexes. Most patients were in the second decade of life and mucoceles were rare (5.6%) for those over the age of 40 years. There was a 3% recurrence rate with surgical excision.

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ORO-ANTRAL FISTULAE

An oro-antral fistula is a complication of extraction of usually either the first or second

upper molars. It has been mentioned elsewhere that this has a chance of occurring in 1:200-300 of such tooth extractions. Lian reported a collection of 21 cases over 10 years at the UH. Flaps for closure had a 90% rate of success.

Reference

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TEMPORPMANDIBULAR JOINT DYSFUNCTION

A series of 50 patients with temporomandibular joint pain was observed by Yaacob and Ling at the UH. Females outnumbered males by 2.6:1. 92% were under 30 years old. Non-professional white collar workers were the largest occupational group (60%). 64% of patients admitted to emotional conflict which the authors thought was the main contributing factor. The majority of patients responded well with reassurance. Dental surgery was reserved only for special cases.

Reference

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BENIGN ENDEMIC PAROTID ENLARGEMENT

This is an asymptomatic condition which has been documented by a few investigators on account of its striking appearance. In certain ways it shows epidemiological similarities to endemic goitres. In a study of lower income groups in 1950, Burgess and Laidin found that 20% of 1,212 Malays, 9% of 430 Chinese and 5% of 715 Indian school children, had enlarged parotids.

The significance of parotid enlargement is poorly understood. The best guess is that it accompanies malnourishment or occurs with recovery from malnourishment. An interesting case in point was in two comparable Malay fishing villages. Parotid enlargement was uncommon in a prosperous one but affected 48% of children in a poor village.

In a study of Orang Asli, Polunin reported parotid enlargement in 69% of a sample of 653 Orang Asli.

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RETROPHARYNGEAL ABSCESS

Retropharyngeal abscesses are uncommon but the diagnosis, like diphtheria, should not be forgotten in a child with stridor or croup. Yeo mentions 3 paediatric cases between 1984 and 1986 seen in Alor Star. Lee reported 2 adult cases of retropharyngeal abscesses that were complications of impacted foreign bodies. A case in a Malay man in Kelantan reported by Elango, Edward and Purohit was complicated by a mediastinal abscess and pericarditis.

Sharma *et.al*. studied a series of 17 cases treated at the HUSM over 10 years. 41% occurred in children below 6 years old. Predisposing factors were upper respiratory tract infections (52%), septicaemia (11%) and foreign bodies (35%). The commonest bacteria cultured were *Klebsiella*, *Staphylococcus* and *Streptococcus*.

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OESOPHAGEAL ATRESIA

Atresia of the oesophagus formed the third commonest cause of neonatal alimentary tract obstruction, after anorectal malformations and Hirshprung's disease, in a series from the UKM peadiatric surgery department from its inception in 1976 to 1981. They observed 30 cases of oesophageal atresia out of 241 neonates with alimentary obstruction. But as the series does not include all cases in the KL area it is not possible to estimate the incidence of the condition from these figures. The authors noted that only 5 cases were referred under 24 hours of life. The average age of babies at referral was 3 days which ideally ought to be less. The oldest was a baby at 14 days.

Maternal hydramnios was noted in 5 cases. Vomiting, excessive frothing at the mouth, cyanotic attack with feeds and the inability to pass a nasogastric tube were the common features noted. 28 babies were operated on with a mortality of 43%.

Tracheo-esophageal Fistula: TEF - without oesophageal atresia, more commonly known as the H-type fistula is rare but usually presents at birth. Quah *et.al*. have reported a case presenting in a 9 year old boy in Kelantan with a right lung abscess. The fistulous opening about 1mm in diameter was seen at bronchoscopy in the posterior wall of the trachea.

References

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CONGENITAL OESOPHAGEAL STENOSIS

Congenital oesophageal stenosis can arise as a result of at least 3 anatomical anomalies. It can be due to tracheobranchial remnants (involving the lower third), fibromuscular stenosis (of the middle third) or a membranous diaphragm. A case of each of these have been reported from the UH.

Reference

Ramesh JC, Ramanujam TM and Jayaram G. Congenital esophageal stenosis: report of three cases, literature review, and a proposed classification. Pediatr Surg Int 17:188-192 2001.

GASTRO-OESOPHAGEAL REFLUX

In small children, gastro-oesophageal reflux can lead to aspiration and respiratory disease. Norzila *et.al*. described 20 patients in 1996, 85% of whom were infants and the oldest 3 ½ years, who had severe respiratory symptoms as a result of gastro-oesophageal reflux. Boys and girls were almost equally represented but 16 of the children were Malays and only 2 were Chinese and 2 Indians. Besides cough, wheezing and stridor, six had apparently life threatening episodes. 14 children required ventilation. 8 children had fundoplication surgery. On follow-up 14 children continued to require inhaled bronchodilator and steroid therapy, including 4 who had fundoplication. Studying 44 patients aged 1-58 months, with chronic respiratory symptoms over 6 months, Siti *et.al*. found evidence of gastro-oesophageal reflux in 71% by pH monitoring.

Rosaida and Goh have mentioned in an abstract that among adults in the UH they found Indian men had a 1.5-1.7 times greater risk of reflux oesophagitis at endoscopy compared to

Chinese and Malays. Indian women also had slightly higher risks than their counter parts but not as much.

References

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OESOPHAGEAL FOREIGN BODIES

It is not uncommon for children to ingest pins, needles and coins. Rounded objects like coins usually get lodged at the oesophageal inlet. Devadason reported a case where a Foley catheter was used to remove a coin successfully in 1976. Goon and Samad have also reported several cases where they safely removed coins using a Foley catheter without anaesthesia.

Among adults, swallowed dentures is a problem which can be lethal due to tears the sharp hooks may cause. Yeoh has written a report of two cases. Out of 200 patients with foreign bodies impacted in the oesophagus, Abdullah found that 11.5% were dental prostheses. 16 had the foreign body removed endoscopically, 5 passed the prostheses through the gastrointestinal tract without serious complications. Elango *et.al*. reported a 60 year old with an obstuction which was caused by a bolus of meat.

An interesting phenomenon where a fish bone extruded itself through the neck has been reported more than once. In one case, described by Huang in 1972 it extruded after 2½ months. Krishnan, on the other hand, reported a case where the fishbone was removed from the subcutaneous tissue one week after the patient swallowed the bone. CT scanning may help in locating these fish bones, which have migrated through the alimentary passage into the neck.

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OESOPHAGEAL STRICTURES

Corrosive oesophageal strictures are the commonest form of oesophageal strictures in Malaysia. Such patients are usually Indian estate labourers who have survived a self poisoning episode. Strictures following peptic oesophagitis are not common. Mekie described the first local surgical replacement of the oesophagus with a segment of small bowel in 1950. Ng had also reported good results with surgery in 8 cases and found that dilatation gave poor symptomatic relief. Balasegaram also reported a series of 6 cases from Seremban between 1962 and 1967.

Osman and Meah reported 19 cases at the UKM over 10 years from 1967 to 1977. Krishnan and Tan collected a series of 40 corrosive strictures from 1968 to 1982 at the UH. 32 patients had either oesophageal bypass or replacement surgery with usually good results.

References

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ACHALASIA OF THE CARDIA

Achalasia of the cardia occurs in Malaysia although we cannot estimate its frequency. Ding reported a series of 15 patients he treated with pneumatic balloon dilatation between 1989 and 1995. They ranged in age from 19 to 66 years. 10 were females and 5 males. All presented with dysphagia, while regurgitation occurred in 73% and weight loss was noted in 67%. From abstract notes, in another series from GH KL, 14 cases were reported over one year in 1999 and one was reported from UH 38 cases from 1991 to 1999.

Reference

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OESOPHAGEAL VARICES

Among the common causes of haemetemesis, oesophageal varices usually carries the poorest prognosis. Balasegaram and Damodaran reported that over 46 months from 1963, 41 cases of bleeding oesophageal varices were diagnosed in Seremban and KL. They accounted for 13% of 326 cases of gastrointestinal bleeding and carried the highest mortality rate (20%) among the various causes of gastrointestinal bleeding. In a series from the UH reported in 1988, it made up 10% of the diagnoses found at endoscopies for upper gastrointestinal haemorrhage. In another series from GH KL of patients seen in 1995, Lakhawni noted that oesophageal varices accounted for 11% of patient with upper gastrointestinal bleeding.

In 70 cases of bleeding oesophageal varices over 6 years from 1963 Balasegaram and Damodaran, performed emergency portocaval shunt surgery on 30 of their patients with a 30% mortality rate. 35 were treated conservatively with a mortality rate of 74%. 5 other patients had other forms of surgery. This was however, not a randomised trial. Cirrhosis of the liver was the underlying cause of the varices in all their patients. 40 (57%) patients gave a history of prolonged alcoholism, while in 8 (11%) cirrhosis was secondary to hepatitis. In the remaining 31% the cause of cirrhosis was not known. The male to female ratio of these patients was 10.7:1 and their aged ranged from 15-73 years. When he extended his series 6 more years to 1975, Balasegaram had a 16% post-operative mortality in the latter half and 8% in the last 15 cases in part due to better patient selection. Altogether in 12 years 211 with bleeding varices were treated conservatively. 35 exsanguinated within hours, 114 died within a week from admission and 62 survived the acute problem, giving a mortality rate of 71%. 13 patients had other operations such as splenectomy, oesophageal transection, gastric vessel ligation or gastrectomy. 6(46%) of these patients died. Of the total 68 patients over 12 years who had emergency shunt surgery, 53(78%) survived. Of these survivors 10 were lost to follow-up. 25 of the remaining 43 died from liver failure (17), recurrent bleeds (6) or liver cancer (2), mostly 2-6 years after surgery. 5 patients were alive 5-7 years after surgery and 8 more alive less than one year from surgery.

In 44 patients who bled from oesophageal varices over 54 months from 1986, seen in GH KL, Tay et al. noted that 43% were Malays, 27% Chinese, 23% Indians and 7% other races. Their mean age was 50 years and the male to female ratio was 2:1. 73% of these patients had cirrhosis, 5 of these 32 (16%) also had a hepatocellular carcinoma. Among the non-cirrhotics 2 had documented portal vein thrombosis and one a pancreatic carcinoma.

Among the cirrhotics, hepatitis B was noted in 41% and alcohol abuse noted in 44%. Alcohol abuse was noted in 70% of the Indians and only 10% of the Malays. 34% of the 44 patients had gastric fundal varices and a third of these bled. Injectionsclerotherapy was performed an average of 4 times for these 44 patients. The rebleeding rate was 4.5%. 8 patients required some form of surgery for their bleeding varies. These procedures included oesophageal transection, splenectomy, underrunning of fundal varix, shunt operation and distal pancreatomy. They had 7 deaths in the acute period, 4 from bleeding, 2 from aspiration and one from encephalopathy.

In the series from 1995 also from GH KL, Lakhawni noted that 9 (64%) out of the 14 patients with bleeding oesophageal varices were Indians. All had blood transfusions and endoscopy in addition to which 3 underwent variceal banding and 8 sclerotherapy. 7 had a Sengstaken tube inserted and 2 had surgery at which oesophageal transection, splenectomy and devascularisaton procedures were performed. Despite this the mortality rate was 43%, in addition to which there were 6 patients during that period who died of torrential bleeding before endoscopy could be done to establish a diagnosis.

Data from UH published only in abstract noted that 30% of varices were alcohol related, 17% related to hepatitis B, 13% were hepatitis C related and a further 6% had 2 of these risk factors. In addition 33% were cryptogenic. There were 138 patients in 19 months. Oesophageal varices in Indian men were alcohol related in 96% (24/25).

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BEZOARS

An accumulation of ingested indigestible material forming a 'foreign body' mass in the stomach is usually referred to as a bezoar. Special terms for example, a trichobezoar, refers to a mass composed of hair. No particular Malaysian peculiar patterns have been observed regarding bezoars but besides a trichophytobezoar, a phytobezoar, that is one composed of plant fibre, and another case involving latex rubber have been reported.

References

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PEPTIC ULCER DISEASE

Although not all dyspepsia is cause by *Helicobacter pylori* the link between this bacteria and peptic ulcer is now an irrefuatble one. As such this topic including its complications is discussed in a section under the bacteria.

INFANTILE HYPERTROPHIC PYLORIC STENOSIS

Hirschsprung, in the latter part of the last century, is credited with our present day understanding of this condition, although Hildanus and Blair, more than a century before him had described it. In Malaysia, Field

estimated the incidence to be 1:100,000 in 1951.This probably was a great underestimate due to inadequate reporting in those days.

Ahmad, Rubaiyat and Mahmud estimated in 1982 that about 10 new cases of this disease was seen each year in the 3 hospitals offering paediatric surgical services in the Kuala Lumpur area. Since there were approximately 60,000 live-births in Selangor yearly, the incidence of the disease was estimated to be about 1:6,000. The incidence in Singapore has been estimated to be about the same. The incidence in Caucasians however, is about 1:400. It is not likely that so many cases are missed in our hospitals to account for the shortfall. It seems almost surely that the condition is in fact 10 times less common here.

The same authors reported that in over 10 years up to 1981 there were 67 infants admitted to the Kuala Lumpur GH with infantile hypertrophic pyloric stenosis. The ratio of males:females was 3:1. Nearly 80% were between 3 to 8 weeks old with the peak incidence at 4 weeks. Indians appear to have a risk twice as high as Chinese and three times as high as Malays of suffering the condition. All patients underwent Ramstedt's pyloromyotomy. 5 had accidental perforations of the duodenal mucosa but came to no harm. There was one death in the series due to renal failure.

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ACUTE GASTROENTERITIS

In many undeveloped countries simple diarrhoea and vomiting constitute a leading cause of deaths among children. Fortunately Malaysia does not fall into that category. At about the time of Merdeka there were about 150 to 200 deaths from gastroenteritis a year but the number now is fewer. It is however a very common cause of morbidity. Returns from the epidemiological unit at the Ministry of Health indicated that in 1973, 131,552 cases of gastro-enteritis were admitted to government hospitals.

Data from the Diarrhoeal Disease Study of the IMR carried out in1980 in 6 districts over one year revealed an overall incidence of 127 diarrhoeal episodes per 1000 population. Of the districts studied the incidence was highest in Sg. Petani (430/1000), followed by Kota Bharu (123/1000), Kuantan (76/1000), Muar (72/1000), Seremban (65/1000) and Klang (10/1000). One year olds (674/1000) were 5.3 times more often affected than the average person. Infants were the next worst affected (490/100). Upwards of 2 years (365/1000) the incidence gradually drops to 5 years after which there is a big drop. Indians (375/1000) seem to be more often affected than Malays (82/1000) and Chinese (68/1000).

Among 4,689 cases of acute gastroenteritis reviewed at the UH over 16 years from 1982, Lee noted 10 deaths, giving a case mortality of 2.1/1,000 admissions. All deaths were seen in infants below one year. 8 deaths occurred in girls. Acute renal failure and pulmonary edema were grave events.

Bacterial, viral and toxic agents plus cow's milk protein sensitive enteropathy combine to give this total and usually cannot be separated. Iyngkaran, Zainal, Lam and Puthucheary were able to isolate pathogens in 50% of 300 infants studied. Viruses made up 24% and bacteria 26% of these cases.

A study by Jegathesan *et. al.* of 3,809 faecal specimens from 19 hospitals all over Peninsula Malaysia in 1972 isolated bacterial pathogens in 16% of specimens. Because of the nature of the study the authors guessed that in half the instances culture may have been unsuccessful for technical reasons, it would mean that bacterial causes was responsible for about 30%

of acute diarrhoeas. It is not unexpected then that Chapman and Lim *et.al*. succeed in isolating bacteria from raw and cooked foods. Dried foods appear to be safer and fresh vegetable most at risk.

The Viruses

Rotaviruses make up the majority of viral cases of acute gastroenteritis (about 80%) and adenoviruses account for the rest. The patients, usually infants, are usually slightly more ill than those with bacteria but they recover faster. Probably between 25-50% of childhood diarrhoeas are due to viruses.

The Bacteria

Salmonella infections form the largest group of bacterial cases of gastroenteritis (about 50%). It has increased over the years due to international transport of man and commercial foodstuff. There are at least 22 serotypes of *Salmonella*, the commonest being *S. typhimurium* (58% of *salmonella* isolates in study by Jegathesan *et.al.*). Chinese appeared to be much more usually affected, especially children. Other relatively frequent isolates were *S. weltevreden* (9%), *S. typhi* (5.5%) and *S. paratyphi B* (4%).

Enteropathogenic *Escherichia coli* accounts for 31-37% of isolates. The 086/B7 and 0119/B14 strains are commonest. In both cases, the highest isolation rates occur in babies less than a week old. In the case of 086/B7, a predilection for Chinese has been noted.

Next *Shigella*, principally *S. flexner* and *S. sonnei*, make up 9-20% of the isolates. Whether enrichment mediums are used or not affects the chances of isolating the bacteria. Children 1 to 5 years old are most often affected.

Latterly, since the 1970s, *Campylobacter* has been recognised as another diarrhoeal agent. Lim, Jegathesan and Wong put its rate of occurrence at about 25-40% of bacteria isolated in KL in a study looking specifically for it. From a total of 281 diarrhoea patients they isolated bacteria in 14%.

Staphylococcus aureus constitutes about a further 5% of bacterial causes. It is often implicated in a group labelled as mixed infections. In an earlier study from 1964, Chan and Lucas reported that *Staphylococci* were responsible in a large number (43%) of gastroenteritis among infants.

Other bacteria that have been isolated as causative agents of diarrhoeal disease include *Vibrio parahemolyticus* (0.5%) and *Plesiomonas shigelloides* (0.2%). In addition *Aeronomas* and other bacteria have been implicated and these are discussed under the bacteria individually.

The Toxic Causes

See Poisoning

References

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Lee WS and Ooi TL. Deaths following acute diarrhoeal diseases among hospitalised infants in Kuala Lumpur. Med J Mal 54:303-309 1999.

NECROTISING ENTEROCOLITIS

This neonatal life-threatening illness is a creation of modern intensive medical care. But this is only in the sense that these babies would previously have died much sooner or died of other causes without the diagnosis being made. Its incidence in developed countries has been estimated at about 1 to 7% of neonatal intensive care unit admissions.

Over a 21-month period, from 1987 to 1988, Boo and Goon studied babies born at the KL Maternity hospital. 108 of 45,770 neonates developed necrotising enterocolitis (NEC) giving an incidence of 2.4 per 1,000 livebirths or 2.7% of special care nursery admissions. There was no significant difference in the incidence between the sexes or among the different races. NEC was most common (9.4%) in the very low birthweight (below 1.5kg) babies and in preterms of less than 34 weeks gestation (8.4%). There did not seem to be a correlation of NEC with most obstetric complications. 55% of the neonates developed the condition during the first week of life.

They recorded a case fatality ratio of 29%. NEC accounted for 5.7% of the hospital deaths of babies.

Reference

Boo NY and Goon HK. Epidemiology of necrotising enterocolitis in Malaysian neonates. Sing.Med.J. 30:444-448 1989.

COWS' MILK PROTEIN SENSITIVE ENTEROPATHY

In one of a few papers on the subject, Iyngkaran *et. al.* at the UH found that 15 out of 19 infants with protracted diarrhoea and 29 out of 41 infants with features indistinguishable from acute infectious enteritis exhibit histologic and enzymatic changes due to cows' milk protein sensitive enteropathy (CMPSE) with or without clinical features on reintroduction of cows' milk. Cows' milk protein is the most important cause for lactose and other sugar intolerance. It not only depletes mucosal oligosaccharidases but it also impairs absorption of monosaccharides. Depressed serum and tissue alkaline phosphatase has been shown to be a diagnostic indicator for CMPSE.

In a survey in rural schools in Sabah, Fong and colleagues detected lactose malabsorption in 321 (48%) out of 675 healthy subjects who were 6 to 13 year olds. Among lactose malabsoptants, 32% were found to be milk intolerant developing abdominal discomfort and/or diarrhoea.

Clinically CMPSE can produce a watery explosive diarrhoea associated with abdominal distension and perianal excoriation and can be confirmed by testing the stools for sugars. In about a third of infants and maybe more than two-thirds of neonates with acute diarrhoeas, cows' milk protein is involved with or without infective agents. On the other hand it may be that gastroenteritis in early infancy predisposes susceptible infants towards the disease.

In protracted diarrhoeas among infants, 75% to 80% exhibit sensitivity to cows' milk protein when it is reintroduced. An additional group may have been sensitive but develop a tolerance by acquiring IgA or IgM antibodies. All patients usually resolve spontaneously within 2 years. Iyngkaran has also shown that the small bowel mucosa of young infants recovering from diarrhoeal disease remains sensitive not only to cow's milk protein but also to soy protein to a variable extent in the majority.

References

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Iyngkaran N, Zainal A, Davis K, Boey CG, Prathap K, Yadav M, Lam SK and Puthucheary SD. Acquired carbohydrate intolerance and cow milk protein-sensitive enteropathy in young infants. J.Peadiatrics 95:373-378 1979

Fong THM, Lee MCC, Campos RL and Chan MKC. A study on the incidence of lactose malabsorption and milk intolerance amongst primary school children in Sabah.

Iyngkaran N, Yadav M, Boey CG, et.al. Causative effect of cow's milk protein and soy protein on progressive small bowel mucosal damage. J Gastroenterol Hepatol 4:127-136 1989.

Yadav M and Iyngkaran N. Transudation of immunoglobulins into duodenal juice of infants with cow's milk protein sensitive enteropathy. Med.J.Mal. 37:239-244 1982

Iyngkaran N, Yadav M and Boey CG. Mucosal and serum alkaline phosphatase activities in milk allergy. Med.J.Mal. 50:21-24 1995.

CONGENITAL CHLORIDE DIARRHOEA

Congenital chloride diarrhoea is a rare autosomal recessive disorder. It is especially rare in Asians and more commonly found in Europe, particularly Finland. Norzila and Azizi found a case in a 6 month old Malay boy, whose parents were second cousins, referred for failure to thrive.

Reference

Norzila MZ and Azizi BHO. Congenital chloride diarrhoea in a Malay child. Med.J.Mal. 49:102-104 1994.

EOSINOPHILIC GASTROENTERITIS

A few cases of thickening of the gastro-intestinal tract associated with diffuse eosinophilic infiltration have been reported in Malaysia. It is important to keep the diagnosis in mind as it may be mistaken for carcinoma, particularly in the stomach where it may lead to unwarranted extensive resection. General opinion is that this is an allergic reaction. Helminth infestations namely, anisakiasis, gnathostomiasis, angiostrongyliasis and filariasis have been mentioned as possible aetiological agents.

References

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Dutt AK, Kutty MK and Tharmaratnam A. Eosinophilic granuloma of the gastro-intestinal tract: three cases with unusual features. Med J Aust 28:1360-1361 1969.

Christophi C, Bahari M and Meah F. Eosinophilic gastroenteritis: report of 2 cases. Southeast Asian J Surg. 8:53-55 1985.

SMALL BOWEL ATRESIA

Together doudenal, jejunal and ileal atresias and stenosis add up to about as many cases as oesophageal atresias and Hirshprung's disease in the UKM experience. What they share in common is probably a common aetiology; which is, disruption of blood supply to a segment of the gut during intrauterine development. Clinical features that are common are that no meconium is passed. The duodenal atresias show more pronounced vomiting whereas abdominal distension is more in ileal atresias. Radiographs help in that no bowel gas is seen distal to the point of the lesion, whereas in the case of duodenal atresias a characteristic double bubble is described.

A case of ileal atresia diagnosed pre-natally at 33 weeks gestation by ultrasound and successfully operated on 36hrs after birth has been reported from UH.

References

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Raman S, Chan LL, Chang KW and Rachagan SP. Prenatal diagnosis of intestinal obstruction due to ileal atresia. Med.J.Mal. 47:228-230 1992.

PEUTZ-JEGHERS SYNDROME

This is an autosomally recessive inherited syndrome that is marked by oral pigmentation and small intestine polyps. It has often been noted as a cause of intussusception in young adults. There have been local case reports.

References

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Joishy SK, Leela MP and Balasegaram M.. Peutz-Jeghers syndrome and its complication. First report from Malaysia with review of literature. Am J Surg. 138:716-720 1979.

GASTROINTESTINAL LEIOMYOMA

Thambi Dorai described a 50-year old female Malay patient with a duodenal leiomyoma presenting with a mass. Ding and Wong reported cases where jejunal leiomyomas caused significant blood losses in two women.

References

Thambi Dorai CR. Leiomyoma of the duodenum: a case report. Med.J.Mal. 43:87-89 1988.

Ding PH and Wong TJ. The role of abdominal angiography in dificult gastrointestinal bleeding. Med.J.Mal. 49:306-309 1994.

PNEUMATOSIS INTESTINALIS

Pneumatosis intestinalis or gas-filled intestinal cysts may be associated with scleroderma, ischaemic colitis, peptic ulcer disease, pulmonary disease, instrumentation, or may have no known cause. Patients may have rectal bleeding, tenesmus, diarrhoea, bowel obstruction or no symptoms. One case from Kota Kinabalu has been reported in 1970. The patient underwent laparotomy for bowel obstruction. Post-operatively he died the following day.

Reference

Kutty MK, Nambiar B and Bau K. Pneumatosis intestinalis: a case report with a brief review of literture. Med J Mal. 24:227-230 1970.

MECONIUM DISEASE

Meconium plug syndrome, meconium ileus and meconium perinotinis all present as neonatal bowel obstruction. It was formerly thought that they were separate entities. Clatworthy coined the term meconium plug syndrome in 1956. Landsteiner first described meconium ileus in 1905 and Morgagni described meconium peritonitis far back as 1761.

Meconium plug syndrome

These patients have mild abdominal distension, bilious vomiting and failure to pass meconium. Relief is obtained after passage of a thick meconium plug either spontaneously or with the help of an enema. A small number are associated with cystic fibrosis but most are not. Ahmad and Madmud reported 3 cases at the UKM from 1970 to 1981.

Meconium ileus

Classically this is associated with cystic fibrosis, however a small group probably less than 5% do not have cystic fibrosis. Symptoms are similar to that above but more severe. Radiocontrast enema will show a microcolon. Enemas usually overcome the problem but there is a mortality risk. This condition is rare in Malaysia. 5 cases were recorded in a 12 year period from 1980-1991 in the UH. 3 neonates were Malays, 2 Punjabis. 4 were full-term, one preterm, and the babies ranged in birth weight from 1.9-3.7kg. There accounted for only 3.7% of all neonatal intestinal obstructions excluding imperforate anus. One of them had a sibling who also had meconium ileus. All of the 5 underwent laparotomy. There was one intra-operative death, 3 succumbed to respiratory infection, but did not have additional features suggestive of cystic fibrosis. One long term survivor also did not have cystic fibrosis.

Meconium peritonitis

This presents as bowel obstruction because adhesions have formed after intrauterine

perforation of the bowel. Meconium may be seen calcified on radiographs especially if the perforation was early on. It is said about half of these babies have cystic fibrosis. Although cystic fibrosis is not seen in Malaysia, Ahmad and Mahmud reported 6 cases of meconium peritonitis in their series from 1970-1981. Ramesh also reported one case in 1999.

References

Ahmad ZL and Mahmud MN. Problems of neonatal surgery in Malaysia. Mal.J.Reprod.Hlth. 1:23-33 1983

Rachagan SP, Lim CT, Chang KW and Kwan BB. Meconium peritonitis due to meconium ileus presenting as fetal ascites: a case report. Asia Ocenia J Obstet Gynaecol 15:117-120 1989.

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Ramesh JC, Chow TW, Yik YI and Ramanujam TM. Meconium peritonitis: prenatal diagnosis and postnatal management – a case report. Med J Mal. 54:528-530 1999.

MECKEL'S DIVERTICULUM

John Meckel described the structure that bears his name in 1809. It probably occurs in 2% of the population in Malaysia as elsewhere. Between 1975 and 1980, 49 cases of complications from Meckel's diverticulum were observed in GH KL.

85% of patients were under 20 years old. There were twice as many males as females. No racial predominance was observed. 19 had diverticulitis. 18 had intestinal obstruction problems, namely volvulus and intussuception. 4 had haemorrhagic manifestations and 8 umbilical associated lesions.

In another report Devadason observed 3 cases where a Meckel's diverticulum caused intestinal obstruction. Lin, Ong and Prathap reported one case where a neonate had a perforation of Meckel's diverticulum.

References

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Lin HP, Ong TH and Prathap K. Perforation of Meckel's diverticulum in the newborn. J Sing Peadiatr Soc 20:54-55 1978.

Meah FA, Ahmad ZL, and Mahmud MN. Meckel's diverticulum in Malaysia. J.Perubatan UKM. 4:75-80 1982.

CROHN'S DISEASE

Crohn's disease is of unknown aetiology. One of its mysteries is why it is rare in some places like Southeast Asia while it remains a common and often intractable problem with protean manifestations in the developed western countries. In a report by Thein-Htut and Kudva at the UKM they mention briefly that over 6 years from 1982 to 1987 they diagnosed only 4 cases in native-born Malaysians. All were males. Two were Malays, one Chinese and one a Sikh.

ACUTE APPENDICITIS

Appendicectomy is the commonest abdominal operation performed in Malaysia. In a review by Lee and Teoh they found that these constituted 55% of emergency surgical operations in GH, KL. As a reason for acute general surgical admission acute appendicitis shares the leading honours with ureteric colic.

As far back as 1931, there were 52 appendicectomy operations performed in Penang. Ipoh, Kuala Lumpur and Seremban combined added a further 138 appendicectomies to the total that year. The rate of operations has progressively increased reflecting not only higher acceptance of surgical treatment but almost certainly an increased incidence of the disease.

A study from Taiping showed that a patient admitted there with a suspicion of appendicitis had a 20-42% chance of having an

appendicectomy.

From a series of 1,000 appendicectomy specimens received in the pathology department of General Hospital Kuala Lumpur over a 9 month period from September 1982, the appendicectomy rate in KL can roughly be estimated at just over 100 per 100,000 a year (estimating the population served by the hospital at just over a million). This rate is comparable to countries with high incidences. Outside Kuala Lumpur the appendicectomy rate is probably lower. The Kuantan district on the East Coast has a rate of 74 per 2100,000 a year and in the adjoining more rural district of Pekan the rate is only 30 per 100,000.

Males are almost equally or a bit more often affected than females as found in two reports in 1990 from UH and Taiping Hospital which showed a male excess of in a ratio of 1.3:1 and 1.6:1 respectively. There does not appear to be any racial predilection for the disease, except one report, from UH, which noted a significantly higher number of Chinese affected. There is nevertheless a trend to suggest that the urban population is more often affected compared to the rural, and Malays where they are a rural population have a lower incidence.

Like in other countries the age group most commonly affected are those in the second and third decade. In two reports from Thanaletchimy in Kuala Lumpur and Hussein and Balasegaram in Seremban, this group accounted for over 70% of their patients. The youngest patient on record in Malaysia was 10 months old and the oldest in the series by Thanaletchimy was 82 years old.

The rate of perforated appendices found and the diagnostic accuracy given in terms of normal appendices removed is given in Table 28.2 below. It should be noted that the column of normal appendices includes cases where a great miscellany of pathology is found and not only where there is no definite pathology. Two of these studies noted that the Indian population had a higher proportion of normal appendices and correspondingly fewer perforated appendices. In most cases of perforation of the appendix the perforation was not diagnosed specifically pre-operatively.

In examining 1,000 surgically removed appendices pathologically Thanaletchimy did not report any unusual pattern of pathology. Worm infestation was present in less than 10% of cases in his series. But from an earlier series of 605 appendices examined pathologically between 1966 and 1974, Kannan Kutty and Balasegaram reported parasites in 14% and ova of parasites in another 12% of specimens. In only 2 out of Thanaletchimy's specimens was a carcinoid tumour found. Other rarer complications of appendicitis like mucoceles and pseudomyxoma peritonei have been reported by other authors in Malaysia. Studying the bacteriology of perforated appendices Lim, Hussin and Yusha found that *E.coli (42%), Streptococci (16%), Bacteriodes (15%), Klebsiella (15%)* and *P.aeruginosa (9%)* were the commonest isolates. The low rate of isolation of *Bacteriodes* was thought to be due to deficiencies in the collection and transport of specimens. A high incidence of ampicillin resistance among *E.coli* and *Klebsiella* was encountered. The aminoglycosides were effective for most Gram negatives. *Bacteriodes* were most susceptible to chloramphenicol and metronidazole.

Table 28.3 Rates of Perforated and normal appendices found at appendicectomy in Malaysia

Authors	Hospital	Year	Rate of Perforation	Rate of normal Appendices
Lee & Teoh	GH KL	1987	18%	19%
Lee, Jayalakshmn Syed Noori	UH	1990	24%	19%
Chua et.al.	Taiping	1990	32%	7%

Acute inflamation of the appendix ccasionally occurs because of diverticula of the

appendix. Chong has noted 9 cases of this among 2,250 appendix specimens at the UH over 8 years from 1967. The patients were adults ranging in age from 19-69 years.

References

Hussein MS, and Balasegaram M. Acute appendicitis in West Malaysia. Med.J.Mal. 27:43-47 1972.

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Chong KC. Diverticula of the vermiform appendix: a report of nine cases. Postgrad Med J. 52:504-510 1976.

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Lim VKE, Hussin Z and Yusha AW. The bacteriology of perforated appendix Med.J.Mal. 38:275-278 1983.

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Lee CM and Teoh MK. Perforated appendicitis - The Malaysian experience. J.R.Coll.Surg.Edinb. 35:93-94 1990.

Lee HY, Jayalekshmi P and Syed Noori SH. Acute appendicitis - The University Hospital Experience. Med.J.Mal. 48:17-27 1993.

Chua MW, Fazidah Y, Khalijah MY et.al. A review of acute appendicitis seen in the Taiping District Hospital from July to December 1990. Med.J.Mal. 48:28-32 1993.

DIVERTICULAR DISEASE

Diverticulosis of the colon can occur anywhere along the entire length of the colon. Classically it happens more in the left colon due to intraluminal pressure causing herniation of the mucosal layer through the serosa at weak points where blood vessels transverse the bowel wall. However, some diverticula are congenital and contain all three natural layers of the gut. Classically diverticulosis leads to bleeding or infection, abscess formation, perforation and adhesions. They are reputedly more common in the West but these problems do occur in Malaysia but have not been reported on. However, a few more unusual problems from diverticular disease have been noted.

Caecal Diverticulitis

Among Asian populations diverticular disease of the right colon has been recognised to be more common in comparison to Caucasians. These diverticula in the caecum are liable to infection that leads to inflammation and even perforation and present clinically very similar to acute appendicitis. In fact, often the diagnosis of caecal diverticulitis is made only at surgery for suspected appendicitis. Lim reported a series of 8 cases in Taiping, noting that one feature that can raise a clinical suspicion is the age of the patient. The 8 patients ranged in age from 30 to 56 years which is older than the typical patient with acute appendicitis. In his series caecal diverticulitis was found in 1:32 cases of appendicectomy compared to a rate in 1:120 noted in a series from New York.

Bleeding

Muthu noted a case of massive bleeding from a right sided colonic diverticulum associated with analgesic (NSAID) use.

Reference

Lim KG. Caecal diverticulitis – a review of eight cases in Taiping, Malaysia. Med J Mal. 54:230-234 1999.

Muthu A, Qureshi A and Ismail MA. Massive bleeding from colonic diverticular disease with NSAID use. Med J Mal. 54:374-376 1999.

ACUTE INTUSSUSCEPTION

Intussusception is one of the common paediatric surgical emergencies. An incidence of 1.9 per 1,000 births has been recorded in Birmingham, UK and 0.77 per 1,000 in Taiwan. In a series reported by Laidin and Goon in Kuala Lumpur they found an annual admission rate of

only 10 cases to the UKM surgical unit. A follow up study of the next 5 years from 1981 to 1985 by Goon found 90 cases. The rate probably does not exceed that in the rest of the country. It is not possible to arrive at the absolute incidence which would no doubt be low in comparison to Western countries where some hospitals have up to 30 to 60 cases a year.

In the series by Laidin and Goon of 104 cases over 10 years they noted a significantly lower rate of intussusceptions in paediatric surgical admissions among Indians. They postulated that the probably lower incidence may be due to the practice of introducing semisolids late, a common practice among Indians.

71 percent of their patients were under one year of age. 66 percent of the intussusceptions were of the ileocolic type. This follows the Western pattern and is unlike the African type of colocolic and caecocolic intussusception that occurs in older children. Vomiting was the commonest clinical feature (82%). More than half the patients had no history of pain, they comprised of mainly the children under one year of age where the classical screaming attacks with drawing up of the knees was absent.

The mortality rate was 14 percent which does not compare well with Western figures. Most of these deaths were in those who presented late. Considering surgical procedures, simple reduction with or without appendicectomy carried a mortality rate of 7%. The mortality rate was 28% when resection had to be performed and in the seven cases where a Meckel's diverticulum was found and resected the mortality was 57%.

44 cases of intussesception were noted in a the Seremban Hospital over 5 years from 1995. Males outnumbered females 3:1. 45% of the patients were between 6-12 months old. Malays formed a great majority (80%) of patients and Indians the fewest. Compared with the ethnic distribution of all hospital admissions Malays had a relative risk of intussuception 12 times greater than Indians. Chinese had a relative risk 5.8 times that of Indians.

Intussusception occasionally occurs in older children and adults. Nuruddin *et.al* have reported one case and Jasmi et al. reported it in a 14 year old Malay boy caused by a polyp in the transverse colon which turned out to be a poorly differentiated mucinous adenocarcinoma. At subsequent elective surgery 3 other benign adenomatous polyps were found.

References

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Ahmad ZL and Goon HK. intussusception among infants and children in Malaysia. Med.J.Mal. 37:150-157 1982.

Jasmi AY, Zain AR and Hayati AR. Large bowel cancer in a young adult presenting as an acute intussusception - a case report. Med J Mal. 47:316-319 1992.

VOLVULUS

Although volvulus of the sigmoid colon is probably the commonest type seen, volvulus of the small bowel has been highlighted in two reports, one case was due to ascariasis.

A number of other exotic cases have been reported. One case involved volvulus of the stomach in a 6 year old child with eventration of the diaphragm. Thambi Dorai described a form of volvulus where the sigmoid and the ileum were involved in a knot. Hisham, Gunn and Jamil described a 48 year old Malay man with a perforated gangrenous small bowel volvulus interposed between the right diaphragm and liver.

References

Balasegaram M. Primary volvulus of the small intestine.

Med.J.Mal. 18:122-124 1963.
Roe TWC, Lal K and Cawkell WA. Three cases of Ascaris lumbricoides small bowel obstruction with volvulus. Med.J.Mal. 23:78-79 1968.

Thambi Dorai CR. Ileosigmoid knot - case report. Sing.Med.J. 29:413-415 1988.

Lopez D. Acute mesentero-axial volvulus of the stomach in a child. Med.J.Mal. 48:351-354 1993.

Hisham AN, Gunn A and Jamil AA. Chilaiditi's syndrome presenting as acute abdomen. Med.J.Mal. 50:281-283 1995.

HIRSHPRUNG'S DISEASE

Next to anorectal agenesis Hirshprung's disease is the commonest cause of intestinal obstruction among neonates. Somasundaram at the UH reported 50 cases from 1968 to 1977, while Ahmad and Mahmud had 47 cases at the UKM from 1970 to 1981. Ramesh *et.al*. had a series of 49 cases over seven years from 1991, in which they advocated a one stage pull through operation. Because the pathology in Hirshprung's disease is not as obvious as in anorectal agenesis, it is likely that some may have gone undiagnosed or were never brought to hospital. Ahmad and Mahmud have noted that less that half were referred at less that 5 days of age and the average age was 9 days.

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Ahmad ZL and Mahmud MN. Problems of neonatal surgery in Malaysia. Mal.J.Reprod.Hlth. 1:23-33 1983

Ramesh JC, Ramanujam TM, Yik YI and Goh DW. Management of Hirshprung's disease with reference to one stage pull through without colostomy. J Peadiatric Surg 34:1691-1694 1999.

ULCERATIVE COLITIS

Ulcerative colitis is a well known disease because it is common among Caucasians. However it is uncommon among Orientals. There have been reports of large series of patients from India but from Southeast Asia, series collected over 10 years or more from places such as Singapore, Hong Kong, Thailand and Burma usually report 10 odd patients or so.

In Malaysia, Ti reported 10 patients with ulcerative colitis from 1968 to 1977 at the UH. Thein-Htut and Kudva at the UKM diagnosed 16 cases between 1982 and 1987 to which they added 7 earlier diagnosed patients in a series of 23 patients. The diagnosis had been delayed for 10 years in four patients. Men outnumbered women 16 to 7. The commonest age of onset was the third decade. There were 10 Malays, 8 Indians and 5 Chinese. 6 (26%) patients had total colitis. Extra-intestinal manifestations were seen in 7 patients. Colorectal cancer was not seen and there was no mortality.

Reference

Thein-Htut and Kudva MV. Ulcerative colitis in Malaysians: a review of 23 patients. Sing.Med.J. 30:385-387 1989.

ANORECTAL AGENESIS

Anorectal agenesis, of which many variants ranging from the more poorly developed 'high' type with one claocal opening, through to the 'low' types with various fistulae to the nearly normal 'anterior anus' covers the spectrum of conditions commonly just referred to as 'imperforate anus'. It is the commonest malformation of the alimentary tract and in local series is 3 to 4 times more frequent than Hirshprung's disease and oesophageal atresias.

Somasundaram collected a total of 67 cases at the UH from 1968 to 1977. 37% were classified as 'high' while 63% were 'low'. Ahmad and Mahmud at the UKM had 158 cases from 1970 to 1981. It is difficult to figure out the incidence of the condition from these series as KL is a referral centre. Koh, however, at the USM hospital in Kelantan collected 23 cases of babies born in 1985 where there were about 40,000 live births in the state. As almost all

cases were local the incidence arrived at roughly is 1:1,700 which is high in comparison to other parts of the world. He reported that 67% of his patients had 'high'/ 'intermediate' lesions while 33% had 'low' ones.

Boys and girls are about equally affected. Koh noted that 7 (13%) patients had Down's Syndrome. In a number of cases in various places, patients have presented in adolesence or adulthood, having survived on a fistula.

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Ahmad ZL and Mahmud MN. Problems of neonatal surgery in Malaysia. Mal.J.Reprod.Hlth. 1:23-33 1983

Koh GC and Jamaludin Z. Anorectal malformation as seen in a new teaching hospital. 20th Annual Combined Surgical Meeting, Academy of Medicine Singapore. 71 1986

DUPLICATION OF RECTUM

Rectal duplications are rare anomalies. Rajah *et.al*. reported 4 cases, presenting as constipation, as a rectal 'polyp', as a 'growth' from the vulva or with acute retention of the urine in Sabah.

Reference

Rajah S, Ramanujam TM, Anas SR et.al. Duplication of the rectum: report of four cases and review of the literature. Pediatr Surg Int 13:373-376 1998.

RECTAL FOREIGN BODIES

Although unusual, doctors in Malaysia ought to be aware that pain in the rectum can be due to strange objects impacted there either after having been ingested or inserted anally. In a perculiar report by Fisher in 1947, he described a Chinese rubber tapper with an impacted mass of latex in the rectum which he succeeded in removing only after lubrication with liquid paraffin. The patient who used his latex collecting pail for food and for washing utensils vehemently denied eating latex. Fisher however, did not fully believe him.

References

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Diong KI. Bone in the anal canal causing acute anal pain. Med.J.Mal. 32:71-74 1977

RECTAL PROLAPSE

Though uncommon and probably less common than in the developed nations, rectal prolapse of the partial and complete types have been noted in Malaysian patients. The elderly, especially women, are at greatest risk. Chronic psychiatric patients appear also to have a higher susceptibility. A non recurrent form of prolapse can happen in children and it is arguable if worms have anything to do with it.

Reference

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THE LIVER

NEONATAL HYPERBILIRUBINAEMIA

This term actually describes a clinical manifestation of a number of causes rather than a disease entity. However, it can be argued that liver immaturity is always present as an underlying entity contributing to the pathology.

Paediatricians generally agree there is a high incidence of jaundice among newborn infants in this region and a higher proportion of clinicians' time is spent doing exchange transfusions here

than in Western countries. Clinical jaundice is estimated to develop in 14% of infants.

Sinniah reported one study where jaundice was severe enough to warrant exchange transfusion in 1 in every 70 babies born. In 38% no other cause besides liver immaturity was found. ABO incompatibility was a feature in 24%, G-6PD deficiency in 16%, Rhesus incompatibility in 8%, sepsis in 6%, prematurity in 6% and for one case there was the respiratory distress syndrome. A study in 1977 reported that of 332 babies admitted to GH KL with severe neonatal jaundice 15% were premature. 178 of these required exchange blood transfusion, 62% of them Chinese, 33% Malay and 5% Indian. G6PD deficiency was found in 21% of the Chinese, 17% of the Malays and 11% of the Indians. In addition to G6PD deficiency abnormal haemoglobins, most noticeably Hb Bart's, contributed to the high incidence of severe neonatal jaundice.

The Ministry of Health reports that there were 70,794 cases of neonatal jaundice in 1990 but the data should be viewed with caution as detection is made only on clinical suspicion. 44% of babies with neonatal jaundice were given phototherapy, 4% were given exchange transfusion with or without phototherapy. The number of kernicterus cases was 60 in 1989 and 42 in1990 and also in 1995.

References

Sinniah D. Neonatal hyperbilirubinaemia. Med.J.Mal. 25:211-214 1971

Lie-Injo LE, Virik HK, Lim PW et.al. Red cell metabolism and severe neonatal jaundice in West Malaysia. Acta Haematol. 58:152-160 1977.

CONGENITAL HEPATOCELLULAR HYPERBILIRUBINAEMIA

DUBIN-JOHNSON DISEASE

This rare autosomal recessive condition was first described in 1954. In Malaysia, it was first seen in a man of Timorese origin in Sabah by Burns-Cox in 1965 and in a Malay man in KL by Dutt *et.al.* in 1968. In 1970, Banerjee reported 9 cases in three generations in one Malay family in Selangor.

References

Burns-Cox CJ. The Dubin-Johnson syndrome in a Timorese. Med.J.Mal. 19:311-313 1965

Dutt AK, Gill SS, Katty MK and Ungku OA. Dubin-Sprinz disease. Med.J.Mal. 23:2-4 1968

Banerjee AK. Dubin-Johnson syndrome: a family study. Med.J.Mal. 25:21-24 1970

BILIARY ATRESIA

Biliary atresia in children takes their lives away when they reach one or two years old, and causes them much suffering in their short innocent lives. The absence of bile ducts may due to agenesis but there is evidence that a destructive inflammatory process in utero may be responsible. The condition is uncommon, not very rare.

In a retrospective study over 10 year from 1982, Karnameedi and Lim noted 35 cases. Alongside these, they found 58 children with neonatal hepatitis. Neonatal hepatitis was used to describe persistent cholestatic jaundice in early infancy associated with abnormal liver function when biliary atresia is excluded. Both these conditions have some similar presenting features. There were no significant sex nor racial distribution of these diseases.

Without treatment biliary atresia is fatal. With operations to drain the bile only 50% of patients survive 5 years free of jaundice. Many develop cholangitis and cirrhosis. Fortunately

liver transplantation has arrived and Tan KC has successfully performed a few cases.

Toufeeq Khan has reported a rare instance of agenesis of the gallbladder, with hard stony faeces in duplication cyst of the hepatic flexure. It was discovered at surgery where it was mistakened for gallstones on ultrasound.

References

Toufeeq Khan TF and Baqai FU. Agenesis of the gallbladder with duplication cysts of the hepatic flexure – a case report and literature review. Sing Med J. 34:181-182 1993.

Karnameedi S and Lim CT. Characteristics of Malaysian infants with biliary atreisa and neonatal hepatitis. Med.J.Mal. 52:342-347 1997.

LIVER TRAUMA

Balasegaram recorded his experience with blunt liver trauma over 7 years from 1961, observing 35 cases in Seremban. He continued his series to 1974 adding 55 more cases from his tenure in KLGH. 79-91% of blunt liver injuries that were operated on were due to road accidents. He judged that a pre-operative clinical diagnosis of liver injury was made in only 46% but diagnostic aids such as paracentesis and imaging improved the rate of correct pre-operative diagnosis to 85%. In 38% of cases the liver injuries were judged extensive at operation. Hepatic resection (36%) and suture with drainage (30%) were the most frequently performed procedures Overall mortality was 14%, but was 11% when cases where tamponade was done were excluded.

Balasegaram also reported on his experience with 89 cases of penetrating liver injuries over 13 years from 1961 to 1974. Similarly 37% of the injuries were judged to be extensive at operation. Suture and drainage (34%), debridement (21%) and resection (19%) were most often performed. Overall mortality was 19%.Tamponade, packing the bleeding liver, had very poor results for both types liver trauma, 83% fatality (10/12 cases), and these survivors faced multiple complications. Excluding cases where tamponade was performed the mortality from penetrating liver trauma was 13%. In both blunt and penetrating liver injuries, Balasegaram noted that there was similarly associated head injuries in about 25%, chest injury in about 30%, skeletal injury in about 15% and other abdominal injuries in over 50%.

A review from the UH of a series 42 patients over 8 years from 1984 found that 88% of liver trauma occurred as a result of motor vehicle accidents. The remainder were due to gunshot wounds, fall from heights and stab wounds. 90% of these patients were men and 74% were between 10-30 years old. 16 (38%) of these patients died. In 7 liver trauma was the main or part of the cause of death while the other 9 died from other organ failure.

Shahrudin reported the very rare occurrence of a gallbladder which detached from the liver bed, cystic duct and artery and was found between intestinal loops following an accident in which the victim was a back-seat car passenger. The liver surprisingly was not severely injured.

References

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Shahrudin MD. A case of traumatic cholecystectomy. Med.J.Mal. 51:158 1996.

LIVER ABSCESS

Da Silva reported 57 liver abscesses as the cause of death in 1,350 necropsies in Singapore in 1950. About one quarter arose from biliary sources especially stones. Another quarter from amoebiasis, another quarter from ascariasis and another quarter from miscellaneous things, including appendicitis, melioidosis and actinomycosis.

In 1981 Balasegaram reported on 442 cases seen over 15 years at KL GH. At the UH Goh *et.al.* reported on 204 cases from 1970 to 1985. Another report by Vijendran from the first Surgical Unit GH KL between 1972 and 1975 had 24 cases. These figures indicate that liver abscesses are still fairly common in KL and the west coast of Malaysia. Most commonly affected were occupationally active adults between 30-50 years. Males were affected 5 to 6 times more than females. Indians accounted for half to two-thirds of the patients.

Evidence incriminating *Entamoeba histolitica* as the causative factor was proven in only 2 patients, in spite of repeated stool examinations in 23 patients in Vijendran's series. Anchovy sauce pus was noted in 12% of abscesses drained. Goh *et.al.* incriminated *E. histolytica* in 44% using a loose criteria including either demonstrating the parasite in the abscess wall, pus or stool, raised antibody titres, having anchovy sauce pus or patients responding to anti-amoebic drugs alone.

Goh *et.al.* considered the abscesses pyogenic in 12% and indeterminate in the remaining 46%. In one case they found tuberculosis and meliodosis in another. Vijendran noted yellow pyogenic pus in 58%. Mortality was 3% at the UH and 12% in the smaller series by Vijendran.

Another series from Kelantan by Sathyamoorthy would suggest that liver abscesses were commoner there. Over 1½ years he found 49 patients with liver abscesses by ultrasound at the Kota Bharu GH. They ranged in age from 11 to 77 years and all were males. 6 patients had more than one abscess.

Reviewing ultrasonographic findings, Sajikan commented that 84% were found in the right lobe, were round and with well defined margins. He also noted that pyogenic ones may contain gas. Sathyamoorthy also concurred, in a report of a series from Kelantan. He found 96% in the right lobe of which most were peripherally situated. They ranged in size from 3 to 12 cm.

References

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Vijendran M. The diagnosis and current treatment of liver abscess. Med.J.Mal. 32:133-138 1977.

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Sajikan AS. Ultrasonographic findings of liver abscess. Med.J.Mal. 43:332-337 1988.

Sathyyamoorthy P. Ultrasound in the diagnosis of liver abscess. The Family Physician. 2:28-31 1990.

Sajikan AS, Zulfiqar MA and Maimunah. Gas-containing liver abscesses: Assessment by ultrasound and computed tomography. Med.J.Mal. 48:33-39 1993.

FOCAL NODULAR HYPERPLASIA

This is an uncommon slow growing benign lesion consisting of liver cells arranged in nodules separated by fibrous tracts within which proliferating bile ducts are included as well demarcated tumour-like areas in normal livers. Several hundred only have been reported in world literature. One such lesion was incidentally found in a 16 year old Malay boy killed in a traffic accident at autopsy in KL.

Reference

Chong KC. Focal nodular hyperplasia of the liver. Med.J.Mal.

28:296-299 1974

HAEMANGIOMA

Cavernous hepatic hemangiomas can be detected on ultrasound and often mistaken for malilgnant tumours. From 1985 to 1992, UKM workers reported 7 women and 2 men, aged between 30-63 years old detected by ultrasound. The diagnosis was confirmed by biopsy in 3 and angiography in the rest.

One case of a patient presenting with thrombocytopenia has been reported in a Chinese female locally.

References

Liam CK and Regina N. Haemangioma-thrombocytopenia syndrome a case report. Med.J.Mal. 44:263-266 1989.

Samad SA, Maimunah A, Zulfiqar and Zaharah M. Ultrasound and computed tomographic appearances of large (giant) hepatic cavernous hemangiomas. Med.J.Mal. 50:82-86. 1995.

PRIMARY BILIARY CIRRHOSIS

Primary biliary appears to be uncommon among Malaysians. Over a 12 year period from 1979 only 7 patients were identified in the UH. All were Chinese females between the ages of 30-55 years. Pruritis was the presenting complaint in 5 patients. All except one was jaundiced when the diagnosis was made. 3 deaths were reported over a follow up period from 1 to 11 years. Two died from liver failure and one from haemetemesis.

Reference

Mohammed R, Goh KL and Wong NW. Primary biliary cirrhosis - experience in University Hospital, Kuala Lumpur. Med.J.Mal. 51:99-102 1996.

CIRRHOSIS

Ross and Dass found that in 1980 there were about 32 male and 4 female admissions for cirrhosis a year at the Penang GH. Of these 60% were from the Indian population who constitute only 11.7% of the local population. The statistics department also note that 40% of deaths due to cirrhosis occur in the Indian community. Of 179 patients over 35 months who had liver biopsy 32 had cirrhosis. 38% had mixed nodular cirrhosis, 28% macronodular cirrhosis, 25% alcoholic cirrhosis and 16% micronodular cirrhosis. When present with chronic active hepatitis cirrhosis was usually of the mixed nodular type. Cirrhosis was commonest in the 50-60 year age group, whilst hepatocellular carcinoma was commonest a decade later.

Kudva and Zawawi reported another series of 80 cirrhotics seen over 6 years at the UKM Department of Medicine from 1982. Alcohol, Hepatitis B and idiopathic causes accounted for about a third of cases each. Again Indians were noted to be significantly more common in the alcohol related cirrhosis while race was not significant in the other causes. Looking at clinical features they noted that acites was that commonest feature at presentation. Common associated conditions included gallstones (37%), diabetes melitus (22%), and peptic ulcer (31%). Hepatocellular carcinoma was found in 10%.

According to Ross and Dass, the high proportion of cirrhotics among Indians was paralleled by a similarly high proportion of Indians with non-cirrhosis alcohol related illness and to a less extent with hepatitis. It most likely that it is the excess in the amount of alcohol ingestion that causes more cirrhosis among Indians. However, there may be a racial predilection towards cirrhosis among Indians as there are genetically determined factors related to histocompatibility antigens that can influence the development of cirrhosis.

In Kelantan, Mahendra Raj looked at the prevalence of peptic ulcer in non-alcoholic

cirrhosis to determine if it occurred more often than in the general population. He found 4.9% of non-alcoholic cirrhotics endoscoped had duodenal ulcers and 7.3% had gastric ulcers. Without a control population it could not be said if this showed that these cirrhotic patients were predisposed to peptic ulcers. Nevertheless from comparative data it may seem that these patients had more gastric but not duodenal ulcers than expected. Hepatitis B surface antigen was documented in 62 of his patients and 76% of them were positive.

There is one report of an unusual association of portal cirrhosis, with multiple nodular fibrotic lesions in both lungs and widespead but moderate haemosiderosis of unknown aetiology in a patient from Klang. The case appears to be rather unique even after reference to international literature.

References

Lau KS, Mukherjee AP, Prathap K and White JC. Portal cirrhosis and idiopathic pulmonary fibrosis with generalised moderate haemosiderosis. Med.J.Mal. 28:253-256 1974.

Ross IN and Dass PK. The spectrum of liver disease in Penang: A clinical and histological study. Med.J.Mal. 40:225-232 1985.

Kudva MV and Zawawi MM. Chronic liver disease in Kuala Lumpur, Malaysia: a clinical study. Sing.Med.J. 31:368-373 1990.

Mahendra Raj S. Prevalence of peptic ulcer in 82 Kelantanese Malaysians with non-alcoholic cirrhosis. Med.J.Mal. 47:208-211 1992.

THE BUDD-CHIARI SYNDROME

The clinical syndrome due to occlusion of the hepatic vein at the junction described by Budd in 1845 and Chiari in 1899 is rare worldwide. One case has been reported by Lee in Malaysia.

Reference

Lee YS. Budd-Chiari syndrome - a case report. Med.J.Mal. 37:80-81 1982

THE BILIARY SYSTEM

CHOLEDOCHAL CYSTS

In a rare condition such as choledochal cysts, we do not yet have any series that can estimate its frequency in live-births. There have been case reports of cases in adults and in one cholangiocarcinoma had occurred. Nah and Wong noted 8 cases in Kuching over 4 years from 1996. Choledochal cysts presenting in pregnancy is rare but Perumal and Balasegaram have observed 3 cases. Hormonal changes may have caused greater cystic dilatation.

References

Krishnan MMS and Couper NTA. Large Type 1 choledochal cyst in adults - a case report. Med.J.Mal. 39:163-166 1984

Yeoh NTL, Somasundran K, Alhady SF and Paramsothy M. Choledochal cyst and cholangiocarcinoma. Med.J.Mal. 41:365-369 1986

Nah SA and Wong LM. Choledochal cyst: a 4 year experience in Sarawak General Hospital. Med J Mal 56sA:120 2001.

GALLSTONES

Extrapolating from ultrasound examination of 728 subjects in Kelantan, of whom 44 had asymptomatic gallstones, Ross and Jayakumar estimated that the prevalence of cholelithiasis was 12% in males and 14% in females in the under 30 year age group. They further estimated that the odds of having gallstones increased by 5% each year of life. There did not seem to be any ethnic variation. The median diameter of stones was 10mm.

Langenbach is credited with performing the world's first cholecystectomy in 1882. Records show that as early as 1931 the operation had been done in Malaysia although we do not know who performed it first here. Today, in most of our hospitals, cholecystectomies are among the 5 leading major elective operations performed. Nevertheless Ross and Jayakumar found the cholecystectomy rate in Kelantan to

be only 6 per 100,000, which is much lower than 70 and 240 per 100,000 in the U.K. and Canada respectively.

In an analysis of the composition of several gallstones, Azman and Halili suggest that local stones have a higher non-cholesterol component and higher concentration of calcium than those elsewhere.

Cholecystitis

Hussein and Balasegaram, while in Seremban and KL GH, have studied the practice of performing routine emergencies cholecyctectomies within 12 hours for all patients clinically diagnosed to have acute cholecystitis. In 218 unselected cases, seen between 1968 and 1973, females numbered 130 compared with 88 males. The average age of patients was 55 years. Calculi were seen on radiography in 18% of their patients. They reported that in only 3 cases was cholecystitis absent at operation. 40 (18%) patients had gallbladder and common bile duct stones, 73 (33%) had stones only within the gallbladder, 31 (14%) had stones only in the common bile duct and 71 (33%) had acalculous cholecystitis. They encountered concurrent peptic ulcer in 11 patients and pancreatitis in 10. 3 patients had a concurrent abdominal malignancy.

In the series only one post-operative death occurred. Post-operative morbidity was also low. Today ultrasonography helps surgeons more accurately diagnose cholecystitis but in most hospitals is it not usually done urgently nor the policy of immediately operating adopted.

Gallstone ileus that results from chronic inflamation forming a cholecystoenteric fistula through which the gallstone passes is rare but because of delay in seeking treatment in our patients, it may be perhaps encountered more frequently here. Low has reported 2 cases.

Kutty studied 327 resected gallbladders, and the patients' case records, over a 4 year period from 1968. 214 (65%) had chronic cholecystitis. In this group 64% were Chinese, 25% were Indians and Malays (11.5%) were under-represented. Among Indians, females were 4 times more often affected than males, whereas among Chinese and Malays women only outnumbered men in a ratio of 1.2-1.5:1. Women tended to suffer the disease younger than men, especially Indian women. 13.5% of the chronic cholecystitis was acalculous. A further 64 (20%) had acute on chronic cholecystitis with a pattern similar to the above.

49 of the specimens were cases of acute cholecystitis. 17(34%) of these were acalculous. The precipitating cause was not obvious in 25 cases, but roundworms were possibly the cause in 2.

Asiatic Cholangiohepatitis

Gallstones or cholelithiasis can also occur in the intrahepatic biliary system. It has sometimes been termed Asiatic cholangitis as it has been reported to be as common as 30% of gallstones among some areas in China. Balasegaram wrote that 10% of biliary calculi in his experience were associated with intrahepatic stones in 1972. Chinese outnumbered Malays by a ratio of 15:1. He also described a number of cases where gallstones were found only in the intrahepatic system or in liver cysts, where there were no stones in the extrahepatic biliary system. A possible reason he offered for the high occurrence of intrahepatic calculi was delay in seeking surgical treatment. He looked for evidence of parasitic infestation in his cases but found none.

The stones in Asiatic cholangiohepatitis are at operation soft brown stones that are mud-like. Repeated infections by bile splitting organisms have been suspected as the cause. At the UH over 4 years from 1986, there were 21 (5%) such cases out of 424 biliary operations. Most were from rural areas. All races and both sexes were affected. Often they were thin and in the third or

fourth decade.

In Kelantan, USM workers reported 20 cases of cholangitis seen over 2½ years from 1990. 80% were females with a median age of 58 years. 11 had also previously documented cases of cholangitis. 14 patients had the friable brown bilirubinate stones in the common bile duct with no gallbladder stones. 2 patients had periampullary carcinoma, in 4 patients *Ascaris* worms were seen, including one of the patients with periampullary carcinoma. Only 2 patients had gallbladder stones.

Over 3½ years from 1993 Din *et al*. reported an experience 49 cases of intrahepatic calculi at the KL GH. 19 of these cases were from gallstone patients from the 647 who had cholecystectomy in the same hospital giving a rate of 3% of hepatic calculi, which is much lower than the 10% Balasegaram reported 25 years earlier. The remaining 30 patients were referred from various parts of Malaysia as KL GH was the referral centre. The median age of patients was 49 years. Females outnumbered males 2:1. 59% of patients were Malays, 27% Chinese and 14% were Indians and other races. In 35% stones were found in the left hepatic duct, 10% they occurred in the right hepatic duct and in 55% the stones were located in both ducts. Benign strictures were observed in 29%, *Ascaris* was found in only 6% (3 patients) and there was one case each of cholangiocarcinoma, Caroli's disease and thalassaemia. Despite various combinations of surgical and non-surgical interventions 57% of patients had residual stones.

Mirizzi syndrome

Mirizzi syndrome is where a gallstone impacted in the neck of the gallbladder causes extrinsic compression of the common hepatic dust followed by a fistula formation between the gallbladder and the common hepatic duct. It is a rather rare complication but HUSM workers reported seeing 3 cases over 2 years from 1992 in Kota Bharu.

References

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Khan TF, Muniandy S, Hayat FZ et.al. Mirizzi syndrome – a report of 3 cases with a review of the present classifications. Sing Med J. 40:171-173 1999.

Din J, Qureshi A, Daud A and Ahmad H. Intrahepatic stones: the UKM experience. Med J Mel. 55:473-477 2000.

LIMY BILE

Limy bile is a rare condition where calcium, usually in the form of carbonates and sometimes bilirubinates and phosphates, accumulates in the gall bladder rendering it opaque on a radiograph. The consistency of bile may vary from fluid to putty-like or even solid, and the colour from white through yellow to brown. One case was reported in Taiping by Thambi Dorai and in a series from UH one case was found in 745 cholecystectomies.

References

Krishnan MMS and Lim KH. Limy bile. Case report and review of literature. Sing.Med.J. 23:374-376 1983

Thambi Dorai CR. "Limy bile" - a case report. Med.J.Mal. 42:119-121 1987

THE PANCREAS

ACUTE PANCREATITIS

Acute pancreatitis is a fairly common acute surgical problem requiring emergency hospital admission, a condition all doctors will have had an encounter with. The local pattern of the disease however has not been very well studied. There has been one study reporting a series of 142 patients in Kelantan in 1995. Females outnumbered males by a ratio of more than 3:1. The incidence among females peaked in the third decade of life. 21% (23/109) of the women were pregnant. Ultrasonography revealed gallstones in only 9.4% but abnormalities of serum transaminases were found in 35% suggesting that occult gallstones/microlithiasis may account for more than that. There was a higher frequency of ascariasis in this group of patients (31%) compared with a control hospital population (13.6%) suggesting that ascariasis may be an important cause of acute pancreatitis in Kelantan. Alcohol was virtually absent as an aetiological factor. Only 8.4% of patients fell into the category of severe pancreatitis and the overall mortality rate was only 2.1%. An abstract by Ridwan et.al. noted 143 cases in Kuala Terengganu over 4 years from 1995 with a similar female preponderance. 9.2% of patients had severe pancreatits and the mortality in this group was 54%.

Another study covering patients seen in UKM over 7 years from 1990 had a collection of 71 patients. There were more males than females in a ratio of 1.5:1. There was a wide scatter of age in the affected patients but the peak age was between 35-44years. Indians were over-represented and Chinese were under-represented. Biliary calculi could be identified as the cause of pancreatitis in 45% of patients and alcohol in 20%. Trauma was the cause in only 2.8%. 30% of patients were classified as severe according to the Simplified Glasgow criteria. The were 2 deaths giving a mortality rate of 2.8%.

There is a suspicion that acute pancreatitis is commoner in the fasting month and thought to be related to a big meal at the breaking of fast but this has not been confirmed in any studies.

Pancreatic pseudocyst: This is not an uncommon complication of acute pancreatitis. In six cases reported from UKM over 3 years, in two the pancreatitis was due to trauma, one to alcohol, one to gallstones and two were idiopathic. All were well after surgical drainage.

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Nadesan MS, Qureshi A, Daud A and Ahmad H. Characteristics of acute pancreatitis in Universiti Kebangsaan Malaysia. Med J Mal. 235-241 1999.

Ridwan As, Mat Sain Ah and Abdullah AJ. Acute pancreatitis – evaluation of management in Hospital Kuala Terengganu from 1995-1998. Med J Mal. 56sA:125 2001.

CHRONIC PANCREATITIS

Chronic calcific pancreatitis presenting with symptoms of abdominal pain, diabetes mellitus and steatorrhoea is not unfrequently encountered in Malaysia. Many are associated with alcohol and affect mainly middle aged males, more commonly Indians. Besides this group some cases have been labelled 'tropical calcific pancreatitis'. In such cases usually young adults are affected. They are non-alcoholic, with a history of malnutrition and usually without marked abdominal pain.

Reference

Tan CT, Kannan P and Sng KH. Tropical calcific pancreatitis. Med.J.Mal. 35:150-154 1980

THE DIAPHRAGM AND ABDOMINAL WALL

CONGENITAL DIAPHRAGMATIC HERNIAS

Congenital diaphargmatic hernias usually bear the name of Bochdalek or Morgagni who first described the two usual variants of the hernia. In the first quarter of this century it was mainly a post-mortem diagnosis as was the case when Shanmugaratnam and Haridas first described it locally in 1948.

In 1973, Damodaran, Nair and Somasundram reported probably the first successful surgical correction of such a hernia in a 2 year 10 month old child in Alor Star. Somosundaram reviewed 20 cases in his experience at the University Hospital KL in 1979. In 1984 Laidin, Zain and Mahmud reviewed 24 cases from the UKM experience. The latter estimated the incidence at 1:10,000 based on the number of deliveries at the KL Maternity Hospital. This is less than the incidence in most advanced countries which is about 1:5,000. We may in fact be missing the diagnosis in some. It was noted in UKM that 29% of their patients were not diagnosed correctly till more than 24 hours after birth. Quah, Hashim and Simpson reported a case presenting at 2½ years old. In contrast, efforts of early diagnosis in some advanced countries lead surgeons even operate on the foetus in-utero when the condition is found, although the results of these cases are not encouraging.

References

Damodaran A, Nair S and Somasundram R. Congenital diaphragmatic hernia: a case report. Med.J.Mal. 28:99-102 1973

Ahmad ZL, Zain AR and Mahmud MN. Congenital (Bochdalek) diaphragmatic hernia: problems in diagnosis and management. Med.J.Mal. 39:185-191 1984

Quah BS, Hashim I and Simpson H. Bochdalek diaphragmatic hernia presenting with acute gastric dilatation. J Pediatr Surg 34:512-514 1999.

GASTROCHISIS

Naidu, Lee and The reported 10 cases of neonates with gastrochisis seen in Alor Star Hospital over 5 years from 1989 to 1993. There were 5 girls and 5 boys. Only 2 had associated anomalies, one a unilateral undescended testes another had midgut malrotation. Nine recovered and survived after surgery.

Reference

Naidu RR, Lee FH and The KH. Management of gastrochisis in a peripheral hospital setting. Med.J.Mal. 51:444-446 1996.

RECTUS SHEATH HAEMATOMA

Hussein has highlighted this condition as a differential diagnosis to entertain in the evaluation of the acute abdomen. Trauma, including 'urut', previous abdominal surgery, and bleeding dyscrasias are underlying causes that should be borne in mind.

Reference

Hussein MS. Rectus sheath haematoma Med.J.Mal. 29:311-314 1975

INGUINAL HERNIAS

Obstructed inguinal hernias used to be the commonest cause of intestinal obstruction in Malaysia and probably still is among Malays and Indians in some rurals areas. Even in an urban setting such as the UH, Ti and Yong have reported in 1976 that for Malays and Indians inguinal hernias was the leading cause of bowel obstruction.

Very large hernias are seen from time to time in rural areas and one treated preoperatively with pneumoperitoneum has been described.

References

Ti TK and Yong NK. The pattern of intestinal obstruction in Malaysia. Br.J.Surg. 63:963-965 1976

Thambi Dorai. Giant inguinoscrotal hernia - a case report.

Sing.Med.J. 27:177-179 1986

FEMORAL HERNIAS

Among strangulated hernias causing bowel obstruction, Ti and Yong at the UH noted that there was one femoral hernia for every 7 inguinal hernias.

Referernce

Ti TK and Yong NK. The pattern of intestinal obstruction in Malaysia. Br.J.Surg. 63:963-965 1976

CONGENITAL INTRAPERITONEAL HERNIAS

Most intraperitoneal hernias remain asymptomatic and even when they cause symptoms, they are not diagnosed until a laparotomy is done. They are usually due to problems of gut rotation during utrauterine growth.

LEFT MESOCOLIC HERNIA - This has also been called a left paraduodenal hernia. It probably occurs when the small bowel moves to the left under the descending colon during Stage II of embryonic gut rotation. With the fixation of the colon the intestines are trapped behind the left mesocolon. The inferior mesenteric vein lies along the anterior rim of the neck of the sac. Kyaw has reported a case and distinguished this from peritoneal encapsulation. In a left mesocolic hernia the intestines enter and exit the sac through one orifice whereas in peritoneal encapsulation there is a separate entry and exit point.

Reference

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OBTURATOR HERNIAS

As in most countries, obturator hernias are rare. The patient is usually a thin elderly female with vague abdominal symptoms or intestinal obstruction. Surgical units in our hospitals are likely to encounter one case every few years.

Reference

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ABDOMINAL COCOON

An abdominal cocoon, was first described in 1978 by Foo in Singapore as a rare condition that mostly affected young Asian girls. It consists of a fibro-collagenous membrane encasing the whole or part of the intestines like a cocoon causing intestinal obstruction due to kinks. The aetiology of the cocoon has not been clearly established. Sporadic cases occur locally. Yip and Lee reported 5 cases in UH and Kyaw has reported one case in HUSM. Peritoneal encapsulation, a membrane covering the small bowel that can easily be removed, is probably a developmental abnormality. It is largely asymptomatic and found incidentally at laparotomy or autopsy needs to be recognised as a different entity.

References

Yip FW and Lee SH. The abdominal cocoon. Aust N Z J Surg 62:638-642 1992.

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HYDROCELES

In the Hikayat Abdullah, the scribe relates

his personal ordeal involving a hydrocele which he blamed the excessive heat of Singapore for. It happened in the 1820s, when he was a Malay tutor to the white merchants. He complained of pain which made him unable to rise sometimes for three days. One day while visiting a friend he just happened to meet a 'general doctor' of the East India Company who was waiting to sail to Europe. The doctor explained surgical aspiration and offered to do it for him. He was both excited and fearful. He gives a captivating account of the debates he had whether or not to undergo the operation. In the end he decided to take the plunge; although not before making out his will! Fortunately, he survived the treatment and lived to tell us about it, and he felt very much better for the cure. In fact he was quite ecstatic. Full of gratitude he bought three hundred mangosteens and four jars of preserved fruits for his doctor, and insisted that the doctor who was leaving to board the ship accept the gift.

Abdullah kept the fluid that was tapped and told the story to his friends who were greatly amazed. He even sent two bottles of the liquid to his parents in Malacca. As the news spread several men came beseeching him to take them to the doctor. Alas, he had sailed and Abdullah tells us some of them wept because he had gone. The account is thoroughly worth reading.

Reference

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CHAPTER 29

THE URINARY SYSTEM

GLOMERULOPATHIES

Glomerulopathy is a histological diagnosis. What the different types have in common is the disease process is centred in the glomeruli; usually immune complexes are deposited on it with an inflamatory reaction. It is not a diagnosis of aetiology and in many cases the aetiology of immune complexes is unclear. It is also not a clinical diagnosis, as clinically glomerular disease can present in several ways. About half present as the nephrotic syndrome, about 20% as asymptomatic proteinuria and/or haematuria and others as nephritis, renal failure etc.. But glomerulopathy or glomerulonephritis is a useful classification of disease because it tells us something of the pathological process.

The pattern of glomerular disease in Malaysia can only be seen from the studies of patients who have clinical conditions that warrant a renal biopsy and present at a referral centre. This is not a representative picture of the disease in the community. The distribution of the various histological types seen in a different studies from KL and Kelantan are given in Table 29.1. Comparison of the studies is difficult because of different terminology, staining tests and observer variation between them. There is general agreement though, that the pattern seen here is closer to the Western than to some other tropical countries like Nigeria or New Guinea. For example malarial nephritis and other tropical nephropathy is not seen. Noteworthy forms of secondary

Table 29.1 Histological types of glomerulonephrites

Author	Prathap & Looi n=1000	Cheong *et.al.* n=133	Zainal *et.al*. n=74
Institution	UH KL	GH KL	HUSM Kelantan
Minimal change	25.7%	16.5%	29.0%
Focal -proliferative	2.9%	21.8%	-
-sclerosis	5.4%	5.3%	19.4%
Diffuse -proliferative	21.9%	28.6%	3.2%
-membranous	5.5%	10.5%	6.5%
Chronic glomerulonephritis	4.0%	14.3%	-
IgA	5.8%*		41.9%
Lupus nephritis	18.4%		
Other	10.4%	3.0%	

(* immunofluorescence was not available in the first part of the series, in the part it was available it accounted for 11% of renal biopsies)

glomerular disease are SLE and IgA nephropathy.

In patients with acute nephritis, D'Cruz *et.al.* at USM in Kelantan remarked that 98% showed evidence of post-streptococcal nephritis. They had 124 children over one year from mid 1987. 54% came from families below the poverty line. 69% had preceding skin infecitons but only 6% had preceding throat infections.

In the subgroup of patients with the nephrotic syndrome clinically, Prathap and colleagues at the UH have reported that histologically 45% of renal biopsies were minimal change glomerulonephritis but all other types were also seen. Renal vein thrombosis is a curious but serious association of the nephrotic syndrome. It is debated whether the thrombosis is the cause or the effect of the nephrotic syndrome, but the latter argument seems to be favoured.

Table 29.2 Histological types of IgA glomerulonephrites

Author *et.al.*	Prathap & Looi n=142	Cheong n=164
Minimal change	11.3%	14.6%
Focal -proliferative	14.8%	17.1%
-sclerosis	4.9%	31.7%
Diffuse proliferative	1.4%	4.3%
Mesangioproliferative	62.7%	31.1%
Mesangiocapillary	0.7%	
Global glomerulosclerosis		1.2%
Chronic glomerulonephritis	4.2%	

In 153 patients presenting with nephrotic syndrome who had minimal change glomerular disease histologically, Looi, Wang, Lam and Chua found that 35% showed mesangial deposits of IgM, but this group had no significant features in presentation or response to therapy.

In the subgroup of patients who present with asymptomatic proteinuria and/or haematuria, Cheong *et.al* reported that of 265 such patients, 23% had lupus nephritis, 40% had IgA nephropathy and 37% had primary glomerulonephritis.

IgA Nephropathy: Such a condition, first documented by Berger in 1968, where IgA containing immune complexes in the glomeruli is probably closely associated with infections of the mucosal systems, principally the respiratory and gastrointestinal. All the different clinical presentations and almost all the histological forms of glomerulonephritis can be seen. A table of the histological distribution in two studies is given (table 29.2). Cheong and colleagues identified 164 cases, in GH KL for the period 1981-1988 accounting for 20% of all glomerulopathies. It did not have any racial predilection and both sexes were similarly affected. Peh and UH co-workers reported 149 cases in 10 years. They noted a Chinese preponderance. In age the peak occurred in the 20-30 year group.

Immunotactoid glomerulopathy: Immunotactoids are fibrillary protein deposits like amyloid but have wider fibrils and have a highly microtubular-tactoid ultrastructure and do not stain similarly with Congo red. Cheah *et.al*. reported a case in a 31-year old woman with nephritic syndrome but without renal impairment.

The role of Hepatitis B (HBV): In countries like Malaysia where the prevalence of HBV carriers is high glomerulonephritis may be caused by immuno-complexes of the HBs antigen. In 259 patients who had renal biopsies over 3 years in the UH, Looi and Prathap found

the 64% (30/47) of patients with systemic lupus erythematosus had HbsAG in in glomerular immune complexes, whereas only 6.1% (13/212) other patients did.

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POLYCYSTIC KIDNEYS

The infantile variety which is fatal is autosomal recessive in inheritance. Raman and colleagues showed that it can be diagnosed antenatally by ultrasound, in their case at 36 weeks of gestation.

The autosomal dominant type that presents later in life has been recorded in a rare association with polycystic ovarian syndrome in a 30 year old female.

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RENAL TUBULAR ACIDOSIS

Renal tubular acidosis is a defect in urinary acidification in the absence of renal failure. It usually presents with symptoms of the consequent hypokalaemia. Devadason reported one case in Taiping in 1976 presenting with periodic paralysis. In 1990 Hanip and colleagues at the UKM reported 2 cases also with severe periodic paralysis which occurred at serum potassium levels of 1.4 and 1.9 mmol/l which were associated with rhabdomyolysis. Zainal reviewed the records of HUSM in Kelantan and noted 16 patients over 5 years from 1986 to 1990. All were women. Their mean age was 29 years and prognosis was good.

Thong reported finding 3 children in a family with distal renal tubular acidosis and co-existent hereditary elliptocytosis in 1997.

Bruce *et.al*. have described 3 mutations associated with distal renal tubular acidosis found exclusively in Southeast Asian populations. The gene affected is the red-cell

anion exchanger band 3 (AE1, SLC4A1). The mutation $Ala^{858} \rightarrow Asp$ appears to be dominant. 2 other mutations $Gly^{701} \rightarrow$ Asp and deletion of Val^{850} appear to be pseudo-dominant and clinically significant only when inherited together or with the ovalocytosis gene.

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RENAL TUBULAR OSTEOMALACIA

Fanconi's syndrome: Characteristically, in Fanconi's syndrome, proximal tubular reabsorption of a constellation of substances are defective, including glucose, amino acids, phosphate and potassium. In some cases as described by Paramaesvaran of an Indian Muslim boy in Penang in 1965, only phosphate and glucose were involved.

Sporadic Adult-onset hypophosphatemic osteomalacia: This is a rare disorder that occurs as a result of either an isolated defect or generalised renal tubular disfunction that includes tubular reabsorption of phosphate. Two cases, a 52 year old Chinese female and a 28 year old Malay male, have been reported who had both undergone laminectomies for intractable low back pain. They had serum phosphate levels below 0.60mmol/l, bone tenderness and proximal muscle weakness and recovered with 1,25 dihydroxyvitamin D and phosphate replacement.

X-linked hypophosphatemic rickets: This is due to an isolated phosphate transport defect at the renal tubule. It is a dominant trait unlike many other X-linked diseases. Yong has described a family with 13 affected persons over 4 generations.

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EMPHYSEMATOUS PYELONEPHRITIS

Emphysematous pyelonephritis is a rare and life threatening form of suppurative infection of the kidneys with gas-producing organisms. Koh, Lam and Lee reported 4 cases seen at the UH between 1986 and 1991. In all 4 cases the infecting organism was *E. coli*, a facultative anaerobe.

Reference

Koh BH, Lam HS and Lee SH. Emphysematous pyelonephritis: drainage or nephrectomy? Br J Urol. 71:609-611 1993.

XANTHOGRANULOMATOUS PYELONEPHRITIS

Xanthogranulomatous pyelonephritis describes an uncommon but not rare form of chronic renal infection. As its name suggests, it destroys the renal parenchyma replacing it with areas of lipid containing macrophages (foam cells), other inflammatory cells, fibrosis and abscesses visible as yellow granulomatous tissue. Patients present with loin pain, recurrent urinary

infections and calculi. Typically the affected kidney is non-functioning when discovered.

Yong and Prathap reported the first series locally from the UH covering 7 years from 1968. They had 8 cases, 6 women and 2 men. 6 were Chinese one a Malay and one Eurasian. All except one had calculi. The patients had a mean duration of 2 years of symptoms. All 8 patients were discharged well after nephrectomy. Puvaneswary *et.al*. reported another case in a 62 year old Indian woman at the UH in 1980. In 1993 Koh reported a further series from the UH of 7 years from 1985. He recorded 10 cases. Again there were more women, 8 compared to 2 men, which fits with experience elsewhere. The patients' ages ranged from 36 to 64 years with a mean of 49 years. 8 patients had calculi, 8 had urine infections (with the expected usual gram negative organisms) and 9 had non-excreting kidneys. The median duration of symptoms was 2 years. Nephrectomy was curative. Early recognition of this condition leads to a nephrectomy sooner that will spare the patient having to endure prolonged suffering.

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Koh KB. Xanthogranulomatous pyelonephritis in a Malaysian population. Sing Med J. 34:341-342. 1993.

RENAL MALACOPLAKIA

Malacoplakia literally means soft plaques. It is a rare lesion that usually occurs in the urinary bladder characterised by numerous mottled yellow and grey soft plaques consisting of macrophages and Michaelis-Guttman bodies or calcospherites which form around intracellular bacteria. Teh *et.al*. have reported an unusual case where the histological features mentioned were found in a large mass in the middle third of the kidney which had infiltrated the ascending colon in a 38 year old woman who had an *E. coli* right perinephric abscess. The patient received a right radical nephrectomy and right hemicolectomy after drainage of the abscess and recovered fully.

Reference

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ACUTE RENAL FAILURE

In a review of patients with acute renal failure seen in the nephrology department of the KL GH in 3 years from 1976, Abu Bakar and Suraini found 152 cases. The age and sex distribution was slightly different. They broadly divided the patients to medical causes (44%) surgical causes (19%) urologic causes (15%) and obstetric causes (22%). There probably was a bias in referral to the unit as 16% of patients had been anuric, 59% were oliguric and only 26% non-oliguric. The mortality rate was 30%, being higher among surgical patients.

In a study to see the pattern of acute renal failure in the entire KL GH, Abu Bakar, Zaki and Prasad prospectively collected a series of patients admitted over a 3 month period in 1987. They found 60 patients out of 22,033 admissions. Acute renal failure was oliguric in 22% and non-oliguric in 78%. Prerenal causes formed the majority; consisting of decreased cardiac output (11), diminished intravascular volume (13) and post-operative (9). Toxic causes accounted for 13 cases, gentamicin being the main drug (8). Another interesting case, not totally uncommon, was due to ingestion of 'jering' (*Pithecellobium lobatum*). Infective causes accounted for 5 cases, obstructive jaundice for 3 and miscellaneous causes another 6. Males slightly outnumbered females and the racial pattern showed no unusual features. 76% of patients were over 40 years, but the paediatric age group was not included in the study. Of the 60 patients 38 were actually

admitted to hospital with a normal serum creatinine value. Of these, 38 with hospital acquired acute renal failure 65% were iatrogenic. Only 18 patients were referred to the nephrology service. Mortality was 18%, but was 54% in the oliguric group and 9% in the nonoliguric group.

Loo and Zainal reviewed patients with acute renal failure in HUSM in Kelantan over 4 years from 1986. They observed 164 patients out of 79,196 admissions, giving a rate similar to the prospective study in KL GH. Similarly 80% of their patients were non-oliguric. Obstructive uropathy was the leading cause (45), followed by infective causes (32). Among prerenal causes there were 10 from decreased cardiac output, 12 from diminished intravascular volume and 11 post-operative azotemia. Obstetric complications excluding obstructive uropathy accounted for 11 cases and aminoglycoside toxicity accounted for 7. The ratio of males to females was 1.6:1. Malays formed 87% of the patients, Chinese 12% and Indians 1.2%, which reflects the general population in Kelantan. The mean age of patients was 50 years. 70% were over 40years old. Acute renal failure was present on admission in 69%. As expected mortality was higher in oliguric patients (56%) compared to the nonoliguric group (19%).

Hooi reported a series of 246 patients with established acute renal failure requiring dialysis in the Hospital Sultanah Aminah, Johor Bharu from 1990-1994. 41.5% of the patients were from outside the Johor Bahru district as the hospital was the referral centre for the whole state. Males outnumbered females by a ratio of 3:2. Chinese who form 35.8% of Johore's population was the only racial group under-represented (21% of patients in the series). Acute renal failure was caused by acute tubular necrosis in 55%, post-renal obstruction in 23%, nephrotoxins in 6% and other causes in 16%. The total mortality rate was 48% but was lower in the group with obstructive causes of renal failure (22%).

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END-STAGE RENAL DISEASE

End stage renal disease (ESRD) without treatment is invariably fatal with a median survival of about 55 days. In a review of ESRD in the nephrology unit in KL GH in 1982, 53% of 174 patients presented for the first time in uremia, without known renal disease in the past. At the time of review, about 1 year later, 21% were dead, 33% were on conservative treatment while 35% went on to a chronic dialysis program and 10% had received a renal transplant.

In a study focusing on analgesic nephropathy as a cause of end-stage renal disease, in 1986, Segasothy *et.al.* noted from the records of 180 patients at GH KL that 31% were due to gromerulonephrites, 14% from tubulointerstitial nephropathies, 6.7% from systemic disease, namely diabetes and systemic lupus erythematosus and 5% were from vascular nephropathies. In 43% (78) the cause was unknown, among these 6 gave a history of excessive analgesic use as did 5 of those with other pathologies.

Hooi estimated the incidence of ESRD in the Johore Baru district from a register of patients at the Hospital Sultanah Aminah from 1990. An incidence of 79:1,000,000 and 86:1,000,000 were obtained for 1990 and 1991 respectively. Using this figure the estimated number of new patients with ESRD for the whole country each year would be about 1,600. In her series males outnumbered females 3:2.

More than half presented with no known cause of the renal failure. Diabetes accounted for about 20%. 65% of patients were between the ages of 31-60years. Malays accounted for 50.4%, Chinese 39.4%, Indians 7.8% and others 2.3% which evenly reflects the population distribution of Malaysia.

Dialysis Provision

Lim *et al*. have reported that the number of publicly funded or subsidised patients on dialysis, *ie*. those managed in the MOH hospitals, increased from 11 per million people in 1990 to 28 per million in 1996. This falls short of the estimated need for dialysis as the need of dialysis for new cases alone is at least 80 per million population a year. With the setting up of the Malaysian Organ Sharing System, Lim *et al*. were able to collect data on dialysis provision throughout the country. Dialysis provision by the private sector and non-governmental organisations (which began only in 1991) saw a dramatic growth in the 1990s. On average 16.5 dialysis centres started up each year, more than doubling the number of dialysis patients from about 2,000 in 1991 to 5,614 in 1999. As in 1999 there were 181 dialysis centres (of which 161 provide haemodialysis and 20 provide CAPD). 52 of these were provided by the MOH, 13 more by other government agencies (Universities and Armed Forces), 73 run by the private sector and 43 by non-governmental organisations. Together they had a capacity for 7,760 patients for haemodialysis.

With 5,614 patients on dialysis in 1999, this meant a rate of 253 per million population, with an estimated new dialysis acceptance rate of 49 per million population. Lim noted some geographical disparity with Penang and KL/Selangor having about 480 dialysis patients per million population whereas Sabah and Kelantan had only 64 and 51 per million population respectively. The trend is strongly towards centre haemodialysis with home haemodialysis declining steadily from 35% in 1994 and projected to be14% only in 1999.

In a study on the cost effectiveness of the MOH dialysis programme as in 1996, Lim *et.al*. found that centre haemodialysis was the most cost effective, followed by home haemodialysis (which cost 1.08 times more), CAPD (1.4 time more) and intermittent peritoneal dialysis (1.7 times more).

Haemodialysis

Maintainance haemodialysis was first introduced by Scribner and colleagues in 1960 and gained acceptance all over the world quickly. In Malaysia it was started in the Department of Urology GH KL in the mid-60s and taken over by the new Department of Nephrology later. In a review up to 1982, 471 had been accepted into the programme. Patient survival was 90%, 77% and 44% at one, three and six years respectively. A home haemodialysis programme was begun in 1977. A review in 1984 showed that of 194 patients accepted into the programme 7 died before the training but patient survival was 93%, 80% and 69% at one, three and five years respectively. A study of rehabilitation in 1984 showed that over 90% of patients achieved good rehabilitation and returned to employment or to household chores.

In a 1999 report, Lim *et.al*. noted that the 2,480 patients on the MOH haemodialysis programme register had a remarkable long term survival. Patients under 40 years old had a life expectancy of 16 years and older patients did as well, when background mortality is adjusted for. Over all the 5 year survival rate was 68% in 1996. Diabetics were the patients who did poorly. 52% of patients were employed in 1996 and 71% reported a normal quality of life index score.

Encephalopathy like that initially reported in Denver in 1972 was first seen in 1976. By 1981, 18 such patients were seen. However, since the aluminium content of water has been

identified as the cause of this encephalopathy, rectification measures have been implemented and there have been no more cases.

Bone changes are potentially serious complications in patients with ESRD and those undergoing dialysis. In some areas it is widespread and disabling but in some localities it remains rare. In Malaysia, Segasothy, Kamal and Abu Bakar have noted that though osteoporosis (76%) was common, significant bone changes was not; being 2-9% at commencement of dialysis, rising to 20% when the total period of dialysis ranging up to seven years was considered.

Continuous ambulatory peritoneal dialysis (CAPD)

Experiments to treat renal failure with peritoneal dialysis go back as far as 1923 with Ganter. But it was only with newly designed catheters and commercially prepared solutions introduced in the 1960s that it started to find its place in the management first for acute renal failure then for ESRD. It is a simple technique free from machines required in haemodialysis but problems with mechanical blockage of catheters, infection and systemic physiological problem have to be overcome and expert supervision is necessary. The UH began a CAPD programme in about 1980 and Chua and Wang reported their initial experience in 1983.

In the 1999 review of outcome by Lim *et.al*. of MOH patients on CAPD which included 732 patients, it was found that patients under 40 years old at commencement had a life expectancy of 18 years. 26% were employed in 1996 and 60% reported a normal quality of life index score.

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RENAL TRANSPLANTATION

The first patient to undergo renal transplantation in Malaysia received a well matched kidney from his brother in December 1975. Both the patient, Martin Rinyeb who was 30 years old then, and his brother, 2 years younger, survived to celebrate the 25th anniversary of the landmark transplant on 13 Feb 2001 with their surgeon and nephrologist. Cadaveric transplantation started in 1976 but the programme did not take off well.

By December 1980, 56 transplants had been performed. The recipients were in the majority males and with a mean age of 30 years. There were 21 parent donors and 35 sibling donors.

The oldest donor was 72 years old and the youngest 17 years old. Patient and graft survival was 83% and 68% at 2 years respectively. By October 1994, a total of 540 renal transplants had been done at the Kuala Lumpur Hospital. Only 9 were cadaveric transplants.

Besides the MOH transplant programme, Malaysians have travelled abroad for renal transplants at first to India for commercial live donor (CLD) transplants. This decreased in the mid 1990s when India imposed restrictions on such procedures. In its place patients for Malaysia have gone to China for commercial cadaveric transplants (CCD). Many of these patients returned for follow up treatment with the MOH hospitals. Morad and Lim reviewed 787 tranplants patients from these 3 sources in the year 2000. 258 (33%) were from their living related donor (LRD) programme, 389(49%) had CLD, and 126(16%) had CCD transplants. Survival with graft function at 1 year was 91%, 90% and 90% respectively. At 5 years the rates were 79%, 72% and 65% respectively. They however said they were in no position to ascertain the incipient cohort for the CLD and CCD patients but had reliable reports of a number of perioperative deaths and early graft failures. They saw no difference in the incidence of fungal and viral infections All 3 groups had also similar rates of tuberculosis, malaria, cytomegalovirus, hepatitis B and C, infection.

Chan *et.al*. reviewed 235 renal transplant recipients who were followed up in MOH hospitals in Johore up to 1999. 78% had their transplants done overseas, 141 had living unrelated CLD transplants in India and 37 CCD transplants in China. Of the remainder, 51 (22%) patients had transplants under the MOH in KL, all LRD transplants except for 2 who had cadaveric transplants. 85% of the patients were Chinese, 7.7% Indians and 7.2% Malays. The primary renal disease was unknown in 69%, was glomerulonephritis in 17% and diabetes in 5.5%. The survival rate at 5 years with graft function was 93% for LRD and 80% for CLD. At 10 years the rates were 72% and 54% respectively.

Complications:

Suleiman *et.al*. reported that out of 237 patients that received a renal transplant between 1975 and 1986, 10 developed tuberculosis. 9 responded well to antituberculous therapy but one patient who also had cryptococcus in his sputum and CSF died 2 months after presentation. Reviewing 434 transplant patients alive up to 1992, they found there were 16 cases, giving a prevalence of 3.6%. The mean period of immunosuppressive therapy before cryptococcal infection was 48 months and the mean duration from symptoms to diagnosis was 13 weeks. The mortality rate was 31%.

Teo and Morad reviewed 106 patients with hepatitis virus who were grafted between 1975 and 1996. 41 patients (39%) had hepatitis B virus (HBV), 9 of them seropositive only after transplantation. 58 patients (55%) had hepatitis C virus (HCV) and the remaining 7(6.6%) had mixed infections. The proportion of these patients developing chronic hepatitis was 32%, 48% and 86% respectively, with a mean onset time which was shortest in those with mixed infections (3.9years) and longest in those with HCV (5.3years). There were altogether 17 deaths among these patients but only 5 were liver related.

Public Attitude

A survey of attitudes of the public towards organ donation done in 1992 gives the prospects of the cadaveric transplant programme a rather grim outlook. In a study of 632 parents of school children across the income groups and races showed that only 22% were willing to be organ donors. Most were also not willing for organs to be removed from a close relative. A survey among professionals, senior government officials and doctors produced such a poor questionaire return that the results could not be meaningfully analysed.

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URINARY CALCULI

Urinary calculi ranks alongside acute appendicitis as the commonest causes of surgical admission for acute abdominal pain, and it ranks alongside peptic ulcers as the commonest problem in general surgical outpatient clinics. In a national survey of hospital admissions for urinary calculi from 1962 - 1976, Sreenevasan found admission rate highest in Selangor and Negeri Sembilan. Nationally yearly admission rates rose from 19 per 100,000 in the period from 1962-1966 to 33 per 100,000 in the period from 1972-1976. Whether there is a real rise in the incidence of urinary calculi or just a greater acceptance of hospital treatmant among the populace cannot be ascertained. All hospital based studies on the incidence of stones also suffer from the fact that many stones remain asymptomatic and many patients resort to traditional and other forms of treatment.

In Sreenevasan's hospital survey upper tract stones accounted for 63 % of calculi. The annual admission rates (per 100,000) were highest in Penang (28), Selangor (25) and Kelantan (23) and were lowest in Kedah (4.6) and Johore (12). Multiple admissions for the same stone, however, is common for upper tract stones and cause admission figures to distort true incidence. In a 2 year study from 1984 in Kelantan, by Lim *et.al.* the operation rate for upper tract calculi was 3.4 per 100,000 a year, accounting for 34 % of urinary stone operations in the state. This underestimates the incidence as patients with upper tract stones are more likely not to come to surgery compared to those with lower tract stones. The incidence peaks among those between the age of 30 to 50 years. Males outnumber females in ratio between 1.5 to 3:1. A follow up study of 183 patients with urinary stones in HUSM from 1985 to 1995 however found that 88% of patients had upper tract stones and 70% of them had chronic renal failure.

Sreenevasan found that admission rates for lower tract calculi were especially high in Negeri Sembilan (26 per 100,000 annually). The rate was 18 per 100,000 in Selangor and between 4 to 9 per 100,000 for the rest of the country. Lower tract calculi are predominantly bladder calculi, only a few calculi are found in the urethra. The operation rate for lower tract stones in Kelantan in 1984-86 was 6.8 per 100,000. Lim, *et al* noted a male to female ratio of 28:1. Adult men were principally affected with a sharp rise in incidence with age. This was in contrast to other areas in the world with incidences as high, such as Thailand, Sumatra, parts of India, Iran and the Middle East, where bladder stones is chiefly a paediatric problem. A follow up report by McAll, Lim and Edward asserted that bladder outflow obstruction was not a feature in a considerable proportion of the men, in contrast to most reports of bladder calculi in the West.

In Limbang, in the fifth division of Sarawak, Lau and Ong retrospectively found 74 cases of urinary calculi over 5 years from 1975 in the hospital which had 10,108 admissions in that

period. There was no noticeable racial difference in frequency of urinary calculi among the 25,630 population of various races including, Malays, Ibans, Bisayas, Chinese, Muruts and Kelabits. No case were seen among the Penans who were a small group numbering 180 living deep in the interior.

There is a general clinical impression that small urinary calculi might increase in occurrence in Muslims as a result of the Ramadan fast, causing ureteric colic and stones that perhaps pass spontaneously. Urine analysis on a small sample of young Malay males have found various changes in urine volume and solute load but the investigators reported that there was no adverse effects on renal function.

References

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Cheah SH, Ch'ng SL, Husain R and Duncan MT. Effects of fasting during Ramadan on urinary excretion in Malaysian males. Br J Nutr 63:329-337 1990.

Nazmi N, Zainal D and Hashim M. Renal stones in Kelantan - has the pattern changed? Southeast Asian J Trop.Med. Pub. Hlth. 29:641-644 1997.

RENAL ANGIOMYOLIPOMA

A renal angiomyolipoma is an uncommon benign mesenchymal tumour of the kidney, first described in 1880 by Bourneville. In one form it is associated with tuberous sclerosis, where the tumours are small, multiple and bilateral. A number of these have been reported in association with tuberous sclerosis in Malaysia. The second form which occurs apart from tuberous sclerosis tends to occur in women, are often large and single. Yip and Lee reported one case and Koh, Wightman and George reported 5 cases, all from the UH. 5 of these 6 cases were in women and all the patients ranged in age from 40-72 years. 5 presented with acute abdominal pain from ruptured renal angiomyolipomas. In one case the bleeding was fatal.

References

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PROSTATE HYPERPLASIA

Lower urinary tract obstruction due to benign prostate enlargement is common in elderly men. It is however difficult to say how common it is. To extrapolate from the number of prostatectomies performed to get an indication of the incidence of the disease is an estimate encompassed by many inaccuracies. Acceptability of such treatment on the part of patients in rural and urban areas change with time at different rates. Availibilty of surgeons and the surgeons' policy on which patients, especially the elderly, are fit for such a previously major procedure also change with advances in anaesthesia. However, this is the best indication we can arrive at for the extent of this condition.

Open prostatectomies were performed in Malaysia as far back as 1932. But it was after the Second World War that a more widespread surgical service was established. Sreenevasan calculated the operation rate per 100,000 population for prostatic hyperplasia in Malaysia as 0.6 in 1950, rising to 3.8 in 1960, 10.0 in 1970 and 12.2 in 1980.

In the Malaysian experience the age range of patients, from 50 to 90 years, is similar to

patients elsewhere. Sreenevasan, Chelvanagam and Vijearasa in a consecutive series of 100 patients in GH KL from 1970 to 1974 found a mean age of 66 years. Cheong in 24 cases in Taiping in 9 months in 1983 and McAll, Lim and Edward in Kelantan in 1984 to 1986 found that nearly half the cases were in the 60 to 69 years age group. Yeoh in Penang collected 100 cases where TURP was performed over 1½ years with a mean age of 70 years. It is generally felt that in the local experience, the big majority of glands removed are benign. Yeoh found 10% of those of which histopathological examinations were done had prostatic carcinoma.

References

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Yeoh NTL. A personal experience with the first 100 TURP at the Penang General Hospital. Med.J.Mal. 44:129-133 1989

URETHRAL STRICTURE

This had been a common problem in the urological and surgical wards in Malaysia many years ago. The majority then were gonococcal in origin which was not treatable before the 1950s. Perineal abscesses, sinuses and cellulitis were common and the strictures often impossible to dilate. Such patients were usually given a suprapubic cystostomy.

HYPOSPADIAS

The pattern of occurrence of hypospadias affects all races and does not appear different in Malaysia from elsewhere. The incidence documented by Goh and Yeo in Alor Star was 0.40 per 1,000 livebirths or 1:2,471. Probably 20-40 odd cases undergo surgical repair each year. Roslan and Proehoeman have described their experience with 68 cases over 5 years.

Reference

Roslan A and Proehoeman F. Further experience with one-stage hypospadias repair. Southeast Asian J.Surg. 9:87-91 1986.

CHAPTER 30

THE REPRODUCTIVE SYSTEM

PRIMARY AMENORRHEA

After the other known causes of primary amenorrhea had been excluded cytogenetic studies were performed on 117 women by Ten, Chin, Jamilatul Noor and Khalid at the IMR. Of these patients 31% were found to have structural abnormalities of the sex chromosome. These were of 4 main types, namely, presence of a Y chromosome (14%), X chromosome aneuploidy (8%), structural anomalies of the X chromosome (7%) and the presence of a marker chromosome(2%). Mosaics constituted 17% of the abnormalities observed.

Reference

Ten SK, Chin YM, Jamilatul N and Khalid H. Cytogenetic studies in women with primary amenorrhea. Sing.Med.J. 31:355-359 1990.

MALE PSEUDOHERMAPHRODITISM

These are conditions where there is defective virilization of the male embryo.

TESTICULAR FEMINISATION SYNDROME

In the testicular feminisation syndrome individuals are phenotypically female but male in genotype. It results from the failure of the gonads to respond to androgens in utero and differentiate into testes. Since the 1950s it has been realised that it is not that uncommon. Wong described cases in Singapore in 1966 and in Malaysia, Teoh described 4 cases in 1976.

PERSISTENT MULLERIAN DUCT

This occurs due to a defect in the action of Mullerian inhibiting substance (MIS) that effects regression of the fallopian tubes, the uterus and upper vagina in embryonic development. It has been found in an 18 month old boy at surgery for a left inguinal hernia and undescended right testes.

References

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AMENORRHOAE GALACTORRHOAE SYNDROME

The amenorrhoea-galactorrhoea syndrome may be idiopathic, associated with certain drugs or the manifestation of prolactin producing tumours. Patients are infertile because of the raised serum prolactin level. Ngan and Wong reported a series of 10 cases from the UH in 1978. Pituitary adenomas were diagnosed in 3. 6 patients had bromocriptine therapy and in 4 women pregnancies ensued. Mustaffa and colleagues at the UKM reported 13 women with a mean period of amenorrhoea of 3 years, who had a mean serum prolactin level of 4,334 mU/l. Their ages ranged from 20-38 years. All managed to conceive after bromocriptine therapy and their mean prolactin level declined to 186 mU/l on treatment.

M.Hamim and co-workers have surveyed the normal levels of serum prolactin in Malay women. The level in premenarchal till the reproductive years ranged from 19 to 23 ng/ml, and fell in premenopausal women (12ng/ml) and fell further in postmenopausal women (9.5 ng/ml.). In menstruating women it varied during

the cycle, but another more pronounced variation was the diurnal cycle which peaked just after midnight with a mean level of 82ng/ml. In pregnancy it rose to a mean level of 242 ng/ml near term.

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MENOPAUSE

The mean age of menopause in Malaysia was found to be 48.7 years, by Hamid, Tey and Nazileh, in a study of 677 women. 18% had menopause before 45 years and in 12% it occurred after 54 years. Race, socio-economic standing and parity did not affect the age of menopause, but if the woman had the birth of her last child after 45 years she tended to have a late menopause.

Reference

Hamid A, Tey NP and Nazileh R. A study on the age at menopause and menopause symptoms among Malaysian women. Mal.J.Reprod.Hlth. 7:1-19 1989.

POLYCYSTIC OVARIAN SYNDROME

This condition was first described by Stein and Levanthal in 1935 as a syndrome involving bilateral sclerotic ovaries, amenorrhoea, hirsutism and obestity. Other endocrine problems are often associated with the condiiton. Tan, Lui, Satgunasingam and Khalid have reported a series of 62 cases seen at the UKM over the period 1982-1988. Indian women seemed overrepresented. A higher proportion of patients (74%) were noted to have acanthosis nigricans than series reported elsewhere. These women were associated with features of a higher body mass index, serum testosterone, hirsutism and non-insulin dependent diabetes miletus. A case with concurrent polycystic kidney disease has been noted.

Reference

Tan TT, Lui SK, Satgunasingam N and Khalid AK. Clinical and endocrine profiles of 62 Malaysian women with polycystic ovary syndrome. Med.J.Mal. 44:302-306 1989.

BENIGN OVARIAN TUMOURS

A twisted ovarian mass is not an uncommon acute surgical problem. Falconer in 1952 reported a case in as young a child as 4 years old.

207 benign ovarian tumours were seen in the UH between 1968 and 1975. They were chiefly mucinous cystaednomas, serous cystadenomas and cystic teratomas. Ovarian fibromas accounted for 3% of all benign ovarian tumours seen in the UH in a 20 year series reported in 1990. For some unexplained reason the left ovary was more often affected – it was affected in 70% of cases. The tumour was rare before the second decade and 77% were in the reproductive age group. Ascites was notes in 13%, but Meig's syndrome was seldom encountered.

In the UKM experience reported in 1992, 69% of ovarian tumours were benign. Benign teratomas accounted for 42% of these, and were the commonest type of ovarian tumour among the Malays and Chinese. Serous and mucinous cystadenomas accounted for another 22% of tumours each and unclassified cystadenomas a further 10%. Among Indians serous cystadenomas (40%) was the commonest ovarian

tumour.

It is a wonder what massive sizes ovarian cysts can sometimes attain. The largest on record in Malaysia are two reported by Ravindran from Seremban weighing 20kg and 28kg.

References

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Ravindran J. Massive ovarian cysts - successful management of two cases. Med.J.Mal. 49:303-305 1994.

ENDOMETRIOSIS

Comparing infertile women undergoing diagnostic laparoscopy in Malaysia and the UK, Arumugam and Templeton reported that 51% of women in Kuala Lumpur compared to only 22% in Aberdeen had endometriosis suggesting it is more common in our population. The 202 Malaysian patients consisted of 32% Malays, 28% Chinese and 40% Indians. Comparing 147 women found to have endometriosis with 281 other women who had laparoscopy but not found to have endometriosis, Arumugam and Wellupilai found endometriosis was significantly associated with women from social class 1 and 2, but there was no association with the severity of disease they developed. There was no difference in age, race and parity between those with and without endometriosis.

References

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Arumugam K and Welluppilai S. Endometriosis and social class: an Asian experience. Asia Ocenia J Obstet Gynaecol 19:231-234 1993.

FALLOPIAN TUBE OCCLUSION

Lim and Ng found that in 129 cases of hysterosalpingography, performed mainly for infertility, in KL, 36% has bilateral tubal occlusion and a further 12% had unilateral occlusion. They found 14 pregnancies occurring after the procedure. Thambu reported that in the treatment of 220 women with tubal occlusion with hydrotubation 29% had subsequent pregnancies after 1-10 hydrotubations.

References

Lim TP and Ng KFT. Certain aspects of hystero-salpingography. Med.J.Mal. 30:121-126 1975.

Thambu JAM. Treatment of tubal occlusion by hydrotubation. Med.J.Mal. 33:4-6 1978.

UTERINE LEIOMYOMATA

Uterine leiomyomata or fibroids are a common problem but there is usually little to report about them in scientific journals. One area in which they cause significant problems is when there is an associated pregnancy. UH workers have reported their finding in 60 pregnant women with fibroids. Their median age was 33 years and 60% were primigravidae. A significant number of them gave a history of infertility (43%) and spontaneous abortions (25%). In patients with fibroids larger than 6cm, malpresentation was a common problem. The Caesarian section rate was 73% most commonly for obstructed labour. Severe haemorrhage occurred in 10 (23%) patients, 3 of whom needed hysterectomy. There were no perinatal deaths.

Reference

Hasan F, Arumugam K and Sivanesaratnam V. Uterine leiomyomata in pregnancy. Int J Gynaecol Obstet 34:45-48 1991.

HAEMATOCOLPOS

Haematocolpos due to an imperforate vaginal septum is an uncommon condition reported elsewhere to occur in 1:1,000-5,000 females. Ooi and Wong noted 7 cases over 6 years at the UH.

Reference

Ooi KC and Wong WP. Imperforate vaginal septum with haematocolpos. Med.J.Mal. 28:279-282 1974.

BENIGN VULVAL TUMOURS

A rare case of a fibroadenoma of the vulva has been mentioned in a local report. It is thought that breast-like tissue could be present there as in certain aquatic mammals.

Reference

Ahluwalia HS, Gopinath A and Kumaradeva. Fibroadenoma of vulva. Med.J.Mal. 32:215-216 1978.

BENIGN BREAST DISEASE

81% of all breast lumps biopsied over 10 years in the Johore Bahru GH between 1971 and 1980 were found to be benign especially in those under 40 years. In contrast to the west fibroadenomas outnumbered cystic hyperplasia (a term to include fibroadenosis, mammary dysplasia and others) and accounted for 76% of the benign lesions. The peak age for fibroadenomas is the third decade, and corresponded to Western findings. The group of conditions lumped together as cystic hyperplasia was also seen in the younger age group in contrast to the West.

Besides the common benign breast lumps, UH workers have reported a series of 16 patients with granulomatous mastitis seen over 3 years. In most it presented as a suspicion of malignancy. They have also reported one case of an ever rarer condition, a plasma cell granuloma of the breast which occurred in both breasts in one patient.

References

Chan KE. Primary carcinoma and benign tumours of the female breast in Malaysian women. Med.J.Mal. 37:217-220 1982.

Yip CH, Wong KT and Samuel D. Bilateral plasma cell granuloma (inflammatory pseudotumour) of the breast. Aust NZ J Surg 67:300-302 1997.

Yip CH, Jayaram G and Swain M. The value of cytology in granulomatous mastitis: a report of 16 cases from Malaysia. Aust NZ J Surg 70:103-105 2000.

TORSION OF THE TESTES

Torsion of the testes is surgical emergency which is important to know about because delay in treatment will lead to loss of one testis. There were 24 cases recorded in the UH over nearly 10 years from its opening in 1967. As might be expected most were young, aged between 14 and 24 years. In this series in 9 patients the testes was saved, two had spontaneous reduction of their torsion on induction of general anaesthesia.

From 1984 to 1994, another 11 years, 80 patients underwent scrotal exploration for presumed testicular torsion in the UH. Of there 67(84%) had a torsion and the testicular loss rate was 51%. However in those who had symptoms for more than 24 hours the testicular loss rate was 71%. The right and left testes were found to have an equal chance of being affected.

References

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