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CONTENTS

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Editorial

Drug Addiction

by A. A. Sandosham

DRUG TAKING for non-medical reasons has become a major source of concern for the world at large and Malaysia is no exception. Hardly a day passes without some reference to drug taking, drug addiction, drug trafficking, etc. in the local press.

The taking of drugs not only to relieve discomfort but also to enhance pleasure and achieve social aims has been the accepted practice in most parts of the world. However, this was largely confined to the more mature members of the community. What is worrying today is the increasing frequency with which younger people are trying these dependence-producing drugs. Unfortunately, there are no reliable data on the prevalence and incidence of the non-medical use of psycho-active substances in this country. But such information as is available from law enforcement agencies, hospital attendances and post-mortem examinations suggests a steady increase in addiction to dependence-producing drugs in recent years.

The Malaysian Medical Association and its Public Health Society have been aware of this problem and during the last decade have set up various Sub-committees, held meetings at Central and Branch levels and organized workshops and seminars (including public seminars) to study and discuss the topic in order to find out in what way the profession could assist in resolving the problem.

Psychologists have tried to analyse the motives associated with the initiation and continuation of drug-taking and find they are many and diverse. Curiosity about the effects of these drugs is a major factor especially among the young. It has been suggested that certain ill-conceived preventive programmes giving information in a dramatic manner about the effects of certain drugs have actually created an interest to the extent of wanting to try out the drug in question. The mass media accounts of drug addiction are daily occurances and could well stimulate an unhealthy interest in wanting to try it. Other motives include the desire to have pleasurable and thrilling experiences, wanting to escape from some undesirable situation, to express independence or to fulfil a need to be accepted. These are particularly characteristic of the young.

It must be remembered, however, that many young persons take these drugs a few times and stop, or use it only intermittently not resulting in the development of dependence. In other words, there is no psychic drive that requires readministration of the drug or that no physical disturbance results when the administration of the drug is suspended. In that case, we may be actually exaggerating the prevalence of drug addiction and by our suspicions unconsciously push the casual drug user deeper into dependence on drugs by generating in him feelings of rejection.

This is not to belittle the seriousness of the situation. There is no getting away from the fact that more and more people in Malaysia are resorting to dependence-producing drugs for various reasons. It is up to the enforcement officers, the social welfare workers, community leaders and educationalists besides medical and health officers to cope with the problems of drug-dependent persons.

While enforcement measures to repress illicit traffic and effect control on the availability should not be overlooked it should be realised that the essential aim should be to reduce the demand for these drugs. There is no evidence that simple information-giving educational programmes is effective in preventing drug dependence. Knowledge does not necessarily provide protection. The social welfare officers are involved in the rehabilitation of the drug dependent and theirs is a formidable task involving not only the addicts but their families and the community as well.

The medical man's responsibilities in establishing early diagnosis, undertaking the correct treatment and helping in the rehabilitation of the drug-addict are very great indeed. Every medical and health officer should be in a position to assist and so it is essential for them to keep abreast with the latest developments in treatment and rehabilitation.

The prevention of drug addiction is a thorny problem and cannot be solved overnight. Changes in cultural attitudes as well as in environmental stresses can only be brought about very slowly. As recommended in a W.H.O. publication, "Everything possible should be done to allieviate environmental conditions that lead to undue stress – discrimination of various kinds, blocked opportunities at work, slum conditions, unfair business and labour practices".

Myocardial Infarct in Young Malaysian Men Forty Years and under: A Retrospective Analysis of Risk Factors

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Summary

MYOCARDIAL INFARCT in Malaysia men forty years and under, is discussed by illustration of clinical cases with reference to risk factors which are analysed retrospectively. Comparison is made with risk factors of Caucasian males in other studies which are discussed to show similar and contrasting characteristics.

It is hoped that preliminary communications such as these may lead to further the understanding that Myocardial Infarct in young men in rapidly developing countries is not uncommon and that prevention programmes could be undertaken to reduce the preventable risks and hence salvage the wastage of valuable man-power at its prime.

Coronary heart disease is known to be common among the three major ethnic groups of Chinese, Malay and Indian in Malaya ((Khaira 1961). In fact, Myocardial Infarct in Malaysian men forty years and under are not unusual. This may be due to the fact that Malaysia is rapidly becoming more industralised and exposed to a more western type of culture and standard of living.

In neighbouring Singapore, Gwee et al (1970) pointed out, that of a total of 183 cases of Myocardial Infarct admitted unselectively to a medical unit over a period of one year, there were only 9 cases falling into the age bracket of 31 – 40 years i.e. 4.9%; comprising all males. This paper records a personal observation of five cases of "premature" Myocardial Infarct occurring over a period of 20 months and reviews retrospectively their coronary profile of risk factors especially that of age and sex, smoking, serum lipid levels, blood pressure, family history of cardiac disease, stress, obesity, diet and other observable physical characteristics and abnormal biochemical findings.

The risk factors in young adults under 40 sustaining Myocardial Infarct in Caucasian countries are well documented [(Blacket & Leelarthaepin 1972) (Valentine et al, 1972) (Oglesby & Seigal, 1972)]. Our preliminary communication is aimed at analysing these risk factors, to determine whether the same factors are present in such young men in the context of an urban area in a rapidly developing country.

Subjects and Methods

The patients selected had confirmed Myocardial Infarct and were 40 years and under.

Confirmation of Myocardial Infarct was made according to the criteria used by Burns-Cox et al (1969) slightly modified for our study, namely:–

(1) History of retrosternal pain at rest accompanied by pathological Q wave in the ECG.

(2) A history of at least one hour's pain at rest accompanied by S.T. segment abnormalities and subsequent evolution; with one or more ancillary evidence of myocardial damage:–

  (a) A WCC of over 11,000/cu. mm.

  (b) ESR greater than 20 mm. per hour (Westegren)

  (c) A temperature rise over 100°F

(d) Characteristic changes in serum Aspartate Aminotransferase (SGOT) showing a rise over 40 Sigma Frankel units and resultant fall to normal of below 28 units.

Cases 1, 2, 3 and 5 were admitted to Our Lady's Hospital between 21/2/71 to 29/10/72. Case 4 was admitted to another hospital but followed up by one of us. All fulfilled the criteria required. During their stay in hospital and after, relavent features of the study comprising history, physical attributes and biochemical investigations were recorded.

Clinical Cases

Clinical cases with details are summarised in Table I, II, III.

Discussion

Myocardial Infarct and Coronary Heart Disease mortality in the younger age groups in affluent countries have shown real percentage increase (W.H.O. 1967). It would be expected that there will be a similar increase of such trends in young men under 40 in Malaysia as the standard of living, dietary habits, economic and cultural changes of the more affluent members of the community are approaching that of its western counterparts. An attempt is made in our small series to observe such risk factors individually, rather than present a statistical analysis.

The definition by the American Heart Association of a Coronary Risk Factor is a "finding associated with at least doubling the risk" (Stamler et al, 1969) or so simply stated (Leading Article BMJ, 1973) that given a set of circumstances "a person will develop a disease in a given period of time" which in this case is Myocardial Infarct.

Numerous risk factors have been cited in premature coronary heart disease, working singly or in conjunction (Blacket et al, 1972). Risk factors implicated have been age and sex, smoking, diastolic hypertension, hypercholesterolaemia, hypertryglyceridaemia, family history of heart disease, diet and obesity, stress, corneal arcus, abnormal glucose and other biochemical abnormalities. These have all been discussed in the Framingham Study (Dawber et al, 1962) and recent prospective studies (Mulcahy et al, 1969).

In considering the age, premature arteriosclerosis in males is considered to have appeared when symptoms and signs have appeared at age 40 and under (National Heart Foundation of New Zealand, 1971). It may be inferred that the subjects in our series have premature heart disease and most likely premature arteriosclerosis as the end stage of their presymptomatic disease state is the development of a myocardial infarct.

Table I

Case No	Sex	Race	Age	Site of Infarct	Previous Cardiac Disease or Hypertension	Family History of Heart Disease	Smoking Habits	Weight in lbs (Ideal weight) (for height) (and build)	Corneal Arcus + = Present	Xanthomas Xanthelesmas
1.	M	Chinese	40	Antero-septal	Nil	Father died of "enlarged heart" age 52	60–70/day	145 lbs (141)	+	Nil
2.	M	Indian	34	Antero-Lateral	Nil	Father died of Coronary Thrombosis (67) Mother died of Cerebral Thrombosis (58)	20–25/day	190 lbs (174)	+	Nil
3.	M	Chinese	35	Posterior Lateral	Nil	Mother died of "Heart Attack"	Nil	148 lbs (141)	+	Nil
4.	M	Chinese	33	Posterior Lateral	Nil	Father had Myocardial Infarct age 60, 1 month previous to Propositus	20/day	148 lbs (137)	+	Nil
5.	M	Chinese	40	Anterior	Nil	Paternal uncle died of "Heart Attack"	20/day	170 lbs (133)	+	Nil

Table II

Case	Occupation During Infarct	Previous Occupation	Months after Promotion to Myocardial Infarct	Possible Prelipitating Stress or Phychological Factors	Clinical Features
1.	Manager of Milk and Food Company	Executive (No Managerial responsibilities)	6	For 2 days previous to infarct unusually vigorous exercise in sports, culminating in heavy Chinese meals. Emotional stress of separation from family life 6 months previously due to shifting to another town. Stress of increased responsibility from promotion.	Woke up on day of Infarct with severe praecordial pain with radiation to neck plus sweating. SGOT 148 units. ECG confirmed Infarct.
2.	Manager of Motor Vehicle Firm	Executive (No Managerial responsibilities)	30	Sedentary worker For 1 week previously, drove long distances up and down Peninsula Malaysia on working holiday. Consumes excess cigarettes and alcohol.	After return, complained of moderate epigastric pain which was detected by SGOT (80 units) and ECG findings of Infarct.
3.	Manager	Executive (No Managerial responsibilities)	10	Sedentary manager; for 2 weeks prior to infarct, made compulsory annual trip to business clients around Malaysia. Increased stress from more resonsibilities of new job.	During return trip, noticed praecordial pain but ignored it. Collapsed the next day but recovered well. SGOT (94 units) and ECG confirmed Infarct.
4.	Sales Supervisor of Liquor Firm	Salesman	3	Psychological stress, father had Myocardial Infarct 1 month previously. Stress of trying to keep up sales figure since promotion and physical stress of excessive travelling to check on his salesmen.	Classical retrosternal chest pains with ECG findings of Infarction and SGOT of 60 units.
5.	Manager of Logging Firm	Clerk	9	Sedentary worker hired to form a logging firm, involving extensive travelling in jungles of Indonesia and under pressure to start the company on schedule.	Typical retrosternal pain not relieved by rest. SGOT 200 units and ECG confirmed infarct.

Table III

Case	Fasting Cholesterol (mg%) (Normal 150–250mg%)	Fasting Tryglyceride (mg%) (Normal 30–150mg%)	Fasting Glucose mg/100ml (Normal 80–110mg%)	Glucosr Tolerance Test (50 G Oral Glucose Load)	Uric Acid (mg%) (Normal 2–7mg%)	Urea Mg% (Normal 20–40mg%)
1.	303	228	104	Normal	9.3	26
2.	360	223	89	Normal	5.7	40
3.	293	88	72	Slightly abnormal 215mg% at 1 hour	7.1	32
4.	348	297	93	Normal	7.2	15
5.	288	230	88	Slightly abnormal 200mg% at 1½ hour	10.0	40

All the subjects are male which fits in with the concept that in younger adults with arteriosclerotic heart disease, the male to female ratio is higher as supported by the World Health Statistic Report (1969), with a male to female ratio of 5 to 1 in younger adults as shown in New Zealand. Various reasons are given for the difference but are beyond the scope of this paper.

Cigarette smoking is considered as one of the 3 "Cardinal Risks" (Stamler, 1971) and may operate by itself as one of the prime factor (Doyle et al, 1964) or in conjunction with other cardinal factors, taking on a multiple increase in risk (Dick and Stone, 1973). This is correlated to the quantity of cigarettes smoked and to a certain extent the amount of inhalation (National Heart Foundation of New Zealand, 1971).

Four of the propositi smoked more than 15 per day (Table I) and one smoked 60 – 70 per day. All are inhalers and started at an early age. Case 3 does not smoke even for social reasons. The Framingham Study (Kannel et al, 1967) found that the risk for manifestation of coronary heart disease including mortality increases with the amount smoked. In assessing the risk, the depth of inhalation may also be significant (Hammond, 1966). Nicotine and carbon monoxide both have effects on the heart and blood vessels, and their actions have been summarised by the Report of An Expert Group appointed by Action on Smoking and Health (1973). It is apparent that our cases who smoked were exposed to such risks pre-infarct.

Elevation of blood cholesterol is part of the coronary profile and a good predictive index of coronary heart disease (Kannel, 1967). In prospective studies Kannel (1971) pointed out that in men aged 35 – 44, all things being equal, there was $5\frac{1}{2}$ times more risk in developing coronary heart disease in those with cholesterol above 265mg/100ml. than in those with figures below 220mg/100ml. The mean value of serum cholesterol in Chinese, Indian and Malay in Malaysia is around 190mg% (Chong et al, 1971). The cholesterol values of our cases are above the national average and above that cited by Kannel, and therefore would fall into the category of increased risk.

Independently raised levels of serum tryglyceride is considered a risk towards development of coronary heart disease, a point which has been raised in the Stockholm prospective studies over a nine year period (Carlson et al, 1972). However combination with high cholesterol carries a greater risk linearly. Elevated blood tryglycerides was found in 2/3 of the cases of myocardial infarct aged under 40 in the report by Oglesby and Siegel (1972). Except for one, all the 4 cases (Table III) have high fasting tryglyceride levels, above 200mg% and wound fit into the coronary profile of young myocardial infarct.

One of the three cardinal risk factors in Western countries is raised diastolic blood pressure (Stamler, 1971). It is one of the best discriminating factor of predisposing causes (Cotton et al, 1972). None of our subjects had hypertension as they had to undergo a pre-employment medical examination nor their blood pressure was high during or after the myocardial infarct. In some populations such as Japan, hypertension and not coronary heart disease is common (Keys, 1970) and hypertension alone is not a causative factor in such places but is a risk only when combined with other factors.

A family history of coronary heart disease (Leading Article BMJ, 1972). In table I, developing the same the family history of all the cases are positive. This correlates well with Blacket et al's (1972) study that half of their young men with coronary heart disease had a positive family history usually ending in death before the age of 65. There is also some evidence that myocardial infarct may occur at an earlier age in those sons whose father had coronary heart disease (Thomas et al, 1964).

Stress is defined as "synomynous with force and pressure exercised upon a person" (National Heart Foundation of New Zealand, 1971). It is a subjective risk but there is evidence to support that psychological and social stimuli contribute to the coronary prone behaviour pattern (Jenkins, 1971). In our cases, there is a distinct relationship between the months in acquisition of the promotion and the myocardial infarct (Table III) which may be due to the psychological and social stress from the new job with more responsibilities. The fact that these people possess driving ambitious personalities may have contributed to the stress mechanism.

Dietary factors in epidemiological studies are linked to coronary disease, by exerting an influence in blood lipid levels especially the quantity of saturated fat eaten (Morris et al, 1969) and to excess carbohydrate consumed which increases in the liver of tryglyceride rich lipoproteins (Fredrickson et al, 1967). Affluent Malaysian indulge in excessive carbohydrate intake and high saturated fat diet with usage of pork oil, peanut and coconut oil for their cooking. In retrospect all five profess to such a diet pre-infarct.

Obesity by itself may not be an independent risk factor (Leading Article BMJ, 1972) but acts as

an adjuvant or secondary risk factor together with excess consumption of food and physical inertia in acting on the primary risk factors of age, blood pressure and cholesterol (Leading Article BMJ, 1973). In table I, cases 2 and 5 are in excess of their ideal weight for that height and the rest are close to normal. Obesity therefore plays a relatively minor role except when it combines with more important risk factors.

Corneal arcus below the age of 50 is one of the observable physical signs in the index of discrimination between patients with coronary thrombosis and those without (Cotton et al, 1972). It may not only be associated with premature manifestation of coronary heart disease but also be seen in normal people (Hickey et al, 1970). However corneal arcus associated with a high cholesterol especially those with a Type II Hyperlipoproteinaemia may be a more valuable predictive tool. All five of the young men have corneal arcus and significantly related to a high cholesterol level, perhaps making this sign a good predictive factor in our case.

None of our subjects had xanthelesma or xanthomas. This is only a valuable sign if associated with hyperlipoproteinaemia. By itself it may be a normal feature and of no serious predictive value.

Overt diabetes is known to increase the risk of incurring a myocardial infarct (Baily, 1968). However impaired glucose tolerance occurs more in frequency in those with coronary heart disease (Wahlberg et al, 1968) and may be related to the development of premature arteriorsclerosis. Only two of the subjects (Table III) have borderline abnormal glucose tolerance tests. None has a family history of diabetes.

No clinical gout was seen but the uric acid was high in two and borderline high in another two (Table III). Serum uric acid was noted to be higher in men under 40 with coronary diseases and this "hyperuraecaemia was related to corpulence and hypertryglyceridaemia" (Blacket et al, 1972) especially Type IV & V. There may be an increased risk of coronary arteriosclerosis in hyperuricaemia without gout (Framingham study).

Conclusion

From this preliminary observation of a small series, there seems to be a pattern of risk factors in our young Malaysian males which fall similar to that of Caucasians. These factors in Caucasians have been proven to be of use for their predictive value in assessing the risk for a coronary and would we feel hold true for young Malaysians as well.

However certain risk factors are more important on the predictive scale namely the cardinal risk factors of smoking, hyperlipoproteinaemia and hypertension (Stamler, 1971) and would be serious if present singly or worse if in combination. These factors have been shown to play a major role in causation of a coronary and our Malaysian subjects share these features to a certain extent except for hypertension. Besides the cardinal factors, the secondary risks factors although not so important, are also present in our subjects in varying degrees. Together, the cardinal and secondary factors form a basis for total assessment of the coronary profile, both for young Caucasians as well as for Malaysian men. It thus seem that exposure to similar enviromental risk factors would bring the same risk for a coronary to different racial and geographical groups.

Certain of these factors can be altered; primarily smoking cholesterol, tryglyceride, obesity, diet, physical inertia and to a certain extent stress can all be reduced.

If the predictive values are reasonably accurate and can even be worked out as a mathematical calculation, (leading Article BMJ 1973) then this will enable an energetic and effective prevention programme to be worked out. This will be especially more urgent in young men of developing countries in reducing the wastage of skilled men in morbidity and mortality.

Acknowledgement

This original article is an everlasting tribute to the late Dr. Francis Chin Gan Fong, who even in his last illness, gallantly and bravely prepared it for the benefit of all his medical friends and patients, towards a specialty he loved best – CARDIOLOGY.

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A Comparative Study of the Prevalence of Adult Obesity in the Three Racial Groups of Kuala Lumpur

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Summary

THE HEIGHTS and body weights have been measured in 550 healthy adults in Kuala Lumpur, and also in another 50 adults with minor disorders. The degree of obesity was determined from the Quetelet index i.e. weight . height^{-2}. Obesity was found to be most uncommon before the age of 30 years, and also throughout life in the Chinese man. After 30 years of age, 21 to 40% of Malay and Indian men and women and of Chinese women were found to be more than 20% overweight. Amongst the women, obesity was particularly prevalent in Indians aged 31 to 40, and in Chinese over 50 years of age.

This pattern of obesity does not appear to be related to differences in diet, but it may well be expected to influence the prevalence of coronary heart disease and diabetes in the adult population of urban Malaysia.

Introduction

Recent population studies in Europe and America show that obesity predisposes to the development of many degenerative diseases associated with the "Western" way of life, including diabetes, coronary heart disease and hypertension, (1,2). These three conditions are now becoming increasingly more common in urban Malaysia and have already acquired a popular name: "tiga serangkai" meaning a collection of three (diseases) forming one bunch.

Consequently it is important to determine the prevalence of obesity in the urban population of Malaysia, and to establish whether obesity carries the same risk for the Asian as already established for the European.

Methods

Heights (without shoes) and body weights (without shoes and in light clothing) were measured on 300 adult women and 300 adult men aged 20 to 70 years. The numbers from the three main racial groups (Malay, Chinese and Indian) were almost equal. Five hundred of these adults were the healthy relatives of patients attending the General Hospital Kuala Lumpur, 50 were technicians and cleaners and 50 were patients with minor complaints, (mostly of the skin). In this group of technicians, cleaners and patients, the skin fold thickness was measured with Harpenden calipers and details of the previous 24 hours' diet were recorded.

The Quetelet index has been strongly recommended as being the most reliable index of obesity (3). It was calculated as weight . height^{-2}, with the body weight measured in kg and the height in m. The significance of the differences between groups was calculated using Wilcoxon's test, the hypergeometric distribution or chi squared as appropriate (4).

Results

Figures 1 to 4 show the body weights ane Quetelet indices for men and women from ths three racial groups. Compared with the "average" American (5) of the same age and height, all groupd are underweight; but in general, all groups after 30 years of age are overweight when compared with the "desirable" (5) weight (and corresponding index) of an American of the same height with a "light

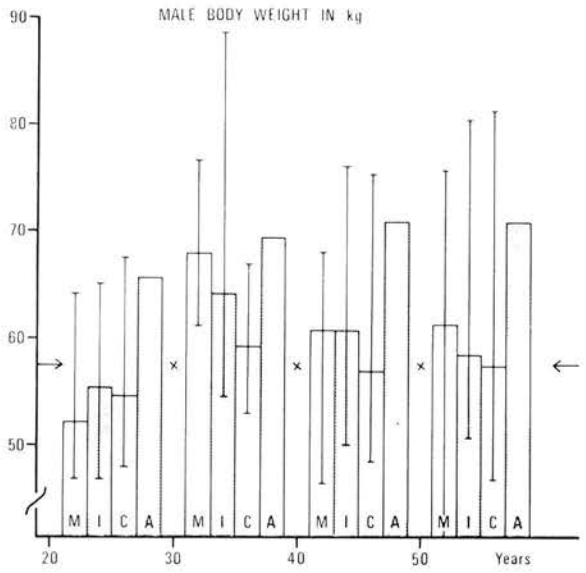

Figure 1

The effect of age on the median body weight (measured in kg) of 300 men from the Malay (M), Indian (I) and Chinese (C) populations compared with the "average" American man (A) of the same height (5). The two arrows and the crosses show the "desirable" weight of the American man of the same height and with a "light frame" (5). The bars show the 10th and 90th percentiles.

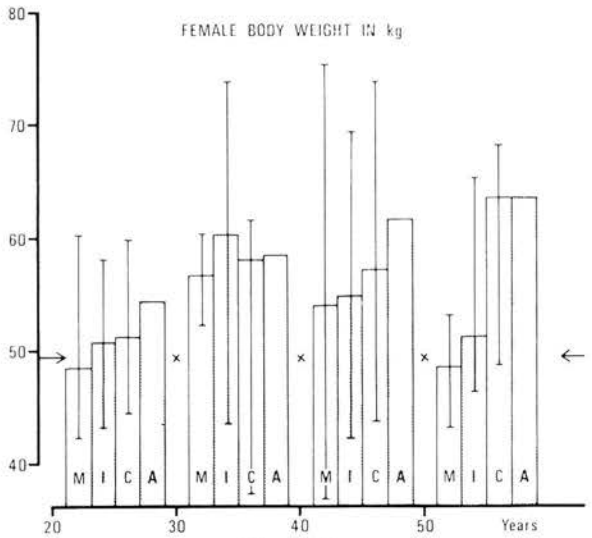

Figure 2

The effect of age on the median body weight (measured in kg) of 300 women from the Malay (M), Indian (I) and Chinese (C) populations compared with the "average" American woman (A) of the same height (5). The two arrows and the crosses show the "desirable" weight of the American woman of the same height and with a "light frame" (5). The bars show the 10th and 90th percentiles.

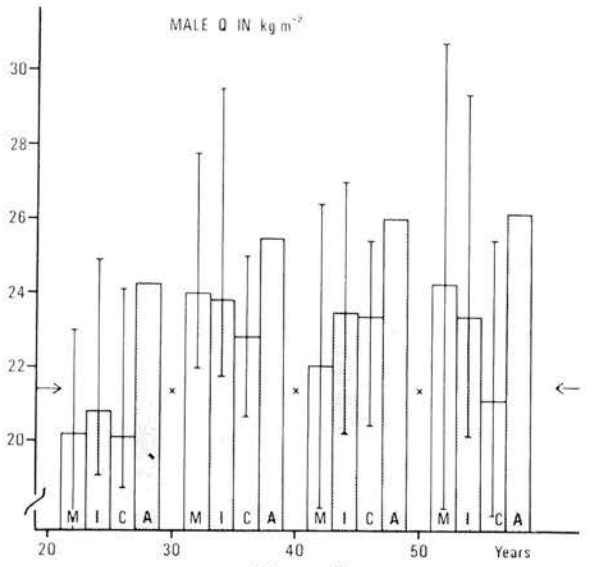

Figure 3

The effect of age on the median Quetelet index (measured in kg.m^{-2}) of 300 men from the Malay (M), Indian (I) and Chinese (C) populations compared with the "average" American man (A) of the same height (5). The two arrows and the crosses show the "desirable" index of the American man of the same height and with a "light frame" (5). The bars show the 10th and 90th percentiles.

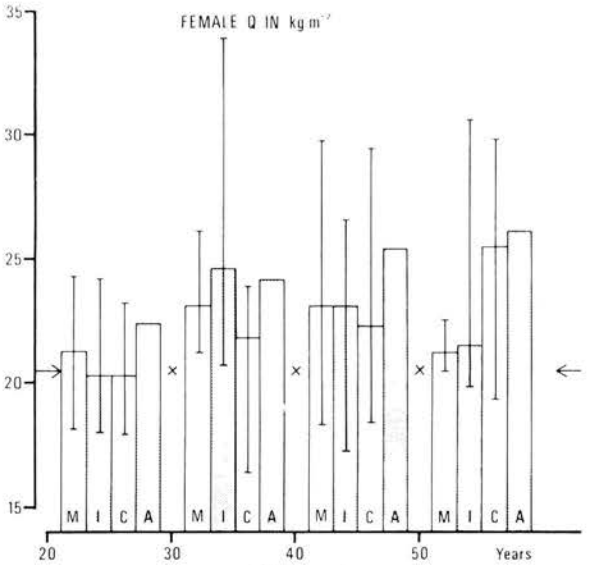

Figure 4

The effect of age on the median Quetelet index (measured in kg.m^{-2}) of 300 women from the Malay (M), Indian (I) and Chinese (C) populations compared with the "average" American woman (A) of the same height (5). The two arrows and the crosses show the "desirable" index of the American woman of the same height and with a "light frame" (5). The bars show the 10th and 90th percentiles.

frame". In the American population, the desirable weight (and index) predict the minimum mortality, particularly from cardiovascular disease.

Table I shows that although there is no difference between the median heights of young men in the three racial groups, young Malay women are significantly shorter than both Chinese and Indian women. In all groups, a loss of height of about 2 cm occurred with increasing age.

women aged 20 to 30, it is probably a valid criterion. below the Americans' "desirable" weight, so that the increase in obesity in the older men is almost certainly underestimated.
On the other hand, the median weight of men aged 20 to 30 from all three racial groups is considerably

Table II shows that in all sections of the urban population, obesity is most uncommon at 20 to 30 years of age. However, after this age obesity

Table I

Height of Men and Women Aged 20 to 30 Years

	MEN (M)			WOMEN (F)*		
	Median	10th %	90th %	Median	10th %	90th %ile
Malay (M)	164	152	170	154	145	157
Chinese (C)	164	160	173	157	152	163
Indian (I)	165	152	170	159	147	165

Height without shoes measured in cm
* FM<FC and FI; P<0.02

If obesity is defined as 20% or more overweight, it will occur when the Quetelet index exceeds 120% of the "desirable" value. Since the "desirable" weight is identical to the median weight for Asian

occurs in 21 to 40% of all racial groups with the notable exception of the Chinese men. Obesity is particularly prevalent in Indian women aged 30 to 40 and in Chinese women over 50 years of age.

Table II

Percentage of Each Group More Than 20% Overweight

	Age in years				
MEN	20 to 30	31 to 40	41 to 50	over 50	over 30
Malay (MM)	2	44	20	33	28 a
Chinese (MC)	3	4	20	8	9 a b
Indian (MI)	6	24 c	27	27	23 a
American	12	25	32	32	30
WOMEN					
Malay (FM)	9	20 d	33	8 c	21
Chinese (FC)	3	7 d	20	56 c	28 b
Indian (FI)	7	50 d e	27	38 c	40
American	12	25	40	45	37

a: MC<MM and MI; P<0.02
b: MC<FC ; P<0.04
c: FC>FM and FI ; P<0.07
d: FI>FM and FC ; P<0.01
e: FI>MI ; P<0.07

Table III shows the skin fold thickness in men and women aged 20 to 30 years. No racial difference could be detected, but as expected, skin folds were thicker in women than in men. No sex or racial difference was found in the ratio of abdominal girth to height: median 0.42 (0.37 to 0.45).

Table IV shows the diet during the previous 24 hours. It can be seen that the only significant differences detected were the smaller quantity of sucrose and larger quantity of meat eaten by the Chinese when compared with the Malays and Indians. All three groups appear to eat the same quantity of fruit (1 per day), vegetables (twice per day), eggs (1 per 5 days), saturated fat (80 g per day) and cholesterol (300 mg per day), but the Indians drink significantly more alcohol ($P < 0.02$).

No differences in blood pressure or plasma cholesterol were found between the three racial groups, but the expected increase with age was detected:
cholesterol 190 mg per dL (160 to 310) at 25 years increasing to 230 (120 to 280) at 55 years
systolic pressure 120 mm Hg (100 to 130) at 25, increasing to 130 (110 to 150) at 55 years
diastolic pressure 80 mm Hg (60 to 85) at 25, increasing to 85 (70 to 100) at 55 years.

No difference with race or age was found in plasma uric acid, but the expected sex difference was detected: men 6 mg per dL (4 to 9) and women 5 mg per dL (2 to 7).

Discussion

With the striking exception of the Chinese men, obesity appears to be equally prevalent in all sections of the adult population in Kuala Lumpur. After the age of 30 years, it is equally common as in America (6), 21 to 40% of the population being 20% or more overweight. In America and Europe, this degree of obesity carries a three fold increase in the risk of developing coronary heart disease (1,2).

Apart from small differences in sucrose and alcohol consumption, diet does not appear to explain the Chinese man's relative freedom from obesity, nor were racial differences in plasma biochemistry

Table III

Skin Fold Thickness Measured in mm

	MEN			WOMEN		
	Median	10th %	90th %	Median	10th %	90th %ile
Triceps	9	6	16	15	11	23
Subscapular	12	8	22	18	11	23
Supra-iliac	11	7	19	14	10	19
Thigh	12	6	19	22	6	40

Table IV

Diet During the Previous 24 Hours

	MALAY (M)			CHINESE (C)			INDIAN (I)		
	Median	10th	90th %ile	Median	10th	90th %ile	Median	10th	90th %
Sucrose (a)	90	30	200	50	0	180	110	60	230
Meat (b)	15	0	50	50	15	150	25	0	80
Fish	160	80	240	120	80	240	160	80	240
Rice	400	300	600	330	150	450	300	0	450
Bread	50	0	120	60	0	120	90	0	250

Food measured in g
a) C<M and I; P<0.02
b) C>M and I; P<0.001

or blood pressure detected. It is therefore suggested that the lower body weight of the Chinese man is most probably associated with a greater degree of physical activity.

If obesity carries the same risk for diabetes and coronary heart disease in the Asian as has already been recognised for the European, the Chinese man would be expected to be relatively free from these disorders when compared with the Malay and the Indian. This possibility is now being investigated.

Acknowledgement

It is a pleasure to thank Datuk (Dr) R. P. Pillay PSD, SPMK, DPMT, JMN, PJK, MB BS, AM, FRCP, FACP, FCCP, FACCP, for allowing me to use the facilities in the General Hospital, and also Encik Harun bin Maadah and Dr. Adnan bin Osman for assisting with the measurements.

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Cervicograms of Normal Labour in Malaysian Women

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MODERN OBSTETRICS has reached a point that a clinical assessment of a patient's progress in labour can be plotted onto a partogram. These partograms aid in the recognition of abnormal labours by simplifying recordings and aid in the correct timing for facilitating labour and for obstetrical interference. Philpott makes use of "alert lines" and "action lines" based on cervical dilatation. These lines were constructed from data derived from the slowest 10% of African primigravidae.

Friedman's sigmoid curve (see Fig. 1) of labour is a valuable pictorial presentation of the progression of normal labour. Friedman's curve was constructed from mean values $\pm$ S.D. for each point of dilatation, but the distribution of the various phases of labour was asymmetrical (Rodesch et al, 1965). Also the curve is inadequate for the management of individual patients because it starts at the undefinable time of the onset of labour of zero centimetre cervical dilatation. Furthermore, the latent period is prolonged and of varying length.

This paper discusses the construction of cervicogram curves showing cervical dilatation of normal labour amongst Malaysian women.

Methods and Patients:

A retrospective study of labour records of patients who delivered at the University Hospital over a 5 month period from November 1974 and March 1975 was made. The progress of labour was studied in patients of all ages and parities who were more than 4 feet 10 inches tall and who had a spontaneous vaginal delivery at 38 – 42 weeks gestation, of a single baby weighing 2280 – 4100 grams, presenting by the vertex. The records of patients who had undergone any previous uterine operations, other than cervical dilatation and uterine curettage, were excluded. Sedation were similar in each group of patients. No epidural or caudal anaesthesia were used in these patients. After case-records scrutiny, there were 644 suitable records for evaluation. These consisted of 286 nulliparous patients on whom 352 vaginal examinations had been done and 358 multiparous patients on whom 411 vaginal examinations had been performed.

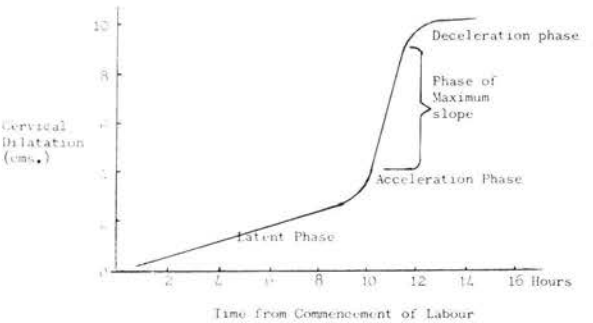

Fig. 1

Friedman's Curve

Cumulative – frequency tables of the dilatation/delivery intervals were prepared for each parity group. A probit analysis of each table was undertaken. Probits corresponding to cumulative – frequencies between 20% to 80% were plotted

against the logarithm of time. A regression line was then plotted and the labour duration equivalent to the probit of 80% was obtained for each cervical dilatation. A cervicogram for each parity was constructed by plotting the time – intervals against actual dilatation from 2 cm. to delivery. As there was no significant difference in the cervicograms obtained for the multiparous patients, all multiparae were lumped together and the progress of labour expressed on one graph.

A prospective study was then carried out and the course of labour of 50 primigravidae and 50 multigravidae were charted on the trial cervicograms. This confirmed the validity of the graphs to accurately chart the progress of labour.

Results:

Some of the clinical parameters of the patients studied were as follows:

		Primigravida	Multigravida
Age	Range	16 – 37 years	16 – 41 years
	Mean	23	26.2
Parity		Para 0 – 286	Para 1 – 148
			Para 2 – 74
			Para 3 – 56
			Para 4 – 33
			Para 5+ – 47
Social class	1 + 2	70	83
	3	82	92
	4 + 5	134	183
Membranes intake at V.E.		48	35
Spontaneous rupture or ARM		238 (83%)	323 (90%)
Birth weight		2300 – 3900	2280 – 4150
Mean birth weight		2795 gms	3150 gms

Discussion:

In view of the difficulty of determining the exact time of onset of labour, particularly in those patients admitted to the labour ward after the onset of their labour at home, it was decided to use the time of admission in labour to the labour ward as the starting point for charting cervical dilatation on the cervicogram. No reference is made to the other qualities of the cervix, namely effacement and position, or the intensity and frequency of uterine contractions which may influence the progress of labour.

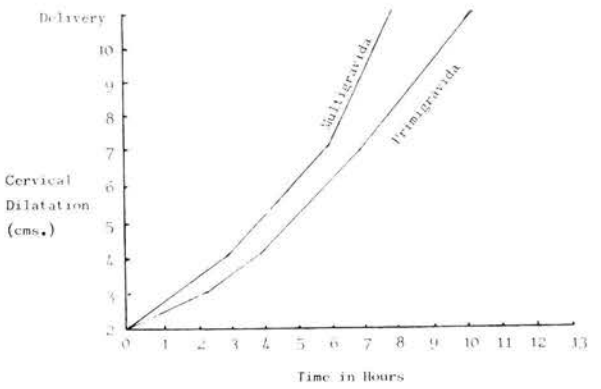

Fig. 2

Cervicograms of normal labour in Malaysian women

The cervicogram is only applicable after the cervix has dilated to at least 2 cm. It ends at delivery and not full dilatation of the cervix, this being a difficult point in time to assess. In the construction of the cervicograms, we have chosen probit of 80% as a highly probable point of normality of the patients reviewed. This was confirmed by the prospective study of 50 primigravidae and 50 multigravidae fulfilling the criteria laid out for the retrospective study.

From the cervicograms constructed, the rate of dilatation of the cervix from 4 cm. to 7 cm. appears similar in both primigravid and multigravid patients. The major difference between the length of labour in primigravid and multigravid patients seemed to be due to a longer latent phase and a longer final phase (i.e. after 7 cm. dilatation) in the primigravid patients. The latter could be related to the failure of the primigravid patients to use her secondary powers to effect delivery of the baby.

Progress of labour can be charted against the cervicograms presented so that any deviation from the normal progress in labour is detected early and appropriate measures instituted (See Fig. 3, 4 & 5). It is hoped that with the introduction of cervicograms in small midwifery centres, abnormal progress of labour can be detected early, even by nursing personnel and referred to adequately equipped Obstetric units for appropriate management, long before fetal demise, and even maternal demise in some cases.

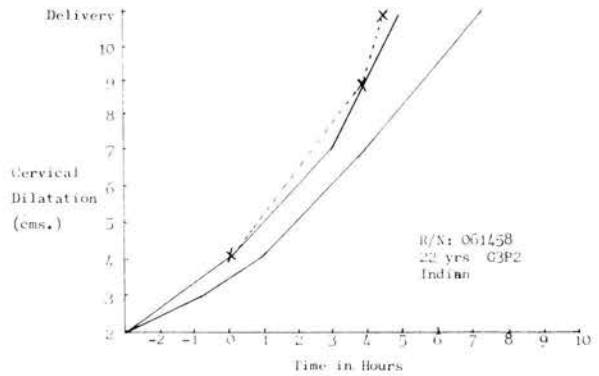

Fig. 3

Normal progress of labour: spontaneous vertex delivery

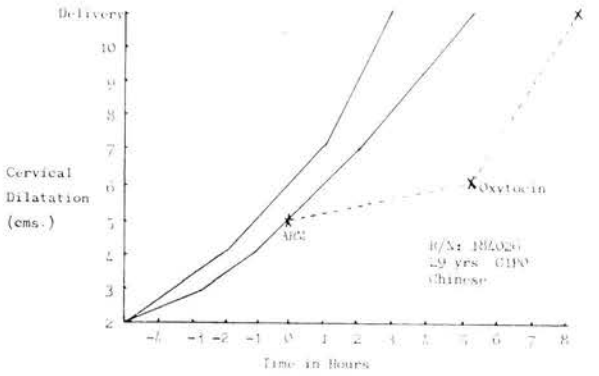

Fig. 4

Slow progress of labour: spontaneous vertex delivery after acceleration with I.V. oxytocin

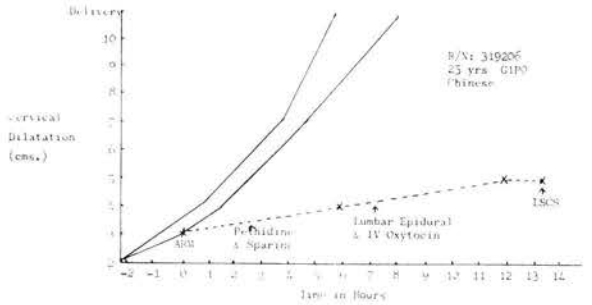

Fig. 5

Poor progress in labour: L.S.C.S. delivery

Summary:

1. Cervicograms showing the rate of cervical dilatation of normal labour amongst Malaysian women are presented in this study.
2. A probit of 80% was used in the construction of these cervicograms.
3. Major differences between the length of labour in primigravid and multigravid women were seen in the initial latent and the final phases.
4. In the active phase of labour, between 4 cm. and 7 cm. cervical dilatation, the rate of cervical dilatation appears similar in both primigravid and multigravid patients.

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Pharyngeal Exudates: Mere Mantle or Menace?

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FOR LONG General Practitioners have held the belief that exudates on the tonsils or other areas of the Pharynx in an acute sore throat were bacterial in origin and that they therefore needed energetic antibiotic treatment. Of recent times many papers have come out proclaiming the paucity of bacterial involvement in acute pharyngitidies (that they are largely viral in origin) but no mention was made of the significance of *exudates* in these situations. Besides, we know of no literature on this subject in the Malaysian Journals.

The purpose of this study was to look into these exudates bacteriologically and see if indeed the General Practitioners' assumption was justified and if not to what extent. In other words we felt there was a need for a study which would enable a General Practitioner to look into an acute sore throat, see an exudate(s) and predict with reasonable confidence the odds on it (them) being of bacterial origin.

We also felt that as a spin off, we would be able to obtain some insight into the degree of streptoccal (Haemolyticus) involvement in these situations which would not only add another dimension to our study but also alert the Clinician to instant and total action to rid this menace. In addition, one of us attempted to describe the exudates in detail (white, yellow or Yellowish white) in the hope that perhaps some useful data might evolve from this exercise.

Materials & Methods

This study was carried out at a General Practice set up having a clientele of all social strata, being situated between a middle class (Home owning) housing Estate and a slum, and lying just within Municipal limits of the capital city of Kuala Lumpur.

All cases presenting with acute respiratory tract symptoms were examined for Pharyngeal exudates, *however small*. Their colour noted, and a swab taken and sent to the Institute for Medical Research for innoculation, culture and identification. All age groups were involved and only cases which had had previous treatment were excluded for fear of culture negative reports making eventual analysis arbitrary.

A total of 51 cases were studied but as no growth was obtained from one of them, this was excluded as due to collection and/or transportation error.

Table I

Total Cultures	= 50
Streptoccus Haemolyticus	= 21
Staphytococcus Aureus	= 4
Staph & Strept	= 8
Diptheria	= 2
Pneumococcus	= 2
No Pathogens isolated	= 13

As the significance of the isolation of Staph aureus and Pneumococcus from throats in terms of pathogenicity is disputed, we are left with a total of 31 Pathogenic isolates (62%).

This is obviously the reverse of bacterial involvement in acute Upper Resparatary Tract Infections as a whole (where viruses are claimed to dominate), and hence significant. The 13 cases

(26%) which grew no Pathogens would largely be due to viruses. Vincent's Angina is a remote possibility.

Table II

Total Cultures = 50
Strept Haemolyticus = 29 (58%)

58% is without doubt a frightening figure in view of the possible serious sequele of Streptococcal sorethroats.

Table III

Total Studied = 50
White Exudates = 23
Yellow or Yellowish white Exudates = 27

Table IV

White Exudates = 23 of which
Strept Haemolyticus = 8
Staph Aureus = 3
Staph & Strept = 3
Diptheria = 2
Pneumonococcus = 1
No Pathogens isolated = 6
Strept Haemolyticus involvement in white exudates = 11/17 (48%).

Table V

Yellow or Yellowish white exudates = 27
Strept Haemolyticus = 13
Staph Aureus = 1
Staph & Strept = 5
Pneumococcus = 1
No Pathogens = 7

Thus strept Haemolyticus involvement in yellow exudates = 18/27 (66.7%).

Discussion

Table I shows that out of a total of 50 throat swabs there were 31 (62%) Pathogenic Bacterial Isolates. This is, of course, not taking into account the other isolates (Staph Aureus and Pneumococcus) whose pathogenicity in acute sorethroats is disputed. If these were included the total bacterial isolates would be 74%. These figures by themselves are meaningful but when one considers them against the background of *all* acute sorethroats where about 50 – 70% are of viral aetiology, then they become even more so and give strong support to the age old belief of the General Practitioner that acute exudative pharyngitis is bacterial until proved otherwise.

A look at Table II shows that no less than 58% of these swabs contained Strept Haemolyticus. This indeed is an alarming figure, though representative of only 50 cases, and warrants further studies from other observers on a larger scale. Meanwhile it will be a brave doctor who withholds immediate and total (i.e. a 10 day course) treatment from an exudative Pharynx, in the absence of culture studies.

Tables IV and V reveal interesting data in that yellow or Yellowish exudates seem to give a much higher yield (66.7%) of Strept Haemolyticus than white exudates (48%). This wide differential in Streptococcal involvement purely on the basis of the colour of the exudates is illuminating and will only remain a viable concept if it is observed on a much larger number of swabs; otherwise it may well peter away into one more of the many moot issues within the medical profession.

Conclusion:

50 cases of acute untreated exudative Pharyngitis were studied in a General Practice situation. Of these 62% proved to be of undisputed pathogenic bacterial aetiology with strept Haemolyticus contributing a menacing 58%. Yellow or Yellowish white exudates gave a much higher yield (66.7%) of Strept Haemolyticus than white exudates (48%). Antibiotic exposure would thus seem justified if only while awaiting culture and more extensive studies.

Acknowledgements

We wish to thank Miss C. Kamala Devi for her painstaking clerical efforts in accumulating and tabulating all the above data. Our thanks is also due to Miss N. Vasantha Devi for her patient secretarial contribution.

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Changes in Body Fluid Distribution in Experimental Protein Malnutrition

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Abstract

The sequential changes taking place in the plasma proteins, blood volume and body fluids in rats during the condition simulating "pre kwashiorkor" is described.

Protein malnutrition was induced in growing rats by feeding them a diet containing **0.5**% *protein. At weekly intervals the total plasma protein and albumin concentrations, hematocrit and the volumes of the different fluid compartments were determined.*

During the eight weeks of study, there was a marked loss in body weights, fall in total plasma protein and albumin concentrations, lowering of hematocrit levels and a slight increase in the plasma and extracellular fluid volumes. The changes in total body water and blood volumes were not significant.

Hypoproteinemia with hypoalbuminemia and an increase in the extracellular fluid volume were not associated with clinical edema, which probably is a late manifestation of protein malnutrition.

Introduction

PROTEIN MALNUTRITION is a problem of major concern to many developing countries in the world today. It is most often due to inadequate consumption of proteins or intake of proteins of poor quality. In protein malnutrition there is no sharp line between health and disease. The scientific study of protein malnutrition in experimental animals has contributed considerably to our understanding of biochemical changes taking place in protein malnutrition. For ethical and humanitarian considerations it is not possible to study the serum protein and body fluid changes during the development of protein malnutrition in man and so an animal model becomes extremely essential. Protein malnutrition in children is invariably complicated by deficiencies of calories, vitamins, minerals and perhaps trace elements, as well as by intercurrent infections and infestations. These alter in endlessly different patterns the basic clinical and metabolic picture seen in the child suffering from protein malnutrition. It is now possible to reproduce in animals the features of the protein deficiency syndrome known as Kwashiorkor (Kirsh, Brock and Saunders, 1968 and Edozien, 1968). In the animal model it is possible to keep to a minimum the individual variations and study the development of fluid changes under carefully controlled conditions.

One aspect in which there is a paucity of information and no general agreement is the fluid and electrolyte changes during the development of protein malnutrition (Gopalan, Venkatachalam and Srikantia, 1953; Picou and Waterlow, 1962; Davidson, 1964). The sequence of changes taking place in serum proteins, blood volume and body fluids have usually been reported after the development of gross edema or manifestations of advanced protein calorie malnutrition. The present study was designed to investigate the sequential changes in serum proteins and body fluids during the early stages in the development of protein malnutrition in rats simulating the condition "pre kwashiorkor".

Experimental

Male Sprague Dawley rats weighing 130 – 160 g were fed freely a diet containing 0.5% lactalbumin. A control group was fed freely a diet containing

18% lactalbumin. The diets were formulated after Edozien (1968). At weekly intervals batches of six rats from each group were weighed and the following determinations carried out:- Total body water, extracellular fluid volume, plasma and blood volumes, total plasma protein and albumin concentrations, and hematocrit values.

Total body water and thiocyanate space (ECF):

An accurately weighed amount (about 1 ml) of 2.5% thiocyanate solution containing 10 μCi of tritiated water was injected intraperitoneally. The accuracy of the amount injected was checked by weighing the syringe before and after injection in a sensitive balance. All food and water were withdrawn from the animals after the injection. Equilibrium of the thiocyanate and tritiated water is known to be complete by about four hours (Smith, 1960), and a sample of plasma can be assumed to be representative of the general body concentration of the labelled water and thiocyanate in the extracellular compartments of the body. Plasma was obtained after the injection of Evans Blue (see plasma volume below).

For total body water determination, the proteins were precipitated from 0.5 ml of plasma by adding 2.5 ml of absolute ethanol and the precipitate removed by centrifugation. One ml of the supernatant was pipetted into 20 ml of Bray's solution (1960) and the activity of tritium counted for 10 minutes in a scintillation counter (Hayes and Gould, 1953). The average of three such counts was taken for calculation of total body water.

The extracellular fluid volume was calculated by the method described by Huang and Bondurant (1955).

The intracellular fluid volume was obtained from the difference between the total body water and the extracellular fluid volume.

Plasma and blood volume:

Exactly four hours after the injection of tritiated water and thiocyanate, the rats were anaesthetized with ether and laparotomy performed. An accurately weighed amount of (about 0.5 ml) a 0.1% solution of Evans Blue was injected directly into the inferior vena cava. Here again this was made possible by weighing the syringe containing the dye before and after injection. After five minutes, as much blood as possible was withdrawn from the inferior vena cava in heparinised syringes and the animal sacrificed. Blood and plasma volumes were calculated using the formula of Loring (1954).

The interestitial fluid volume was obtained from the difference between the extracellular fluid volume and the plasma volume.

Hematocrit:

Hematocrit was determined by transferring heparinised blood to a Wintrobe tube with a Pasteur pipette and centrifuging at 1500 $\times$ g for 30 minutes. The level of packed cells was expressed as a percentage of the total volume of blood.

Plasma proteins:

The total plasma protein concentration was calculated from the micro-Kjeldahl determinations of plasma nitrogen using a factor of 6.54 (Sunderman, Sunderman, Flavo and Kallick, 1958). Electrophoresis of the plasma on cellulose acetate was performed and the percentage distribution of albumin calculated. The absolute amount of albumin was obtained by multiplying the total plasma protein concentration by the relative percentage of albumin (Chandrasekharan, 1969). The total amount of protein and albumin in the circulation was calculated.

Results and Discussion

The absolute volumes of the different fluid compartments and the total circulating plasma proteins are given in Table I.

The changes in the body weights, plasma proteins and hematocrit are illustrated in fig. I.

The changes in fluid volumes are shown in fig. 2.

Body weights:

The animals on the 0.5% lactalbumin diet lose weight progressively, the loss being greatest during the first week (25%) and at the end of eight weeks the rats had lost 45% of their initial weights. The overall severity of malnutrition may be assessed from the loss in body weights. During the same period of time the control animals gained over 125% in body weights (Fig. 1a). The experimental animals looked emaciated, but there was no evidence of edema or accumulation of body fluids during the two month period of experimentation. In Enwonwu's study (1971) 5% of the animals fed the low protein diet developed edema after six weeks and by 10 weeks 18 – 25% were grossly edematous.

Plasma proteins:

There was a gradual diminution in the total plasma protein concentration especially after the fourth week (Fig. 1b). With low protein levels edema formation is to be expected according to the

Table 1

Changes in body fluid volumes and plasma protein content in rats during protein malnutrition*

Duration: (Weeks)		1	2	3	4	5	6	7	8
Experimental rats (0.5% Lactalbumin diet)									
Plasma vol. (ml)	M.	3.69	3.79	3.45	3.83	3.97	4.32	3.84	3.82
	S.D.	0.33	0.14	0.36	0.36	0.53	0.34	0.40	0.22
Blood vol. (ml)	M.	8.31	7.39	5.95	7.13	6.73	6.97	5.99	6.28
	S.D.	0.68	0.48	0.61	0.42	0.74	0.18	0.65	0.28
Total body water (ml)	M.	73	82	75	70	62	74	58	54
	S.D.	7	5	7	5	5	3	4	3
Extracellular water (ml)	M.	23.44	18.27	22.51	17.80	19.46	19.25	18.05	19.11
	S.D.	2.83	2.08	1.45	1.92	1.46	1.43	1.08	1.20
Total circulating plasma protein (mg)	M.	165	192	166	161	169	166	159	154
	S.D.	35	12	24	25	13	23	23	11
Total circulating albumin (mg)	M.	84	102	91	88	90	104	91	76
	S.D.	22	17	10	25	14	10	25	11
Control rats (18% Lactalbumin diet)									
Plasma vol. (ml)	M.	5.62	7.06	7.45	8.76	9.76	12.17	12.49	12.18
	S.D.	0.44	0.67	0.43	0.91	1.02	0.89	1.38	1.21
Blood vol. (ml)	M.	12.03	12.11	14.55	17.86	18.84	23.83	24.11	24.01
	S.D.	1.01	1.27	0.99	2.01	1.76	0.98	2.33	2.22
Total body water (ml)	M.	107	144	176	196	174	214	260	214
	S.D.	12	11	5	11	42	12	15	24
Extracellular water (ml)	M.	36.77	27.78	43.48	52.82	42.91	62.86	56.82	65.51
	S.D.	2.85	0.84	4.67	2.20	9.77	6.96	4.00	6.37
Total circulating plasma protein (mg)	M.	338	420	487	558	660	840	890	822
	S.D.	16	57	56	52	37	90	72	90
Total circulating albumin (mg)	M.	187	236	247	307	400	431	506	417
	S.D.	17	27	35	37	39	85	42	103

*Each result is the mean of six rats

classical hypothesis of Starling (Landis and Pappenheimer, 1963), as a result of the reduced colloid osmotic pressure of the plasma. A deficiency of colloid osmotic pressure would lead to escape of fluids into the tissues. In infants with protein malnutrition edema is almost invariably accompanied by hypoproteinemia (Waterlow, Cravioto and Stephen, 1960). Enwonwu (1970) observed that the development of edema was always preceded by a large drop in the serum protein concentration. He also suggested that "the association between hypoproteinemia and edema does not in any way imply a cause and effect relation." In the present study there was a decrease in the total circulating plasma proteins inspite of an increase in the plasma volume and this is probably due to a greater fall in the plasma protein concentration (Fig. 1c). However, it is observed that in protein malnutrition, even when there is no hypoproteinemia, there may be a decrease in plasma volume and so in the total circulating plasma protein (Waterlow, *et al,* 1960).

The plasma albumin concentration in rats fed the low protein diet was consistently lower than the control group, and so was the total amount of circulating albumin. However the relative amount of albumin remained rather unchanged. It is interesting to note that a significant fall in the concentration of albumin occurred after one week on the low protein diet and decreased further only towards the end of the study. It is possible that mobilisation of albumin from the extravascular compartments prevent marked dimunition in the albumin concentration in animals fed a low protein diet in the intervening period (Fig. 1d and 1e).

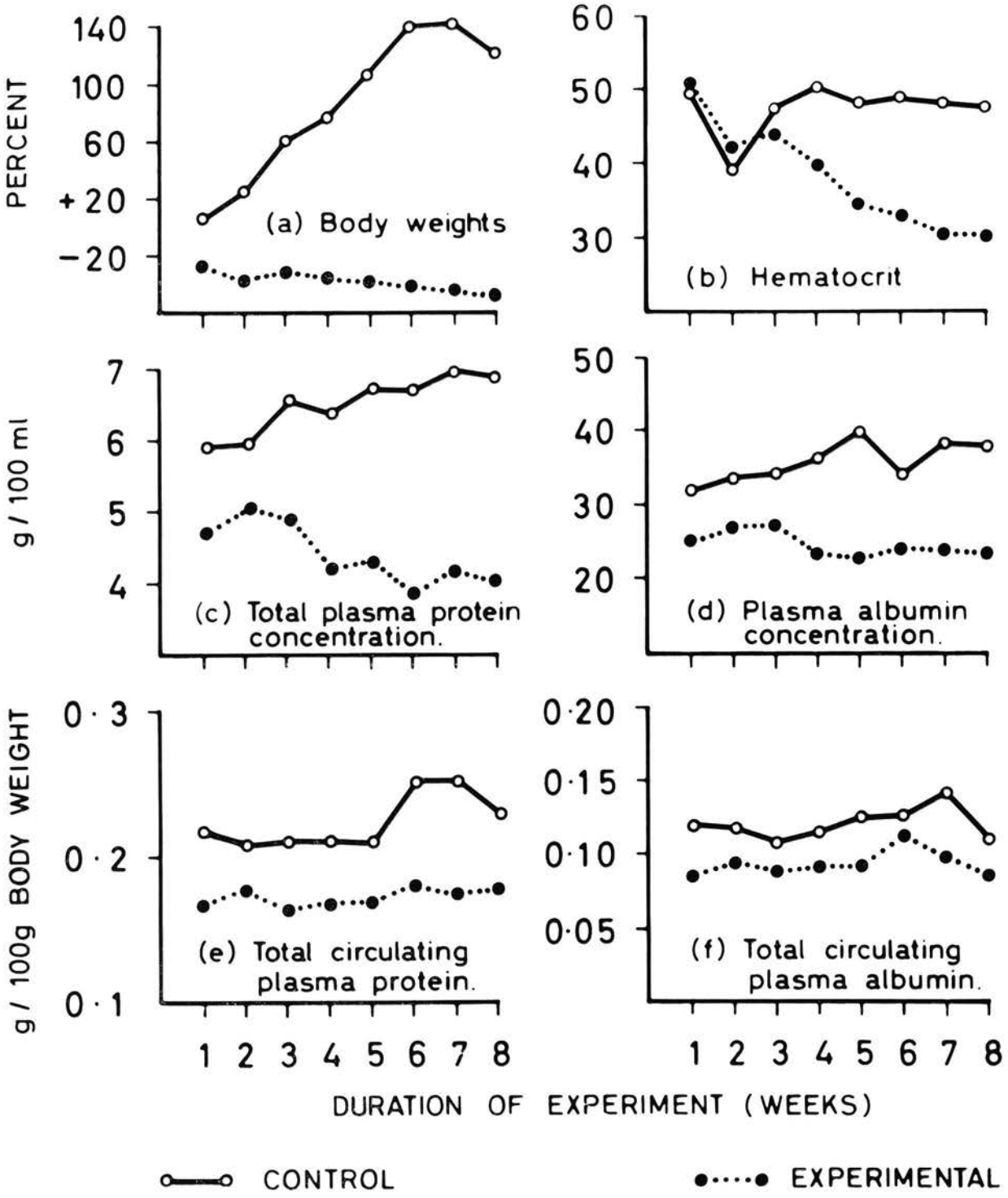

Fig. 1

Changes in body weights, hematocrit, and plasma proteins during experimental protein malnutrition in rats. The results for body weights are expressed as percent change from initial body weights. Each point is the mean of six rats. The lines joining the points are not meant to represent the changes in the intervening period, but merely to indicate general trends.

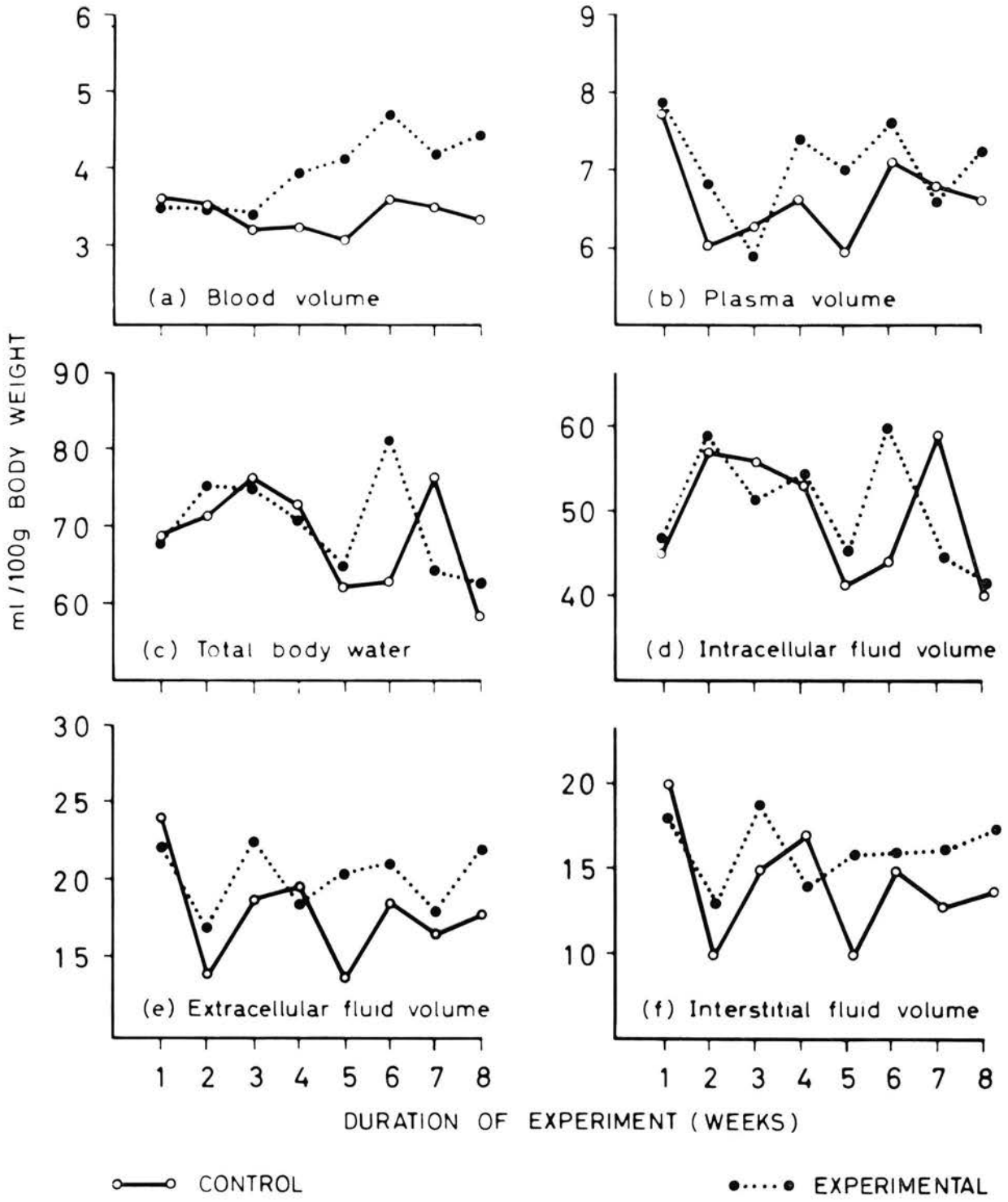

Fig. 2

Changes in the blood and plasma volumes, total body water and intracellular, extracellular and interstitial fluid volumes during experimental protein malnutrition in rats. Each point is the mean of six rats. The lines joining the points are not meant to represent the changes in the intervening period, but merely to indicate general trends.

Hematocrit:

There was a gradual fall in the hematocrit value as the duration on the low protein diet increased (Fig. 1f). This is most likely due to the development of anemia and an increase in the plasma volume.

Plasma volume:

The plasma volume per unit of body weight increased and was relatively greater, the higher the loss in body weight. In the present study the increase was evident from the 4th week onwards (Fig. 2a). There are many conflicting reports, some workers claiming that in nutritional edema the plasma volume is actually increased (Waterlow *et al,* 1960; McLaren, 1969), while others report that it is stationary (Keys, Bronzek, Henschel *et al.*; 1950). In nutritional edema at the height of the disease there is an absolute diminution in plasma volume (Gopalan *et al,* 1953).

Blood volume:

There was a fall in the relative blood volume towards the end of the 7th and 8th weeks of the experiment (Fig. 2b). Blood volume varies, on the whole, directly with the body weight, especially to the metabolically active body mass. During growth total plasma and blood volumes increase slowly according to the surface area until adult volumes are reached. After cessation of growth the blood volume remains unchanged in the rat. A decrease in plasma protein concentration may influence the blood volume through colloid osmotic pressure. In cases of malnutrition the blood volume seems to decrease at the same rate as the serum proteins (Walters, Lehman, and Rossiter, 1947). The fall in blood volume towards the end could possibly be explained by the development of anemia and this is substantiated by the low hematocrit findings in the present study.

Total body water:

There were no significant changes in the total body water during the first six weeks. Towards the end there was a very slight increase in the total body water (Fig. 2c). In malnutrition the water content of the body tends to be increased even without clinical edema. Clinical edema, as occurs in kwashiorkor, appears only after a considerable degree of water retention (Dean, 1962). In Edozien's study (1968) edema developed only about the 4th month. Perhaps the onset of edema marks a transition from the mild to the severe state of the disease (Enwonwu, 1970).

Intracellular water:

The intracellular fluid volume did not show any significant alterations, except for one observation each in the control and experimental group. It is suggested that protein malnutrition does not affect the intracellular fluid volume at least during the early stages.

Extracellular water:

There was a slight increase in the extracellular water content (thiocyanate space) after the 4th week (Fig. 2d). The volume of extracellular fluid is often high in malnutrition, and a consequence of this is the appearance of edema. Many explanations have been brought forward to account for the increased extracellular fluid volume in malnutrition (Widdowson, 1968). None of them explains all the facts, there are probably several causes. The more important ones seemtobe:-a) Fall in the oncotic pressure of the plasma and the resulting flow of fluid to the extracellular compartment (Picou and Waterlow, 1962). b) Alterations in the relative proportions of the three great components of the body due to malnutrition. The replacement by water of body space previously occupied by fat and cellular tissues is probably an important cause. Diminution is total body solids by providing space for the accumulation of excessive extracellular fluids may tend to mask the severity of the edema (Waterlow *et al,* 1960). c) Protein malnutrition can also result in diminished renal blood flow and glomerular filtration resulting from diminished cardiac output. This would presumably lead to sodium retention and edema (Davidson, 1964). d) Increased concentration of a substance with anti diuretic activity (Srikantia and Mohanram, 1969).

Interestitial fluid:

There was a small increment in the interstitial fluid volume after the fifth week, but not significant enough to manifest itself as clinical edema. This finding is consistent with the absence of clinical edema during the early stages of protein malnutrition.

Conclusion

The severity of protein malnutrition as gauged by gross alterations in body weights are not paralleled by equally significant alterations in the volumes of the fluid compartments of the body during the early stages. The classical edema so often associated with protein malnutrition is not evident during the early stages in the development of protein deficiency.

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Occupational Health in West Malaysia

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1. Introduction

THE FEDERAL GOVERNMENT has placed much emphasis on industrial growth and development of new industries since the introduction of the General Plan of Development in 1956. This was continued through the second five years of the Social and Economic Development plan for 1961 – 1965. The specific objective in all these plans in relation to occupational health is the development of industries designed to be labour-intensive so as to generate employment opportunities and reduce unemployment. Essentially these development plans were formulated to promote the economic welfare of all people in general and the workers in particular.

Recognising this fact, the Cabinet in June 1966 made a decision to establish an Industrial Health Unit. This unit was initially to be based in the Ministry of Labour and Manpower with the specific objective of evolving a nation-wide Occupational Health Service. It was also envisaged that this scheme would stimulate interest and the need for such a service among the management, workers and the medical profession in general. In conjunction with the Ministry of Labour, particularly the Factory Inspectorate, the unit had the task of assessing the cost to the national economy of industrial diseases and accidents.

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In June 1970, the unit having completed its initial task requested the formation of a joint committee in occupational health of members of the Ministries of Health and Labour to further intensify its activities and co-ordinate overlapping objectives. Further, the Ministry of Health in consultation with the Ministry of Labour and Manpower, obtained the services of a World Health Organisation consultant on occupational health from Canada. After careful study of the existing facilities, especially the infra-structure for Health Care Delivery System, he recommended the transfer of the unit to the Ministry of Health, basing his recommendations on the desirability of developing the unit into an occupational health facility within the health centre based medical care.

The scope and magnitude of the task before the Occupational Health Unit can be judged from Table 1 which gives the number of work establishments and structure of the economically-active population in 1973. The effectiveness of the unit will depend on the health care it can provide for a known population of 2.9 million work force. However, this figure does not include the self-employed and the numerous cottage industries scattered all over the country.

2. National occupational health and safety legislations

The responsibility for safety, health and welfare of the working population is distributed essentially between the Ministry of Health and Labour. Other ministries involved are the Ministry of Local Government, Agriculture, Transport and Communication. Table 2 gives a comprehensive list of all legislations

Table 1

Distribution of national work force by branch of economic activity, 1973

Branch of economic activity	Number of establishments	Total economically active population (in thousands)	%
Agriculture, forestry, hunting and fishing	12,324	1,359.1	46.8
Mining and quarrying	1,156	55.2	1.9
Manufacturing	3,074	251.9	8.7
Construction	1,390	92.4	3.2
Electricity, gas, water and sanitary services	108	19.7	0.68
Commerce	20,331	274.6	9.43
Transport, storage and communication	1,561	97.9	3.37
Services	14,432	472.6	16.3
Activities not adequately described	Na	101.3	3.5
Persons seeking work for the first time and unemployed	Na	178.4	6.15
TOTAL	54,378	2,903.1	100.0

operative and their functions as indicated by appropriate code number below the table. It is not possible in this general review to discuss in detail all the legislations but the major ordinances, namely the Rump Labour Code 1933, Workmen's Compensation Ordinance 1952, the Factory and Machinery Act 1970 and the recent Employees' Social Security Act 1967 will be briefly summarised.

The Rump Labour Code 1933: This code deals primarily with the provision of accommodation, sanitation, health requirements and the provision of hospitals and medical care services in the estates and mines. It also provides generally for inspection by labour officers of conditions of work, maternity benefits and, to some extent, wages. Medical officers of health are gazetted under this code and are responsible for the health provisions.

Factories and Machinery Act 1970: The act was initially introduced in 1967 and further modified in 1970 forms the major legislation regulating health, safety and welfare in all places of work. This act provides for the appointment of the Factory Inspectorate and the appointment of any other officers from time to time as deemed necessary by the Director-General of Factories and Machineries. One such officer gazetted as an inspector is the Industrial Health Officer. He then deals primarily with prescribing health and welfare requirements such as sanitation, preventive measures including health screening, medical examinations – pre-employment, periodic of workers exposed to special risks and toxic substances, and the provision of treatment services. Though this is a comprehensive legislation, as far as safety and welfare is concerned, the main deficiency as regards health is in the requirement for notification of occupational diseases. The act requires the employer, not the attending physician, to notify such diseases. The employer notifies as required to the Director-General of Factories and Machineries and not to the Occupational Health Unit in the Ministry of Health. Secondly, not all work places are covered by this act, as it excludes premises where less than five employees work and those in which no machinery is used.

The Workmen's Compensation Ordinance 1952: This provides for compensation to workmen for injury and diseases in the course of employment. It however, excludes workers who work under a direct contract of services, casual labour, domestic servants and those whose income exceeds $500 a month. The ordinance defines the legal liability of employers and the quantum of compensation to be paid. It also spells out the role of the Ministry of Health in the provision of medical examinations, treatment of injured workmen and designation of approved hospitals. Finally, it outlines procedures of arbitration proceedings in cases of disagreements between employer and employees. The second schedule of the ordinance provides a list of compensatable occupational diseases. The list, perhaps comprehensive in 1967, has omitted occupational lung disorders especially in relation to lung dust diseases.

Table 2

National occupational health and safety services (administration)

Sector	Institution responsible	Relevant legislation(s) (title, year)	Functions*
Health	Ministry of Health	The Poisons (Sodium Arsenite) Ordinance 1949 and Regulations.	1
		The Radioactive Substances Act 1963.	
		The (Draft) Public Health Act.	
		The Hydrogen Cyanide (Fumigation) Ordinance 1953	1
Labour	Dept. of Labour	The Factories and Machinery Act 1970	1, 14
	Dept. of Factories and Machinery	The Rump Labour Code 1933	1
		The Workmen's Compensation Ordinance 1952	1, 11
		The Employment Ordinance 1955.	1
		The Children and Young Persons (Employment) Act 1966 and Regulations.	1
		The Workers' (Minimum Standards of Housing) Act 1966 and Regulations	1
Social Security	Dept. of Social Security	The Employees' Social Security Act 1969.	9, 10
Non-governmental	Local Authority	By-laws of municipalities, town boards (or councils) and local councils	1, 5 6
Other	Dept. of Mining.	The FMS. Mining Enactment 1926	1, 2
	Petronas.	Air Navigation Ordinance 1952, The Air	1, 4
	Dept. of Agriculture	Navigation Order 1953, The Air Navigation	1
	Ministry of Transport	(General) Regulations 1953, The Air Navigation (Radio) Regulations 1953	
		The Railway Ordinance 1948	1
		The Road Traffic Ordinance 1958	1
		Road Traffic (Amendment) Act 1964	
		The Merchant Shipping Ordinance 1952	1
		The Port Authorities Act 1963	
		The Pineapple Industry Ordinance 1957	1
		The Dangerous Trades (Calcining or Roasting of Sulphurous or Arsenical Ores) Rules 1924.	5
		Environmental Quality Act 1974.	4

*** Appropriate code number of functions**

1. Inspection and enforcement
2. Advisory
3. Surveillance
4. Norms, guides, criteria, standards
5. Health licensure of work places
6. Sanitary supervision
7. Pre-employment examination
8. Periodical examination
9. Curative care
10. Rehabilitation
11. Workmen's compensation
12. Education of workers
13. Education of employers
14. Registration of notified occupational accidents/diseases

The Employees' Social Security Act 1969: This act provides for benefits to employees in case of invalidity and employment injury including occupational diseases. However, it excludes all workers earning more than $500 a month, agricultural workers and also all enterprises employing less than five workers.

The act provides for methods of administration involving the handling of funds contributed by the employers and employees, appointment of inspectors and medical officers for the purposes of the act. The constitution of the Medical Board and the Appalate Medical Board are also defined. Occupational diseases are covered in the fifth schedule. The list is not comprehensive and requires further addition of recognised occupational diseases.

Initially the act was introduced on a pilot basis in five selected areas and is being progressively

extended to other parts of Peninsular Malaysia. It is envisaged that the act, when fully operational, will by and large replace the Workman's Compensation Act.

3. Health manpower, training and education in occupational health and safety

The distribution of the estimated total medical and other health personnel by the type of employment in Peninsular Malaysia is shown in Table 3. Out of a total of 17,154 health personnel, over a third are employed in the provision of medical and health services in the private sector which includes plantations and industries. Most of the 901 physicians in the private sector do provide treatment services to the industries and plantations. Only a handful have had any form of training in occupational health. In the Government sector, i.e., the Ministry of Health, there are three physicians with occupational health training and one health inspector with some experience.

Occupational health is still in its infancy and little emphasis is placed on it in the training institutions of the country. The undergraduate medical students are given eight hours lecture with a factory visit, while the postgraduate trainees in the Master of Public Health programme devote a total of 18 hours with a limited number of factory visits.

4. Health services for workers

It is not possible to obtain figures to estimate the percentage of work establishments where health services are provided at plant level but my impressions are that in most some form of first aid is available. In some, curative care with diagnostics and referal system have been developed through the utilisation of hospital assistants and nurses. A few establishments have the services of a part-time medical practitioner who is retained by the firm to provide essentially curative service. Some industrial concerns employ their own physician who provides pre-employment, periodic medical examinations with diagnostic and curative care. It is discouraging to note that none of the establishment provides any form of health education to workers on occupational hazards or monitor the working environment.

However, estates and mines have evolved a more comprehensive medical facility for their workers mainly to satisfy the Rump Labour Code which requires employers to provide free medical, health and housing facilities. Most establishments have the services of a visiting medical officer who visits periodically, usually at intervals of a week. He examines all cases referred to him by the resident medical assistant and, if necessary, refers the more complicated cases to government hospitals. Preventive activity is usually confined to sanitation, anti-larval control, and immunisation. Provision of family planning and health education, though minimal, is being attempted in many estates.

Larger establishments provide and maintain hospitals usually individually or as a group to cover estates within a given area. Such hospitals have the services of a full-time resident medical officer supported by para-medical staff. With fragmentation of estates into small holdings, most group hospitals are increasingly difficult to finance and provide the required comprehensive medical care.

5. Occupational health diseases and problems

Available statistics do not reflect existing occupational diseases because none has been systematically notified, recorded or compensated. The Factories and Machinery Act requires notification of occupational diseases but unfortunately no diseases have been reported by the employers. On

Table 3

Distribution of estimated total medical and para-medical personnel by type of employment

	Total	Employed by government	Employed by private and/or State enterprise in any kind of economic activity		Private
			Full-time	Part-time	
Physicians	2,167	1,266	NA	NA	901
Nurses	7,830	3,621	155	NA	4,054
Medical or health assistants	2,837	1,463	NA	NA	1,374
TOTAL	17,154	9,410	155	NA	5,329

the basis of available clinical evidence from hospital records, the following diseases: silicosis, stannosis, asbetosis, occupational dermatitis, kerato conjunctivitis and noise-induced deafness to mention a few have been diagnosed not infrequently.

6. Occupational accidents

Available data on accidents are insufficient for statistical analysis, especially in relation to frequency and severity rate. This is probably due to poor reporting and lack of an acceptable definition of accidents. Occupational accidents are defined as those occurring at the place of work; the degree of severity is usually specified since trivial occurrences are often unrecorded. In Table 4 accidents reported in 1968 are being compared with those of 1972 and 1973. The total number of accidents seems stable. However, the number of accidents giving rise to permanent disability has increased from 377 in 1972 to 923 in 1973. The highest accident rates are generally among agriculture, forestry and fishing industries.

Table 4

Number of reported industrial accidents in 1968, 1972 and 1973

Branch of economic activity	1968	1972	1973
Agriculture, forestry hunting and fishing	5,407	5,952	6,902
Mining and quarrying	1,028	1,292	1,086
Manufacturing & processing	1,969	3,321	2,650
Construction	1,330	966	765
Electricity, gas, water and sanitary services	130	114	81
Commerce	443	737	592
Transport, storage and communication	1,253	694	408
Services	435	386	254
Activities not adequately described	NA	NA	5
TOTAL	12,595	13,462	12,743

The highest fatality rate is experienced by the agricultural sector, possibly from saw-milling and logging establishments. This is followed closely by manufacturing and quarrying activity. Fatal accidents have risen from 40 in 1972 to 370 in 1973 indicating a 60% rise. This is a grave situation requiring immediate governmental enquiry.

7. Workmen's compensation and sickness absence

The quantum of compensation paid depends on the number of accidents and their severity. It is evident that accidents, especially the more severe resulting in permanent disability and fatality, are on the increase. This is reflected in the amount of compensation paid. This experience is reflected in Table 5 which shows the amount of compensation paid in 1968, 1972 and 1973. Though the breakdown for 1972 is not available, it is discouraging to note that the total amount of compensation paid in 1973 has trebled the amount paid out in 1968. This clearly indicates that there is unnecessary, avoidable loss of labour and enormous loss of potential production. This economic burden imposed on the nation through compensation needs careful study.

Table 5

Workmen's compensation paid in cases of accidents, occupational diseases and sickness absence 1968, 1972 and 1973

Branch of economic activity	1968	1972	1973
	Amount in $	Amount in $	Amount in $
Agriculture, forestry, hunting and fishing	931.83	NA	1380582
Mining and quarrying	571.839	NA	832417
Manufacturing	810.390	NA	1536993
Construction	678.336	NA	617002
Electricity, gas, water and sanitary services	47.762	NA	44721
Commerce	373.439	NA	891153
Transport, storage and communication	465.847	NA	590441
Services	207.705	NA	251008
Activities not adequately described	NA	NA	6211050
TOTAL	4087,131	1219299	12355367

8. Obstacles in occupational health

The main obstacle in developing and implementing an occupational health and safety programme is the lack of a comprehensive legislation and a single authority to regulate and enforce. Secondly, the lack of trained personnel in both the government and the private sector. Last, but not the least, is

the apathy among workers towards individual health and possibly lack of interest in occupational health among the trade unionists.

9. Conclusions

An important task of the occupational health service will be to improve and strengthen the training and teaching of medical graduates (undergraduates and postgraduates), health inspectors and nurses in the principles of occupational health practices.

ii) Develop guidelines, standards and threshold limit values for the country, taking into consideration local and ethnic factors.

iii) Conduct operational surveys throughout the country to identify the nature and magnitude of the incidence and prevalence of occupational diseases.

iv) Present industrial hygiene activity in relation to monitoring and surveillance be intensified.

v) The list of occupational diseases in the second schedule of the Workman's Compensation Act and the fifth schedule of the Employee Social Security Act be reviewed and enlarged.

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Brief Psychotherapy with Children

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Introduction

SHORT-TERM THERAPY has been found effective in the treatment of behaviour disorders of children and adolescents.[2,4,5,8] Rosenthal[8] defines brief psychotherapy as limited to a maximum of ten calendar weeks. His technique involves a case formulation at the initial interview, the setting of realistic treatment goals and collaboration of the family as an essential part of the therapeutic process. In addition the therapist plays an active and often directive role. On account of the time constraint in brief psychotherapy, more planning and treatment strategy is involved and there is a constant focuss on the issue of termination. According to Barten[2], short-term therapy utilizes a health-oriented outlook emphasizing the assets and strengths of the child and parents. Hence with the family adopting more positive expectations, a change in other areas of behaviour would continue even after the therapeutic process has been concluded. The results of the above studies indicate that short-term treatment is as effective as traditional long-term treatment besides the economy of time and personnel. Philips[7] attributes the feasibility of short-term treatment in children to their natural forward surge – growing and changing, and the fact that parents respond better as parents than they do simply as adults seeking help.

Based on these findings, when the Child Guidance Clinic in Assunta Hospital commenced about two years ago, I decided that as far as possible, brief psychotherapy would be the treatment of choice. Thus all children with behaviour disorders who required therapy were given short-term treatment, hence excluding older children and adolescents with deep seated personality disorders and those who were psychotic. This paper reports my experience with the use of brief psychotherapy in a multiracial group of children.

Procedure

Child Guidance is a new concept in Malaysia and since I conducted the clinic alone, I planned a gradual approach to diagnosis and therapy, which would be more acceptable to the parents. Even among the Caucasian parents, only two had any knowledge of Child Guidance. Thus all parents were informed at the first interview that the diagnostic sessions would involve weekly visits for a total of three weeks. On each occasion, the mother was interviewed, a few of the fathers were also seen individually and the therapist had a play session or an interview with the patient, depending on the age. If psychological testing was indicated, it was done during this period. At the end of these sessions, a diagnostic formulation was made and the course of treatment planned. The parents were then informed of the child's problem, if psychotherapy was deemed necessary, the specified period not exceeding ten visits, preferably weekly sessions was then decided. In addition parents were counselled as to what role they play in the therapeutic process. I did not have the services of a psychiatric social worker to see the mother, at the same time, the child came for therapy. In order to maintain confidentiality of the patient so essential in the treatment process, mothers of children in therapy were seen every two weeks at a different time. This also enabled the therapist to keep track of behaviour at home and take appropriate steps.

The Patients

Of the 15 patients, 8 were Malaysians and 7 Caucasians. All were referred by Private Practitioners or were from the Paediatric and Medical wards of this hospital. The majority were from middle class homes and spoke either English, Chinese or Malay. Their ages ranged from 3 – 17 years. All were from intact families.

Diagnosis

After 3 weeks of initial evaluation, a diagnosis was arrived at together with predisposing causes or circumstances of the behaviour disorder. The classification of psychopathological disorders of childhood proposed by the group for Advancement of Psychiatry[3] was used. The patients fell into the following groups:–

Reactive disorders	10
Developmental deviations	1
Psychoneurotic disorders	3
Personality disorders	1

Table 1 sets out particulars of the patients together with their modes of presentation and symptoms.

Psychotherapy

The form of psychotherapy depended on the developmental level of the patient. Using non-directive play therapy, the younger children invari-

Table 1

Patients & Their Presenting Symptoms

	Name	Nationality or Race	Sex	Age	Presenting Symptoms	Other Symptoms
1.	Siti	Malay	F	3 yrs.	Oppositional behaviour	Regressive behaviour, aggression directed towards mother.
2.	Ravi	Indian	M	4 yrs.	Night terrors	Temper tantrums, oppositional behaviour in school & at home, sibling rivalry.
3.	Karen	Chinese	F	4 yrs.	Socially withdrawn	Temper tantrums, regressive behaviour, oppositional behaviour in school.
4.	David	American	M	4 yrs.	Encopresis	Regressive behaviour.
5.	James	British	M	6 yrs.	Urinary urgency & frequency	Irritability, provocative behaviour.
6.	Paul	Aust.	M	6 yrs.	Marked aggressive behaviour in school	Nocturnal enuresis, difficult school adjustment, profane speech, destructive behaviour.
7.	Charles	French	M	7 yrs.	Nocturnal enuresis	"too good" behaviour, hypersensitivity, social withdrawal.
8.	Cara	Swedish	F	8 yrs.	Social withdrawal	Underachievement in school, temper tantrums, hypersensitivity.
9.	Anne	British	F	8 yrs.	Frequent headaches	Difficult school adjustment, insomnia, overly dependent behaviour.
10.	Mary	Aust.	F	9 yrs.	School failure	Temper tantrums, sibling rivalry overly dependent behaviour, low frustration tolerance.
11.	WKY	Chinese	M	9 yrs.	Separation anxiety	Regressive behaviour, overly dependent behaviour, seductive behaviour.
12.	Maniam	Indian	M	10 yrs.	Acute anxiety attacks	Confused and irrational, regressive behaviour, insomnia.
13.	KEK	Chinese	M	15 yrs.	Acute anxiety attacks	School failure, nightmares, giddiness & palpitations.
14.	WPC	Chinese	F	16 yrs.	School phobia	Freezing sensation in chest, distractibility, insomnia.
15.	TSK	Chinese	F	17 yrs.	School phobia	Severe headaches, depression, forgetfulness, distractibility.

ably acted out their anxieties in doll play. The role of the therapist involved interpretation, reflection and reinforcement of more mature forms of behaviour. With the older children, anxiety problems were very pronounced, in fact 4 of them were hospitalised in acute panic states associated with multiple somatic complaints. They were placed on mild tranquilisers for a short duration, at the same time psychotherapy was commenced. During their stay in hospital, intensive psychotherapy was given every other day. The period of hospitalisation in all cases was short – less than one week. Upon discharge psychotherapeutic interviews were continued on a weekly basis. The time limit of brief psychotherapy still applied – not exceeding 10 visits. The older children tended to be more inhibited, hence more "therapeutic pressure" was involved. During the treatment sessions, the therapist focussed on the presenting symptoms, other problems that the patients or their parents brought forward and also dealt with any underlying psychopathology in the patient.

Increasing self-esteem was another treatment goal particularly for the older patients.

Duration of Treatment

Number of patients	15
Completed treatment	11
Definite to marked improvement	10
Relapse	1
Defaulted	4

The length of therapy ranged from 4 – 10 weeks with a mean duration of 6.6 weeks. If the diagnostic sessions were included, the total attendance at the Clinic came to an average of 9.6 weeks.

Termination

The duration of therapy, within the ten week limit, was specified before short term treatment commenced. This was stressed to both parents and patient initially, and as treatment progressed, the prospect of termination in the near future was brought up again as a reinforcement for further behaviour change. Then two weeks before termination, the question of adequacy of present functioning was discussed together with the information that there were only two more sessions left.

Follow-up

This was done through a follow-up interview with the mother or by telephone at 3, 6, and 12 month periods. Queries were made concerning the child's present social adjustment, school performance and any recurrence of the former behaviour problems. Parents were also asked to give an appraisal of psychotherapy – in what manner this was of help to their child. Relapse in the one patient occurred 4 months after the family left Malaysia.

The following case presentations show the type of problems encountered in brief psychotherapy:–

Case 1. School phobia

S. K. a 17 year old Chinese girl complained of severe occipital headaches for the past 3 months as a result of which she only attended school for 3 days in the whole of the previous term in Form 4. She had been admitted into the medical ward for investigation, EEG and skull x-rays were normal. She was then referred to the Child Guidance Clinic for management of school refusal.

S. K. was the only girl in the family with 4 brothers all of whom were high achievers. Her father was a clerk and mother a housewife. Both appeared detached and seldom visited her in hospital. S. K. came from a traditional extended family. The paternal married aunt dominated the family and S. K. was very attached to her. During hospitalization, this aunt was her constant companion.

S. K. completed primary school in Chinese medium and did extremely well. She was then placed in an English medium secondary school when she did not perform as well. However, she passed the L.C.E. examination and was placed in the Arts stream. While in Form 4, during the mid-year examinations, she passed in Maths., English and Bahasa Malaysia but failed all the other subjects.

Soon after that, her symptoms appeared – severe headaches, difficulty in concentrating on studies, forgetfulness and increasing anxiety as she felt progressively less capable of coping with her school work. When she felt better she would attempt to go to school, accompanied by her aunt, but would panic when the car approached the school and she would refuse to enter.

During the diagnostic sessions, S. K. appeared depressed and apprehensive, somatic complaints dominated the interviews. Since hospitalization, she was placed on small doses of Diazepam. She communicated almost entirely in Cantonese which she spoke very well. It was obvious that she had a very poor command of English and hardly up to Form 4 level. By the 3rd visit, S. K. expressed a desire to return to school when she was fully recovered.

In the diagnostic formulation, her aunt was told that S. K. had a strong attachment to her and ambivalent feelings towards her parents. She attempted to resolve this by moving into their room since her illness but still they did not alter their attitude toward her. School phobia was related to separation anxiety from her aunt together with an impending fear of failure in school and a complete loss of face at home. It was further explained that S. K. would require psychotherapy over an eight to ten week period. The focus of therapy would be to help S. K. work through her ambivalent feelings towards her parents, to enable her to accept her illness as having an emotional basis, to help her return to school as soon as possible and to improve her self-esteem. The role of the family, particularly her parents, was to be supportive of her efforts to resume studying and to obtain for her the services of an English tutor. As therapy progressed, there was a perceptible improvement in affect, at the same time, somatic complaints decreased. By the 5th visit, S. K. was well enough to contemplate returning to school after the Chinese New Year holiday. I arranged with her headmistress to permit her to return to school on a gradual basis, initially confining herself to a few classes – Bahasa Malaysia, English Language, Maths and Art, the latter two being her best subjects. Her social relations had also improved. Together with some classmates, she visited a local orphanage to distribute toys and sweets to the children.

The following week, S. K. reported that she was attending school daily and could easily cope with the four subjects specified. In fact she was coping so well that she started to sit in on all the other classes. She looked very attractive in a new long dress and her headaches had largely gone. Her aunt reported that at home she was completely changed. She was now assertive, verbally aggressive to her younger brothers, and often pestered her aunt to go shopping for new dresses for herself. She was happily attending school daily. Her family was pleased with the change. On that note therapy was terminated after 10 weeks.

At the follow-up interview, one year later, S. K. had completed the Form 5 examinations and obtained four distinctions but failed in Bahasa Malaysia. She intended to repeat the examination and possibly go for further studies. There was no recurrence of school refusal.

Case 2. Urinary urgency and frequency

James W, a 6 year old English boy, was referred by the paediatrician because of frequency and urgency of micturition for which no physical cause could be found. For the past year he had 3 attacks of frequency each lasting only a few days. Sometimes he received treatment from the family doctor, at other times symptoms would spontaneously subside. On this occasion however frequency had lasted 3 weeks, urinanalysis was normal and medications were of no avail. Mrs. W reported that James went to the toilet every few minutes even while he was enthralled in play or watching T.V., he awoke 2 – 3 times at night for this purpose and lately was more irritable and provocative towards his elder brother.

James was the younger of two boys in the family, his father was a mining engineer and mother a housewife. Both parents had a close and warm relationship with the children. Mrs. W had been unwell for the past few years and had had several operations but was now fully recovered. Mr. W. spent a lot of time with the boys and rarely punished them.

James was a very intelligent, verbal and imaginative child. In the first play session, the repeated bashing together of the heads of the parent dolls and later interlocking of the boy and father dolls was very suggestive of the primal scene. No comment was made at that juncture as I was unsure of the significance of this play. James also played a game of hide and seek in the adjoining bathroom but managed to withhold micturition throughout the entire 45 min. session.

The following week Mrs. W confirmed that about 10 months ago on a Sunday afternoon, the boys were found peeping through the keyhole of their parents' room, while they had intercourse. The boys giggled a lot, acted sheepishly and subdued for the rest of the day. They were told off but no other punishment was meted out. The key hole was then sealed! Soon after this incident James' attacks of frequency began, the present attack being the longest. Mrs. W reported that since the previous visit, James had made a lot of progress and day-time frequency was much less.

During the second play session, James was seen tugging at his penis on several occasions. He made a doll using plasticine then fiercely smashed it very flat with a rolling pin saying "my father says some people have to be squashed." When queried by the therapist, he replied "because they are bad." He then proceeded to describe how some people were squashed and full of blood. I felt this was related to his witnessing the primal scene and fear of punishment. When asked what would make

him scared, James replied with a lot of bravado that he was not scared of anything except some crocodiles he saw in the zoo.

In the diagnostic formulation, Mrs. W was informed that James' problem specifically castration anxiety was aroused by the primal scene. This is particularly traumatic in a child during the period of oedipal conflicts, and in this case, the added anxiety connected with his mother's several operations. Anger and at the same time fear of the father's power was very real. Treatment would entail play sessions for 5 more weeks to enable James to work through his anxieties and fears with respect to his father and so prevent further recurrences of this problem.

By the 4th week, Mrs. W stated that James was fine and micturition back to normal. In play he was still preoccupied with killing all the fierce animals and protecting the good ones. During the subsequent sessions, father doll continued to receive rough treatment. Snakes were twined round his head and neck "so he can't see because he is bad." On another occasion, father doll was so bent and distorted in the legs "so he can't walk." When reflections were made of the boy's anger toward the father, James' answer was to bash the heads of the parent dolls together and throw them in the basket.

By the 5th session, James seemed to have worked out his anger on the father doll and play was back to normal. Mrs. W reported that he was much happier in school and at home. The entire duration of treatment was 8 weeks. At the 3 month follow up, there was no recurrence of frequency of micturition, he was performing very well in school and given the leading role in the annual school concert.

Conclusion

Case 1 illustrates how a common problem like school phobia can be helped through brief psychotherapy. The emphasis is on initial case formulation, realistic treatment goals and participation of the family in the therapeutic process. For the adolescent, Kerns[5] is of the opinion that "the time limit mitigates some of the fears of his own normal functioning, that he is not so badly off, and frees him to work on his problem." The therapist too working within this time constraint has to plan before hand the treatment focus for each session, with the ultimate aim of helping the adolescent adapt to his internal needs and to reality.

Case 2 is an example of the use of non-directive play therapy within the brief psychotherapy set. Within the span of 8 weeks, the patient expressed his anxiety, hostility and aggression in spontaneous doll play and was able to resolve his conflicts. In all cases, the duration of therapy is always specified and reemphasised in the course of treatment. The therapist attempts observations, reflections and interpretations for the child. According to Axline[1] "it is not necessary for the child to be aware that he has a problem before he can benefit by the therapy session." Further Woltman[9] states that "free play of itself has decided cathartic value."

In the treatment of behaviour disorders of children it is a debatable point where diagnosis ends and therapy begins. According to Masterson[6] even with the first phone call for appointment the therapeutic process has begun. Hence the separation of diagnostic and therapeutic sessions is a mere convenience for explaining to parents. With many of the children in this study improvement was shown after the first session. Technically the duration of therapy should be reckoned from the initial visit. Even then in this study, the average length of treatment is still less than 10 weeks.

The results of this study indicate that brief psychotherapy is suitable for the treatment of a variety of behaviour disorders in children. Hopefully there will be a greater awareness of behaviour problems in paediatric practice. The child's developing personality is more flexible and responsive to therapy. Brief psychotherapy with the economy of time and personnel would extend help to a greater number of children.

Summary

Child Guidance is a new development in Malaysia. This paper records my experience of brief psychotherapy with a multiracial group of children. Though the numbers are small, results are encouraging. In Malaysia with the acute shortage of personnel in this field, greater use of brief psychotherapy is advocated.

Acknowledgement

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Serum Insulin Secretion by Adult Malaysians

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Introduction

IT HAS RECENTLY been suggested that an excessive and prolonged secretion of insulin after oral glucose, often precedes the development of maturity onset diabetes (1,2), and that an over-secretion of insulin may also lead to coronary heart disease (3). It may therefore be possible to identify individuals and even populations (4) susceptible to diabetes and coronary heart disease by the determination of serum insulin.

We wish to report a comparison of insulin secretion in the three main racial groups in Kuala Lumpur.

Methods

All subjects were patients attending the General Hospital with minor complaints, mostly with skin disorders. After an overnight fast, venous blood was collected and each subject drank 50 g glucose dissolved in 200 mL water. Further venous blood samples were collected at 30 min intervals for two hours. Serum was separated from the fasting, 60 min and 120 min samples and stored at -30° for insulin determination by radio-immuno-assay (5). Blood glucose was measured immediately from all samples which were collected into fluoride containers using a Technicon Autoanalyzer and the neocuproine method (6).

Results

Table I shows the number of adults in each racial group with their ages and Quetelet indices. This index is recommended for the accurate assessment of obesity (7) and is calculated from (body weight in kg) . (height in m)$^{-2}$. It can be seen that the Chinese adults were significantly less obese than the Malays and Indians, which corresponds to data from 500 healthy adults visiting the General Hospital (8).

With the exception of obesity, all other significant differences detected follow the same trend with the Chinese occupying an intermediate position between high values for the Indians and low values for the Malays. Table I and Figure 1 show that during the glucose tolerance test, the Indians have the greatest and most prolonged rise in both serum insulin and in blood glucose concentration.

Discussion

The excessive sustained rise in serum insulin and blood glucose concentration shown by the Indians compared with the Malays cannot be explained by differences in age or obesity (9,10) since both the age and the Quetelet index was found to be higher in the Malay than in the Indian, whereas both age and obesity show small positive correlations ($r = 0.2$) with blood glucose and serum insulin.

The difference may be related to diet (4,8) and also to the greater prevalence of consanguinity in this Indian population, and it would be expected to be associated with a higher incidence of both coronary heart disease and diabetes in the Indian compared with the other racial groups.

This possibility is now being investigated.

Table I

The number of adults from each racial group with their age in years, the proportion of men, their Quetelet Index in kg . m^{-1}, fasting blood glucose concentration, changes in glucose during the oral glucose tolerance test in mg . dL^{-1}, area under the glucose curve in mg . hr . dL^{-1}, fasting serum insulin concentration, changes in insulin during the oral glucose tolerance test in μ- unit . mL^{-1}, area under the insulin curve in - unit . hr. mL^{-1}. The median is followed by the range in parenthesis and the significance of the differences was tested by the Kruskal-Wallis method.

	MALAY (M)	CHINESE (C)	INDIAN (I)
Number	9	7	11
Percentage of Men	78	57	73
Age	45 (21 to 55)	46 (21 to 57)	31 (25 to 52)
Quetelet Index (a)	25 (20 to 30)	22 (16 to 24)	23 (20 to 35)
Fasting Glucose	90 (80 to 110)	90 (90 to 100)	90 (70 to 100)
Maximum Change in Glucose (b)	+30 (+20 to +90)	+60 (+50 to +80)	+70 (+20 to +90)
Change in Glucose at 120 min (c)	..20 (..60 to 0)	..10 (..40 to +20)	+10 (..30 to +20)
Area under Glucose Curve (d)	20 (5 to 85)	50 (30 to 75)	70 (25 to 85)
Fasting Insulin	1 (0 to 8)	1 (0 to 10)	1 (0 to 10)
Change in Insulin at 60 min (e)	+15 (+2 to +30)	+18 (+5 to +50)	+22 (+8 to +60)
Change in Insulin at 120 min (f)	0 (0 to +6)	+2 (0 to +14)	+6 (0 to +16)
Area under Insulin Curve (g)	15 (1 to 33)	25 (5 to 50)	28 (15 to 65)

a) C <I + M : P<0.05
b) M<C + I : P<0.02
c) I C + M : P<0.02
d) M<C + I : P<0.01
e) Not Significant
f) I >C + M : P<0.01
g) M<C + I : P<0.01

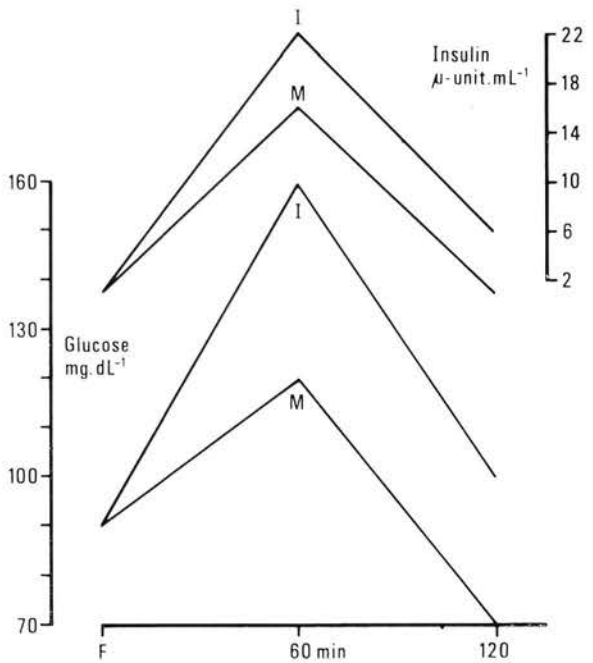

Figure 1

Serum insulin concentration and blood glucose concentration during a 50 g oral glucose tolerance test in the Malay (M) and Indian (I) adults.

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Screening for G. 6-P.D. Deficiency

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IN MALAYSIA AND SINGAPORE, red cell glucose-6-phosphate dehydrogenase (G.6-P.D.) deficiency is common (Vella, 1959; Wong, 1974, 1975). It is a major cause of neonatal hyperbilirubinaemia and kernicterus in this region (Wong, 1964, 1965; Sinniah, 1971), in addition to being responsible for drug induced haemolytic anaemia. It is most important to detect G.6-P.D. deficiency in newborns in the population so that morbidity and mortality from neonatal hyperbilirubinaemia may be reduced. Many tests for G.6-P.D. deficiency have been devised. Of these, the earlier Heinz body test (Beutler, 1955) and the glutathione stability test (Beutler, 1957) were too non-specific for screening purposes. The more specific and highly sensitive tests, which have been used require specialized equipment, are very tedious for screening and are reserved for detecting mildly deficient heterozygotes. These include spectrophotometric assay of the enzyme; methaemoglobin elution test and the G.6-P.D. tetrazolium cytochemical method. Screening tests were developed which are equally specific but are much less sensitive, viz, brilliant cresyl-blue method (Motulsky, 1961); methaemoglobin reduction test (Brewer, 1962) and the MTT spot test (Fairbanks, 1962). These however are not entirely satisfactory for screening G.6-P.D. deficiency in Malaysia, especially in the rural areas where difficulties may arise in the collection and despatch of blood specimens to the nearby hospital.

In 1966, Beutler devised a fluorescent screening spot test based on the fact that reduced nicotinamide adenine dinucleotide phosphate (NADPH) fluoresces under ultra violet light. In the presence of G.6-P.D. glucose-6-phosphate (G-6-P) is oxidised to 6-phosphogluconate, this being associated with the reduction of NADP to NADPH which fluoresces (Figure 1). With G.6-P.D. deficiency NADPH is not produced in sufficient quantities to cause fluorescence. Beutler (1968) improved its sensitivity by adding oxidised glutathione (GSSG) to the

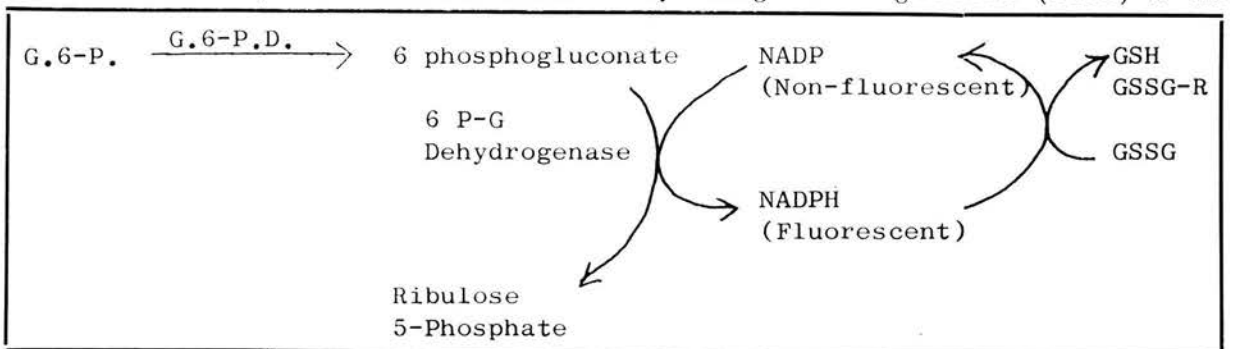

Fig. 1 Part of Hexose-Monophosphate Shunt to illustrate the principle underlying the fluorescent screening test for G. 6 - P. D. deficiency.

reaction mixture, eliminating almost entirely the slight fluorescence which sometimes appears in the presence of mild G.6-P.D. deficiency. When GSSG is present, NADPH is oxidised through the action of glutathione reductase (GSSG-R). He also enhanced the initial intensity and stability of the fluorescence by substituting tris-hydro-chloride buffer for phosphate buffer.

White (1972) reported that the test could be accurately performed with blood applied on blotting paper instead of being collected in a tube or bottle. This clearly simplifies the collection and despatch (to a distant laboratory, if necessary) of such blood specimens.

We have found this modified fluorescent spot test to be very useful for screening G.6-P.D. deficiency in Malaysia.

Method

A. Specimen collection

Whole blood is applied directly to the end of a filter paper strip, allowing it to soak through completely. Sufficient blood is smeared to allow a $\frac{1}{4}$ inch diameter disc of the blood-soaked paper to be punched out. Preferably one inch of the filter paper should be blood-filled to enable subsequent checking, if necessary. The filter strip is then mounted on a data card as shown (Fig. 2).

When the specimen is air dried, it may be stored for at least two weeks so that results may be checked if necessary or performed when convenient if results are not urgently required. Storage for this period of time has not reduced the accuracy of the test.

B. Reaction mixture:

This is made up of equal parts of the following:

1. Glucose-6-phosphate (G-6-P) 0.01 molar solution (molecular weight 358.2) in tris-hydrochloride buffer, 0.75 molar solution (molecular weight 121.1).
2. GSSG (oxidised glutathione) 0.008 molar solution (molecular weight 612.7).
3. NADP – 0.0075 molar solution (molecular weight 765.44). This should preferably be freshly prepared though when stored deep frozen, it remains stable for not less than one week.

0.1 ml of the reaction mixture is placed in a 10 × 75 mm labelled test tube. A $\frac{1}{4}$ inch single-hole paper punch is used to punch out a disc of blood-soaked paper which is then placed in the reaction mixture and incubated at 37°C for 15 minutes.

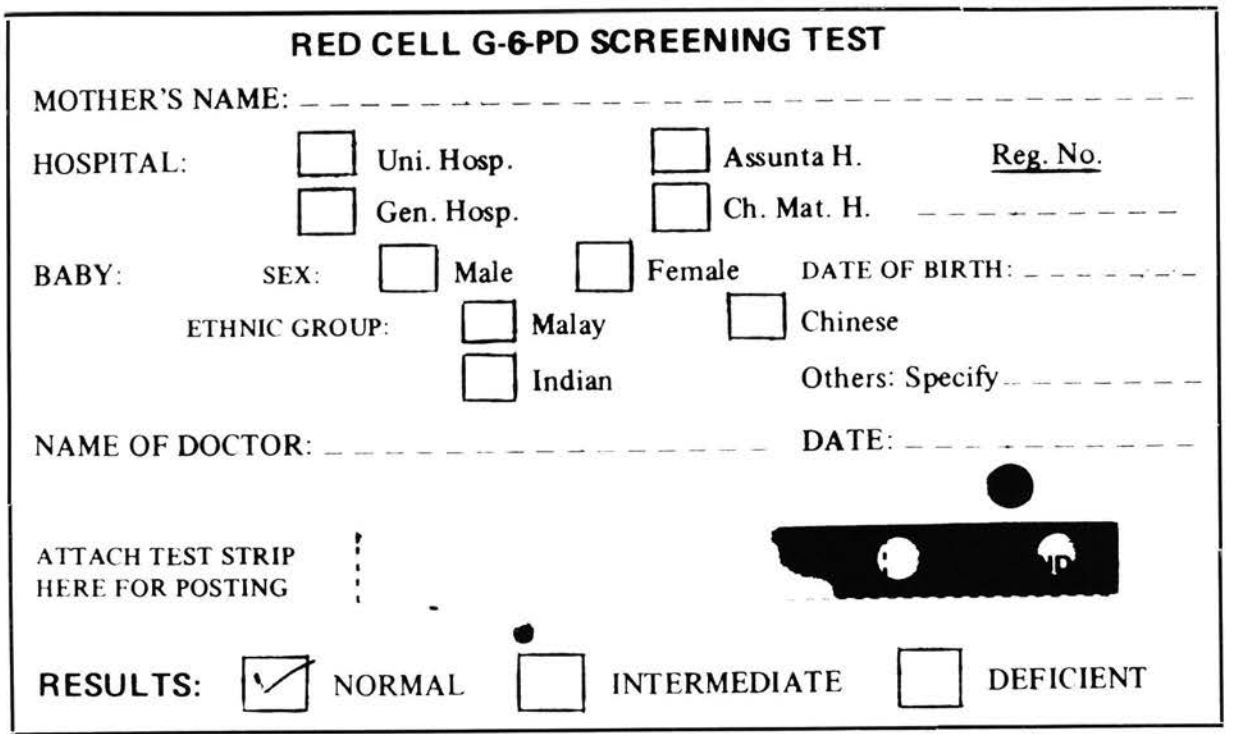

Fig. 2 Data card sample showing attached filter paper strip with punched-out discs.

Using a capillary tube, the test mixture is spotted on a filter paper and allowed to dry after which it is examined under a source of long ultra-violet light for fluorescence. It is most important to allow the spot to dry thoroughly to obtain suitable fluorescence. Large numbers of similar test mixtures may be spotted at the same sitting.

Interpretation

Spots which contain normal G.6-P.D. activity fluoresce brightly under ultra-violet light, contrasting sharply with those deficient in G.6-P.D. which show almost no fluorescence. Those intermediate in G.6-P.D. activity fluoresce less brightly. It is to be noted that this test has not been evaluated for heterozygote detection (Beutler, 1966).

Using the above test, the incidence of G.6-P.D. deficiency was determined on 2,049 cord blood specimens, collected as described and despatched by post from four other hospitals in Kuala Lumpur and Petaling Jaya. The results are shown in Table I.

Comments

The test described requires only one or two drops of blood (cord blood or blood from a heel prick) and the collection of specimens is simple and convenient. However, by far the greatest advantage of the test is that specimens can be despatched from outlying areas by post as they remain stable for as long as 3 weeks. In Malaysia, many deliveries are still conducted at home, often in remote rural areas where nearby hospital facilities are not available. It is not uncommon to find that babies born in these areas develop hyperbilirubinaemia due to G.6-P.D. deficiency and that kernicterus is not a rare complication. As it is possible to reduce morbidity and mortality from this cause by avoidance of certain "trigger" drugs, phototherapy, exchange transfusion and genetic counselling, this high-risk group must first be identified. The method described, because of its simplicity, is particularly suitable for use in remote rural areas to detect G.6-P.D. deficiency. Cord blood may be collected as described with the help of midwives (bidans) who may then despatch them to an appropriate centre. Infants who are found to be G.6-P.D. deficient can then be rapidly identified and appropriately treated.

The test itself is simple to perform. The only "specialized" equipment required is the long-wave ultra-violet lamp which is inexpensive if bulk purchases are made. It is estimated that each test costs between Malaysian five and ten cents. Up to two hundred specimens can be tested in less than half an hour, inclusive of the time required to prepare the reagents. Its reliability has been tested elsewhere (Beutler, 1966; White, 1972; Fairbanks, 1969). Fairbanks et al. (1969) in an analysis of published methods of detecting G.6-P.D. deficiency found that the fluorescent spot test is as specific and sensitive as the other currently available screening test, for example the Motulsky's dye – decolorisation method. The incidence of G.6-P.D. deficiency in cord blood of newborns among the major races in Kuala Lumpur and Petaling Jaya as detected by the fluorescent screening test is similar to that reported by Wong (1964) in Singapore using the brilliant cresyl blue decolorisation method (Table II). It is higher among the Chinese (3.1%) and the Malays (1.4%) than among the Indians (0.2%). We have also compared this test with the Prankerd's modification of Motulsky's dye decolorisation test (1962) on 20 known G.6-P.D. deficient patients and 20 other G.6-P.D. normal subjects and have not found any discrepancy in the results.

Conclusion

This is a simple, cheap, reliable and rapid test for G.6-P.D. deficiency. We recommend it as a screening test, especially for newborns and is particularly suitable for us in remote rural areas in Malaysia.

Table I

Incidence of G.6-P.D. deficiency in cord blood of newborns in Kuala Lumpur and Petaling Jaya as detected by the Fluorescent Screening Test

	Total tested	G.6-P.D. Deficient				Female heterozygotes
		Males	Females	Total	%	
Chinese	931	26	3	29	3.1	5
Malays	629	9	0	9	1.4	4
Indians	487	1	0	1	0.2	—
Others	2	2	0	2	—	—

Table II
Incidence of G.6-P.D. deficiency in Malaysia and Singapore (%).

	Wong (1964)	Robinson, Lau, Lin & Chan (1975)
Chinese	1.9	3.1
Malays	1.5	1.4
Indians	0.5	0.2
Aborigines	–	–

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Ovarian Tumours Complicating Pregnancy in a Malaysian Study

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THERE IS a wide variation in the incidence and pathological characteristics of ovarian tumours complicating pregnancy throughout the world. This paper reviews the pattern of this complication in pregnancy in Malaysian women.

Materials and Methods

This study was undertaken in the University Hospital, Kuala Lumpur, Malaysia. During the period May 1968 to October 1973, there was a total of 13,845 deliveries. During the same period 27 cases of ovarian tumours in pregnancy were diagnosed. Cysts less than six centimeters in diameter were excluded as they were assumed to be non-neoplastic as in the other series (Booth, 1963; Tawa, 1964; Sinnathuray, 1971). All the ovarian tumours removed at laparotomy were subjected to careful histological examination.

Results

Incidence

The incidence of this complication was one in 512 deliveries. This is compared with the results of other workers in Table I. There is thus a wide variation in the incidence reported. Although neighbouring Singapore has a population whose ethnic groups are similar to Peninsular Malaysia, these tumours appear to be less frequent in Singapore. A possible reason is that a large proportion of the patients were unbooked or booked late in pregnancy (Sinnathuray, 1971). The University Hospital, Kuala Lumpur, serves as a referral centre for almost the whole of Peninsular Malaysia; and further has a higher proportion of booked patients. All obstetric patients at booking, are subjected to a routine pelvic examination at this Institution, thus allowing for the early detection and hence a higher yield of ovarian tumours in pregnancy.

Table I

Incidence of Ovarian Tumours in Pregnancy

Study	Year	Incidence
Hass	1949	1 : 330 Pregnancies
Grimes et al	1954	1 : 81 Pregnancies
Booth	1963	1 : 591 Pregnancies
Sinnathuray	1971	1 : 6226 Pregnancies
Present Study	1974	1 : 512 Pregnancies

Racial Distribution

As shown in Table II, the highest proportion of patients was Chinese. However, this distribution is similar to that of patients attending the antenatal

Table II

Racial Distribution

Race	Number of cases	Percentage
Chinese	15	55.5
Malay	5	18.5
Indian	5	18.5
Others	2	7.5
Total	27	100.0

[1]Lecturer
[2]Lecturer
[3]Professor and Head

clinic at the hospital. This was also a similar finding in Singapore (Sinnathuray, 1971). There is, therefore, no racial bias in the incidence of ovarian tumours in Malaysian pregnant women.

Parity and Age Pattern

Seventeen patients were multiparous, with an average age of 31 years (range 21 – 43). The average age of the primiparas was 23 years (range 17 – 30). As shown in Table III, 20 patients (74 percent) were below the age of 30.

Table III
Maternal Age Pattern

Age in years	Number of cases	Percentage
Less than 20	2	7.4
20 – 30	18	66.6
31 – 40	6	22.3
More than 40	1	3.7
Total	27	100.0

Time of Tumour Detection

As shown in Table IV, one-third of the cases was diagnosed in the first trimester at routine pelvic examination. Another one-third was diagnosed in late pregnancy either at labour or at lower segment Caesarean section. Seven out of these nine patients were first seen at the ante-natal clinic at period of gestation ranging from 24 to 39 weeks, when detection of asymptomatic adnexal masses is difficult. A significant number (22.3 per cent) was discovered in the puerperium. These patients had booked late in pregnancy after the 33rd week of gestation.

Table IV
Time of Tumour Detection

Gestation	Number of cases	Percentage
1st trimester	9	33.3
2nd trimester	3	11.1
3rd trimester	9	33.3
Puerperium	6	22.3
Total	27	100.0

Location of Tumour

Grimes et al (1954) found that of the unilateral cysts, nearly twice as many were found on the left, whilst the reverse was found by Haas (1949) and Booth (1963). In this series 14 (51.8 per cent) were on the left, and 10 (37.1 per cent) were on the right; three (11.1 per cent) were bilateral.

Complications

One of the complications most feared in pregnancy is torsion of the pedicle of the ovarian tumour. In the present study, this complication occurred in three cases (11.1 per cent) at the tenth, eleventh and fifteenth week of gestation respectively. None of these patients aborted.

Three patients presented with obstructed labour due to an impacted ovarian tumour in the pelvis and were delivered abdominally (Table V).

Table V
Complications of Ovarian Tumours in Pregnancy

Nature of Complications	Number of cases	Percentage
Torsion of pedicle	3	11.1
Impacted tumour causing obstructed labour	3	11.1
Malignancy	2	7.4
Total	8	29.6

Management

In 11 patients (40.7 per cent), the ovarian tumours were removed electively between 8 and 28 weeks gestation. Of the six emergency laparotomies, two were performed before the twelth week, one in the fifteenth week and three at lower segment Caesarean section for obstructed labour. In one patient, the cyst was discovered at 14 weeks gestation, but was assessed to be less than six centimeters in diameter and was left alone. At subsequent lower segment Caesarean section for contracted pelvis, this cyst was found to have grown to about twice its original size. In the remaining nine patients, the cysts were an incidental finding either at lower segment Caesarean section or at laparotomy for post-partum sterilization. Table VI shows the type of surgery performed. In the majority of cases

Table VI
Type of Operation for Ovarian Tumours in Pregnancy

Type of Surgery	Number of cases	Percentage
Cystectomy	17	62.9
Unilateral salpingo-oophorectomy	9	33.3
Total hysterectomy and bilateral salpingo-oophorectomy	1	3.8
Total	27	100.0

(62.9 per cent), the tumours appeared benign and a cystectomy was performed. In nine patients a unilateral salpingo-oophorectomy was done. In two of these patients the tumour was gangrenous following torsion of the pedicle, in one the tumour was solid, and the remaining six patients had already completed their families and had requested sterilization earlier. One patient had a total hysterectomy and bilateral salpingo-oophorectomy because of features at laparotomy which were strongly suggestive of malignancy.

Pathologic Findings

All ovarian tumours removed were subjected to careful histological examination. The results are shown in Table VII. Twenty-five tumours (92.6 per cent) were benign, the commonest ovarian tumour in pregnancy being benigh cysttic teratoma

Table VII

Pathology of Ovarian Tumours in Pregnancy

Type of ovarian tumour	Number of cases	Percentage	
Benign			
Cystic teratoma	12	44.5	
Mucinous cystadenoma	5	18.5	
Serous cystadenoma	5	18.5	92.6
Parovarian cyst	2	7.4	
Luteal cyst	1	3.7	
Malignant			
Granulosa cell tumour	1	3.7	7.4
Dysgerminoma	1	3.7	
Total	27		100.0

(44.5 per cent). Such a pattern has been reported by other workers (Booth et al, 1963; Tawa, 1964; Sinnathuray, 1971). Of the three patients with bilateral ovarian tumours, two had dermoid cysts and one bilateral serous cystadenoma. Although Booth and Sinnathuray had no malignancies in their respective study, in the present study two cases of malignant ovarian tumours, namely dysgerminoma in a 17-year old primigravida, and malignant granulosa cell tumour in a 33-year old multipara, were encountered, giving an incidence of 7.4 per cent. The incident of malignancy in ovarian tumours complicating pregnancy has been quoted to range from 2 to 5% (Jubb, 1963). The relatively high malignancy rate of 7.4% in our study is unusual. Probable explanations are chance occurrence, or the fact that being a major referral centre, there is a tendency for complicated pregnancy cases to seek delivery at this institution.

Pregnancy Outcome

In 21 patients (77.7 per cent) pregnancy continued to 37 weeks or more. Three patients were delivered between 28 to 34 weeks; in one of these there was acute hydramnois with hydrops foetalis and in another a macerated intra-uterine death with advanced ovarian cancer. One patient aborted at 11 weeks, four days after ovarian cystectomy. Another presented as incomplete abortion at 11 weeks gestation and the ovarian tumour was detected on admission. One patient was lost to follow-up.

Mode of Delivery

Fourteen patients (51.8 per cent) had spontaneous vaginal deliveries. In six of these the tumours were undetected prior to delivery. Nine patients were delivered by lower segment Caesarean section. In three of these, the reason was an impacted tumour in the pelvis causing obstructed labour. A Caesarean hysterectomy was performed in one patient who had advanced ovarian carcinoma.

Maternal and Foetal Mortality

There was no maternal mortality in our series. One of the abortions could be attributed to the ovarian surgery. This was the patient in whom a luteal cyst was removed at 11 weeks gestation.

There were two stillbirths; one was the result of hydrops foetalis secondary to maternal and paternal alpha-thalassemia traits; in the other a macerated stillbirth was present in association with advanced ovarian tumour.

The absence of maternal mortality and the extremely low foetal wastage in our series can be attributed to the early detection of the tumour during pregnancy at this hospital, enhanced by routine vaginal examination at the booking visit.

Discussion

Based on the records of 13,845 consecutive pregnant women seen throughout pregnancy and puerperium, 27 cases of ovarian tumour complicating pregnancy were noted, giving an incident of 1 in 512 deliveries. Reported incidence of this complication has varied in different series from as high as 1 in 81 pregnancies (Grimes et al, 1954) to as low as 1 in 6226 pregnancies (Sinnathuray, 1971). The possible reasons for this wide variation in incidence are the inclusion or exclusion of cysts smaller than six centimeters in diameter, the variable time of booking patients and whether a routine pelvic examination was done at booking. Grimes

included all cysts irrespective of their sizes. Sinnathuray pointed out that only half of his cases had ante-natal care and even amongst these patients a significant number was booked late. An additional factor of importance is the generally symptomless nature of the condition unless complications set in. The importance of a bimanual examination in the first trimester is emphasized by the fact that not less than one-third of the tumours in our study were discovered at this time.

When an asymptomatic ovarian tumour is discovered in the first trimester, it usually should not be removed until the second trimester. Operation during the first trimester has been found to be associated with a high incidence of abortion of 35 per cent (Buttery et al, 1973). In our series one out of the three cases operated-on in the first trimester aborted. Buttery further found that if the tumour were operated on in the second trimester only two per cent aborted. In our study, none of the patients operated upon in the second trimester aborted. The high incidence of abortion in the first trimester of pregnancy may be related to the function and integrity of the corpus luteum of pregnancy. Csapo (1972) has shown that the pregnancy is dependent upon the corpus luteum before the seventh week of gestation and that it becomes dispensable after that due to the luteo-placental shift. Since a functional cyst will usually become smaller and disappear by the sixteenth week, this seems to be a reasonable time to remove the tumours that persist; for at a later date the increased size of the uterus may require its manipulation or make the surgical approach mechanically difficult.

If a tumour is discovered above the pelvic brim in the last five weeks of pregnancy, Holland (1945) advocates ovariotomy and subsequent vaginal delivery. The procedure however, is technically difficult at this time because of the enlarged uterus. If labour starts soon after, the patient may also have a painful abdominal scar during labour. We would, therefore, advocate waiting till term and then perform a Caesarean section together with removal of the tumour. When a tumour praeva is discovered in labour as in three of our cases, a Caesarean section should be performed, followed by the removal of the tumour.

The fact that one-third of the tumours in our study were an incidental finding at lower segment Caesarean section or at post-partum sterilization stresses the importance of routine inspection of the ovaries during these operative procedures.

There is no doubt that an ovarian tumour discovered in pregnancy should be removed as this removes a potential cause of dystocia in labour. There is also a greater liability to complications in pregnancy. Although Booth et al (1973) and Sinnathuray (1971) have not found any malignant ovarian tumours in their series, the significant incidence of malignancy of 7.5 per cent in our experience emphasizes that ovarian tumours in pregnancy should be treated surgically.

Creasman et al (1971) reported a series of 17 patients with ovarian carcinoma in pregnancy. Unusual ovarian tumours, such as dysgerminoma and granulosa cell tumour, account for a higher proportion of neoplasms than the overall ovarian cancer population. It is not surprising, therefore, that the two cases of malignancy in our series turned out to be a dysgerminoma and a malignant granulosa cell tumour. Creasman et al contend that since ovarian carcinoma is highly malignant and can grow rapidly, a patient who is found to have such a tumour antenatally probably should have the pregnancy sacrificed. In all but one patient he performed radical surgery followed by radiation and/or cytotoxic therapy. All their 10 patients in stage I A were alive and well at five years. One of our patients with granulosa cell tumour had a radical surgery (total hysterectomy and bilateral salpingo- oopherectomy) followed by chemotherapy. She was lost to follow-up two months later. The other, who had a stage I A dysgerminoma of the ovary, had a unilateral oophorectomy at 23 weeks gestation and the pregnancy went on to term and she had a normal delivery. She is alive and well five years after the initial surgery and has had three more spontaneous vaginal deliveries at term. It would appear, therefore, that sacrifice of the pregnancy need not improve the maternal prognosis and that unilateral oophorectomy may be employed in the patient with a mobile unilateral tumour with an intact capsule.

Summary

An analysis of 27 cases of ovarian tumours diagnosed in pregnancy and puerperium is presented. The incidence was I: 512. One-third of the tumours was diagnosed in the first trimester. Ninety-two per cent of the tumours were benign of which dermoid cysts were the commonest. In three of these patients torsion of the ovarian pedicle occurred and in another three, pelvic impaction caused obstructed labour. Two patients (7.4 per cent) presented with malignant ovarian tumours. The management of these tumours is discussed.

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Inhibition of Post-partum Lactation with Quinestrol

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OVER THE last two decades, there have been an increasing resort to bottle feeding in place of breast feeding. This has been especially obvious among urban mothers in the Malaysian Singapore region (Mills 1955, Dugdale 1970, Wong 1971). Inhibition of post-partum lactation can be achieved by various methods, namely varying doses of stilboestrol, analgesia and restriction of fluid, injection of hexoesterol, plentiful of water, Vitamin B6 and various practices that are used in the local communities. In general, the more successful ones are the use of hormones. In practice, stilboestrol in varying schedules are used for suppression of post-partum lactation. Because of the need of constant supervision, attempts have been made to suppress lactation with single dose hormones. Loke and Lean (1970) and Kuah (1975) have given single injection of ablation and found it to be highly effective. The aim of the present study is to determine the effectiveness of a single dose of *oral* long acting oestrogen, namely, quinestrol in the inhibition of post-partum lactation. This was compared with a placebo in a double blind trial.

Quinestrol is a 3-cyclo-pentyl ether of ethinyl oestradiol. Clinical studies have already shown it to be a potent, orally effective oestrogen with a long duration of action. This has been shown to be due to quinestrol being stored in body fat depots. The compound is well tolerated and has minimal gastrointestinal side effects. Extensive blood coagulation studies performed in patients receiving quinestrol did not reveal any significant alterations.

Materials and Methods:

A double blind trial of quinestrol with a placebo was conducted in 120 women who delivered vaginally at the University Hospital, Kuala Lumpur between April 1973 to September 1973 and who had expressed the desire not to breast feed. Patients with any complications associated with the pregnancy were excluded.

Identical capsules containing 4 mg. quinestrol and lactose were prepared. These capsules were coloured pink and a capsule was given within 6 hours of delivery. Patients were given these capsules in a random manner. A total of 60 patients received quinestrol while the remaining 60 patients were treated with placebo capsules containing lactose.

Daily records were kept of the condition of the breasts with regard to consistency, lactation and comfort. The character of the lochia, rate of involution and any side-effects were also noted. In addition to the clinical assessment, the mother was questioned about breast comfort. The patients stayed in hospital for a period of 5 – 7 days.

If increasing lactation became established or if severe breast engorgement or pain occurred the patient was commenced on a course of stilboestrol to suppress lactation.

In order to assess the results after discharge from hospital, these patients were advised to return to the post-natal clinic 6 weeks after delivery, when they were questioned on breast engorgement, pain, lactation, increase in lochial flow or any further treatment by a general practitioner after they had been discharged from hospital.

Results:

There were 60 patients who were given quinestrol and 60 patients who had the placebo. The results of the double blind trial were evaluated during the patients' stay in hospital as well as after discharge from the hospital.

The criteria for a successful result were absence of pain, lactation or engorgement. A satisfactory result was achieved if there was mild discomfort, mild engorgement or mild lactation which did not require the use of another lactation suppresant, namely, stilboestrol. If there was moderate to severe engorgement with pain and lactation, which necessitated the administration of stilboestrol, it was considered a failure.

The immediate results are as shown in Table 1. Lactation was successfully inhibited in 46 of 60 patients who had quinestrol while they were in hospital. A success rate of 76.7 percent. Satisfactory results were obtained in 6 of 60 patients (10 percent). Eight patients who were considered to have failed with quinestrol had to be given stilboestrol. In contrast, only 6 patients (10 percent) who were given the placebo had their lactation suppressed. However, in a large number of patients (51) who were on placebo, there was no suppression with the placebo and stilboestrol had it be administered.

Table I

Assessment of Effects of Quinestrol and Placebo

	Quinestrol	Placebo
Results/No. of Patients	60	60
Success	46*	6*
Satisfactory Result	6	3
Failures	8	51

*$p > 0.01 < 0.05$

After discharge from the hospital, the patienst were interviewed and assessed during their post-natal visit. If the patients had no pain, engorgement or lactation after discharge from hospital it was considered that suppression has been successful. A satisfactory result was obtained if there was slight engorgement or discomfort with slight lactation which did not require the use of stilboestrol. Those patients who needed a further course of stilboestrol after discharge from hospital because of engorgement, lactation or severe pain were classified as failures. The follow-up was assessed at the first post-natal visit at the end of the 6th post-partum week. The results are as shown in Table II.

Table II

Follow-up Results of Breast Suppression with Quinestrol, Placebo, Stilboestrol

	Quinestrol		Placebo	
	Immediate	Late	Immediate	Late
Success	32	31	4	4
Satisfactory	4	3	1	0
Failures (Had Stilboestrol)	5	—	30	2
Total of Patients	41		35	

Of the 60 patients who were on quinestrol alone only 41 patients returned for their post-natal follow-up. Of the 36 patients who had good and satisfactorily suppression with quinestrol, in the immediate post-partum period, only 2 (5.5 percent) needed a course of stilboestrol after discharge. These were considered late failures.

35 patients who had been given a placebo initially were seen in the post-natal clinic. Of the 4 patients who had immediate good result, none needed further suppresant in the late post-partum period. One patient who was considered to be satisfactorily suppressed during her hospital stay had increased breast engorgement and lactation and needed a course of stilboestrol. Of the 30 patients who lactation was not suppressed with the placebo and who had a late course of stilboestrol, two needed further suppression with stilboestrol.

Discussion:

The use of a simple oral dose of quinestrol in the inhibition of post-partum lactation has been described by Barbour and Barush (1968), Kuku (1968) and Ng and Lee (1972). Results of these studies have shown that quinestrol was highly effective (67 percent to 80 percent) and this has been confirmed in the present study where 86 percent successful suppression was achieved.

The single oral dose of quinestrol has been shown to be less frequently associated with rebound breast engorgement and withdrawal bleeding (Barbour and Baruah 1968, Ng & Lee 1972) 5.5 percent of the patients whose lactation were initially successfully suppressed with quinestrol had further milk leakage. This was contrasted to the two patients who had rebound breast engorgement with stilboestrol, giving an incidence of 6.6 percent (Table II). Lee (1971) showed that oral stilboestrol was associated with rebound breast engorgement in 65 percent of patients and with withdrawal vaginal

bleeding in 25 percent of patients. There seemed to be no adverse effect on the lochia or rate of involution of the uterus in the present study.

Also, stilboestrol administration seemed to be associated with a statistically higher incidence of puerperal thrombo-embolism in Western communities (Daniel, 1967). This risk seems to be greater with age and greater parity. Consideration should be given perhaps in with-holding this preparation in high risk patients. However, puerperal thrombo-embolism is known to be among Asians (Jones, 1964; Srivasata, 1964; Tinckler, 1964; Wong & Teoh, 1975). Of the 4 cases presented by Wong & Teoh (1975), two patients had puerperal inhibition of lactation with stilboestrol.

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Goldenhar's Syndrome

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THE oculo-auriculo-vertebral dysplasia syndrome of Goldenhar, (Goldenhar 1952) is characterized by three main features.

1. Epibulbar dermoid or dermolipoma of the eye
2. Auricular anomalies
3. Vertebral anomalies

Besides the above constant features, other associated anomalies may be present. Two cases are presented.

CASE REPORTS

Case 1.

H.K.L., 19 year old Chinese female was referred to the Eye Clinic, University Hospital, Kuala Lumpur, in July, 1975, with a mass below the right zygomatic arch and a fleshy dermolipoma in the right eye. There was no relevant family history.

She was found to have the three characteristic features of Goldenhar's syndrome.

Ocular findings in the right eye were an epibulbar dermolipoma covering the temporal half of the cornea (Fig. 1) and a concomitant divergent squint with amblyopia. The visual acuity was reduced to counting fingers.

General examination showed a right hemifacial microsomia, five preauricular skin appendages placed along a line extending from in front of the

Fig. 1.
Right hemifacial microsomia, with skin appendages, dermolipoma in right eye with divergent squint.

ear to the angle of the mouth and a mass with overlying hypopigmented skin below the right zygomatic arch (Figs. 1 & 2).

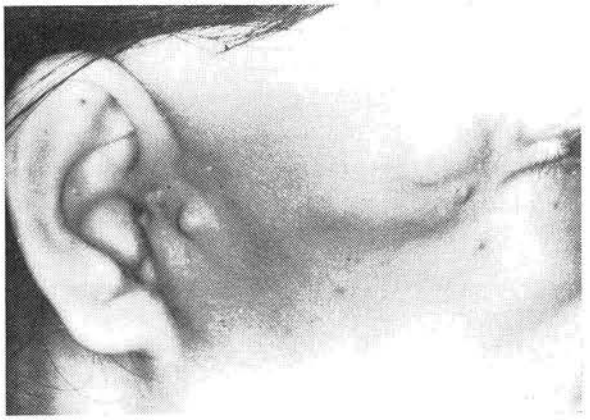

Fig. 2
Mass below right zygomatic arch and preauricular appendages.

Neurological examination revealed exaggerated knee and ankle jerks and bilateral positive Babinski. The reflexes of the upper limb and abdomen were normal. There was no sensory and motor involvement nor any sphincteric disturbances.

Radiographs of her facial bones and jaw demonstrated a right hypoplastic maxillary antrum and nasal cavity, a deviated nasal septum (Fig. 3) and three unerupted right upper molar teeth (Fig. 4). Radiographs of the cervico-dorsal spine revealed scoliosis of the dorsal spine with thinning and flattening of the pedicles of C_7 to T_5 vertebrae (Fig. 5) and the lateral view showed an increased

Fig. 3 Occipito-mental view of facial bones. Note the deviated nasal septum, hypoplastic right maxillary antrum with three unerupted molar teeth and hypoplastic right nasal cavity.

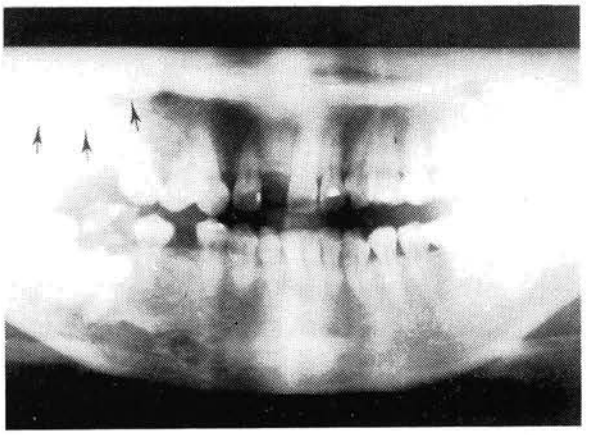

Fig. 4 Panoramic tomogram of the mandible. Note the three unerupted right upper molar teeth (indicated by arrows).

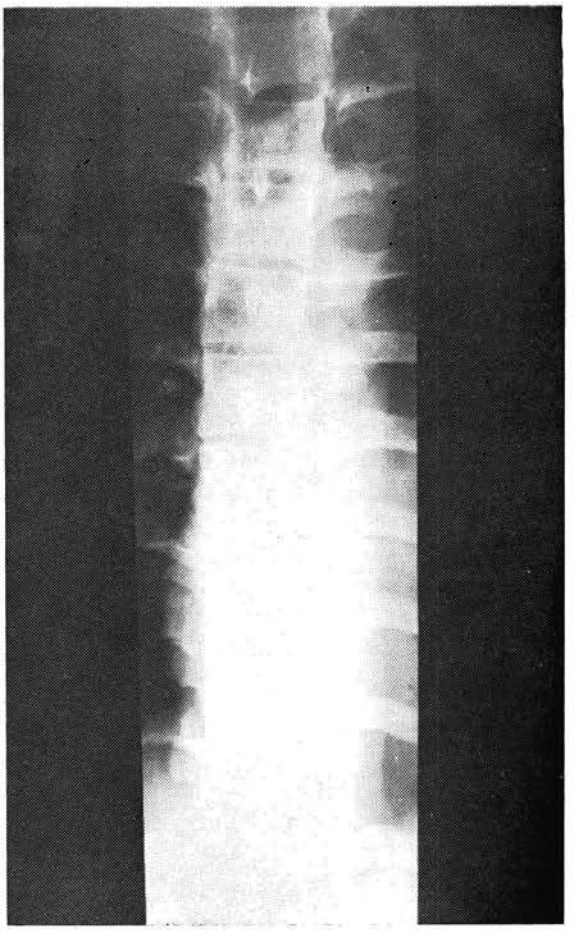

Fig. 5 Anteroposterior projection of dorsal spine. Note the flattened and thinned pedicles of C_7 to T_5 vertebrae and the increased interpedicular distance at the vertebral levels.

sagittal diameter of the spinal canal (Fig. 6). These radiographic findings suggested the presence of an intramedullary tumour of the spinal cord. A myelogram (Fig. 7) confirmed the intramedullary tumour extending from C_7 to T_5 vertebrae.

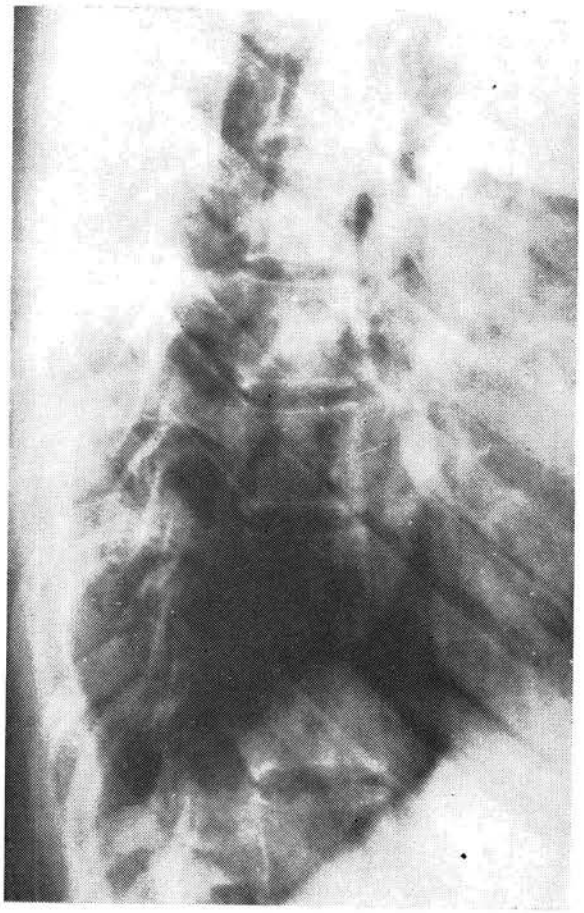

Fig. 6 Lateral projection of dorsal spine. Note the increased sagittal diameter of spinal canal from C_7 to T_5 vertebral levels.

Case 2

M.S., a six months old female Indian child was seen at the Eye Clinic, in August, 1975. There was no history of maternal illness during pregnancy. She was a normal full-term delivery. Her developmental milestones were slightly delayed. There was no relevant family history.

The eye examination showed a left inferior limbal dermoid (Fig. 8).

General examination revealed four left preauricular skin appendages and a left hare-lip with an anterior cleft of the hard palate (Fig. 9).

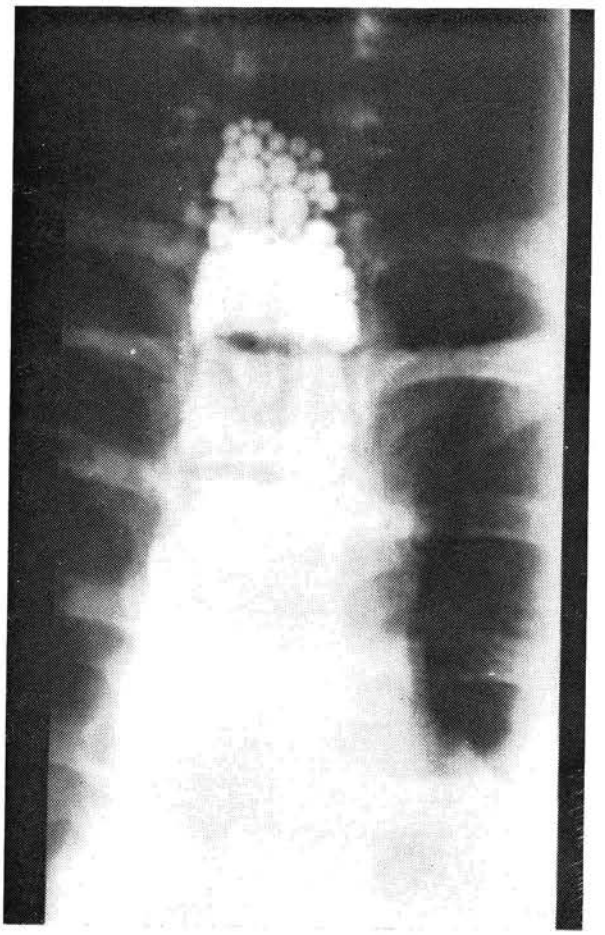

Fig. 7
Antero-posterior spot view of myelogram done in prone position shows a widened half shadow of spinal cord from C_7 to T_5 vertebral levels.

Radiographs of the facial bones and jaw were normal. Her chest radiograph revealed no abnormality.

Radiographs of her spine (Fig. 10) revealed spina bifida of T_1, T_2 and T_3 vertebrae with a hemivertebra at T_4 level.

Discussion

Goldenhar's Syndrome presents with three essential features which are ocular, auricular and vertebral. Other associated anomalies that have been described are varied in nature.

Ocular Anomalies. In the series by Baum et al (1973) a dermoid cyst or dermolipoma was bilateral in 23% and unilateral in 53% of the cases. Upper

lid colobomas were found to be unilateral in 21% and bilateral in 3% of the cases. Other ocular abnormalities described are Duane's retraction syndrome, anophthalmos, corneal anaesthesia and decreased tear formation.

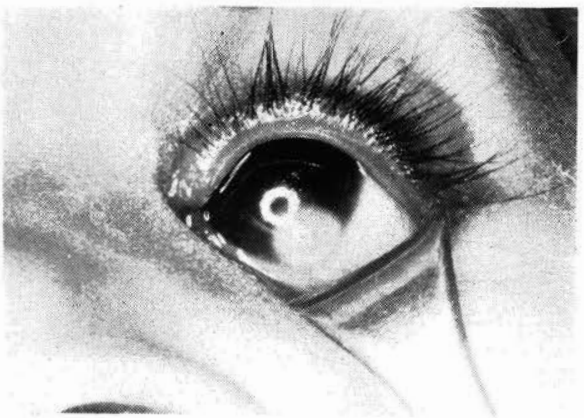

Fig. 8 Case 2
Inferior limbal dermoid of left eye.

Fig. 9 Case 2
Left harelip with cleft palate and preauricular skin appendages.

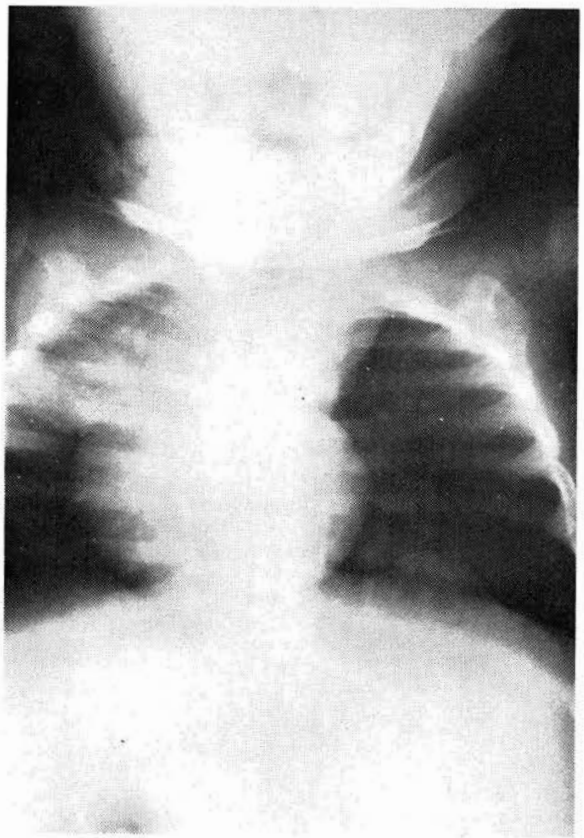

Fig. 10 Case 2.
Antero-posterior projection of dorsal spine shows spina bifida of T_1, T_2 and T_3 vertebrae and hemi-vertebrae at T_4, level.

Auricular Anomalies. The most constant feature is preauricular appendages of which 70% are unilateral. Other anomalies are posteriorly placed ears, microtia, aplasia or stenosis of the external auditory meatus. Hearing loss mainly unilateral, is usually a conduction defect (Baum, 1973).

Vertebral Anomalies. Vertebral anomalies vary; commonly seen are hemi-vertebrae, cuneiform vertebrae, narrowed disc spaces, spina bifida, scoliosis, and supernumerary thoracic or lumber vertebrae (Bowen, 1971).

Associated systemic manifestations. The cardio-vascular system is most commonly involved. Ventricular defect, Fallot's tetralogy, patent ductus

arteriosus, coarctation of the aorta and right bundle branch block have been described (Baum, 1973). Inguinal hernia, umbilical hernia, rectovaginal fistula, imperforate anus, high arched palate, bifid tongue and uvula and cleft palate have all been noted. Other associations include hydrocephalus, mental retardation and epilepsy (Bowen, 1971).

The first patient had an intramedullary spinal lesion. This association has not been previously repo rted. Syringomyelia and glioma of the spinal cord were considered but the absence of a definite sensory level, the site and extent of the lesion together with the lack of symptoms make the diagnosis of syringomyelia unlikely. The aetiology of this lesion is not confirmed as the patient was reluctant to undergo further investigation.

Summary

Two cases of Goldenhar's Syndrome are reported. Both cases presented with the three classical features of the syndrome together with associated anomalies. An intramedullary spinal tumour as an associated anomaly, as seen in Case 1, has not been reported previously.

Acknowledgements

The authors are grateful to the Medical Illustration Department, University of Malaya, for the photographs and Mrs. T. C. Lai for secretarial assistance.

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Benign Intracranial Hypertension in Infants due to Tetracycline

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Introduction

SIDE EFFECTS associated with tetracycline therapy are well known (Pflug, 1963). The commonest are gastro-intestinal effects such as nausea, vomiting and diarrhoea. Others include photosensitive skin rashes, fatty "degeneration" of the liver, especially in the pregnant woman, renal effects such as a high blood urea due to a negative nitrogen balance, and a transient renal tubular disorder mimicking the Fanconi syndrome. The last has been attributed to the effect of outdated tetracycline.

In addition, there are a number of side effects peculiar to the neonate and infant. Amongst the better known of these are the yellow-green pigmentation of decidous teeth seen in infants given tetracycline (Davies et al., 1962) and the inhibition of normal skeletal growth of the premature infant during tetracycline administration (Cohlan et al., 1963). It is less well known that benign intracranial hypertension occasionally occurs. This is indicated by a bulging anterior fontanelle in an infant receiving tetracycline therapy (Millichap 1959, Fields, 1961). Although benign in itself, these infants should all be admitted to hospital in order to exclude a more serious cause of the bulging fontanelle.

The following case is reported as an example of this complication.

Case Report

The patient, a 7 month old, Indian female infant was well till eight days prior to admission when she developed a fever, cough and coryza. She was seen by a general practitioner who commenced a course of oral tetracycline (dose not known). The fever and cough subsided but five days after tetracycline had been commenced the anterior fontanelle was noticed to be bulging. On admission to hospital the child was active and fed well. Her temperature, pulse and respirations were normal. The head circumference was 42 cm. (normal for her age). The anterior fontanelle was bulging but not tense. There was no nuchal rigidity and muscle tone and deep tendon reflexes were normal. The pupils were equal and reacted to light and the fundi were normal as was the remainder of the physical examination.

Investigations

Blood count and an X-ray of the skull showed no abnormalities. A lumbar puncture was unsuccessful but a ventricular tap showed a pressure of 100 mm and clear CSF with 2 RBC, 2 WBC, sugar of 80 mg% and protein of 10 mg%. No organisms were detected and culture showed no growth. Subdural taps were dry on both sides.

Following the ventricular tap, the anterior fontanelle was less full but it was another twenty-four hours before it returned to normal. No therapy was given and on discharge three days after admission, the infants's general condition was satisfactory. At follow-up 2 months and 4 months later there were no neurological deficits and the baby appeared to be developing normally.

Discussion

The history of tetracycline therapy followed by a bulging fontanelle in an otherwise well baby

suggested that the raised intracranial tension was due to tetracycline. However the possibility of an acute meningitis, a partially treated meningitis or a subdural effusion could not be excluded clinically.

Other causes of a bulging anterior fontanelle in a newborn or infant include, Nalidixic acid (Boreus and Sundstrom, 1967, Deonna and Guignard, 1974), Corticosteroids, particularly when reduced or withdrawn (Greer, 1963, Neville and Wilson, 1970), Vitamin A in excess, (Marie and See, 1954) and also in deficiency, (Keating and Feigin, 1970) and otitis media, (Symonds 1952, Greer 1962).

Our patient had received none of the above drugs and showed no evidence of otitis media, hypocalcaemia or avitaminosis. The anterior fontanelle returned to normal following cessation of tetracycline therapy.

The pathogenesis of benign intracranial hypertension due to tetracycline is uncertain but is probably due to a number of factors. Sereni et al., (1965) were able to show that an analogue of tetracycline, namely tetracycline-1-methylene-lysine is excreted more slowly by the human newborn baby than by an older infant, and that the plasma concentrations 6 and 12 hours after oral administration of a single dose (12 mg/kg) of the tetracycline analogue were always significantly higher in newborn babies than in infants more than 2 months old. It was concluded that this was because of the lower glomerular filtration rate of the neonate. The same paper also reported that the brain tissue concentration of the tetracycline analogue in newborn rabbits was approximately ten times higher than that in 2 month old rabbits given the same dose weight for weight. Among the tissues examined only the brain showed a marked accumulation of the analogue in the newborn rabbit. It is postulated that similar results would probably be found with tetracycline.

In the case reported here, the dose of tetracycline given was not known but signs of a raised intracranial pressure were only noticed on the fifth day of administration. It is possible that the accumulated doses of tetracycline given to this infant produced a high plasma tetracycline concentration. If the brain of the newborn infant also shows preferential concentration of tetracycline, the bulging fontanelle might have been the result of a local reaction to this unusually high concentration.

Although not a common side effect of tetracycline therapy, the possible development of intracranial hypertension following its use is a further reason for avoiding this drug in the treatment of infections in infants and young children.

Summary

An infant was given tetracycline for a febrile illness. Five days later she developed a bulging anterior fontanelle which subsided on cessation of tetracycline therapy.

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Micromethod for the Measurement of Renin Activity

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Abstract

A micromethod for the measurement of renin concentration was described for plasma and renal lymph of cat. It involved the preparation of renin substrate free from renin and from angiotensinase. Renin from 0.1 – 0.2 ml of plasma or renal lymph was made to react with the prepared renin substrate in a incubating medium. Incubation of renin from plasma or renal lymph in the presence of excess substrate was done at pH 7.0 in a polythene tube. To each incubation mixture neomycin sulphate, 2 mg/ml and a kallikrein inhibitor trasylol, 100 units/ml were added and all incubations were done at 37°C for a period of 12 hr with constant rate of agitation. The angiotensin so formed during the period of incubation was absorbed on a column of 1 ml prepared Dowex 50W – X2 (NH_4^+), 100 – 200 mesh and thereafter eluted and freeze-dried. The extracted angiotensin fraction in its freeze-dried form was dissolved in 1 ml of 0.9% NaCl and bioassay was done on the mean systemic arterial blood pressure of ganglion-blocked rats against Val^5-angiotensin II-asp-β-amide. The method measures the angiotensin generating capacity of renin in a controlled environment and can be adapted for the measurement of plasma renin concentration in man.

Introduction

THE PROTEOLYTIC ENZYME RENIN (Munos et al., 1939) is secreted from the juxtaglomerular apparatus of the kidney into the blood stream (Cook & Pickering, 1962) and into the renal lymph (Lever & Peart, 1961; Gan & Lockett, 1973). Renin interacts with its specific alpha-2-globulin substrates (Plentl et al., 1943) from the liver to liberate angiotensin I (Elliot & Peart, 1956) which is then converted to angiotensin II by a converting enzyme (Skeggs Jr. et al., 1956). Conversion of angiotensin I to angiotensin II takes place mainly in the pulmonary vascular bed (Ng & Vane, 1967). Angiotensin II, the active end-product of renin is a very potent vasoconstrictor, evokes aldosterone secretion (Davis, 1962). Renin is known to play a role in certain pathological conditions.

High plasma renin levels are commonly found in association with renal hypertension involving stenosis of the renal artery (Woods & Michekalis, 1968), in pheochromocytoma (Maebashi et al., 1968) and in hepatic cirrhosis with edema (Imai & Sokabe, 1968). Low plasma renin levels are associated with primary aldosteronism (Brown et al., 1968).

In essential hypertension, renin levels can either be high or low (Fasola et al., 1966; Weidmann et al., 1968; Creditor & Loschky, 1968). The β-adrenergic blocking agent is effective in treating essential hypertension with abnormally high renin level. Whereas the aldosterone antagonist spironolactone is particularly good as an anti-hypertensive agent in essential hypertension patient whose renin levels are low (Simpson, 1974). It is apparent that knowledge of exact plasma renin concentration will be useful in studying and treating these pathological conditions.

This paper describes the development of a sensitive micro-method for the measurements of renin concentration from the plasma and renal lymph of cat. With appropriate modifications, it can be adapted for the routine measurements of human plasma renin concentration.

METHODS

Preparation of standard cat renin

Standard cat renin was prepared according to the method of Katz et al., (1966) from 45.5 g kidneys of one animal which had been decapsulated and frozen immediately after removal from the anaesthetized animal. The frozen kidneys were later thawed at room temperature. Freezing and thawing was repeated three times in the same day to increase cell rupture and the availability of renin for extraction (Haas et al., 1954). Thereafter, the rest of the procedure was carried out in a cold room at 5 – 10°C. The kidneys were homogenized using a Waring Blendor in 0.05 M Na_2HPO_4, 3.5 ml per g of tissue. The homogenate was transferred to a sac of Visking tubing (size 24/32 in) and dialyzed for approximately 20 hr against 0.1 M lactic acid buffered to a pH within the range, 3.50 to 3.55 by addition of solid $NaHCO^3$. This process also inactivades angiotensinases (Skinner, 1967). The residual solids removed from the dialysed homogenate by centrifugation for 20 min at 2,000 r.p.m. The supernatant, adjusted to pH 7.0 by the addition of a few drops of 3.5% $NaHCO_3$, was centrifuged for 10 min and the pH of 7.0 was reconfirmed.

This supernatant was put into 130 ampoules each containing 1 ml of standard cat renin. The air in the ampoules was displaced with dry nitrogen, and the ampoules sealed and stored at −20°C.

Preparation of cat renin substrates

Renin substrates were prepared by the method of Haas et al., (1966) from arterial blood of cat which was nephrectomised under chloralose anaesthesia and bled 10 hr later whilst still under anaesthesia. The blood was collected into a chilled heparinised flask and the plasma was separated at once by centrifugation at 2,000 r.p.m. and 4°C, for 20 min. Solid ethylene-diamine tetraacetic acid (EDTA) 1.88 g/100 ml, was added to the plasma and dissolved at room temperature. The solution was stirred and brought to pH 8.0 by the cautious dropwise addition of 5 N NaOH. After cooling to approximately 5°C the pH was adjusted to 5.3 by the slow addition of 2.5 N H_2SO_4 while stirring continuously. Renin substrate was then salted out by the addition of solid $(NH_4)_2SO_4$, 30.4 g/100 ml plasma, and stirred for 10 min, then capped stood overnight at 4°C.

After 14 hr, the renin substrate was obtained as a centrifugate of the mixture. The substrate was extracted twice with distilled water (2 × 12 ml per 100 ml plasma). The combined extracts were then centrifuged. The supernatant was dialyzed in sacs of Visking tubing against 6 changes of distil water in 24 hr in the cold room at 5 – 10°C. After centrifugation, the residue was discarded and the solution of substrate was freeze-dried and stored at −20°C.

Measurement of renin activity

A micro-method, modified from the method of Boucher et al. (1967) was developed for the measurement of renin concentration in plasma.

Plasma or standard renin, 0.1 to 0.2 ml, was added to 3 ml isotonic saline (0.9% NaCl at pH 7.0, unless otherwise stated) containing neomycin sulphate (Andrew Laboratories) 2 mg/ml, and a kallikrein inhibitor, trasylol 100 units/ml (Skinner, 1967) in a polythene tube. All tubes were immediately capped and incubated, with uninterrupted vigorous and standardized agitation, in a water bath at 37°C for 12 hr before cooling rapidly to 4°C. The tubes were stored at 4°C after incubation before the isolation of angiotensin.

The isolation and elution of angiotensin so formed was carried out in approximately 1 ml prepared Dowex 50W – X2 (NH_4^+) resin, 100 – 200 mesh (Bio-Rad Laboratories), contained in a glass column 14 cm long with an internal diameter of 1.25 cm. Each Dowex column was prepared by washing with 10 ml 0.2 M ammonium acetate at pH 6.0, then with 20 ml 10% (V/V) aqueous acetic acid and finally with 30 ml distilled water before the cold incubate was passed through the column. The angiotensin was adsorbed on the column and was then eluted by passage of 7 ml 0.1 N diethylamine followed by 7 ml 0.2 N ammonia in a Erlenmeyer flask and was freeze-dried. The dry residue was dissolved in 1 ml 0.9% NaCl immediately before assay against Val^5-angiotensin II-asp-β-amide (Hypertensin, Ciba).

Bioassay

Female rats, 150 – 200 g, of an inbred Wistar strain, were anaesthetized by intraperitoneal (i.p.) injection of pentobarbitone sodium, 40 mg/Kg (Nembutal, Abbott Laboratories). The trachea, an external jugular vein and a common carotid artery were cannulated with polythene tubes. Mean arterial blood pressure was recorded from the carotid cannula through an E & M pressure transducer coupled to a Nesco Recorder. Injections were made through the cannula in the external jugular vein in volumes not exceeding 0.15 ml. Each injection was washed with 0.1 ml 0.9% NaCl. Ganglionic blockade was induced in all rats before the assay commenced by injection of pentolinium (Ansolysen, May & Baker), 0.5 mg intravenously followed by 2.0 mg subcutaneously to give a more stable basal blood pressure (Peart, 1955).

All assays were of 4 × 4 Latin square design. The two doses of standard Val[5]-angiotensin II-asp-β-amide most commonly used were 0.5 and 2.5 ng. The two doses of extract were selected to give comparable responses to those elicited by the two standards. The assay were designed and analyzed by the method as described for posterior pituitary extract by Holton (1948). Typical tracings from assays of renin activity in both the renal lymph and arterial plasma are shown in Figure 1.

Collection of blood and renal lymph

For the measurement of renin activity, blood is collected from the carotid artery via a polythere cannula. Collection of renal lymph from cat was previously described (Gan & Lockett, 1973).

Preparation of isotonic buffered incubation salines

Terminology

The Terms renin activity and renin concentration are treated as synonymous. Renin activity is computed as ng angiotensin formed per hr. when 1 ml plasma/lymph or standard renin is incubated with an excess of substrate under standard conditions for 12 hr.

RESULTS

Effects of changes in renin substrate concentration

Different concentrations of renin substrate were incubated, each with 0.1 ml standard cat renin. Figure 2 shows that a maximum yield of angiotensin

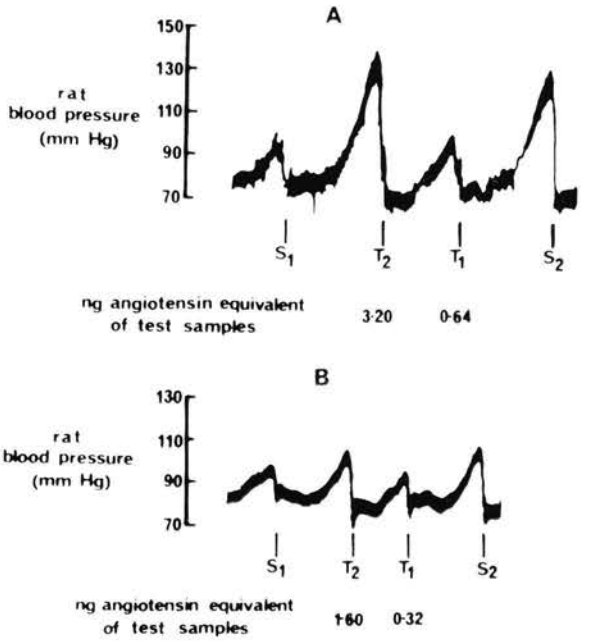

Figure 1

Tracings from two assays of renin activity on the blood pressure of pentolinium-treated rats

A: Assay of renin activity from renal lymph
S = standard angiotensin, S_1 = 0.5 ng, S_2 = 2.5 ng
B: Assay of plasma renin activity
S = standard angiotensin, S_1 = 0.4 ng, S_2 = 2.0 ng
Values indicated beneath T_1 and T_2 show the ng angiotensin found in the injected volumes of the test samples. The calibrated pressure (mm Hg) is shown on the left of each tracing.

Table 1

The composition of isotonic buffered incubation salines

pH	Solution A (ml)	Solution B (ml)	NaCl added (g × 100 ml^{-1})
	0.055M citric acid	**0.055M Na_2HPO_4**	
3.9	50	50	0.48
	0.0016M citric acid	**0.00346M sod. citrate**	
5.0	67.9	32.1	0.54
	0.067M NaH_2PO_4	**0.067M Na_2HPO_4**	
5.9	90	10	0.52
6.5	70	30	0.50
7.0	40	60	0.46
8.0	5	95	0.42

was obtained by the use of approximately 80 mg renin substrate per incubating medium for 12 hr of incubation. To ensure that the substrate presence is in excess, 90 mg of substrate was employed for each measurement of renin activity in plasma and in lymph under the standardized conditions.

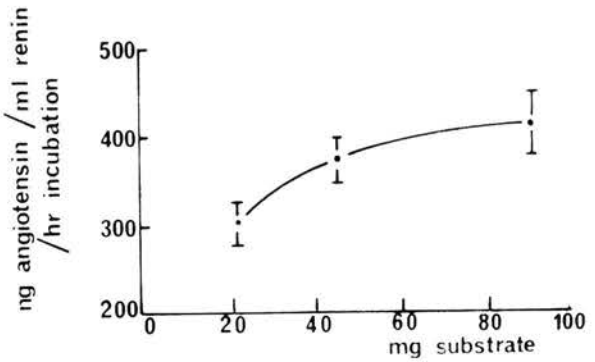

Figure 2

Effect of varied concentrations of renin substrate on the generation of angiotensin by standard cat renin

The vertical bars show the fiducial limits of assays, P = 0.05.

Effects of changes in renin concentration

Figure 3 shows the rate of interaction of standard cat renin with renin substrate with varying concentrations of cat renin. The relationship between ng angiotensin generated /ml renin/hr incubation with different dilutions of renin was linear for up to 12 hr incubation period.

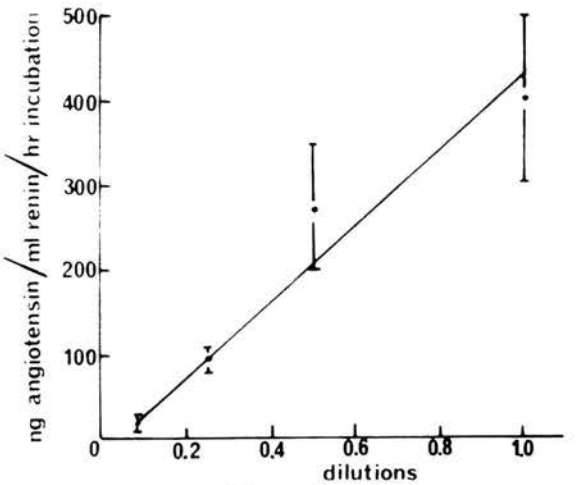

Figure 3

Rate of interaction of standard cat renin with renin substrate

In each case 90 mg of substrate was used. Vertical bars as in figure 2.

Relationship between the quantity of angiotensin generated and the duration of incubation

Standard cat renin was incubated under standard conditions with excess renin substrate. Angiotensin was formed at a constant rate throughout the first 12 hr of incubation as shown in figure 4.

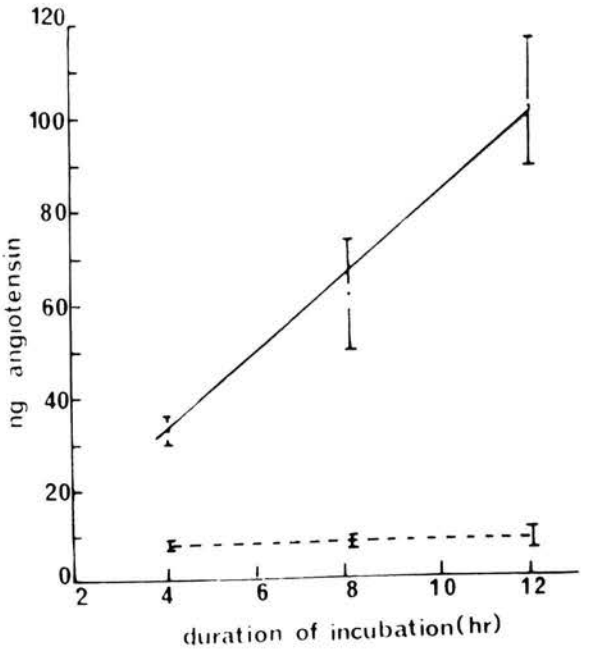

Figure 4

Relationship between the total angiotensin formed and the duration of incubation

The continuous line represents the cummulative total of ng angiotensin generated per ml cat renin incubated with excess substrate and the broken line shows the rate of formation of angiotensin in ng per ml cat renin per hr of incubation. Vertical bars as in Figure 2.

Effects of pH on angiotensin generation

Isotonic buffered incubation salines for various pH values are prepared as shown in table 1. The curves relating pH to ng angiotensin formed per hr in the presence of excess renin substrate was determined for standard cat renin as shown in figure 5. The optimum pH was 7.0. A small hump seen in the curve at pH 3.9 was attributed to the presence of pseudo-renin (Skeggs et al., 1969). Since these authors report that pseudo-renin is almost inactive at pH 7.0 all incubation for the determination of true renin activity should be carried out at pH 7.0.

Recovery studies

Duplicate samples of known concentration of synthetic angiotensin when subjected to the same

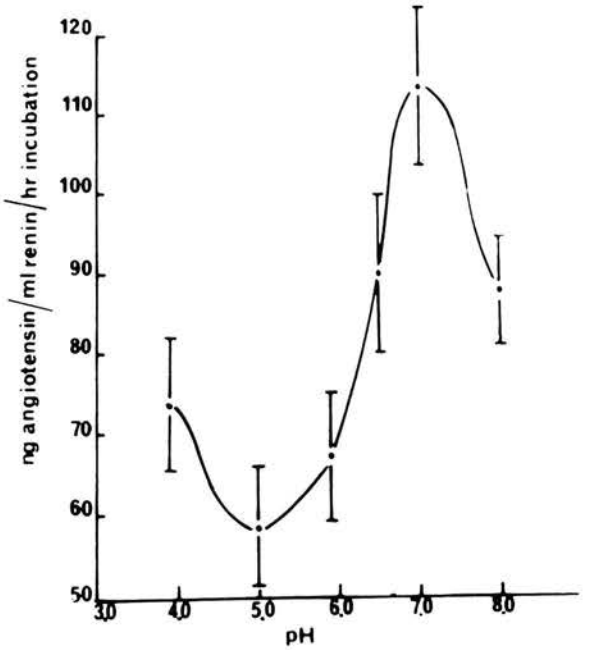

Figure 5

pH curve for the interaction of standard renin with renin substrate

Figure shows the curve relating the rate of formation of angiotensin by renin in 0.1 ml of cat plasma incubated with excess substrate (as ordinate) to pH (as abscissae). In each case 90 mg of substrate was used. Vertical bars as in Figure 2.

isolation process carried out in 1 ml prepared Dowex 50 W – X2 (NH_4^+) renin, 100 – 200 mesh and thereafter freeze dried and assayed give not less than 80% recovery. Results of duplicate samples assayed was in agreement within the limit of ± 5%.

DISCUSSION

The method presented measures the angiotensin generating capacity of renin in a suitably controlled environment. The initial requirements in the development of the method is to prepare renin free from angiotensinase and from substrate, and then to prepare substrate free from renin and from angiotensinase. Proof of the absence of angiotensinase in renin and in substrate was obtained by continued incubation of standard renin with limited amounts of substrate for several hours after the maximum yield had been obtained. The constancy of the maximum yield for several extra hours on incubation demonstrated the absence of angiotensinase activity. Proof of the absence of substrate in renin preparations was obtained by demonstration of the absence of angiotensin formation on incubation of renin without addition of substrate. Proof of the absence of renin from preparations of substrate was made by demonstration of the absence of angiotensin formation when the substrate was incubated without the addition of renin.

The interactions of renin with renin substrate and the subsequent measurements of angiotensin generating capacity of renin assumes that renin substrate is always present in excess. Thus each batch of substrate prepared was interacted with standard renin to ensure that the amount of substrate used was in excess. The simplest way to calibrate substrate was to measure the maximum amount of angiotensin that could be formed from it by a fixed amount of standard renin, and adjustment made if necessary so that the substrate used each time is of equal concentration to the 90 mg shown in figure 2.

The incubation of renin with its substrate was carried out in the presence of a kallikrein inhibitor, trasylol, 100 units/ml and neomycin sulphate, 2 mg/ml in 0.9% NaCl. Both trasylol and neomycin sulphate in the concentrations used had no effect on the reaction rate between renin and its substrate, nor had they any effect on rat blood pressure (Skinner, 1967). Neomycin sulphate was employed to prevent bacterial contamination of the incubation medium because it had been shown previously that bacterial contamination could lead to destruction of angiotensin II (Lever, et al., 1967).

Interaction of standard renin or of plasma/lymph with excess renin substrate under standardized conditions was followed by absorption of the angiotensin so formed on a Dowex column and thereafter eluting and freeze drying. Since injections of freshly prepared solutions of these residues produced clean pressor responses of the mean systemic arterial blood pressure of ganglion-blocked rats, and duplicate incubates yield residues of similar activity, the extraction procedure was also deemed reliable. Moreover, the pressor response elicited in the rat by the injection of extracted angiotensin fractions from both lymph and plasma was of a similar shape and indistinguishable from the pressor responses induced by synthetic angiotensin II (figure 1).

The method allowed detection of renin activity in relatively small volumes of plasma or lymph. Coupled with its relative rapidity and reproducibility, the method was particularly suited to measure small volume of test sample. With appropriate modifications the method can be used to measure renin concentration in human plasma.

SUMMARY

A micro-method was developed for the measurement of renin concentration in the plasma and renal lymph of cat. The method involved the interaction of renin from plasma or from renal lymph with excess renin substrate in a controlled environment in the presence of neomycin sulphate and trasylol for a period of 12 hr. The angiotensin so formed was absorbed onto 1 ml of prepared Dowex 50W – X2 (NH_4^+), 100 – 200 mesh and elution of angiotensin was done by using 7 ml 0.1 N diethylamine followed by 7 ml 0.2 N ammonia in a Erlenmeyer flask and freeze dried. The freeze dried residue was dissolved in 0.1 ml 0.9% NaCl and bioassayed against Val^5-angiotensin II-asp-β-amide on the mean systemic arterial blood pressure of ganglion-blocked rat. The optimum pH of incubation was found to be 7.0 and hence this pH was recommended for incubation purposes. Recovery studies by using synthetic angiotensin was found to be extremely good. The method is reproducible and sensitive enough to detect the renin concentration in 0.1 ml of cat plasma/lymph. The method can be easily adapted to measure the plasma renin concentration in man.

ACKNOWLEDGEMENT

I thank Emeritus Professor M. F. Lockett, Department of Pharmacology, University of Western Australia for her useful suggestions when this work was undertaken. I should also like to extend my thanks to Professor Chan Kok Ewe for reviewing the manuscript in the preparation of this paper and Miss Siti Eshah for typing the manuscript.

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Craniocerebral Injuries

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Abstract

Definitive diagnostic procedures and appropriate therapy have been developed for approximately twenty-five percent of patients with craniocerebral injuries of sufficient severity to warrant their hospitalization. The remaining seventy-five percent represent those with damage of the brain resulting from blunt injury followed by drowsiness;-stupor;-coma; as consequence of cerebral contusion-laceration, multiple small hemorrhages, axial distortion, cerebral edema, and increased intracranial pressure. Many of these pathophysiological alterations present unsurmountable therapeutic problems. Increases to an undesirable level of intracranial tension may be effectively managed, and this in turn have a beneficial bearing on some of the other undesirable pathological processes.

THE DEVELOPMENT OF various modes of rapid transportation and the relatively unrestrained manner of deportment of the citizenry of most industrialized nations, has resulted in a progressively increasing number of bodily injuries. Multiplicity of lesions of traumatic origin, in particular those sustained in motor car accidents, is the rule and not the exception. In sophisticated medical institutions groups of surgeons have been formed to accord the injured skillful diagnostic and therapeutic considerations. This widespread development of the Surgery of Trauma has had general acceptance by both the laity and the medical profession. It has resulted in substantial decrease in the morbidity and mortality directly related to injury. Interestingly enough, the care of patients with the sole or principal traumatic lesions being located in the intracranial cavity, remains the responsibility of the neurosurgeon. They have made advances in definitive diagnoses and surgical treatment, however, there still remains many unknowns concerning the pathophysiology of these intracranial lesions of traumatic origin.

Presented as an invited lecturer at the Tunku Abdul Rahman Institute for Neurological Sciences, August 1975.

As obtains in most segments of medicine, the interpretation of the clinical features of patients with craniocerebral injuries and their correlation with the pathological state constitutes our basic knowledge of those with this type of lesion. It has become conventional to classify these for facility of presentation, however, it is recognized that more often than not the classes fuse or meld. Moreover, some of these categories in common use are based on abnormal clinical features alone whereas others are derived from demonstrable anatomical derangements.

A. Laceration of Scalp

B. Simple Fracture of Skull (linear or depressed)

C. Compound Fracture of Skull (vault and base)

D. Penetrating Missile Wound of Head

E. Closed Head Injuries
   1. Mild Cerebral Injury (concussion)
   2. Moderate Cerebral Injury (cerebral contusion)
   3. Severe Cerebral Injury (cerebral laceration)

F. Intracranial Hemorrhage:
   1. Extradural Hemorrhage
   2. Subdural Hemorrhage
   3. Subarachnoid Hemorrhage
   4. Intracerebral Hemorrhage
   5. Intraventricular Hemorrhage

In some instances the location and extent of the intracranial lesion or lesions is evident upon routine examination, whereas in others the pathophysiological factors are obscure. Under the latter circumstances in particular, one should accord "little things" full consideration. A few examples: the determination of the site of impact to the head by the inflicting object is quite important. Here there is frequently transitory deformation of the skull, with or without resultant linear fracture but sufficient to detach the dura mater. Crossing vascular channels from the diploic to the dural circulation are interrupted thus setting the stage for the development of an extradural hematoma; the relatively rapid appearance of a swollen upper eyelid with the overlying skin having a blue tint and this associated with evidence of a blow to the occipital scalp commonly signifies multiple parallel linear fractures in the bony roof of an orbit and a concomitant homolateral contusion-laceration of the frontotemporal region of the brain; ataxic breathing associated with stupor and paucity of muscular movements strongly suggest impaired medullary function resulting from pressure by a hematoma within the posterior cranial fossa; excessive sweating associated with generalized stiffness of the extremities, but not evident decerebration, appearing shortly after injury suggests intraventricular hemorrhage. In all events, every abnormal feature that can be demonstrated in each patient should be assessed and recorded even though it may require repetative examinations to determine the relative significance of these in the total clinical picture.

A cursory appraisal followed by cerebral arteriographic examination is to be condemned. This somewhat definitive examination does serve as an excellent diagnostic adjunct but should be used with discretion. It serves as an aid in establishing the presence of or excludes the possibility of a mass lesion of surgical significance. It is to be recognized that only about one-fifth of the total group of patients who have sustained some type of craniocerebral trauma are in need of surgical therapy. These consist of those with open wounds of the vault of the skull, an occasional instance of compound fracture involving the nasal cavity and/or ears, a variety of blood collections or hematomas of the intracranial compartments, and focal contusion of the brain with edema adjacent to the lesion. Even though surgical elimination of such focal lesions may be considered adequate, this frequently resolves only a segment of the total problem. It is, therefore, necessary to maintain an attitude of expectancy interlarded with repeated observations, throughout the patient's illness.

Information regarding the details of the accident, obtained on entry to the hospital, is often fragmentary, second handed, and frequently unreliable. The victim, commonly a young to middle aged male, is transported by ambulance from the site of accident to the hospital. Even the attendant in charge of the ambulance may not be able to give an accurate account of the sequence of events that ensued enroute to the emergency area of the hospital, in particular changes in the state of awareness or consciousness. It is, therefore, mandatory that the doctor in attendance be familiar with abnormal physical features that may indicate the site of dysfunction of the brain. He should also be sufficiently versatile to make a determination of the nature and extent of damaged parts other than the head and assign those so injured to appropriate members of the surgical team.

Those with lacerations of the scalp, compound fractures of the vault of the skull and the patients who have had a period of unconsciousness followed by a lucid interval and subsequent drowsiness to stupor, should have definitive diagnostic procedures as indicated and prompt surgical attention. The remaining group consists of those with stupor to coma without abnormal physical features suggesting a focal lesion.

There are three important abnormal findings to be looked for during the initial as[essment: degree of alterations in the conscious state, the status of the eyes, especially the pupils and alterations, usually diminution, in movements of the extremities. Among these three the state of consciousness of awareness stands preeminently. Conventionally five grades have been recognized, i.e. alert, drowsy, stuporous, coma, and moribund, however, sharp lines of distinction do not separate these stages. A complete understanding of the changes in the complex cerebral mechanism that results in loss of awareness and contact with surroundings remains obscure. The accumulated evidence indicates that the function of the reticular formation of the upper brain stem is in part at least to regulate the state of consciousness. The clinical evidence in the human suggests more widespread nuclear areas of influence. The conscious state varies from patient to patient. In general the more profound the loss of awareness the more severe the cerebral injury. Furthermore improvement is usually estimated by the patient becoming more

responsive to all types of stimuli, remaining on a plateau when reaction to surrounding remained unchanged and worsening if the altered state of unconsciousness become more profound. Consequently the clinician relies heavily on this index in estimating the extent of the cerebral damage. In some patients of the moderately to severely injured group treatment is instituted immediately upon entry before embarking on the examination. This therapeutic urgency is posited on the presence of excessive bloody secretions which partially obstruct the airway. This complication may be corrected by positioning the patient on one side and complete toilet of the nasopharynx by suction. If this is not successful, tracheostomy should be performed forthwith.

After mandatory emergency issues have been resolved, a careful and thoughtful examination should be made. Usually drowsiness to stupor prevails. The status of the pupils is determined. The central pathways for both pupilloconstrictor and pupillodilator effects course through the upper brain stem. Lesions rostral to the diencephalon have little influence on pupillary and ocular functions. More caudally situated lesions are not infrequently associated with significant pupillary changes. Importantly, among these are the dilatation of a pupil secondary to compression of an oculomotor nerve by laterally located hematoma and constriction of the pupils in patients with pontile lesions. Observation of other oculomotor nerve dysfunctions may aid in diagnosis, in particular a laterally rotated optic bulb. In addition oculocephalic and oculovestibular reflexes may furnish information regarding the neural level of the traumatic lesion implicating the mesencephalic-hindbrain complex.

The third of the aforementioned trio of areas to be critically examined namely the motor components of the extremities frequently show unilateral dimunution of spontaneous and/or limited movements subsequent to noxious stimuli. Hemiparesis to paralysis is not difficult of demonstration. Stretch reflexes are variable consequently alteration of these may not represent valid evidence of damaged myoneural connections, however, the sign of Babinski if present on the side of suspected paresis, is an important finding. Mild to moderate rigidity of all extremities suggests impending decerebration secondary to uncal herniation. The frequently quoted "flexion posture" of the upper extremities representing decortication and the "extension posture" with internal rotation of these parts as indicative of decerebration does not hold in clinical practice. One of these attitudes may alternate with the other in a matter of seconds in patients who subsequently are shown to have tentorial herniation of the mesial posterior temporal lobe of the brain.

If after careful assessment of the evidence derived from repeated observations and examinations a decision regarding surgical therapy cannot be reached, arteriography should be performed. Although a subdural collection is demonstrated by the examination this does not necessarily settle the issue of therapy. It is to be remembered that in most instances the subdural hematoma represents a complication of a surface brain lesion and that its surgical evacuation in some way not be followed by appreciable change in the course of the patient's illness. Surgical mortality remains high in the group with so-called acute subdural hematoma consequently serious consideration should be accorded the possible effectiveness of this therapeutic approach during the early phase of illness. This viewpoint does not hold for extradural hemorrhage which should receive surgical attention prior to the appearance of decerebration or fragments of this posture. Evacuation of the hematoma in this anatomical position should be followed by prompt recovery.

After resolving a part of the total problem of some patients by surgical evacuation of a blood clot and/or this in combination with removal of contused and/or macerated brain, factors which are instrumental in the production of stupor to comatose in many with closed head injury still persist. The two outstanding ones are damage to important cell masses of the brain stem and cerebral edema. Dehydrating chemicals may be beneficial in some instances, however, in others the effects are transitory at best. The major problems are said to be brain swelling and cerebrovascular congestion associated with an increase in intracranial pressure. Accumulated experimental and clinical evidence indicates that uncontrolled intracranial hypertension is a major contributing cause of death in patients with craniocerebral trauma. The anatomicophysiological basis for this is that the intracranial volume is essentially fixed. These constituants are blood, brain, and cerebrospinal fluid consequently an increase in the volume of one is at the expense of the others. Swelling of the brain following cerebral injury results from brain edema. As a consequence of this, intracranial tension is increased thus imposing cerebrovascular congestion which in turn adds to the total intracranial volume. At some point the intracranial pressure rises beyond that compatable with life. Imposing a relatively high degree of intracranial pressure on a normally functioning brain is quite different from creating a comparable set of intracranial circumstance in a patient with

contusion of the brain implicating the upper brain stem. Adding even small increments of pressure may produce medullary failure. Untreated compression of the brain by an extradural hematoma resulting in a fatal outcome has been cited by some as an example of death due to intracranial hypertension. This oversimplified examination does not take into account the concomitant edema of the white matter underlying the area of compressed brain, the axial shift of the upper brain stem with the herniation of the uncus through the incisura tentorii and the resultant mesencephalic hypoxia. No doubt the accompanying increase in intracranial pressure under the conditions aforementioned should be regarded as a component of the complex mechanism that resulted in death, however, several pathophysiological mechanisms are brought into play. Since our knowledge is grossly defective regarding the interplay of these pathophysiological processes, treatment of a relatively large segment of patients with closed head injuries is largely empirical. There is ample clinical evidence to support the notion that dysfunction of the brain consequent to blunt trauma of the head becomes less in evidence if the cerebrospinal fluid pressure is maintained within normal limits. During the past six decades various methods have been developed and used to effect this end result, however, none of these have proved to be a therapeutic answer to the multiple problems presented. For the past fifteen years, it has been recognized that continuous recording of the intracranial tension furnishes a more knowledgeable approach to maintaining the intracranial pressure at a normal or physiologically acceptable level.

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Lumbar Epidural Anaesthesia in a Solo

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Introduction

THE PAUCITY OF specialist anaesthetic services in Sarawak does tend to test and at times strain the resilience of the single-handed surgeon in practice. Lumbar epidural anaesthesia has proved both safe and useful in the surgery of the lower abdomen in preselected cases. This report represents the first hundred cases in such a practice, using this form of anaesthesia.

Historical Survey shows that early experimental work was done by Corning, Cathelin and Sicard at the turn of the century. Clinical application is generally accredited to Pages (1921) and Dogliotti (1931). Dawkins (1945) and Bromage (1961, 67) are among the more recent workers who have helped to consolidate the scientific basis and expand the clinical usage of epidural (extradural) anaesthesia.

Anatomically, the dura mater is attached above to the margins of the Foramen Magnum and ends at the lower border of the second lumbar vertebra. The epidural or extradural space is thus between the dura and vertebral canal. It extends from the base of the skull above to the sacro-coccygeal membrane below. It contains areolar tissue, fat and vessels, and has a negative pressure. All spinal nerves must of necessity traverse this space on their way out of the spinal canal. In the lumbar region, this space is 2 – 3 mm in width and is 4 – 5 cm from the skin.

Materials and Methods

For inclusion both the patient and the pathology must be suitable. All the patients were thought fit apart from the disease needing operation. The procedure is explained and only those patients who appeared calm and co-operative were chosen. The surgical condition should be confined to the lower abdomen and the pelvis, such that the operative procedure would be limited to below the umbilicus, i.e. T10 dermatome.

The sex and age distributions are as follows:

There are thirty-two (32) males and sixty-eight (68) females.

Age:

9 – 1.

10 – 19 – 13.

20 – 29 – 31.

30 – 39 – 31.

40 – 49 – 12.

50 – 59 – 8.

60 – 69 – 2.

70 – 2.

The operations performed are as follows:

Type of Operations	*Number.*
Appendicectomy	44.
Bilateral Tubal Ligation	29.
Ing. Herniorrhaphy	9.
Hysterectomy	8.
Ovarian Cystactomy	3.
Gilliam's Operation	2.
Varicocoele	1.
Orchidopexy	1.
Laporatomy	1.
Ectopic Pregnancy	1.
Sigmoid Colcectomy	1.

Anaesthetic Solution used:

Basically, only Lignocaine and Prilocaine (Citanest) were used, with or without Noradrenaline I in 200,000:-

Leostesin 2% – plain – 32.
\+ – Noradrenaline – 8.

Xylocaine 2% – plain – 29.
\+ – Noradrenaline – 11.

Citanest 2% – plain – 15.
\+ – Noradrenaline – 5.

Site of Lumbar Puncture:

The space between the spines of the second and third lumbar vertebrae was preferred, although when necessary the more accessible adjacent spaces were used:-

L1 – 2 – 8.
L2 – 3 – 80.
L3 – 4 – 12.

Technique:

This technique was first introduced to me by McCaul (1966) and is basically similar to that described by Boulton (1968) and by Lee and Atkinson (1968). A Gordh's needle is put into a forearm vein and secured. An ampoule of Aramine, Magill's laryngoscope and an endotracheal tube were put on the anaesthetic machine in readiness. The patient is put in the lumbar puncture position with the side of the intended incision lowermost. The lumbar area is sterilised and draped. A long 19 G needle with a short bevel, attached to a 2 cc. syringe with about 1.5 cc. of air, is then pushed into the L2 – 3 interspace until sudden increased resistance is felt as the needle hits the ligamentum flavum. The plunger of the syringe is pushed and the rebound sensation is quite characteristic. Slow steady pressure is then applied to advance the needle about 1 mm at a time, with frequent test for 'rebound'. A sudden give is felt when the extradural space is entered and the air is injected with ease after negative aspiration for C.S.F. The syringe is disconnected and the needle rotated to make sure that it has not entered the dura. The patient's back is straightened and he is asked to move his toes when a test dose of 5 cc. of anaesthetic solution is injected. After five minutes, if there is no giddiness or tingling in the legs, the remaining 15 cc. of the solution is injected slowly, with the patient continuing to move his toes. The patient then lies on his back with 10 – 15 degrees of Trendelenburg tilt. After 10 – 15 minutes, the incision can usually be made, and only then is the patient told to stop moving his toes.

Results and Discussions

The criteria of a successful block are:

(1) Surgical analgesia of up to T10.

(2) Muscular relaxation below the umbilicus.

(3) Absence of serious side-effects.

98 cases fulfilled these criteria. There were two failures. It is interesting to note that both had acute appendicitis: Case 1, a young woman had uncontrollable quite gross tremors after 20 cc. of 2% Lignocaine, which made operation difficult. In Case 2, a young man aet. 34, the lumbar epidural anaesthesia just refused to rise above L1. General anaesthesia was used instead.

Inadvertant intradural injection is of course the most serious complication; it did not occur in this series. Prophylaxis by attention to details of puncture is of utmost importance. Voluntary movement of the patient's toes throughout the procedure and up to ten minutes after injection of the anaesthetic solution is a useful & visible guide that nothing untoward has happened. Preparation for dealing with apnoea and hypotension from a 'massive spinal' cannot be overstressed.

The blood pressure changes during lumbar epidural anaesthesia have been analysed by Wong et al (1975). The important thing is the pulse

(i.e. perfusion pressure), which is generally maintained, even though there is often some drop in both systolic and distolic pressures. Thus, if the pulse is easily palpable and less than a hundred per minute and the patient is comfortable, the slight hypotension can be ignored.

Transient tremors were seen in 10 cases. If the aspiration test is negative for blood, further injection was continued slowly, with safety.

Some mesenteric traction sensation was felt nearly in all cases of appendicectomy. Discomfort or pain was only felt when there had been undue traction on the caecum, particularly when bound down.

The upper level of block cannot as yet be predicted with certainty. Apart from volume there are so many other factors involved in the spread of anaesthetic solution (Lee and Atkinson, 1968). In general, 2 – 3 cc. will be needed to block one segment. Put in another way, 10 – 15 cc. of solution will be needed to block four segments on each side of the point of injection (Lee and Atkinson, 1968). The rationale of using 20 cc. of solution is to block about six segments above L2, i.e. T9. Roughly, this is true in this series: in all cases the epigastric skin sensation had remained normal (and the mesenteric traction sensation tended to confirm this) implying that the upper level was somewhere between T7 and T10. The lower level invariably went down to S1, as in all cases the legs were completely paralysed toward the end of operation. This suggests that downward spread of epidural solution is favoured.

For procedures of up to $1\frac{1}{2}$ hours, plain Lignocaine 2% or Prilocaine 2% had been found adequate. The solutions with 1 in 200,00 Noradrenaline were used for longer procedures, or when the 20 cc. limit was likely to be exceeded to ensure a high enough block, e.g. tall persons. Probably the 1.5% solution of Lignocaine or Prilocaine as recommended by Boulton (1968) and Lee (1968) would be better, as greater volume can be used. Unfortunately, this strength is not available in the Malaysian market and dilution of the 2% solution could compromise sterility. The long acting Marcaine 0.5% had not been used for the relatively short operations reported in this series.

Conclusion

Lumbar epidural anaesthesia has been found to be effective and safe for a wide range of lower abdominal operations in a solo surgical practice. With careful attention to details regarding the selection of patients and the actual technique if needle puncture and injection, it is relatively free from serious side-effects. Until specialist anaesthetic services become freely available in the whole of Malaysia, I would recommend that epidural anaesthetic techniques, both lumbar and caudal, be included in the post-graduate curriculum for all surgical aspirants.

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Granuloma of The Larynx Following Intubation

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Introduction:

ENDOTRACHEAL INTUBATION has been known to produce various local complications, one of which is post-intubation granuloma, first described by Clausen in 1932. Howland and Lewis (1956) estimated it occurred once in every 800 to 1,000 cases of intubation. Although endotracheal intubation has become a commonly used method of establishing and insuring an effective airway since its introduction into anaesthesia by Elsberg in 1910, a review of the literature showed only few reports of post-intubation granuloma. Many cases might be missed unless specific questions are asked and the larynx examined post-operatively.

Case One:

O.L.S., a 34 years old Chinese housewife was first seen in May 1975 with a complaint of a low pitched hoarse voice since she had a General Anaesthesia for Caesarean Section $2\frac{1}{2}$ months earlier. She was unable to sing.

The only significant abnormality found on indirect laryngoscopy was a small granulation tissue seen on the anterior 1/3 of her left true vocal cord. On direct laryngoscopy and removal, it measured 0.2 cm x 0.5 cm x 0.3 cm and histological examination confirmed the finding of granulation tissue. Her voice has become normal since the removal.

Case Two:

B.A.M., a 38 years old English housewife, was referred to the ENT clinic on May 1975. She complained of hoarseness after vomiting with migraine 4 weeks earlier. She has regained her usual voice during the visit. Upon specific questioning, she admitted she has a slight change in her voice since she had a General Anaesthesia for hysterectomy 3 years ago, but she did not pay much attention to it.

On indirect laryngoscopy, a typical laryngeal granuloma was seen on the posterior aspect of her left true vocal cord, it was sessile and arose from the vocal process of the left aryteroid. Upon removal, it measured 1 cm x 0.4 cm x 0.4 cm and proved to be granulatous tissue on histological examination. Her voice has improved since the removal.

Discussion:

The significant of duration of the tube in the larynx seems to have been over-rated in the production of post-intubation granuloma. Wylie (1950) reported a case of post-intubation granuloma, discovered 3 weeks after tonsillectomy (a 15 minutes operation). Bergstrom (1964) described 3 cases of post-intubation granuloma of considerable variations in the duration of intubation (1 hour to 39 hours). He had earlier reported an incidence of one in 176 cases of prolonged intubation (Bergstrom, 1962). He considered epithelial scrapping of the vocal cord during intubation to be the principal reason for formation of granuloma. The period of intubation varied from $\frac{1}{2}$ to 4 hours in our cases.

Both our cases are females; post-intubation granulomas are known to occur more common in female than in male. Howland and Lewis (1956) reported a ratio of 7 to 1 in favour of female. They

attributed the higher incidence in female to smaller larynx and mucosa of true cord to be approximately half as thick as in male.

Classically post intubation granulomas are invariably found on the vocal process of the arytenoids (Epstein and Winston, 1957). However, in the 50 cases reported by Howland and Lewis (1956) 3 were found to be on anterior 1/3 of the true vocal cord, 10 middle 1/3 and 37 vocal process of the arytenoids. Our case one of granuloma in the anterior 1/3 of the cord, tends to support Howland and Lewis' results.

Although the incidence of post-intubation granulomas is low, patient with laryngeal symptoms following intubation should be examined by laryngologist to establish its diagnosis. Case two was diagnosed 3 years after intubation. Early treatment with voice test and anti-biotics may favour regression of granuloma (Bergstrom, 1964). However, the main treatment is by careful removal and histological examination to exclude malignancy.

Summary:

(1) Two cases of post-intubation granulomas are described.

(2) Short duration of intubation may cause granuloma, in contrast to the popular belief that it recurs only in prolonged intubation.

(3) Post-intubation granulomas occur more commonly in females.

(4) Post-intubation granulomas may be found at any site of the true vocal cord, though it is commonest at the vocal process of the arytenoid cartilage.

(5) Patient with laryngeal symptom after intubation should be seen early to establish diagnosis and treatment.

Acknowledgement:

Acknowledgement is made to Miss A. M. Tan for her secretarial assistance.

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Removal of Blunt Oesophageal Foreign Bodies from Children Using a Foley Catheter.

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P.A. and Lateral Chest X-rays are taken to confirm the diagnosis that the blunt foreign body (in our case Fig. 1 a 20 cent coin swallowed by a 6 year old Malay girl on 9.7. 75) is in the oesophagus.

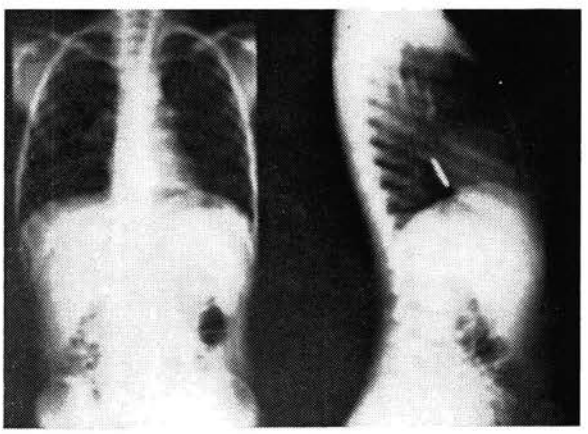

Fig. 1
Chest X-ray. Coin at lower end of oesophagus.

Method.

After preliminary sedation (not always necessary), the child was placed in the lateral decubitus (or oblique) position with the foot of the x-ray table slightly elevated to prevent aspiration of foreign body, or oesophageal or gastric contents. A sucker and emergency trolley with laryngoscope, endotracheal tube etc., were kept available.

The Foley Catheter was passed through mouth (or nose) into the oesophagus. A few ml. of Urografin 60 were injected into the catheter to assist fluoroscopic positioning and when the catheter was distal to the foreign body, the balloon was inflated.

The oesophageal lumen thus enlarges and the foreign body dislodges to rest on the inflated balloon and thus reduces the risk of perforation. The foreign body is pulled ahead of inflated balloon and removed from the mouth – see Fig. 2.

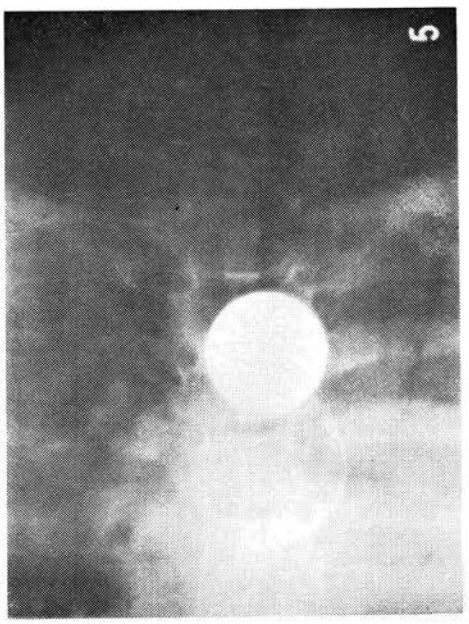

Fig. 2
Demonstration of removal with inflated balloon of Foley Catheter below coin.

If the nasal route is used, the balloon has to be deflated before removal. If the balloon slips past the foreign body, the procedure is repeated.

Discussion.

Oesophagoscopy has been the usual method of removal of foreign bodies and still has to be used for sharp foreign bodies and probably if the period after ingestion is greater than 48 hours. However, there is the hazard of general anaesthesia, hospitalisation, and a small risk of oesophageal perforation.

This technique of using a Foley Catheter is simple, safe and successful if there is no history of *underlying oesophageal disease*. If this is suspected when foreign body impaction is not at the points of physiological narrowing (thoracic inlet, aortic arch, left main bronchus, or oesophagogastric junction) a Dianosil swallow (precaution against aspiration) should be done. A dionosil swallow also localises and stains non-opaque foreign bodies for removal.

Acknowledgements.

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Brufen in Conditions Allied to, but Excluding Rheumatoid Arthritis and Osteoarthrosis – Open Study

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A CLINICAL TRIAL OF Brufen (ibuprofen-2-(4-iso-butyl phenyl) propionic acid) in conditions allied to, but excluding Rheumatoid Arthritis and Osteoarthrosis was undertaken at the Orthopaedic Department, University Hospital, during the period from January 1974 to October 1974. The patients attended the above department on an outpatient basis during this period. Those with proven rheumatoid arthritis were excluded, but all other allied conditions of joints and periarticular tissues where anti-rheumatic therapy was indicated were included in the trial.

Method

A group of fifteen patients were selected from those attending the outpatient department with recent complaints and mostly untreated by any effective anti-rheumatic therapy. The study was at first conducted by a Double-blind Cross-over technique using placebo capsules supplied by Boots Research Department. The technique involved giving the drug Ibuprofen 1200 milligrams in three divided doses daily for the first two weeks and a Placebo over the next two weeks in a group of patients, and then reversing the procedure in the same group of patients. After three months of this technique, the trial was changed in favour of Open study in a similar group of patients. Brufen capsules were administered orally. The treatment period in any one patient lasted from two weeks to two months, and in one patient for three months. The duration of treatment was dictated by the clinical response in a given patient.

The conditions treated were varied, but a common factor of pain in and around joints were chosen, and investigations that were carried out included Haemoglobin estimation, total and differential white cell count, erythrocyte sedimentation rate, serum uric acid, blood urea, faecal occult blood, and a complete urinalysis including glucose, and protein, cells and casts. Serum rheumatoid factor was tested by the Rose Waaler and Latex adhesion methods. The patients had a complete physical examination, including fundoscopic examination of the eyes. A pretreatment assessment of pain was made by the patients' subjectively into the following categories: very severe, severe, moderate, and slight. (The Practitioner)[1] Objective assessment included articular or periarticular swelling, tenderness, range of movements of the affected or neighbouring joints.

Brufen was initially given in doses of 200 milligrams, four times a day, but later the dose was increased to 400 milligrams three times a day, this being found to be the optimal dose for clinical effect. Follow-up of the patient was done at two-weekly intervals, up to two months for the purpose of the trial initially. Later on the trial period was extended to three months; the first month being the period of double-blind cross-over technique and the next two months being the period of open study. All the patients in the trial were re-examined after an interval of six-months from the end of the trial period to find out if they were taking any Brufen or other pain-relieving drugs, whether there was any re-currence of the original conditions and to record their subjective impression about the drug given to them. The patients did not keep any record of the pain, but were thoroughly questioned at each two-week period. It was felt that daily record keeping would subjectively make the patient too self-critical.

Pain is to some extent is a personal experience and a daily reminder was not considered proper. However, for subjective assessment of pain, the following criteria was offered to the patient (The Practitioner)[1]:–

Very severe:	Continuous severe pain, requiring pain-relieving drugs continuously.
Severe:	Pain present continuously, with periods of reduced intensity, but requiring continuous use of pain-relieving drugs.
Moderate:	Bouts of pain, bearable, but interfering with daily activity, and requiring pain-relieving drugs.
Mild:	Pain, which is not constant and bearable requiring only occasional use of pain-relieving drugs.
No pain:	Complete relief of pain, for an interval of six weeks after stoppage of drugs.

The objective assessment of pain was done by doctor and patients, as follows: Much better, Better, No Change, Worse and Much Worse. In addition clinical assessment of part affected in terms of tenderness, range of movement and inflammation was made at each visit. Laboratory investigations were repeated after an interval of one month to six weeks. Any additional therapy, during this period such as anti-rheumatic drugs and physiotherapy was also noted. Opthalmological examination was also repeated.

Results

The patient characteristics is given in Table I. The diagnoses is summarised in Table II. This included conditions like peri-arthritis of the shoulder, non-specific synovitis of the knee, non-specific articular pain in the hands including the thumb, Tennis elbow, and Cervical spondylosis and Poly-arthralgia with negative rheumatoid factor. The subjective assessment of pain by the patients, both before and after treatment is given in Table III. All the patients were objectively assessed by one doctor (author) and the results are given in Table IV. It will be seen from Table III that four patients were still in pain after six weeks, though mild, but three out of these were satisfied with daily Brufen of 800 milligrams in four divided doses. The doctor's grading of patients' pain as seen in Table IV compares well with that of the patients', especially in the severe and very severe grades, indicating thereby the milder nature of the drug in question. The side-effects were noticeably absent, except in two patients; patient number 2 complained of increased thirst and patient number II complained of an uneasy feeling in the 'stomach'. Blood sugar estimation in the former was within normal limits and occult faecal blood tested in the latter was negative. These two patients continued to tae the drug, after reassurance.

Discussion

The purpose of the study was to assess the efficiency of Brufen (Ibuprofen) in terms of degree and duration of analgesic activity; anti-inflammatory effects and to ascertain the nature and incidence of adverse reactions in conditions allied to but excluding rheumatoid arthritis and osteo-arthrosis. Strict selection of patients, resulted in a total of only fifteen patients who could be given the drug with the certainty that they will take it regularly for the prescribed time. In view of this, the small number was not felt to invalidate the results obtained. In addition these patients attended the trial on an outpatient basis intentionally, in order to remove any "ameliorative effects that a hospital admission may produce". (Mills et al 1971)[2].

There is an immense amount of western literature reporting on clinical trials conducted with Ibuprofen, since 1967, but very little from this country itself. Its efficacy has been compared with other anti-rheumatic drugs like aspirin (Chalmers 1969)[4], (Jasani et al, 1967)[5], (J.B. Dick-Smith 1969)[9], indomethasin (Shridhar D. Deodhar et al, 1973)[7], phenyl-butazone (Cardoe N. 1969)[3], (Pavelka K. et al 1973)[8], Butacote (Regaldo R.G. and Fowler P.D. 1974)[6], Prednisolone (Shridhar D. Deodhar et al 1973)[7], and Ketoprofen (Sarah B. Mills 1973)[10], in the treatment of rheumatoid and non-rheumatoid conditions. The opinions stated are at best still controversial and inconclusive. That Ibuprofen does possess anti-inflammatory effects, there does not seem to be any doubt (Dick-Smith J.B. 1969)[9], but its pain relieving effects in conditions studied here is not very un-equivocally stated. Hence the justification for our trial, of the drug.

During the course of this trial, it was found that the objective assessment of anti-inflammatory response was not satisfactory. Grip-strength, joint tenderness and joint swelling were measured in all the patients where relevant. There was no dramatic alteration in these clinical features and it was felt that a subjective element of patient responsiveness is involved, especially in the former two signs. Although clinical indices of joint tenderness, joint 'dolorimeters', measurement of digital joint size, hand grip and various composite laboratory indices

Table I

Patient Characteristics

No.	Name	Age	Sex	Race	Diagnosis	Duration of Complaint	Previous Treatment
1)	L.L.P.	31 yrs.	M	Ch.	Articular pain in both hands, nausea on taking Indocid capsules.	three months	Indocid 25 mg three thrice daily.
2)	N.P.	50 yrs.	F	Ind.	Articular pain left thumb. metacarpo-phalangeal and inter-phalangeal joints.	four months	Paracetamol irregularly.
3)	R.A.	35 yrs.	M	Ind.	Traumatic synovitis right knee.	one month	Knee bandage and aspiration of the joint.
4)	C.C.K.	52 yrs.	M	Ch.	Right Tennis elbow and polyarthralgia.	one month	Physiotherapy only.
5)	J.L.	26 yrs.	F	Ind.	Non-specific synovitis both knees.	two years	Intra-articular Hydrocortisone.
6)	S.L.	47 yrs.	F	Ind.	Cervical spondylosis.	three months. previous episode four years ago.	Physiotherapy.
7)	J.L.	33 yrs.	F	Ind.	Cervical spondylosis.	two months	Paracetamol irregularly.
8)	J.J.	36 yrs.	F	Ind.	Cervical spondylosis.	four months	Intermitant neck traction.
9)	T.S.	26 yrs.	M	Ch.	Polyarthritis with negative rheumatic factor.	one month	– Nil –
10)	A.G.	55 yrs.	M	Ind.	Periarthritis right shoulder.	three months	Physiotherapy only.
11)	M.A.	20 yrs.	F	Ind.	Articular pain in both hands, rheumatic factor negative.	four months	Paracetamol irregularly.
12)	M.T.	40 yrs.	F	Ind.	Non-specific synovitis both knees.	two months	No treatment.
13)	S.B.	54 yrs.	F	Ind.	Periarthritis right shoulder; diabetic. post-mastectomy right side for Ca. Breast three years ago. X'Rays R. Shoulder negative.	six months	Physiotherapy, Paracetamol irregularly.
14)	A.P.	55 yrs.	F	Ind.	Polyarthritis with negative rheumatoid factor; pain both heels; Obese.	one year	Physiotherapy; one course of Butazolidine six months earlier caused anaemia.
15)	T.S.K.	18 yrs.	F	Ch.	Polyarthritis with negative rheumatoid factor; severe low-back pain.	three months	Bed-rest; aspirin Hospitalised for three months.

Ind.: Indian
Ch. : Chinese

have all proven useful in assessing new anti-inflammatory and anti-rheumatic drugs, none has proved superior to simple demonstration of pain-relief. (Shridhar D. Deodhar and Carson Dick W. et al 1973)[7]. A satisfactory assessment of pain-relief could be made in all our patients and this is the index used in this study. Additional treatment in the form of short-wave diathermy, wax baths and active assisted movements were given where indicated, as physiotherapeutic measures.

One of the problems faced during the period of double-blind cross-over technique was that, many patients had recurrence of pain while on placebo and declined the offer of further supply of medicines. Once a patient's confidence in the

Table II

Diagnosis	Number of Patients
Articular pain in Hand including metacarpo-phalangeal joint of Thumb.	3
Tennis elbow with polyarthralgia.	1
Periarthritis shoulder.	2
Cervical Spondylosis.	3
Polyarthritis without rheumatoid factor.	3
Non-specific synovitis of the Knee.	3
TOTAL	15

Table III

Patients' assessment of pain before treatment and after treatment

Grade of Pain	Before Treatment	At Four Weeks	At Six Weeks
Very severe	3 patients	3 patients	1 patient
Severe	3 patients	3 patients	2 patients
Moderate	9 patients	2 patients	2 patients
Slight	—	—	3 patients
TOTAL	15 patients	8 patients	8 patients

Three patients at the end of three months still had slight pain; but were satisfied with daily Brufen of One Tablet (200 milligram per tablet) four times a day.

Table IV

Doctor's assessment of patients' pain taking into consideration the findings on clinical examination and interrogation

Grade of Pain	Before Treatment	At Four Weeks	At Six Weeks
Very severe	3 patients	2 patients	1 patient
Severe	3 patients	2 patients	1 patient
Moderate	6 patients	2 patients	—
Slight	3 patients	—	—
TOTAL	15 patients	6 patients	2 patients

At the end of six weeks two patients in the very severe and severe categories still had slight pain, and were on a maintenance dose of Brufen one tablet (200 milligrams) four times a day.

efficacy of a drug was shaken, it is never easily restored. This was the reason for the abandonment of the double-blind cross-over technique and institution of an Open Study. With respect to the dosage of Brufen, initially an attempt was made to co-relate pain relief with the amount of drug. The optimal clinical effect was obtained between dosages of 1200 milligrams to 1600 milligrams of Brufen, in four divided doses daily.

The main value of the drug Ibuprofen, was observed to be good relief of 'moderate' pain. Patients with 'severe' pain did not get a satisfactory response. In these patients additional treatment with another analgesic drug was required, in full dosage. Once the severity was lessened, Brufen reduced further pain. The time at which optimal effect of the drug began to be noticed was about two weeks, reaching full effect of pain relief in three weeks. In those, who still had pain, exhibition of the drug produced an effect up to six weeks, after which the drug had to be discontinued. Curiously, after an interval of two weeks, when Brufen is again taken, pain relief was better. Other than a subjective phenomenon it is difficult to explain this feature. The best feature of this drug is in respect of side-effects, which are virtually negligible. In this series, one patient complained of increased thirst and another complained of an uneasy abdominal sensation. Blood sugar in the former was normal and faecal blood in the latter negative. Several previous workers with this drug have similarly commented upon the side-effects, but tended to question the therapeutic efficiency. (Owen-Smith and Burry, 1972)[11]. It is interesting to note, that long after the trial has ended, we still get some patients requesting "those tablets you used to give before"!

Summary

In conclusion, it is felt that, despite a plethora of anti-rheumatic drugs available, some of which are undoubtedly effective, Ibuprofen is a valuable, pain-relieving drug in moderately painful non-rheumatoid articular and periarticular conditions. The optimal dose appears to be 1200 milligrams in four divided doses daily and satisfactory clinical response takes at least two weeks. The complete absence of side-effects makes this the drug of choice in long-term therapy.

Acknowledgements

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colleague Dr. S. Sengupta, in the Department who referred some of his patients to me for inclusion in this trial.

The Research Division of The Boots Company Ltd., provided the Brufen tablets and Placebo, as well as the format of the trial protocol.

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T3 Toxicosis – a case report

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Introduction

TRIIODOTHYRONINE (T3) THYROTOXICOSIS has been accepted as a distinct variant of thyrotoxicosis in adults since it was first documented by Hollander et al in 1971. Patients with Graves disease, autonomous hyperfunctioning adenomas, or multinodular toxic goiter may present with hypertriiodothyronemia without elevation of serum thyroxine (T4) levels. Although serum thyroxine levels are normally 50 times higher than serum triiodothyronine (T3) the latter is 3 to 4 times as potent biologically with a free T3 fraction 1/7 that of free T4. T3 has a direct biological action independant of T4. A compensatory elevation of T3 may occur in subclinical hypothyroidism (Evered 1973), endemic goiter (Kochipillai 1973) and Pendreds syndrome (Gomez-pan 1974). High T3 levels in the presence of a normal T4 may occur as a precursor of relapse of hyperthyroidism (Hollander 1971), in opthalmic Graves disease (Ormston 1973) and in autonomous thyroid nodules (Evered 1973). The criteria for the diagnosis of so called T3 toxicosis are (1) clinical hyperthyroidism. (2) normal serum total T4. (3) normal free T4. (4) normal or increased radioactive iodine uptake which cannot be suppressed by adequate doses of T3. (5) increased total T3. (6) normal TBG.

Case report

The patient, a housewife (Z bte A.R.) was first seen in Hospital Daerah Kuala Pilah on 19.9.1973 with a history of chest pain on the left side more on breathing. However this history was changed to that of left loin pain while patient was in the ward and the patient was diagnosed on discharge as urinary tract infection and later readmitted for I.V.P. The I.V.P. was normal. The E.C.G. on 19.9.1973 showed a sinus tachycardia of about 100/minute. Chest X'Ray was normal.

On 12.6.1974 she was readmitted with right sided chest pain and she was diagnosed as bronchitis on discharge. Chest x-ray was normal but the E.C.G. still recorded a tachycardia of 100/minute.

She was admitted again on 9.9.1974 again complaining of chest pain and a pericardial rub was heard at this stage. E.C.G. on 11.9.1974 showed a trial fibrillation with a rapid ventricular response but no evidence of pericarditis is seen. Chest x-ray showed an enlarged heart. She was given digoxin and Eraldin (practolol) and Lasix. On discharge she had sinus rhythmn but the rate was still 100/minute.

She was seen by one of us (N.T.S.) on 31.5.1975. This time she again had left sided chest pain. On further questioning she admitted that she felt palpitations in the left side of the chest off and on and this gives her a distinct discomfort but there was no relation to exertion. Direct questions showed that she had weakness in the girdle muscles; had normal bowel habits and felt warm most of the time. She did not feel cold in the early hours of the morning. She had a normal appetite and did not lose weight recently. Clinical examination revealed a thin lady in no obvious distress but with difficulty in getting up from the squatting position. There were no eye signs of thyrotoxicosis. The thyroid was clinically enlarged but there was no bruit. The hands showed only minimal tremor

and was warm and wet. The resting pulse was 100/minute regular with BP 150/90. The heart was not enlarged but there was a soft systolic ejection murmur at the left sternal edge. E.C.G. again showed a sinus tachycardia of 100/minute. A tentative diagnosis of thyrotoxicosis was made. The sleeping pulse was 80/minute, and on reviewing the history the inescapable facts emerged that here was a woman of 50 with a tachycardia and an enlarged thyroid gland and has been complaining of palpitation for almost two years; a study of the thyroid function was clearly indicated.

20 Microcuries of I^{131} was given orally for uptake on 30.7.1975.
4 hour uptake 60%
24 hour retention 78%
T3 – RU 88%
T4 – ETR 1.03
Serum T4 level 11.3 Ug %
Raised uptake & retention; normal RU, ETR, & T4
Scan – slightly enlarged thyroid gland
Comment – Enthyroid
However radioimmunoassay of T3 was done and the level of T3 was 4.8 nanogram/ml. and a diagnosis of T3 toxicosis was made.

The patient was treated with carbimazole and after two months she was clinically much improved and a repeat T3 value was 2.6ng/ml.

Discussion

The mean value of serum T3 measured by radioimmunoassay in normal subjects has been reported as being between 1 and 2 ng/ml the actual value depending on the particular laboratory. The T3 estimation was done using an RIA kit from Radiochemical centre, Amersham.

	Normal values	Patient on 30/7/75
Total serum T4 (mcg %)	4 – 12 mcg%	11.3 mcg%
UTBG index (%)	75 – 112%	88%
Effective Thyroxine Ratio	0.82 – 1.16	1.03
Free Thyroxine Index	5.3 – 12.5	12.5
Serum Triiodothyronine (ng/ml)		
(female non pregnant)	0.66 – 1.86 ng/ml	4.8 ng/ml.
Ratio of T4:T3	70:1	23:1

Table 1

Summary of in vitrio thyroid levels in normals and patient

Hypertriiodothyroniemia may be a premonitary manifestation of thyrotoxicosis (Hollander 1971). However in this lady the symptoms of thyrotoxicosis could be noted from September 1973 almost 2 years before the diagnosis was made. The predominant cardiac presentation of this patient with hardly any other features of thyrotoxicosis is noteworthy. A pericardial rub was heard and this is due to a scratching systolic sound along the left sternal border which is often mistaken for a rub in cases of thyrotoxicosis. There was no other evidence of a pericarditis. Eye signs were significantly absent in this case although there is some evidence for a correlation between triiodothyronine (T3) and eye involvement. All the criteria for T3 toxicosis namely clinical hyperthyroidism, normal total T4, normal free T4, increased radiactive iodine uptake, increased total T3 and normal UTBG are fullfilled. The serum T3 concentration is usually increased in all cases of thyrotoxicosis but in T3 toxicosis the magnitude of this discrepancy is greatly exaggerated. The elevated serum T3 possibily arises not from peripheral conversion of T4 to T3 but from the predominant hypersecretion of T3 relative to T4. In support of this view is the finding that hyperfunctioning thyroid nodules a relatively common cause of T3 toxicosis frequently contain an abnormally high T3: T4 ratio in their thyroglobulin.

The presence of T3 toxicosis is common in patients after 131 I therapy and surgery. In the case described there was no prior therapy of relevance. T3 toxicosis among hyperthyroid patients in New York was reported as 4% (Hollander, 1972) and a similar figure was reported from Canada (Tremblay, 1972). In this area T3 toxicosis was reported as a rarity in Singapore (Tan BY er al., 1975) and most of their cases were those with relapse following 1311 therapy or surgery. In Kuala Lumpur at the department of Nuclear Medicine at least 3 cases have been seen in a survey of over 200 cases of thyrotoxicosis examined. However hypertriiodothyronemia in association with normal or reduced T4 levels appear to be extremely common after 131^{I} therapy for thyrotoxicosis (Mahadev et al., 1975).

With more widespread availability of RIA T3 estimation more exact information on the incidence of T3 toxicosis in this area will be available soon but current evidence suggests an incidence of 1% or less. It is well known that elevated T3 levels may precede the development of over† hyperthyroidism and elevation of T4 values. It is likely that patients are examined at a more late stage of their disease here than in more advanced countries accounting for the relative rarity of T3 toxicosis. The incidence of T3 toxicosis appears to be also correlated with dietary iodine. Thus a high inci-

dence of 12.5% was reported from an iodine deficient area in Chile (Hollander, 1972). The low apparent incidence of T3 toxicosis in this area may well be a consequence of high dietary iodine.

Summary and comments

This is a report of a 50 year old housewife who had a number of admissions for palpitations and one episode of paroxysmal atrial fibrillation for which a cause was not looked for but when thyroid enlargement was noted the pieces fell in place. It is seen that T3 toxicosis in middle life also gives rise to symptoms referable to the heart. T3 toxicosis is perhaps a rare form of thyrotoxicosis in this area but it has to be kept in mind in all cases with clinical features of thyrotoxicosis and normal T4 values.

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Mass Rearing of Mites Collected from House-Dust Samples

*by Vijayamma Thomas** *Tan Bock Hay***
*and Yap Pak Leng**

Introduction

HOUSE-DUST MITES have been recognised as an important source of allergen from the beginning of this century (Storm Van Leeuwen, *et al* 1925). Among the several mites present in house-dust samples, the "European" house-dust mite *Dermatophagoides pteronyssinus* which has world-wide distribution (Spieksma and Spieksma-Boezeman, 1967), was found to be the most important allergen (Voorhorst *et al*, 1967). A significant correlation between "North American" house-dust mite *D. farinae* and human hypersensitivity to house-dust was found by Larson *et al* (1969). Miyamoto *et al* (1970) found that house-dust was one of the most important causative antigens in bronchial asthma and allergic rhinitis in Japan. They found very close co-relation between house-dust extracts and house-dust mite extracts in skin tests (1968). Nayar *et al* (1974) found that these two species play a significant role in the etiopathogenesis of bronchial asthma in India. Pepys *et al* (1968) found a good co-relation between a history of house-dust allergy, prick tests and inhalation test reactions to an extract of a culture of *D. culinae* in asthmatic subjects. They found that most of the patients reacting to *D. culinae* reacted at a weaker level to extracts of cultures of *G. domesticus* as well as *A. siro*.

Although bronchial asthma and allergy to house-dusts are quite common among Malaysians, no work has been done so far to study the mites present in house-dust. This work was therefore undertaken to determine the common species of mites present in the dusts collected from houses of patients who suffer from bronchial asthma and nasal allergy.

In a study of this nature, the most important prerequisite is to have a technique to rear the mites in large numbers and harvest them with ease so as to be able to prepare sufficient quantities of extracts for skin tests. The paper lists various species of dust-mites isolated and a technique for mass-rearing and harvesting mites isolated from the dust samples collected from patients' houses.

Collection of House-dust Samples

A total of 98 samples of house-dust were collected from houses of patients who live in Petaling Jaya and who have complained of nasal allergy or bronchial asthma. These dust samples were collected from mattresses and furniture and were sent within 24 hours of collection to the Department of Parasitology, Faculty of Medicine.

Two amounts of about 0.2 gms. each of fine dust were examined upon receipt of the samples. The remainder of the samples were placed in plastic tubes with screw caps and were coded. These were provided with a pinch of sterile food consisting of a mixture of well ground farex and dried ox liver in the ratio of 1: 1. These were then incubated from 2 weeks to 4 weeks at room temperature (27° – 28°C) with relative humidity of 75 percent. After incubation, two other samples of about 0.2 gm. each were again examined. Those samples in which no mites were noticed were considered as negative.

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Live mites were easily detected in dust samples examined under a low-power binocular microscope. Individual mites were removed with fine moistured camel hair brush and identified.

Mite Fauna

Of the 98 samples examined, 92 samples had one or more species of mites. The number of mites in 1 gm. of dust varied from 1 to 65. The following mites were identified:

1. *Glycyphagus geniculatus* (Vitzthum)
2. *Glycyphagus spp.*
3. *Tyrophagus putrescentiae* (Schrank)
4. *Blomia* sp.
5. *Suidasia medanensis* (Oudemans)
6. *Dermatophagoides pteronyssinus* (Trouessart)

In addition to these, there were a few other mites which were not identified. Of these, in addition to *Dermatophagoides* spp. *Glycephagus* spp. and *Tyrophagus* spp. have been found to provoke allergic reactions in patients by Maunsel, *et al* (1968) and Pepys *et al* (1968).

Culture Procedures

Cultures of *Dermatophagoides pteronyssinus, Glycyphagus* spp. and of *Tyrophagus* sp. were maintained in the laboratory.

It took about 3 to 5 months to establish stock cultures from positive dust samples and to produce large numbers. For this, about 150 to 250 mites were picked up with fine camel hair brush from the original samples. These were then introduced into clean tall plastic cups provided with 10 gms of sterile mite food consisting of a mixture of ground farex and dried ox liver in the proportion of 1: 1. The plastic cups were then closed and were kept in large jars at room temperature at a relative humidity of 80 per cent.

These cultures were then left undisturbed. After 3 to 4 weeks, these were examined. By this time, healthy cultures showed increase in the number of mites. These cultures were then left without any further addition of food. After 3 – 5 months, when mites increased gradually in numbers and the food became scarce, many active mites crawled up the sides of the plastic container. As the movement started, the lid of the plastic container was unscrewed and left loose on the cup and the container was left on water in enamel dishes. From the rim of the rearing jars the mites moved down along the outer surface (Plate I) and fell into the water. Within 2 or 3 days, very large numbers of mites fell into the water and these were collected using a fine muslin strainer. These harvested mites were used for subcultures.

Plate I.
Large numbers of mites that crawled out of the rearing cups and fell on to the water in which the rearing cups were placed.

It was noticed that under identical rearing conditions and food supply *Tyrophagus* sp. produced the most prolific and healthy cultures followed by *Glyceyphagus* spp. *D. pteronyssinus* took a longer period of time to establish in cultures and the multiplication was not very prolific.

Due to certain technical difficulties extracts of these mites were not taken for skin tests.

Discussion

Mites of the genus *Dermatophagoides* have been shown to be the main source of house-dust allergen by various investigators (Voorhorst *et al* 1967, Maunsel *et al* 1968, Larson *et al* 1969).

However, Maunsel *et al* (1968) found that extracts of other species like *Glycephagus* spp., *Tyrophagus* spp. and *Acarus siro* also provoked a lesser response. Pepys *et al* (1968) found that extracts of cultures of *A. siro* and *G. domesticus* gave reactions in patients. Miyamoto *et al* (1970) showed that from among a total of 36 species of mites which he isolated from house-dusts, no single mite was particularly related to the results of the skin tests. They came to the conclusion that the allergenicity of house-dust was largely determined by the total number of mites contained in the dust rather than by the presence of any single species. They ascribed this phenomenon to the complexity of house-dust mites and the several common antigens which these mites have.

In any future work in Malaysia on house-dust allergy, the allergenic potency of various mites present in the house-dust samples must be studied. An easy technique of mass production of various mites therefore would be of great advantages to any one who intends to work on it.

Acknowledgements

The authors wish to express their thanks to Dr. D. Macfarlane, Acarologist, Commonwealth Institute of Entomology, British Museum (Natural History), England for identifying the mites in the house-dust samples.

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Book Reviews

CLINICAL TESTS BY OESOPHAGEAL FUNCTION by Richard Earlam, *Crosby Lockwood Staples, Lond.* **1976. p.p. 383. 131 figs. £12.00 net.**

THIS IS one of a series of books, the purpose of which is to provide the clinical worker with a background knowledge of the principles behind functional tests in use and an explanation of the useful data to be derived from the tests.

The text incorporates all that is new and useful in analysing the patient with oesophageal disease. It will be of interest not only to surgeons but also to gastro-enterologists and students and should benefit most those patients who are unfortunately disabled by one or more of the debilitating symptoms due to inability to swallow properly.

RADIOTHERAPY IN MODERN CLINICAL PRACTICE. Edited by H.F. Hope-Stone, *Crosby Lockwood Staples, Lond.* **1976. p.p. 358. £10.00 net.**

ELEVEN AUTHORITIES who are active in the field have combined to highlight some of the advances that have been made in the past decade in the treatment of malignant disease by irradiation. This is a subject of growing importance in the practice of medicine today, and it will continue to be so in the future, with increasing incidence of neoplastic disease.

The book stresses the importance of collaboration with physicians and surgeons so that the best form of treatment of each patient can be formulated. The book indicates which patients should be referred to a radiotherapist for active treatment and points out at what stage of various diseases such referrals should be made.

The book should be of great assistance to physicians, surgeons and medical officers.

Error Correction

RE : HOMOCYSTINURIA - A CASE REPORT

Med. J. Malaysia Vol. XXX No. 3 March, 1976 pg. 216

In Figure 9, the numbering should have been from left to right on the photograph, ie 8 should have been 1 and 1 should have been 8.

Index to Vol. XXX - June 1976

SUBJECTS

AUTHORS

Recent Publications of W.H.O.

The following recent publications of WHO are available at the office of WHO Representative, Room 1004, Fitzpatrick Building, Jalan Raja Chulan, Kuala Lumpur.

PROMOTING HEALTH IN THE HUMAN ENVIRONMENT — Geneva, World Health Organization, 1975. A Review based on the Technical Discussions held during the Twenty-seventh World Health Assembly, 1974. 69 pages – Sw.fr. 12.—

COMMUNITY WASTEWATER COLLECTION AND DISPOSAL
by D.A. Okun & G. Ponghis — Geneva, World Health Organization, 1975. 287 pages – Sw. fr. 42.—

HEALTH BY THE PEOPLE — edited by Kenneth W. Newell
Geneva, World Health Organization, 1975.
206 pages – Sw.fr. 36.—

THE WORK OF WHO 1975 — Annual Report of the Director-General to the World Health Assembly and to the United Nations. *Official Records of the World Health Organization* No. 229 – Geneva 361 pages – Sw.fr. 18.—

ALTERNATIVE APPROACHES TO MEETING BASIC HEALTH NEEDS IN DEVELOPING COUNTRIES
by V. Djukanovic & E.P. Mach — Geneva, World Health Organization, 1975. A joint UNICEF/WHO study.
116 pages – Sw.fr. 24.—

THE SCIENTIFIC BACKGROUND OF THE INTERNATIONAL SANITARY CONFERENCES 1851 – 1938
by Norman Howard-Jones — Geneva, World Health Organization, 1975.
History of International Public Health No. 1.
110 pages – Sw.fr. 12.—

EXPANSION OF THE USE OF IMMUNIZATION IN DEVELOPING COUNTRIES — Geneva, World Health Organization, 1975. *WHO Offset Publication* No. 16. 32 pages – Sw.fr. 12.—

SMOKING AND ITS EFFECTS ON HEALTH — Geneva, World Health Organization, 1975. Report of a WHO Expert Committee – *Technical Report Series* No. 568 100 pages – Sw.fr. 9.—

EVALUATION ON FAMILY PLANNING IN HEALTH SERVICES — Geneva, World Health Organization, 1975. Report of a WHO Expert Committee – *Technical Report Series* No. 569. 67 pages – Sw.fr. 7.—

VIRAL HEPATITIS — Geneva, World Health Organization, 1975. Report of a WHO Meeting – *Technical Report Series* No. 570. 51 pages – Sw.fr. 7.—

EARLY DETECTION OF HEALTH IMPAIRMENT IN OCCUPATIONAL EXPOSURE TO HEALTH HAZARDS — Geneva, World Health Organization, 1975. Report of a WHO Study Group – *Technical Report Series* No. 571. 80 pages – Sw.fr. 8.—

ADVANCES IN METHODS OF FERTILITY REGULATION — Geneva, World Health Organization, 1975. Report of a WHO Scientific Group. *Technical Report Series* No. 575. 45 pages – Sw.fr. 6.—

CONTROL OF NUTRITIONAL ANAEMIA WITH SPECIAL REFERENCE TO IRON DEFICIENCY — Geneva, World Health Organization, 1975. Report of an IAEA/USAID/WHO Joint Meeting – *Technical Report Series* No. 580. 67 pages – Sw.fr. 7.—