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Have We Conquered the Communicable Diseases?

Dr. Paul C. Y. Chen

IN THE developed countries, the bulk of communicable diseases have been controlled. As a result, the three leading causes of death in young children are accidents, congenital anomalies and malignant neoplasms, which for example accounted for 59% of all deaths in 1971 among children aged one to four years in Australia. On the other hand, the diseases in a developing country such as Malaysia are most commonly the set of communicable diseases that are faecally-transmitted or air-borne. Thus, in Malaysia, pneumonia, diarrhoeas, home accidents and diphtheria accounted for 54% of all deaths among children aged one to four years of age (Chen, 1975). The World Bank (1975) in its Health Sector Policy Paper notes that the most widespread diseases in developing countries are the faecally-transmitted diseases the most common of which are the intestinal parasitic and infectious diarrhoeal diseases including poliomyelitis, typhoid and cholera. In Malaysia the infection rates for round worm, whipworm and hookworm in rural children aged seven to twelve years of age were found by Bisseru and A. Aziz Ahmad (1970) to be 86%, 88% and 54% respectively. Such intestinal parasitic diseases are frequently chronic and debilitating rather than causes of acute illness or death. Nonetheless, they are important since infestation by 13 – 40 round worms can result in a loss of 4 gm. of protein each day (W.H.O. 1967).

Much improvement in the health of the rural people of Malaysia has been made since Independence, particularly in the field of maternal and child health. Some of the communicable diseases, such as diphtheria, have been reduced to a great extent. Thus, the incidence of diphtheria which was 28 per 100,000 population in 1959 dropped to a low of 3.7 per 100,000 population in 1972 (Fig. 1). This is partly due to the development of the maternal and child health services and partly to a change in the schedule of immunizations made available to children (Dugdale, 1969; Chen & Choong, 1971).

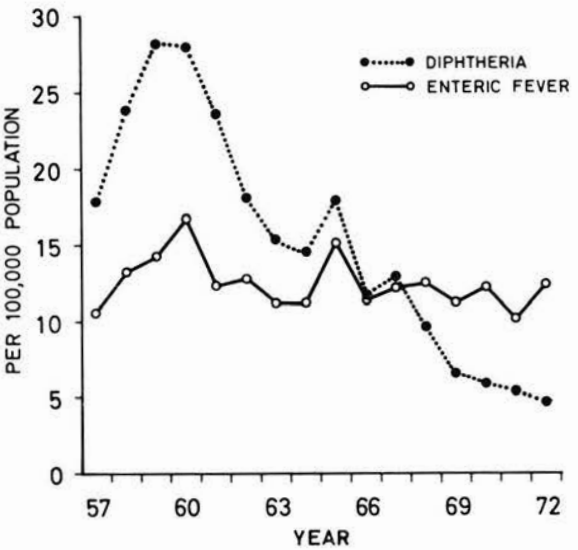

Fig. 1
Reported incidence (notifications) of diphtheria and enteric fever per 100,000 population in Peninsular Malaysia, 1957 to 1972.

However, the incidence of many of the faecally-transmitted diseases has remained unchanged. For example, the incidence of enteric fever (typhoid) has continued at a steady rate of about 12 per 100,000

population throughout the 15-year period from 1957 to 1972 (Fig. 1). This is related to the fact that faecally-transmitted diseases share a common origin – the contamination of food, water and soil with human waste. If water is not safe for drinking or is insufficient for personal hygiene and sewage disposal, diarrhoeal disease will continue to spread easily. Consequently, even though much has been achieved against some of the air-borne diseases such as diphtheria and tuberculosis, the problem of the faecally-transmitted diseases such as enteric fever, dysentery, diarrhoeas and other intestinal infections has continued to affect the people particularly the children.

The 1970 Housing Census (Malaysia, 1973) showed that 52.5% of living quarters in Peninsular Malaysia did not receive a piped water supply and that in the rural areas such quarters constituted 67.7% of rural dwellings (Table I). It also indicated that 10.4% of rural dwellings obtained their water supplies from rivers, canals and drains. In other words, it was observed that piped water was not available to the vast majority of rural living quarters which account for almost two-thirds of the living quarters in Peninsular Malaysia. In the same report it is noted that 40.3% of rural dwellings had inadequate toilet facilities, made up of 13.1% whose latrines discharged into rivers and 27.2% which had no latrines at all (Table II). These two factors combine to create the environmental situation that facilitates the spread of faecally-transmitted diseases particularly those associated with contaminated water supplies (Fig. 2).

Table I

Percentage Distribution of Water Supply by Strata and Type, Peninsular Malaysia, 1970

Strata	Piped water	Wells, pumps	Rivers	Canals, drains	Others
Metropolitan	89.6	8.9	0.2	0.3	1.0
Urban large	71.4	26.3	1.2	0.3	1.2
Urban small	61.5	34.5	1.9	0.4	1.6
Rural	32.3	54.4	8.1	2.3	2.9
Total	47.5	43.0	5.6	1.6	2.3

Source: West Malaysia Census of Housing, 1970, Final Report.

Table II

Percentage Distribution of Toilet Facilities by Strata and Type, Peninsular Malaysia, 1970

Toilet facilities	Metropolitan	Urban large	Urban small	Rural	Peninsular Malaysia
Adequate	**95.1**	**84.6**	**83.4**	**59.7**	**69.8**
Flush	52.3	28.9	16.4	10.3	18.6
Bucket	34.8	37.6	45.8	5.0	17.2
Pit	8.0	18.1	21.2	44.4	34.0
Inadequate	**4.9**	**15.4**	**16.6**	**40.3**	**30.2**
Over rivers	3.2	4.5	6.4	13.1	10.1
None	1.7	10.9	10.2	27.2	20.1

Source: West Malaysia Census of Housing, 1970, Final Report.

Fig. 2

The ecological setting against which faecally-transmitted diseases are spread. The cultural practice of using river waters, which is often contaminated, is an age-old practice that must be taken into account in the control of such diseases.

Studies in several developing countries in Latin America have indicated that health improvement results from better water supplies and sewage facilities (Van Zijl, 1966). In the Philippines improved water supply and toilet facilities reduced the incidence of cholera by 70%. Some studies, on the other hand, do not show that improved water supplies and sewage facilities result in improvements in health. This is due to the fact that the cultural practices of the people may interfere. Drinking water may continue to be stored in contaminated jars. People may continue to prefer contaminated river or well water because of greater convenience, taste or other cultural reasons (Chen, 1971). However, it has been noted that by connecting the water supply system into individual homes, not only is the water readily and conveniently available, but also it is unnecessary for water to be stored in jars – a practice that used to result in the contamination of the water and in the breeding of vectors of diseases such as the Aedes mosquito. The W.H.O. Expert Committee on Enteric Infections (1964) underlined the importance of health education in the prevention of enteric fever. It noted that the customs, beliefs and cultural practices of a people must be heeded and woven into the fabric of any preventive programmes.

Health education and efforts to change the behavioural patterns of people are difficult tasks fraught with many pitfalls. Thus the fortunately rare instances of failure do not mean that improvement in water supplies and sewage facilities are futile but merely indicate the difficulties that are likely to be encountered when attempts are made to change behaviour patterns.

The cost of providing water supplies is usually very high. However, relatively simple techniques of providing water supplies are nowadays available. Several very effective rural water supply systems have been constructed in rural Sarawak. Nonetheless, even these simple techniques are relatively costly – each gravitational water supply system to a village of about 100 homes can cost $20,000 or more. In view of the limited resources of individual states, the responsibility of providing financial and manpower resources to construct such supply systems should obviously be a federal one.

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Some Aspects of Prevention of Coronary Artery Disease*

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Introduction

LADIES & GENTLEMEN, I consider it a great honour to have been invited to deliver this lecture before such a distinguished gathering, The subject of my talk this morning is "Some aspects of prevention of coronary heart disease". As you are all aware, the whole subject of prevention is an immense one, and cannot justly be covered in 20 minutes. I shall, therefore, only highlight some of the impressions I have had over 20 years, practising cardiology.

About 10 years ago I met an old friend, a prominent cardiologist, at a conference like this, and during a discussion on the management of coronary artery disease he commented, "I fear that our therapeutic measures are more impressive than helpful to our patients. We should consider this whole problem in terms of preventive cardiology and seek to obtain the help of the paediatricians".

I recall pondering over these words at the time, because it appeared strange, coming from him, a practising physician like myself, whose philosophy and training have traditionally involved attempting the cure of a disease as and when it presented itself. Yet it was true, that though we saw hundreds of patients with the disease, and our hospital statistics were beginning to show this to be the leading cause of death and distressing morbidity, we were adopting a stereotype attitude which underscored our helplessness. Many of us did realise that there were many unsatisfactory aspects about our management, but we consoled ourselves that we were doing the best under the circumstances, and no other physician could do more.

Over the last two decades, as a result of intensive work in the Laboratories and in the field, it has become quite clear, that what we were seeing in our patients, was the end-stage of a disease process, that started many years earlier. We have come to realise that moderately advanced lesions appear to be obstinately irreversible, and cannot regress, despite the intense application of current methods of therapy. It was also clear that for every patient who developed symptoms, there were hundreds more who showed no overt clinical evidence of this dangerous disease.

Our performance record, also in terms of salvage of lives of these patients was a dismal one, in spite of rapidly improving medical and surgical capabilities, often involving the application of expensive technology in coronary care units and other areas.

Logically then, our attitudes and our emphasis had to move towards those areas in time, when control or manipulation of probable causes may be effectively applied. I hope to deal in this paper, within the time available with the question of primary prevention of atherosclerosis, by which I mean, the attempt at control of those aspects of the disease that begin early in life, and are probably responsible for the later serious coronary artery lesions in adult life. It would be impossible to provide a simplified formula, or a dognatic programme, for general application. And as I proceed,

* Guest lecture delivered at the ASEAN Congress of Cardiology in Bali on 18th October, 1975.

it may be obvious to you, that the recommendations I make, would be coloured by my own experiences and philosophy, in dealing with this problem. For I speak, not as an epidemiologist or a public health worker, but as a practising cardiologist.

First, we need to ask our pathologists if they can tell us when the initial lesion, if any, begins. To me, one of the most amazing aspects of the anatomy of the coronary blood vessels is that their location, unlike that of any other artery elsewhere in the body, causes them to undergo twisting, turning, buckling and telescoping, with every single heart beat, so many thousand times per day. I cannot think of any metal, or man-made tube, that could withstand this type of pressure for more than a reasonable length of time. There must be little tears or injuries that occur over the many years of a life time. But repair and regression does occur, in an orderly fashion. We are told by some, that atherosclerosis is a result of a possible abnormal reaction to such injuries.

In the view of most investigators, the evolution of the adult plaque starts from fatty streaks, probably in the second decade. They can reduce in size or even regress, to judge from experimental lesions. The critical time of life, for such possible regression, appears to be towards the end of the second, or perhaps, the third decade. In the presence of certain known risk factors, the critical point in the evolution of atherogenesis appears to shift into the paediatric years. Hence, all measures to control or reduce the factors that fuel the progression of such lesions, would have to take into consideration these age groups.

To me, there appears to be a strong genetic factor in the causation of coronary artery disease. In the words of Sir William Osler we inherit a 'tube', by which he means the vascular tree.

We have considered marriage guidance, for genetic reasons, for people with thalassaemia and other genetically transmitted disease – why not then, for possible risks of coronary heart disease? Perhaps in the light of modern knowledge, we should advise against intermarriage amongst families, in whom there are two or more coronary risk factors, and we should strongly discourage families, with hereditary hyperlipoproteinemias from intermarrying into similar groups.

Perhaps there is something to be said in the old fashioned practice of "arranged marriages" in this part of the world, where the background of prospective partners, both socio-economic and medical are studied by the elders of the families concerned, to see if there is "compatibility". It is common knowledge, that these family elders, scrutinise the family histories of the intending bride and bridegroom carefully, looking for diseases like diabetes, hypertension and so on. It would, thus, appear unfortunate, that as western influence erodes further into our society, this practice becomes less common.

Since the observations of the Framingham Project, much data has been extracted by so many different groups, and so many statements made, that I wonder sometimes if a state of confusion is produced not only the lay public, but also to doctors.

Briefly however, to look at these studies positively, significant contributions have been made, establishing an association between certain characteristics of individuals and environmental factors in the development of atherosclerosis. These "risk factors" have been evaluated as indicators of atherosclerosis, and the generally accepted view is that their elimination will alter the course of the disease.

A careful look at these risk factors reveals that, though much remains unknown, the etiological relationship of *elevated serum lipids, cigarette smoking, hypertension, diabetes* and *obesity* in coronary heart disease can no longer be doubted. The applicability of adult risk factors to children, at present rests on *belief,* but not on absolute proof: *belief* that life-long reduction of serum lipids and hypertension, will carry with it reduced risk of atherosclerosis: *belief* that childhood habits of *diet, exercise* and *abstinence from smoking* will carry over into adult life. Thus, primary prevention will call for the identification of a particular type of child and the young adult, at risk.

Such a search implies a more thorough form of medical examination, including attention to family history. There should be at least one medical examination of all children at primary, secondary and tertiary levels of education. This should also apply to those seeking employment. It is surprising that, although, these are usually done in most countries, nobody has given serious attention to estimation of serum lipids, the blood sugar and the serum uric acid, in these medical examinations, especially when all that is required is only one specimen of blood. The possible expense and value, in terms of cost benefit in developing countries, like ours, for any type of screening, has to be considered, but to me this is not prohibitive. These are practical, albeit, very necessary measures, if we are at all serious, in tackling the very grave problem of coronary artery disease. Biochemical and other disorders, detected at these examinations should be

treated on an individual basis. The long term effects of such therapy on the growing child cannot be known with certainty. It may also carry implications we have so far not considered, because our ideas of abnormal values in young age groups, is not well established. We must also remember that the consequences of diagnosing an abnormality, could affect career choices, employment possibilities and even insurance premiums.

Inspite of the tremendous work done, and the evidence that has been gathered, as to the role of saturated fat and cholesterol in the incidence of coronary artery disease, it is shocking to note that most nutrition programmes in our countries, advocate a diet that encourages the development of atherosclerosis. Perhaps our public health colleagues should be orientated towards current views on nutrition.

There have also been recommendations, for a general change in diet for the entire childhood population. Laboratory and field studies leave no doubt, that we could lower cholesterol and lipid levels, and control obesity, by diet alone. Such a general change in diet, as opposed to a selective change, for those with abnormal lipid levels and other metabolic abberations, is based on the belief, that at the adult level, established habit patterns are notoriously difficult, if not impossible, to change.

To me the best results are obtained, if health education on the role of an appropriate non-atherogenous diet, is aimed primarily at the mother and housewife, who has the greatest influence on the education of their children and their diets. In this connection, radio programmes boomed into the kitchen, often produce salutary effects. I hold the belief, that no serious harm can result, if we advocate for our people, a commonsense diet – i.e. a diet moderate in calories, moderate in total fats, moderate in polyunsaturates, and low in saturated fats and cholesterol. Further, I feel there is more than sufficient evidence to show, that advocacy of such a diet from infancy or early in life, will contribute to good health generally, and lower the incidence of coronary artery disease.

I have over the last 10 years or so, talked to student groups, civil servants' organisations, teachers' institutions, Rotary Clubs and so on, on the importance of a non-atherogenous diet, so much so, that in the city where I live in, particularly everyone is now on low animal fats and on moderate calories. Practically every family you ask in Kuala Lumpur will tell you, that they use corn oil or sunflower oil for cooking, instead of coconut oil, which is much cheaper, and has been for centuries the cooking oil of choice in Asia. Kuala Lumpur has become now so medically sophisticated, that patients come to my clinic and demand, an estimation of fasting lipids. In fact, estimation of fasting lipids, blood sugar and serum uric acid, has now become a routine procedure in the annual examination of all government servants over the age of 40. In addition an electrocardiograph is always included for the 40+ groups. We have also to persuade our public health colleagues not to be unduly preoccupied with infections and communicable diseases – in view of the rising incidence of coronary artery disease.

We must also realise that, in a consideration of the risk factors in the natural history of coronary artery disease, some important pieces of information are lacking. . *The first,* is what causes coronary artery disease in the 20 – 30% of patients, who during life, lack any of the major risk factors. Secondly, why is it that women who were supposed to be relatively immune during their reproductive lives are now beginning to show an increased incidence of the disease?

With regard to the first question, I recall one day telling the wife of one of my patients, that we have found none of the currently associated risk factors in her husband, who had just suffered an acute myocardial infarction. She replied, 'I told you right from the first that you would find nothing in all the tests that you have done. If you really want to know what has caused this heart attack, I will tell you'. I asked somewhat patronizingly, what this was, and she replied quickly 'it is stress, the stress of his work, stress of his social obligations and even the stress of his pastimes'.

There is no doubt that many of us do have patients, with a kind of aggressive, driving personality, that we believe are the characteristics of a successful person in modern society. These are individuals with excessive competitive drive, aggressiveness, impatience, and a sense of time-urgency. It is highly likely that such behaviour influences currently known risk factors.

Friedman has called this, the "Type A" personality and makes out an interesting and provocative thesis to show its major role, as an important risk factor. I feel we must include this type of personality, and the stresses of modern living, into our repertoire of risk factors. I have always believed that hard work never killed anybody, but we are developing into a group of individuals with the inability to relax in between such hard work. Although it is difficult to quantitate stress or psychological factors, in relation to coronary artery disease,

most of us have seen ample evidence of its role in our clinical practice. There is no doubt in my mind that the stresses and tension of modern living, in our urban society, are significant contributory factors, and that our contemporary mode of living, with its pace and turmoil, have additive effects on other risk factors.

With regard to the second question why there has been an increase in coronary artery disease in women of reproductive age, I suspect that the oral contraceptive pill may have a large role to play. While not decrying the immense amount of benefit that has resulted from its use, I cannot in all honesty believe, that the use of progesterogens and oestrogens for such a long period of time, is without serious harmful effects. Over the last 7 or 8 years I have seen women in the reproductive part of their lives with coronary artery disease who have had no other risk factors other than the fact that they have been on the 'pill' for many years.

I feel that the role of endocrine and sex hormones in the pathogenesis of coronary artery disease requires closer scrutiny, and much more research needs to be done. Besides, the 'pill' is not the answer to family planning. It would perhaps be preferable, to ask our young women to have the number of children they require in early life, where the risk of congenital defects in the offspring is much less, and then have their tubes ligated, instead of being for practically a lifetime on sex hormones.

In the short time available I have discussed some aspects of the prevention of coronary artery disease, largely from the experience I have gained and the impressions I have formed over a period of 20 years. I have proposed *medical examinations* or screening of children and adults at certain definite intervals.

I have suggested *genetic counselling,* in predisposed groups, and those with increasing number of risk factors. I have advocated *health education* of our public health personnel, our mothers and housewives, and our children, on the value of an *non-atherogenous diet*. I have made my observations as a clinician on the role of stress and tension as strong contributory factors, despite a lack of concrete scientific evidence. Lastly, I have made a plea to make a close look at the oral *contraceptive pill* as a contributory factor for the increase incidence of coronary artery disease in women.

At this juncture, I would like to sound a word of warning. If we are to prevent in this part of the world, the epidemic of coronary artery disease which has been ravaging the West, a *well planned* and *well organised,* preferably *government-sponsored* effort should be made now. We cannot afford to wait for 100% scientific proof. There is more than enough experimental and epidemiological evidence for us to justify embarking on a widespread social effort to curb this dreaded menace. The prevention of coronary artery disease will be the *No. 1 medical problem of the century* and is bound to tax the ingenuity and wisdom of the medical profession to the limit. The time to act is *now.* In the words of Samuel Johnson "Nothing will be attempted if all possible objections must first be overcome".

It is perhaps opportune for countries in the Asean region to pool their resources and conduct epidemiological and field studies in collaboration, for we do not have the finances to conduct research on such large scales, in our own individual countries.

Before I conclude, I would like to make a plea to our governments and universities in this region to make more funds available for fundamental basic research. Whilst money for applied research is not difficult to come by, we are faced with the reluctance of governments and institutions of higher learning to spend money on basic research. However, it is from this, and from this alone will our knowledge of this disease be further enhanced.

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Malaria

by *Prof. H. Gilles*
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IN THIS COMMUNICATION I intend to review, discuss and critically evaluate certain aspects of malaria which have exercised me for some years and which I hope will be of interest to an audience of physicians. I shall deal with the following topics –

1. Misconceptions in clinical malaria.
2. Controversial aspects in the treatment of cerebral malaria.
3. Treatment and prophylaxis of chloroquine resistant malaria.
4. Genetics and malaria.
5. Malaria; anaemia and pregnancy.
6. Quartan malarial nephrosis of childhood.

The geographical distribution of malaria still covers a very considerable area of the world and in some Asian countries – India, Pakistan and Bangladesh, the incidence of malaria has recently shown a considerable rise not only in rural but also in urban areas (Bruce-Chwatt, 1974). Over the past five years there has been a striking increase of malaria imported into the United Kingdom from Asia (Brit. med. J. 1974) and consequently in 1974 *P. vivax* represented 66% of all infections (Bruce-Chwatt, 1975); fortunately vivax malaria is not a directly fatal disease. On the other hand, fatal cases of malaria in visitors, especially to Africa, have averaged 6.5% of reported infections due to *Plasmodium falciparum* (Bruce-Chwatt *et al.*, 1974).

Misconceptions in Clinical Malaria

The three most common misconceptions relating to the clinical picture of falciparum malaria as it presents in Britain are – 1) the pattern of the fever, 2) the appearance of jaundice, and 3) an appreciation of the time interval between treatment and clinical and parasitic response. The *fever* in *P. falciparum* malaria, especially in primary attacks, is irregular rather than tertian; its pattern is in fact unpredictable with a daily swinging fever not uncommon, which may or may not be accompanied by rigors and profuse sweating.

Jaundice frequently occurs in severe attacks. The diagnosis that is often made, even when a history of travel to the tropics has been elicited, is infectious hepatitis. Although the latter is a very common disease, *falciparum malaria* should always be excluded first. Moreover, in infectious hepatitis the fever usually subsides with the appearance of jaundice while in *P. falciparum* infections the temperature remains elevated (Gilles, 1974).

After a successful therapeutic course of antimalarial drugs the average time interval between the onset of treatment and the clearance of fever is about 62 hours, while the average parasite clearance time is around 77 hours (Hall *et al.*, 1975). Unless this is recognised, premature condemnation of a perfectly effective and adequate therapy is made. Careful monitoring of parasitaemia is a mandatory concomitant investigation when assessing treatment.

In severe falciparum malaria, mental confusion is a very important prognostic sign necessitating emergency treatment while careful daily assessment

of renal function is mandatory to anticipate impending renal failure and institute prompt dyalisis.

Controversial Aspects in the Treatment of Cerebral Malaria

Punyagupta *et al.,* (1974) reported on 12 patients with severe falciparum malaria, all of whom had received heparin as well as other drugs. Haemoptysis was observed in 4 patients, severe gastrointestinal bleeding in 8; 9 out of 12 patients died – a staggering mortality by any standard! Neither severe gastrointestinal bleeding nor haemoptysis are common complications of acute *P. falciparum* malaria; yet the authors concluded their paper as follows – "We feel strongly that in addition to effective antimalarial drugs, adequate doses of heparin, steroids and low molecular weight dextran should be given at the earliest moment to patients with acute *P. falciparum* who present with one or more severe clinical complications, or with early laboratory evidence suggesting D.I.C., whether or no coagulopathy is evident".

Although severe falciparum malaria may be associated with intravascular coagulation, its pathogenic significance remains uncertain and it could even be a protective reaction (Reid and Nkrumah, 1972); moreover, therapeutic defibrination by ancroid ('Arvin') benefited neither patients with cerebral malaria (Reid and Nkrumah, 1972) nor monkeys with knowlesi malaria (Reid and Sucharit, 1972). In human falciparum malaria heparin has caused haemorrhage which may well have contributed to death (Borochovitz *et al.,* 1970; Smitskamp and Wolthuis, 1971). Like Reid (1975) I feel that heparin is unlikely to benefit patients with cerebral and other forms of severe malaria. In this context, it is interesting to record the findings of Elmes (1975) in Belfast who reported that heparin headed the list of iatrogenic admissions to hospital due to drugs.

Clinical or pathological evidence in favour of cerebral oedema in cerebral malaria is unconvincing yet it has been claimed that steroids benefit such patients by relieving this oedema. Since a short course of dexamethasone (or any other steroid preparation) is unlikely to harm the patient and may possibly give some benefit, I think it is justifiable to give steroids, as adjuvant treatment in cerebral malaria on empirical grounds. I have certainly witnessed a few African children recover from a 3 day coma due to *P. falciparum* when parenteral chloroquine alone was administered; nor should one ignore the fact that both quinine and chloroquine have well known anti-inflammatory properties.

Genetics and Malaria

At least two genes affecting red cells confer relative resistance against *P. falciparum;* the autosomal gene for haemoglobin S and the sex linked gene for the glucose-6-phosphate-dehydrogenase variant named A^-. Whereas for these genes malaria selection can be regarded as established, it is still a hypothesis for some other polymorphic traits of red cells (Allison, 1954; Allison and Clyde, 1961; Gilles *et al.,* 1967; Edington and Gilles, 1975).

Intracellular parasitism brings about an extreme degree of contact between two completely different genomes. Therefore, it is not surprising if sometimes unusual features arise. A case in point is that of malaria infection of G-6-PD-normal and G-6-PD-deficient red cells. Here it is found that, in heterozygous females who have in their blood a mixture of these two cell types, the G-6-PD-normal cells are infected preferentially (Luzzatto *et al.,* 1969), and these persons enjoy relative protection against *P. falciparum* (Bienzle *et al.,* 1972). However, in homozygous males having only G-6-PD-deficient cells no protection is apparent. These findings have led to the suggestion that adaptation of the parasite to a particular cell type may place it at a disadvantage when confronted alternatively with two different types of erythrocytes (Luzzatto, 1972).

Allison (1957) suggested that the increased levels of fetal haemoglobin (HbF) which are associated with some form of thalassaemia might protect against malaria, and there is data to suggest that falciparum malaria infection correlates inversely with the level of HbF in infants during the first 3 months of life (Gilles, 1957). We have approached this problem in two ways. First, we have examined the red cells of infants with *P. falciparum* infection to see if there is any difference in the distribution of parasites between cells carrying predominantly HbA as compared with HbF; secondly, we have looked at the relative degree of parasitization of fetal and adult cells in tissue culture. The preliminary results indicate clear-cut differences in both distribution and degree of parasitization of fetal as compared with adult haemoglobin-containing cells (Pasvol *et al.* 1976).

Miller *et al.* (1975) have recently suggested that Duffy blood groups determinants (Fy^a or Fy^b) may be erythrocyte receptors for *P. vivax,* and that this phenomenon may explain the insusceptibility of West Africans to vivax malaria, since Duffy negative erythrocytes occur in high frequency in West Africa.

Treatment and Prophylaxis of Chloroquine-resistant Malaria

Chloroquine-resistant *Plasmodium falciparum* strains are known to occur in various parts of South America, e.g. Brazil, Colombia, Venezuela and in Southeast Asia, e.g. Thailand, Vietnam, Laos, Cambodia, Malaysia, Indonesia, West Irian and the Philippines. Any patient who has contracted falciparum malaria in these areas should be considered for practical purposes as having been infected by a chloroquine resistant strain and treated as such whether seriously or moderately ill. Until recently, 16 different regimens involving 12 drugs administered over 1 to 14 days were recommended (WHO. 1973). A recent paper by Hall *et al.,* (1975) has improved matters considerably and has rendered the treatment of chloroquine-resistant malaria simple and effective. It consists of quinine (at least four doses given at intervals of 8 to 12 hours) followed by a single dose of sulfadoxine-pyrimethamine (Fansidar). A slight modification of this regimen for adults who are not severely ill is given below –

Day 1. Quinine sulphate (orally) 540 mg. base (2 tablets) 12 hourly.

Day 2. Quinine sulphate (orally) 540 mg. base (2 tablets) 12 hourly.

Day 3. Quinine sulphate (orally) 540 mg. base (2 tablets) 12 hourly.

Day 4. Pyrimethamine 75 mg. + Sulfadoxine 1500 mg. (Fansidar: 3 tablets)

The reasons why I advocate 3 days of quinine instead of 2 are as follows – a) in 82% of Hall's series at least one dose of quinine was given by intravenous infusion thus ensuring optimal absorption which cannot be guaranteed with oral therapy, especially in the first days of malarial illness when gastrointestinal disturbances are not uncommon, b) in Hall's own series the *average* course of quinine was 3 days. The dose of Fansidar can also be given on Day 1.

For severely ill patients, parenteral quinine given by slow intravenous infusion is mandatory and will have to be continued until oral therapy (as above) is possible. The progress of the parasitaemia should be monitored twice daily.

Malaria. Anaemia and Pregnancy

In areas where falciparum malaria presents a 'stable' pattern, adults usually suffer little overt disease because of their acquired immunity. However, during pregnancy, and especially in primiparae there is a temporary loss of this immunity manifested by certain specific features. Firstly, there is a dramatic increase in both parasite rates and densities (Kortman, 1971). Secondly, a very marked haemolytic anaemia occurs which bears little relation to the density of the falciparum parasitaemia and it is thought that the effect might be immunologically mediated. However, there is no doubt that malaria is implicated, since prophylactic antimalarial treatment results in a dramatic fall in the incidence of anaemia of pregnancy in primiparae (Gilles *et al.,* 1969).

The mechanisms involved in this loss of immunity to falciparum malaria in pregnancy are not known, although Cohen and McGregor (1963), found that turnover rates of IgG were much lower in pregnant women than in other adult Gambians. A baffling feature of this temporary loss of immunity is that it seems to be selective to the haemopoietic system, since the other severe manifestations of malaria, e.g. cerebral, are not usually seen.

Quartan Malarial Nephrosis of Childhood

The tropical medical literature contained many references regarding some association between quartan malaria on the one hand and nephrosis on the other (Atkinson, 1884; Giglioli, 1930). Unfortunately, many of the early workers often made free and interchangeable use of terms such as 'nephritis' and 'nephrosis', and differentiation between the nephrotic syndrome in children and in adults was frequently ignored; moreover, the epidemiological evidence produced for the association was not devoid of flaws. Thus, in the first edition of the texbook 'Diseases of Children in the Tropics and Subtropics' (Trowell and Jelliffe, 1958) the following paragraph appears – "there is considerable disagreement in the literature concerning the incidence and nature of nephrosis in malaria ..... the question of an association must, therefore, still be considered unproven".

Irrefutable proof of this association came from the studies of Gilles and Hendrickse (1963) who found that almost all of their West African children with nephrosis also had demonstrable *P. malariae* infection. In contrast, in only a small minority of the non-nephrotic children could quartan malaria be detected. In both groups, however, the prevalence of *P. falciparum* was not significantly different (Fig. 1.). Hendrickse and Gilles (1963) first advanced the suggestion that the nephrotic syndrome might be due to glomerular damage caused by the deposition of immune complexes. There is now much evidence to support this point of view (Ward and Conran, 1969; Allison *et. al.,* 1969; Houba *et al.,* 1971; Voller *et al.,* 1971).

Conclusion

Malaria still remains the most important of the acute imported diseases into the United Kingdom and the dictum first pronounced by Maegraith in 1963 'Unde Venis' – where have you come from – remains as pertinent as ever.

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Some Characteristics and Services of Chinese Medical Practitioners in Malaysia

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THE EXTENSION OF cosmopolitan (Western-style) health care to increasingly more remote areas and traditional populations around the world has faced many of the same problems that its intensification is facing in the most industrialized and urbanized countries. These problems are especially those of high cost, inadequate skilled manpower, and acceptability to and trust by the population. One response in the United States has been an increased interest in paramedical services such as midwives and upgraded nurse training and responsibility, the models and experience of these services being largely sought abroad. Another response has been an increased awareness of the role that folk medicine has to play in health care. The problem, as Chen has noted, is to separate those traditional practices which are helpful or at least neutral from those which are demonstrably harmful, and to encourage the former as well as discouraging the latter in the interest of public health (Chen, 1973).

Malaysia offers what must surely be one of the most diverse set of options for health care in the world. People frequently consult several types of folk practitioners, pharmacists, and physicians at the same time. Traditional beliefs concerning diet, exercise, child birth, and folk medications are vital and continuing influences on the health of the public in Malaysia, and the traditional practitioner needs to be considered as he fits within the broader system of health care (Dunn, 1974). Yet, little is factually known about the status of non-cosmopolitan medicine, especially in the cities (Chen, 1971).

It is the object of this paper to summarize some basic statistics on the characteristics of Chinese practitioners *(sin-seh)* and the services that they offer in Malaysia.

General Information

There are twenty-six associations of traditional Chinese practitioners in Malaysia, gathered into the Federation of Chinese Physicians and Medicine Dealers Association of Malaya. The Federation estimates that there are a total of about 1,000 Chinese practitioners in Malaysia. Less than half of these are recognized by their fellows as fully qualified or are affiliated with an association. The remainder, largely trained by apprenticeship and self-study, are specialists in such things as the treatment of piles or setting of bones. Questionnaires were sent out to 370 affiliated practitioners nation-wide, and an unusually cooperative response for a mail questionnaire, sixty-two per cent, was received.

The continuing vigor of the Chinese medical tradition in Malaysia is indicated by the support of active medical schools in Kuala Lumpur, Penang and Ipoh. The school in Kuala Lumpur presently has eighty students taking a four-year course at night, and in recent years it has graduated several hundreds of practitioners. Students study traditional medical theory and diagnosis, and techniques of acupuncture, moxibustion, and herbal treatment. At the Tong Shin Hospital in Kuala Lumpur, an option of Chinese-style care is offered by the Central Chinese Physicians Association. In addition, the Association maintains a free public clinic which in 1975 treated 10,860 patients.

Characteristics of Chinese Practitioners and Their Practice

Chinese practitioners are more than 95 per cent male. A full third of them are over sixty years old, but the success of the schools is indicated by the fact that almost another third are under forty. Almost equal numbers of practitioners have now been educated in Malaysia as educated in China. There is a statistically significant association of medical school training with training in Malaysia, and apprenticeship with training in China. Nationally, only one-third of practitioners are school-trained; but, the proportion so trained rises to over two-thirds in states with medical schools. Of the responding practitioners, 53 per cent were Cantonese, 23 per cent Hakka, 16 per cent Hokkien, and 8 per cent of other dialect groups. The dialect group of the practitioner correlated only with the state of residence, however, and not with specialization, country of training, type of education, or size of practice. Half of the practitioners are in private practice and the other half are associated with a medical hall. A significantly larger proportion of cases involving pediatrics, gynecology, and treatment for injury are handled by the latter group than by those in private practice. The third who specialize in acupuncture are almost entirely graduates of a medical school and tend to be in private practice.

Table I
Specializations Among Chinese Practitioners in Malaysia, 1974

Specialization	Percentage of respondents indicating specialization[a]	Specialization as percentage of total specializations cited
Internal medicine	83.8	27.7
Gynecology	66.0	21.8
Pediatrics	61.8	20.4
External medicine	24.6	8.1
Injury	19.4	6.4
Piles	9.9	3.3
Acupuncture	37.2	12.3
Total numbers	19.1	57.8

[a]Indication of multiple specializations, to a maximum of three, was allowed.

Patients are male or female in almost equal proportions. Their dialect group composition corresponds closely with state distribution, but half of responding practitioners claimed that at least 10 per cent and up to 25 per cent of their patients were non-Chinese. The patients are of all ages, but about one-third are under twenty.

The major conditions treated are listed in Table II. Their relative importance was remarkably constant from state to state. Bronchitis-emphysema was especially low in Pahang and high in Kedah, and heart disease was only mentioned in Selangor, Sabah and Sarawak.

Table II
Relative Importance of Illnesses Treated by Chinese Practitioners in Malaysia, 1974

Illness	Points[a]	Percentage of total points
1. Rheumatism	725	19.9
2. Gastric complaints	596	16.3
3. Gynecological complaints	545	14.9
4. Bronchitis and emphysema	478	13.1
5. Colds or influenza	293	8.0
6. Nerve complaints	224	6.1
7. High blood pressure	185	5.1
8. Kidney and urinary complaints	159	4.3
9. Heart disease	122	3.3
10. Diabetes	98	2.7
... Other complaints[b]	232	6.3

[a]The questionnaire asked practitioners to list and rank the five most common illnesses that they treated and to mention others commonly seen. The answers were weighted by multiplying the first rank listings by six, second by five, down to unranked complaints which were weighted by one.

[b]Commonly mentioned other complaints included bone fractures, skin diseases, piles, paralysis, and venereal disease.

There are concentrations of practitioners in the major cities of each state, but practitioners are also widely dispersed in small towns throughout the country. With regards to their distribution, the states of Selangor, Pahang and further north may be distinguished from states to the south and in Sabah and Sarawak. There are between 16 and 20 association member practitioners per 100,000 Chinese population in Selangor, Pahang, Perak, Penang, and Kedah, but between 37 and 43 in Negri Sembilan, Melaka, Johore, Sabah and Sarawak. This distributional pattern holds when practitioners per 100,000 total population is considered, there being under 15 in the northern states and over 20 in the southern states. The states of Perlis, Trengganu and Kelantan have only one or two practitioners each. Within the capital city of Kuala Lumpur, there are an estimated 200 practitioners of all background, 68 being affiliated with the Chinese practitioners' association. They are highly concentrated in the old Chinese downtown, where they reach a density of 93 per 100,000 Chinese (70 per 100,000) population, and in Pudu district (59/100,000 Chinese) (Meade and Wegelin, 1975).

The average responding practitioner sees between 280 and 570 patients a month. Forty per cent of practitioners see under three hundred

patients a month, but fourteen per cent see over 600, and four per cent, over 1000. Generalizing to include practitioners who did not respond, it is estimated that between 100,000 and 200,000 people a month consult a Chinese practitioner. The proportion of these patients who are chronically ill and seen repeatedly varies greatly from one practitioner to another according to specialization. The median is between 70 and 75 per cent, which accords with the importance of complaints treated (Table II).

Comment and Conclusion

It is obvious from the data collected that Chinese medicine in Malaysia remains a vital tradition providing medical treatment to substantial numbers of people throughout the country. Some of these people, of course, are seeing other doctors as well and are taking advantage of the diverse types of health care available in Malaysia. Experienced practitioners frequently noted that for the last twenty years, cosmopolitan medicine has been preferred for cases of acute infection and for obstetrical care. It is generally after the hospitals and private doctors have failed to provide relief that the patients turn to traditional medicine, it is said, which they find helps them. Some support for this view can be found in the importance of such conditions as rheumatism, emphysema, "nerve complaints" (including back pain and paralysis) and high blood pressure in present practice. It is noteworthy, however, that children are also well represented in traditional practice, and that cases of menstrual irregularity, influenza, malaria, ear and nose diseases, leukemia and dengue fever are also treated. Those practitioners interviewed consistently said that whenever a condition failed to respond to treatment, they referred the patient to a physician. For some conditions, however – such as nasopharyngeal cancer within the general nose complaints – detection may be seriously delayed. In the People's Republic of China, the appropriate usage of different treatments and approaches apparently has been advanced by mutual study, but in Malaysia there is little basis today upon which the Chinese practitioner can differentiate those cases for which his treatment is beneficial from those before which it is impotent and therefore, by delaying other treatment, dangerous. Given the opportunity to develop the knowledge for such discrimination, the service performed by the Chinese practitioner might be upgraded to constitute a continuing contribution to health care in Malaysia's plural society.

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The Improvement of Immunization Coverage by Early Immunisation of Children in Malaysia

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Introduction

ONE OF the major problems of any immunization programme concerns the extent of coverage of the population. In Malaysia the bulk of the immunization to infants and preschool children is largely performed at the child health clinics (infant welfare clinics), both in the urban as well as in the rural areas. In 1969, although approximately 50% of infants born in Peninsular Malaysia attended child health clinics (Mettrop 1970), only 33% of infants less than one year of age were fully immunized with triple antigen (DPT). One of the reasons for this poor coverage in children attending clinics is that 50% of them drop out by the age of six months (Dugdale 1969 & Chen 1975a). Therefore in the Malaysian context, in order to increase the rate of immunization of infants attending child health clinics, the primary series of immunization should be completed within the first six months of life. With this in view the University Hospital, Malaysia, has adopted the following programme of immunization since 1968. (1) simultaneous B.C.G. and smallpox vaccinations to the newborn. (2) administration of DPT and poliomyelitis vaccines commencing at the age of six weeks, when the mother comes for her post-natal check up. By this means the primary immunization is completed by the age of six months. The efficacy and safety of such a schedule has been discussed in an earlier paper (Chen 1971). Along similar lines in 1972, the Ministry of Health, Malaysia, recommended the commencement of DPT in the second month of life whereas previously it was begun during the fourth month of life.

The purpose of this paper is to exrmine whether there is a change in the immunization coverage of children in Peninsular Malaysia with this change of immunization schedule.

Methods

Yearly records of the number of doses of BCG, smallpox, DPT and poliomyelitis vaccines given to children in Peninsular Malaysia for the years 1968 to 1974 were examined. From the above the coverage of immunization of infants less than one year of age was then obtained.

Results

Table I shows the immunization coverage by year for children less than one year of age in Peninsular Malaysia from 1968 to 1974. For BCG, which was given soon after birth, the coverage was high (72 – 81%). The coverage for smallpox, which was given between three to five months of age, was between 44 – 50%.

Prior to the onset of the new schedule the coverage with respect to DPT immunization was between 29 – 36%. Currently with the change in the national schedule of immunization DPT being commenced at the second month and the third dose at the fourth month, the coverage for full DPT immunization increased to 51%. The coverage for poliomyelitis immunization for the year 1973 and 1974 was similar to that of DPT.

Discussion

The results clearly show that coverage is improved when immunization is given early in life.

Table I

IMMUNIZATION COVERAGE BY YEAR

(For children less than one year of age)

PENINSULAR MALAYSIA

Type of vaccines	% and number of children immunised													
	1968		1969		1970		1971		1972		1973		1974	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
BCG	39*	(120,829)	37*	(109,270)	41*	(122,888)	53*	(163,745)	72@	(221,706)	74@	(232,395)	81@	(251,362)
Smallpox	49	(151,596)	50	(150,042)	50	(149,412)	48	(147,452)	44	(135,318)	47	(147,722)	49	(152,182)
DPT														
1st dose	46	(142,856)	49	(145,117)	50	(149,131)	51	(157,756)	54	(166,836)	59	(185,150)	63	(193,368)
3rd dose	29	(88,386)	33	(99,490)	35	(104,560)	36	(111,171)	36	(112,370)	48	(150,160)	51	(155,874)
Poliomyelitis														
1st dose		—		—		—		—		—	59	(186,063)	62	(191,270)
3rd dose		—		—		—		—		—	45	(141,990)	49	(150,963)

* refers to newborns only.
@ refers to all infants below one year of age.

Dugdale (1969) observed similar findings in the Kuala Lumpur Municipal clinics. 80% of these clinic patients were immunized with BCG but only 20% of the patients were fully immunized with DPT by the age of one year. As a result, in 1970, the schedule of immunization in the Kuala Lumpur Municipal Clinic was revised and DPT was began at two months of age instead of four months. This resulted in the doubling of the coverage of the clinic patients for full DPT immunization. (Pathmanathan 1973).

Thus in Malaysia it seems that the rate of immunization of children, attending child health clinics, can be increased by (a) starting immunization as early in life as is possible, (b) giving simultaneous administration of several antigens, thus providing maximal protection within the fewest number of visits, and (c) completing the primary series of immunization (other than measles and reinforcing doses of DPT and poliomyelitis) by the age of six months.

As only 50 – 60% of infants in Peninsular Malaysia attend child health clinics, in order to increase coverage, efforts should be directed to increase the attendance of children to these clinics. But until such time as health education to women folk in the importance of continuous health supervision and immunization can be achieved one has to depend on other measures in increasing the rate of immunization. This can be done by immunizing children whenever they are available. In Peninsular Malaysia 73% of all births are delivered in hospitals or at home by trained midwives (Malaysia 1975). Immunization with BCG and smallpox can be given at all these maternity hospitals and at home by trained midwives and *jururawat-desa* (community nurses). In Peninsular Malaysia, since approximately 50% of mothers attend post-natal clinics, they can be asked to bring along their babies for immunization at these post-natal clinics.

However, many children, especially those from lower income families, do not attend child health clinics, they do come to the hospitals or health centres when they are sick. This opportunity should be taken to immunize such children when immunization is not contraindicated e.g. in the presence of minor afebrile illnesses. Further, patients who are admitted to hospitals are often fit for immunization on discharge. However, few have been immunized as exemplified by the fact that of the toddlers admitted to the University Hospital, Kuala Lumpur only 25% of them were fully immunized with D.P.T. and 11% with poliomyelitis vaccine (Chen 1975b). Therefore it is possible to raise the coverage by immunizing children seen in hospitals and in health centres.

Summary

The coverage of immunization of infants less than one year of age for the years 1968 to 1974 in Peninsular Malaysia is presented. Immunizations given early in life achieve a much higher coverage than that given later in childhood. With the change in the national schedule of immunization, when DPT is given earlier in life i.e. at the second month the coverage for full DPT immunization increased by 15%.

In the Malaysian context, where 50% of the infants attending child health clinics drop out by the age of six months, it is crucial to complete by the age of six months the primary series of immunization (other than measles and reinforcing doses of DPT and poliomyelitis vaccines). This can be done by immunizing children as early in life as is possible and giving simultaneous administration of several antigens, giving the maximal number of immunizations in the fewest number of visits.

The rates of immunization of the community can further be improved by immunizing children in the post-natal clinics and also in the outpatient clinics of hospitals and health centres and in the hospital wards.

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I am grateful to the Director-General, Ministry of Health, Malaysia, for permission to publish this paper and to Professor M.J. Robinson for advice.

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Study of One Hundred Cases of Typhoid Fever in University Hospital Kuala Lumpur (October 1967 to July 1972)

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Historical Background

THE FIRST STUDY OF typhoid fever in West Malaysia, was reported in a bulletin from the Institure of Medical Research by William Fletcher[1] in 1927. This report was made to determine if enteric fevers were common in the country as there was an increase in the number of positive Widal tests. There was no epidemic reported; the carrier rate determined from faecal smears was less than 0.08 per cent and the author concluded that enteric fever was not common. The probable reasons postulated were the "evenly distributed heavy rainfall, the excellent water supply of the towns, the scarcity of flies, the absence of large milk-distributing companies and the presence of colloidal clay in the rivers." During 1925-1926 one hundred and eighty-two cases of typhoid fever were diagnosed either by examining the excreta bacteriologically or by three successive Widal tests.

Green and Mankikar[2] (1949) reported an epidemic of typhoid fever due to ice-cream. The infection first showed itself in epidemic form mainly among school children in a town with a population of 5,000. The ice-cream manufacturer was found to be "a fairly constant excretor of virulent typhoid bacilli" but was a "particularly healthy looking and active individual."

Introduction

The clinical features of epidemic typhoid differs from endemic typhoid in various aspects. Textbook descriptions refer to epidemic typhoid, hence the admitting medical officer at the emergency room or medical clinic for the first time experience special difficulty in making an accurate and prompt diagnosis of endemic typhoid fever. (Wicks, Holmes, Lindsay, 1971)[3].

In 1962 Huckstep[4] described typhoid fever in East Africa as "the king of actors on the stage of disease." He noted that "a case of typhoid fever may present as a disease clinically indistinguishable from malaria, progress to a bacillary dysentry, mimic a case of acute bronchitis, simulate a full-fledged lobar pneumonia, cause an acute abdomen with perforation and then finally in convalescence, with its evil spent, linger on as an orchitis, a myocarditis or a peripheral neuritis."

This paper examines the clinical manifestations and the diagnostic difficulties of the disease as encountered in a teaching hospital.

Material and Methods

The cases were studied retrospectively. The first one hundred cases where the diagnosis was made by isolation of S. typhi either in the faeces, urine or blood were analysed. There were 62 males and 38 females. The ethnic distribution is as seen in Table I. The youngest patient was aged one year and the oldest was 80 years of age. Mean age was 23 years (See Table II).

Information like history of T.A.B. vaccination, contacts or possible sources of infection were not available. The average duration of hospitalization was 24 days, the shortest stay being 4 days and the longest 67 days. 86 cases were admitted into medical, 11 into paediatric and 2 cases into surgical

Table I
Ethnic group distribution of typhoid cases

Ethnic Group	No. of cases of typhoid fever
Malays	27
Chinese	31
Indians/Ceylonese/ Pakistanis	41
Others	1
Total	100

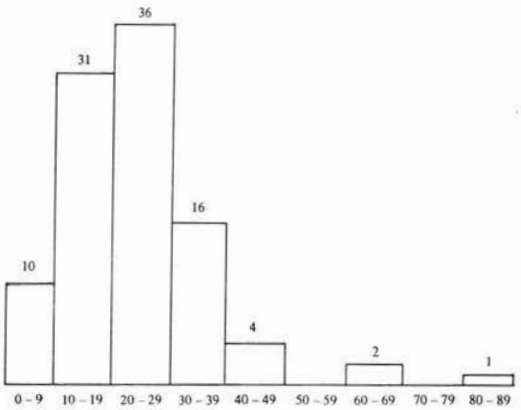

Table II: Age distribution of typhoid cases

wards. There was no statistical difference in the number of admissions by months in a year (See Table III).

Clinical Features

The symptoms and signs are summarized in Tables IV and V respectively. In the majority of cases (91%) the onset of illness was insidious. The most common symptoms were a triad of fever, chills/rigors and sweats. Headaches were described as generalized, constant and worsened as the fever rose. The step ladder type of fever described in textbooks as typical of typhoid was seen in only five cases. The patients had either intermittent, remittent or continued fevers. In fifty-one patients the spleens were palpable and in four the spleen was tender. Sixty-one patients had enlarged palpable livers of which fourteen had tenderness on palpation. Mental confusion were present in eight patients of whom four were severely toxic.

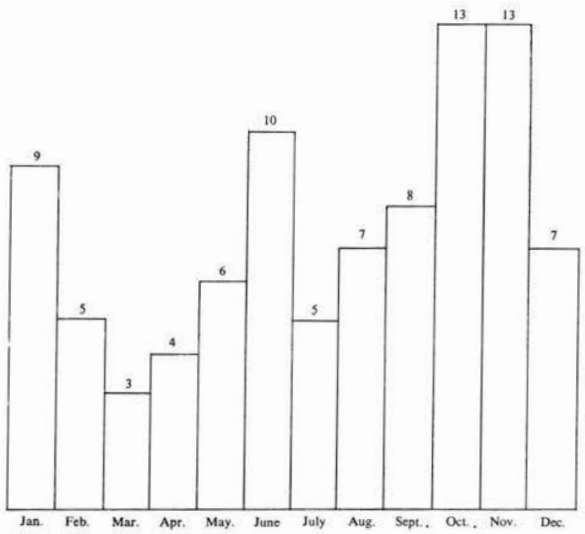

Table III: No. of typhoid cases distributed monthly.

Table VI
Diagnoses on admission

Diagnoses	Percentage of Cases
Typhoid	61%
Possible typhoid	22%
Urinary tract infection (all female patients)	5%
Malaria	3%
Amebiasis	2%
Infective hepatitis	2%
Pneumonia	2%
Pulmonary tuberculosis	2%
Meningitis	1%
Total	100%

Diagnosis on Admission

As seen in Table VI the initial diagnosis of typhoid was correctly made in sixty-one and the disease was suspected in another twenty-two cases. Of the other 17% a variety of diagnoses were made.

Investigations

In only half the number of cases was there any change in the nature of the stools. Microscopic

Table V

Signs on admission – comparing with studies in Africa

Signs on admission	Percent of Cases		
	A	B	C
General			
Fever	100%	98%	No data
Fever and Rigors	74%	No data	No data
Relative bradycardia	93%	33%	No data
Jaundice	6%	No data	No data
Rash (Rose spots)	8%	0%	5%
Toxaemia	4%	No data	54%
C I T			
Abdominal tenderness	No data	33%	61%
Palpable spleen	51%	No data	No data
Palpable spleen with change in size	9%	No data	No data
Tenderness in spleen	4%	No data	14%
Enlarged liver	61%	No data	No data
Tenderness in liver	14%	No data	No data
R.S.			
Bronchitis	11%	33%	56%
Lobar consolidation	No data	3.5%	No data
C.N.S.			
Mental confusion	8%	33%	29%
Meningism	No data	8%	No data
R.E.S.			
Tender Lymphadenopathy	1%	No data	No data

A = present study of 100 cases
B = study of 243 cases in Rhodesia, 1966-1969 (Wicks, Holms, Lindsay)
C = study of 975 cases in Kenya and Uganda, 1954-1961 (Huckstep)

examinations of urine revealed three cases of haematuria and twenty-eight with albuminuria. The mean haemoglobin value on admission was 12.2 g % (PCV 37.4%). There was a range of 2,300 to 14,300 WBC/cmm. Leucopenia (<5,000 WBC/cmm.) was present in 37% of cases, while a leucocytosis (<10,000 WBC/cmm.) was found in 6% of cases.

The Widal test was not done in twelve cases and in sixty-six a repeat titre was not obtained. Of the eighty-eight cases where the first three was performed, thirty-six (41%) had H or O titre 1/250 dilution. In sixty-four the H and O titre were the same, twelve where the H antigen titre was greater than the O titre and another twelve where the reverse was noted. In only thirty-four was a repeat test performed.

S. typhi was isolated in forty-one cases in faeces alone, in thirty-one in blood alone and in twenty-five in both faeces and blood (See Table VII). In two cases *S. typhi* was isolated in the urine as well. The percentage of positive blood and/or stool cultures

Table IV

Symptoms on Admission – comparing with studies in Africa

Symptoms	Percent of Cases		
	A	B	C
Fever, chills/rigors and sweats	76%	No data	No data
Diarrhoea without blood	35%	37%	30%
Headaches	32%	75%	75%
Cough	23%	53%	22%
Abdominal pain/discomfort	22%	52%	61%
Constipation	15%	17%	No data
Anorexia	14%	No data	No data
Vomiting	12%	24%	25%
Muscle or bone aches or joint pains	7%	18%	54%
Jaundice	5%	No data	No data
Fever	19%	39%	No data
Chest pain	No data	27%	20%
Dysuria	No data	24%	No data
Sore throat	No data	6%	7%
Epistaxis	No data	1%	No data

A = present study of 100 cases
B = study of 243 cases in Rhodesia, 1966 to 1969 (Wicks, Holmes and Lindsay)
C = study of 975 cases in Kenya and Uganda, 1954 to 1961 (Huckstep)

Table VII

Confirmation of diagnosis by Isolation of Salmonella typhi

Number of Cases where Salmonella Typhi was isolated

Week	Blood	Urine	Faeces	Bl + Fe	Fe + Ur.	Total
1st	1	0	2	1	0	4
2nd	II	0	12	15	1	39
3rd	10	0	13	2	0	25
4th	9	2	14	7	0	32
Total	31	2	41	25	1	100

was evenly distributed amongst patients in the second, third or fourth week of illness.

In all cases *S. typhi* was sensitive to chloramphenicol in the antibiotic sensitivity test. Next highest in sensitivity was cephaloridin and ampicillin (45% in blood, 42% in stool). Only 22% were sensitive to kanamycin and less than 3% were sensitive to penicillin, streptomycin, tetracycline or erythromycin.

Treatment and Response

There was an average of twenty days delay after the onset of the patient's illness before specific drug therapy was commenced. This was largely due to the delay in patients coming for hospitalization.

After chloramphenicol was started it took an average of 5.3 days before the patients became afebrile for at least twenty-four hours.

The average dose of chloramphenicol given before clinical defervescence was achieved (i.e. afebrile for at least twenty-four hours) was 10.35 gms, – approximately 2 gms per day or 500 mgm four times a day for five to six days. The highest dose was 32 gms and lowest 1gm before clinical defervescence.

The average total dose of chloramphenicol used was 22.6 gms. In the majority of cases chloramphenicol was continued for ten days after clinical defervescence at an average of 1.25 gms/day i.e. 250 mgm five times a day.

Most cases convalesced in hospital for an average of five days after chloramphenicol medication was stopped. This was also the waiting period for at least two negative stool cultures before the patient was discharged. Only one case required surgical intervention for terminal ileal perforation. 67% of cases had three negative stool cultures before discharge.

Recurrence of Symptoms

There were 10% of cases with recurrence of symptoms in this series, half of which occurred before the patients were discharged from hospital. The other five cases had recurrence of fever at the follow-up clinic and were promptly readmitted. The relapse usually occurred nine days after cessation of chloramphenicol therapy.

Six cases with recurrence were treated with both chloramphenicol and amipicillin, two had only chloramphenicol whilst the other two had only ampicillin.

Mortality

Only one death occurred in the series. The patient was twenty-three years of age, had a prolonged fever with chills and rigors and after one month of severe illness was admitted in a state of confusion and dehydration. He was diagnosed as a case of septicemia due to typhoid. On admission he was treated with intramuscular chloramphenicol and subsequently intravenous hydrocortisone and ampicillin. On the fourth hospital day he was hypotensive and had haemetemesis which proved fatal. Postmortem findings showed generalized fulminating typhoid lesions. There was lymphoid hyperplasia and ulceration of the gut with congestion and hyperplasia of spleen and lymph nodes.

Comments

Comparing the symptomatology of patients in this series with those of Wicks et al and Huckstep there were some notable differences. Headaches, abdominal pain, discomfort and muscle/bone/joint pains were much less common amongst this group of patients whereas chest pain and dysuria which occurred in about a quarter of the cases studied by Wicks et al was not noted.

It would appear that the cases of typhoid studied in Rhodesia, Kenya and Uganda were more fulminating in severity; 54% of Hucksteps cases had toxemia (compared to 4% in this series) and 33% of Wick's cases had mental confusion (compared to 8% in this series). Also, bronchitis as a complication occurred more frequently in the African patients (33% and 56% of cases in the two studies) whereas it was detected as a clinical sign in only 11% of this series.

A relative bradycardia was recorded in 93% of the patients under study whilst this was found in only 33% in Wick's group. No data were available with regards to splenic and hepatic enlargements in the other two studies but 51% and 61% of our patients had enlarged spleens and livers respectively.

The results of the Widal tests will depend on the stage of illness when the blood sample was taken. The Widal tests performed in this series showed that a single Widal test had little diagnostic value (Christie 1969). Where a repeat test was performed, less than a third showed a significant rise in titre to confirm the clinician's suspicions in doubtful cases. Three-quarters of the cases were treated with chloramphenicol based on clinical diagnosis before the Widal reaction results were known and only a quarter had therapy withheld until the Widal tests results were available.

With regards to isolation of salmonella typhi, this study showed the importance of culturing blood and stool samples. These samples should be taken regardless of the stage of the illness because results from this series demonstrated the even distribution of the number of positive cultures during the second, third or fourth week of illness. The belief that the organism is present only in the first week in the blood stream and thereafter disappears is not borne out in this study. With current bacteriological methods positive cultures of faeces and urine occur earlier than the third week of the disease.

There were ten percent of cases with recurrence of symptoms in this series, half of which occurred before the patients were discharged and the other half had recurrence of fever when seen at the follow-up clinic. Osler[6] found that the relapse rates varied in different clinics and in spite of application of various antibiotic regimes, relapses occurred in twenty percent of cases. However it must be pointed out here that it is difficult to determine whether a case has relapsed, has a re-infection or a recurrence of symptoms. In all the ten cases with recurrence of symptoms, antibiotic treatment with chloramphenicol and/or ampicillin was effective.

Summary

This is a retrospective study of the clinical presentation, physical findings, differential diagnosis, investigations, treatment and response of 100 cases of bacteriologically proven typhoid cases. The symptomatology and clinical signs are compared with two other studies and reference is made to the problem of diagnosis. The value of the Widal test and culture for isolation of the bacteria is examined and emphasis is placed on the importance of blood and stool culture. All cases responded to chloramphenicol therapy.

Acknowledgements

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Vasectomy

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Summary

A SERIES OF vasectomy carried out in private practice is recorded. After two unintentional pregnancies in the early months of this series the technique of managing the cut ends of the vasa is modified. There has been no unwanted pregnancy since.

The complication rate in this series is low.

The majority of the operations is carried out through a single mid-line incision.

Introduction

It is becoming very obvious that population control, and in particular the permanent methods of population control is the answer to this ever growing population and ever decreasing food supply. The argument for and against the above statement can be carried on ad infinito. However two facts have to be borne in mind. One, based on the present 2% growth rate in population, the projections indicate that there will be 8 billion people on this earth by the year 2005. It has also been estimated that the earth will support no more than 10 billion people. At the present rate of population growth this will be attained just 50 years from now. There is yet another way to look at this. The average time for the world population to double itself is 35 years. At this rate there will be one billion billion people on earth in 1,000 years. This amounts to 2,030 people per square meter (1,700 people per square yard.) (Wallace & Riddle 1971.) Secondly, inflation and stagflation apart, the pundits tell us that the world today has a food reserve of 7 days.

Temporary methods of birth control have been used for many decades all the world over. In many countries legal abortion has been allowed to help curb population growth. As yet, the countries that need population control most, countries that are termed under-developed or developing, are the countries that still show a population growth of more than 2 percent.

Legal abortion is unlikely to be introduced in Malaysia for some years. Sterilization seems the best answer for population control for the time being. Female sterilization has been practised and is widely practised today. Vasectomy, male sterilization has been practised for a decade or so, but is less well-known. A statement from a certain organisation recently gave the impression that only doctors from that particular organisation are qualified to perform vasectomy. In fact, general surgeons, gynaecologists and general practitioners with appropriate training should be able to perform this simple operation and contribute to the population control program.

The primary objectives of voluntary vasectomy is to block the vas completely with minimal mobidity, immediate and long term, while at the same time avoiding any procedure which will make subsequent reanastomosis technically impossible.

History of Vasectomy

Vasectomy has a long and interesting history. The first recorded reference to the occluded vas was made by John Hunter during his disections in 1775. He observed a case in which a vas deference was obstructed and replaced by a fibrous cord while the corresponding testicle was of normal size and appearance. Sir Astley Cooper, in 1830 noted that

ligation of the vas in dogs had no effect on spermatogenesis and the epididymis became enlarged to accommodate the sperms. (Quoted by: Hackett & Waterhouse 1973.) There was considerable controversy as to the clinical effects of vas ligation in the latter part of the 19th century. Vasectomy was also advocated in the treatment for benign prostatic enlargement during this time. In the early part of this century, vasectomy was used for eugenic purposes.

The popularity of vasectomy as a mode of population control is of shorter history. India and the Peoples Republic of China are reputed to be the leading countries to carry out vasectomies on a large scale.

Preoperative Interview

Obviously, the surgeon has his indications before a man is considered for vasectomy. As a general rule, if the couple are absolutely sure they no longer want any additional children they should be considered for vasectomy. Some surgeons may insist on a minimum age in addition to the minimum number of live children. Once a couple has been ear-marked for vasectomy, the surgeon should have a full discussion with the patient as well as his wife. It is essential that the couple understand that the operation will not affect their pattern of sexual behaviour in any way. The commonest misunderstanding in this part of the world is that vasectomy is equated with castration, by the public. They should be made to understand that the hormones which play some part in controlling sexual behaviour are released and carried by the blood stream and this is not affected by the operation. It should also be made clear that the testes contribute only a small proportion of the volume of the ejaculate. One of the more convincing proof of this, is that even with his trained eyes, the surgeon is unable to differentiate an ejaculate specimen from a vasectomised patient and one from a non-vasectomised patient.

The question most commonly asked by patients is, 'what happens to the spermatozoa that continue to be produced?'. Physiologically, the normal process of reabsorption are accelerated. The other important question is that of reanastomosis. As a basic rule if the patient is truly concerned about this, I discourage him from the operation as I feel that he is not ready for such an operation. Technically, vasovasectomy is possible. The results depend entirely on the person performing the operation. It must be remembered that anatomical success does not go hand in hand with physiological success. The effects of antibodies formation has to be borne in mind also; Kleinman 1972 and Phadke and Pudukone 1964.

Anaesthesia

There may be some differences of opinion but the majority of surgeons carrying out vasectomy are satisfied with local infiltration analgesia. This seems adequate for most patients and has two big advantages

1. It is safer than general anaesthesia.
2. It is cheaper than general anaesthesia.

In the present series, all operations were done under local infiltration analgesia. The agent used is 2 percent lignocaine without adrenalin. Usually 2 to 4 mls of this agent is used.

Principles of Technique

Figure 1 shows the male reproductive system. Spermatogenesis takes place in the testes and the spermatozoa are then transferred to the seminal vesicles. They are stored here until ejaculation when they are transferred into the urethral passage. Here, prostatic discharge is secreted and this forms the bulk of the ejaculate. Vasectomy aims at interrupting the transfer of formed spermatozoa from the testes to the seminal vesicles. Hence, a man is not immediately sterile following vasectomy as there will be a store of spermatozoa already in the seminal vesicles. These have to be discharged before the man can be proclaimed sterile. The ligation of any rigid tube like the vas is almost impossible. Ligation with cat-gut or any other surgical suture will only hold this temporarily. Non-absorbable materials tend to cut through the thick wall of the vas if tied too tightly. Diathermy fulguration has been found reasonably effective. However, it sometimes produces pain along the cord. Furthermore, the vas is notorious for spontaneous reanastomosis. To this end the best technique is to divide the vas and then somehow prevent the mucosa of the two free ends from coming into contact with each other. There are various ways to achieve this. In this present series, the free ends are turned away from each other and secured upon itself.

Preparation: The anterior aspect of the scrotum is shaven of any hair that may be present. The whole pubic area is then thoroughly cleansed with an antiseptic solution, Salvon. The operation area having been draped, the vas on each side is palpated between the thumb and the index finger as shown in figure 2. Thereafter the local anaesthestic agent is injected as shown in figure 3. The vas of the selected side is then localised using a fine towel clip or a 21G injection needle. (See figure 4)

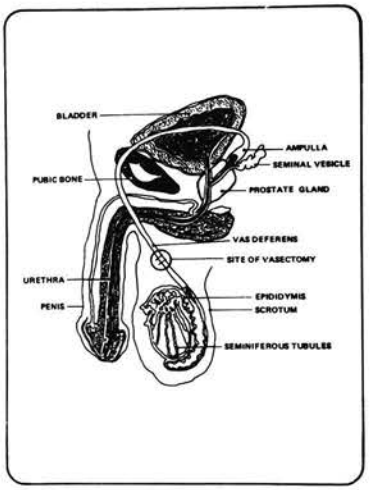

Fig. 1 Male Reproductive System showing the area of Vasectomy.

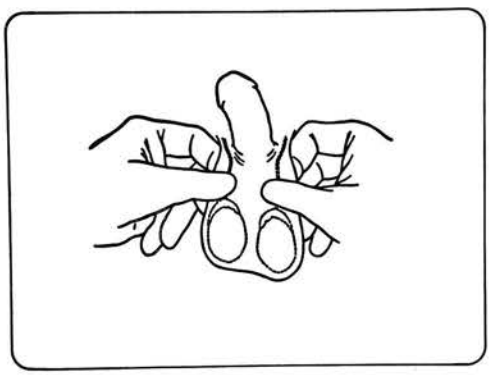

Fig. 2 Feeling to locate vasa deferentia.

Incision: In this series a single incision technique is employed. This incision is made transversely in the midline of the scrotum. It needs be only 1 centimeter in length and no more. This is shown in figure 5. Some surgeons prefer to carry out the operation through two incisions. This seems unnecessary, as both the right and the left vas are accessible through a midline incision.

Ligation: Having made the incision across the localised vas, the vas is easily isolated. The vas is separated from the leach of blood vessels (testicular artery, (see fig. 6) spermatic artery, artery to the vas and the Pampiniform plexus) that accompanies it.

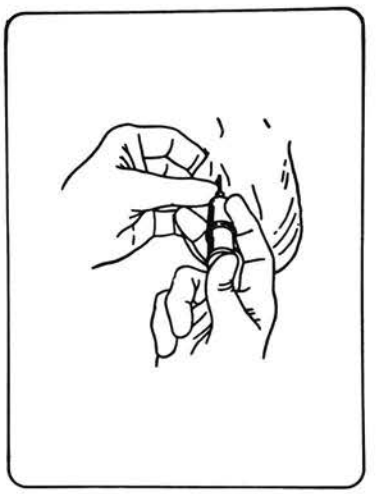

Fig. 3 Injecting Local Anaesthetic.

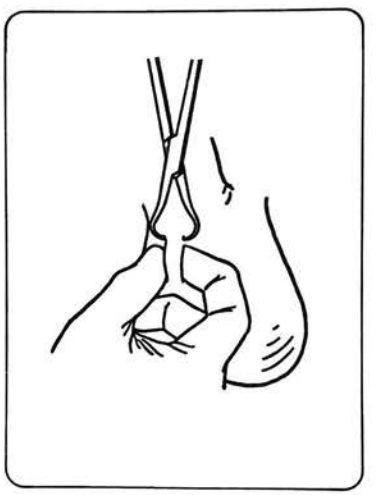

Fig. 4 Vas deferens localised with towel clip.

Thereafter the vas is sectioned and the free ends are ligated and each is turned upon itself away from the other (figures 8, 8 & 9). The small incision is then closed with continuous subcuticular stitches or through and through stitches. (figure 10.)

Materials and Methods

A total of 450 vasectomies was carried out in the 6 years period between 1970 and 1975. All the patients were aged between 30 and 45 years old. There were 403 Chinese, 30 Indians, Pakistanis and Ceylonese, 15 Malays and 3 Caucasians. The patients have all had a minimum of two children each. In the first 35 patients a two incision technique was employed. One centimeter of the vas was

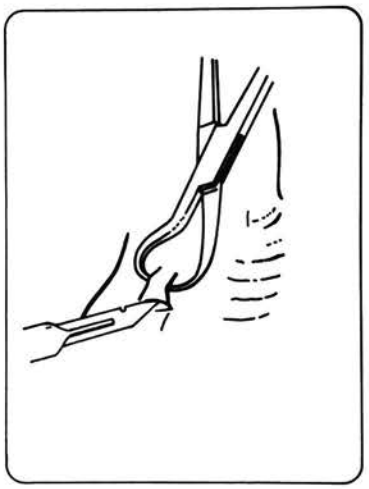

Fig. 5 Tranverse incision (1 cm) made.

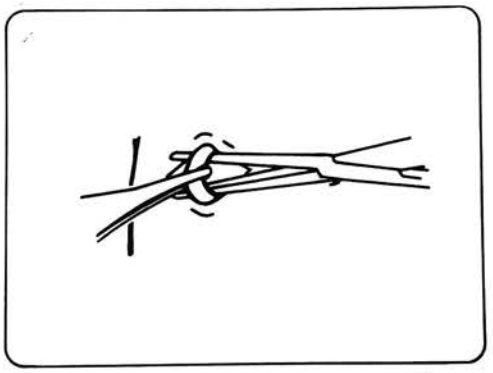

Fig. 6 Vas isolated.

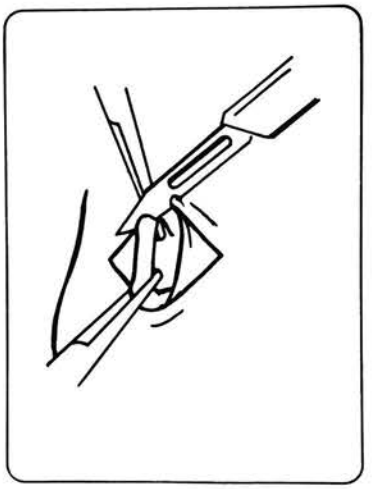

Fig. 7 Vas clamped and cut.

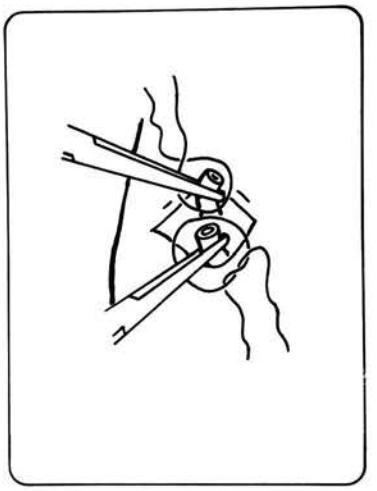

Fig. 8 Cut ends of vas ligatured and turned upon itself.

removed, and the free ends of the vas were left in situ. Thereafter the operative technique as outlined above was followed.

In the follow-up patients were advised to have a minimum of 10 ejaculations before they submit a specimen of ejaculate for microscopic examination. If any evidence of spermatozoa is found the examination is repeated after another 5 ejaculations.

Results:

There were 2 failures in this series. Both these occurred following techniques in which the free ends of the vas was not treated. In the first instance, the patient never had a negative semen following vasectomy. In the second instance, the patient failed to turn up for semen examination. Four months following vasectomy, he presented himself and informed that his wife was pregnant. This was confirmed when an examination of his semen showed the presence of active spermatozoa. A repeat vasectomy was carried out.

The follow-up rate is very poor indeed. Only about 10% of vasectomised patients turned up for follow-up examination. However, it could be safely presumed that had there been any other failure, the patient would have reported the same complication. Following vasectomy the patient is given

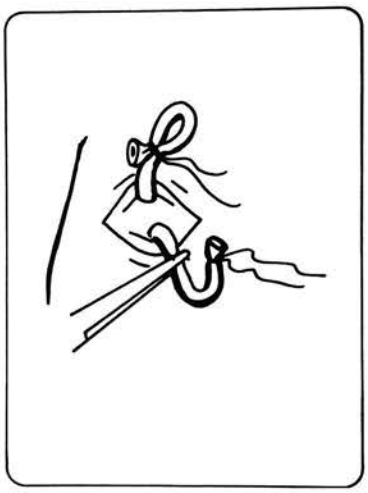

Fig. 9 Ligature of free ends of vas completed.

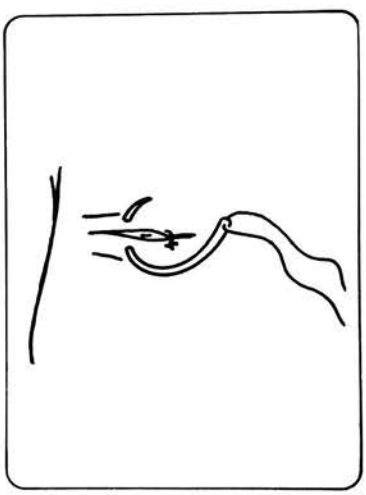

Fig. 10 Skin closure.

instructions that he should report back to the clinic should there be any pain, swelling, bleeding and/or fever. Only 2 patients reported with complications. One reported the day following the operation complaining of pain. Examination did not reveal any significant degree of swelling or any evidence of infection. He was given analgesics in the form of paracetamol and a day's medical leave. The second patient reported at the end of a week following the operation. He had a poor healing of the wound which soon responded to the usual treatment.

One patient presented 17 months following the operation complaining of a lump on each side where the operation had taken place. This was found to be a fibrous nodule which formed over the cut-end of the vas. The patient was reassured and no treatment was given.

Discussion

Vasectomy is a relatively simple procedure which could be carried out as an office procedure. It is associated with minor complications such as bruising, swelling, pain, wound infection, non-specific epididymitis, pain on ejaculation, haematoma sperm granuloma and post-operative psychological effects. Recanalization is certainly a factor to be considered but with careful treatment of the free ends of the divided vasa, this could be reduced to a minimum. In this series there was no incidence of recanalization after the technique of folding the free ends of each vas upon itself was adopted. Recanalization is a failure of technique. The other failure that has to be borne in mind is one where the patient resumes intercourse without any any protection before a negative sperm count has been attained. Whilst this may be said to be a failure due to the patient it is also the duty of the surgeon to give careful and precise instructions to the patients before the operation. This is where the question of the pre-operative interview becomes very important. This is even more so in Malaysia where the procedure is relatively unknown and often misunderstood. Many males and some females still imagine that following vasectomy, the man would become feminised.

In the present series the complication rate is certainly very low. This is in agreement with results published by Livingstone 1971, Schmidt 1966 and Leader et al 1974. The long term complication rate is also minimal. The first patient in the series was done in 1970 and those done in that year have now had the operation performed for a period of 5 years. Whilst haematoma is a problem in many series it is found that careful attention to control bleeding at the site of operation can reduce, or prevent haematoma formation. In this series, there is one case of sperm granuloma. This is thought to be the result of an inflammatory reaction due to extravasated spermatozoa. The first description of such a complication was by Grunberg 1925. Thereafter Steinberg and Strauss 1947 collected three such cases from the literature.

Recanalization is the commonest cause of the failure of vasectomy to render a man sterile. Other causes include the ligation and section of a structure other than the vas e.g. a thrombosed testicular artery. However this is not common in the hands of trained surgeons. Studies started in late 1960 reported

failure rate of up to 4 percent (Pressar 1973). However the more recent studies show that the failure rate is less than 1 percent; Davis 1972, Gould 1974, Klapproth and Young 1973, Muangman 1974. The decline is probably due to improvement in the technique of vasectomy as is the case in this series. However it is essential that a candidate for vasectomy should know of this small percentage of failure before he submits himself to the operation. Marshall and Lyon 1953, reported an illustrative case, "... recanalization took place after a section of vas had been removed, the lumina had been coagulated with diathermy, and the ends ligated with silk after being turned back." The surgeon just cannot win in all the cases he operates on.

The possibility of the existence of a third vas, though not common must be considered in cases where the sperm count does not get to negative. Cases have been reported by Getze (1959) and Tuffill (1970) as mentioned by Wallace & Riddle (1971).

In all his enthusiasm to prevent recanalization, the surgeon must bear in mind a resolution passed at the second International Conference on Sterilization, Geneva, February 1973. "The operation must always be done bearing in mind the possible necessity for future reanastomosis should the patient re-marry, and it thus follows that a minimal amount of vas must be destroyed compatible with an effective operation .....".

Infection at the site of operation is a complication seen in less than 1 percent of vasectomy. In this series one patient had the operation site infected. This did not present any problem in management. Infection could also affect the vas itself, the epididymis and the testis. In this instance it is noted that the case of total gangrene following vasectomy was reported by Pryor et al (1971). The use of non-absorbable material to ligate the free ends of the vas can promote chronic and troublesome infection. Five deaths due to tetanus infection of the vasectomy site were reported amongst 62,000 men who had vasectomies done at the family welfare festival in India during 1971. This was published in the National Herald, Lucknow, India on April 3rd, 1972. Although the cause of the tetanus infection was not established there were circumstances which give rise to suspicion with regards to sterility when these procedures were carried out. However no record of death from tetanus has been reported in connection with vasectomies done under proper aseptic conditions. In many of these no routine antibiotic was given to the patients.

Other infections such as epididymitis and orchitis are not commonly seen. One of the most important factors that is worrying the Malaysian males as well as females, and for that matter other Asians, is whether the operation is going to lead the man into a state of feminity and sexual impotence. Basically this fear stems from the misconception that vasectomy is the same operation as castration. In controlled series as well as in animal experiments it has been shown that no significant side effects follow vasectomy. Where changes occur these were usually within normal limits and were not harmful. For example a 1973 study of 32 men one year after vasectomy reported no changes in the blood levels of sodium, potassium, chloride, carbondioxide, albumin, calcium, cholesterol, alkaline phosphatase, glucose, creatinine and bilirubin and no significant change in uric acid. This study was conducted at the Battelle Memorial Institute. Gregoire and Moran (1972 and 1973) found no significant change in either protein, fructose, lactic dehysrogenase or glucose-phosphate isomerase, in the seminal plasma of post-vasectomised patients. Studies conducted at the George Washington University Medical Centre by Derrick et al (1974) showed that there is a temporary suppression of spermatogenesis and an arrest of sperm maturation immediately following vasectomy. However, normal spermatogenesis soon resumes. There is also evidence to show that there is no change in the level of pituitary gonadotropins (F.S.H. – L.H.) or testosterone. (Smith et al 1974 and Speidel et al 1973).

Conclusion:

It is generally accepted that family planning is necessary in Malaysia as in many countries in the world. The backbone of family limitation is built around the condoms, the oral contraceptive pills and the intrauterine contraceptive devices. The condoms still carries a high rate of failure as experienced by the local population. Male and female sterilizations are essential for more reliable and permanent family limitation.

The experiences elsewhere and locally have shown that male sterilization is cheap and suitable for family limitation. It can be implemented in large campaigns such as the vasectomy camps in India. The complication rate is very low.

There is also an urgent need for the training of more doctors to provide this service to patients who need it. Studies should be intensified to develop a vas valve. If this reversibility can be assured the popularity of this simple procedure will increase.

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Occurrence of Opium Alkaloids in Commercial Herbal Stomach Remedy Preparation

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Abstract

Nine different brands of commercial herbal stomach remedies were screened for the presence of morphine. Detection of morphine was done by thin layer chromatography followed by gas chromatography. It was found that one of the nine brands screened contained morphine. The amount of morphine present in this particular brand was estimated to be 1.2 mg.

Introduction

STOMACHACHE PREPARATION OF various types are used very widely in South East Asia, in particular by the people of Chinese origin. In Malaysia these stomach preparations can be obtained freely from Chinese druggist and sundry shops.

The purpose of the present investigation is to discover if any of these commercially available preparations contain morphine.

Materials and Methods

Nine different brands of stomachache preparations were obtained from the Chinese druggist shop. All nine preparations had been claimed to be effective in relieving stomachache and vomiting, while a few preparations claimed to be additionally useful in relieving cough, dysentry, indigestion and seasickness. The nine brands are assigned names ranging from brand A to brand I and the weight of each single dose is as shown in table 1.

Extraction – Single doses of the individual preparations were each digested with 25 ml dilute hydrochloric acid (1N) at 60° – 80°C for three hours. The aqueous suspension was filtered and the filtrate treated with solid sodium carbonate until the final solution acquired a pH of 8.6. The alkaline solution was then extracted with a chloroform: isopropyl alcohol (IPA) mixture (3:1) twice (1 × 50 ml, 1 × 25 ml). The combined organic phases was concentrated to 1.5 – 2.0 ml under reduced pressure after drying (anhydrous Na_2SO_4). This fraction was expected to contain any phenolic alkaloids that might be present in the original dose.

Table 1
Sample Identification and Their Corresponding Weights

Brand	Weights (g)
A	1.36
B	2.15
C	1.82
D	1.29
E	1.24
F	1.13
G	1.19
H	1.28
I	1.34

Table 2
Morphine Rf Value on Silica Gel TLC (0.1 mm Plates)

Solvent System	Rf Value
$CHCl_3$: IPA, 3: 1, with 1% conc. ammonia	0.45
Benzene: methanol, 4: 1	0.31

Identification – Morphine was identified by means of thin layer chromatography (TLC) on silica gel GF_{254} using the solvent systems indicated. Morphine spots were visualised with iodine vapour (brown spots) and Dragendorf's reagent (orange spots). Only the extract from brand E showed an equivalent spot with identical characteristics (figure 1).

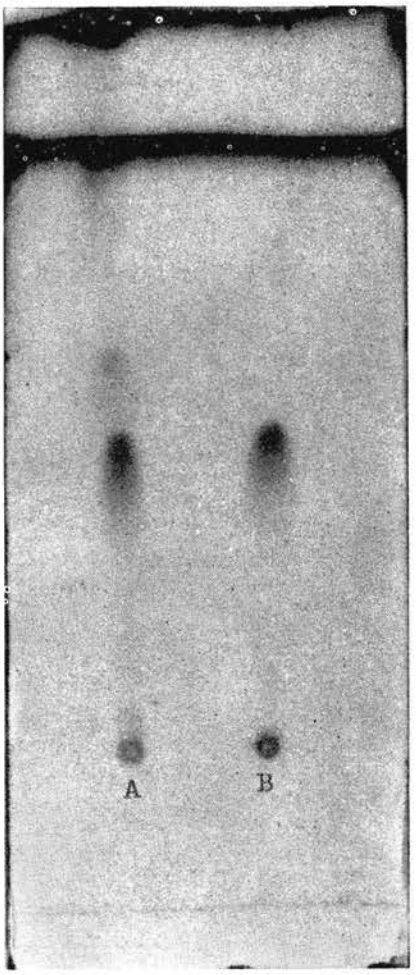

Figure 1
TLC Chromatogram of Sample E (A) and Morphine Standard (B).

Morphine was further confirmed in sample E by conversion of the alkaloid present to its diacetyl derivative (heroin) which was identified separately by comparison on gas chromatography with an authentic sample prepared from morphine.

Quantitative estimation – A quantitative estimation of the amount of morphine present in a single dose of brand E was carried out by measuring the spot

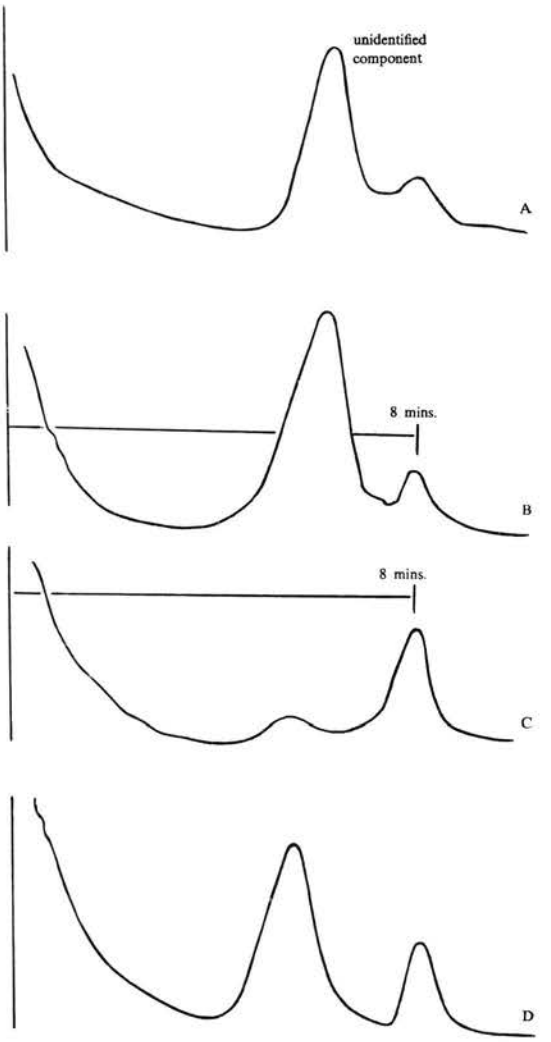

Figure 2
Gas Chromatograms Indicating Presence of Diacetylmorphine.

A = Sample before acetylation
B = Sample after acetylation
C = Diacetylmorphine (heroin)
D = Peak enhancement

areas for known aliquots of a standard solution of E in chloroform. The areas were then compared on a calibration curve obtained with an authentic sample of morphine, figure 3.

Acetylation of morphine standard and of the alkaloid extract from brand E – Morphine sulphate (8.2 mg)

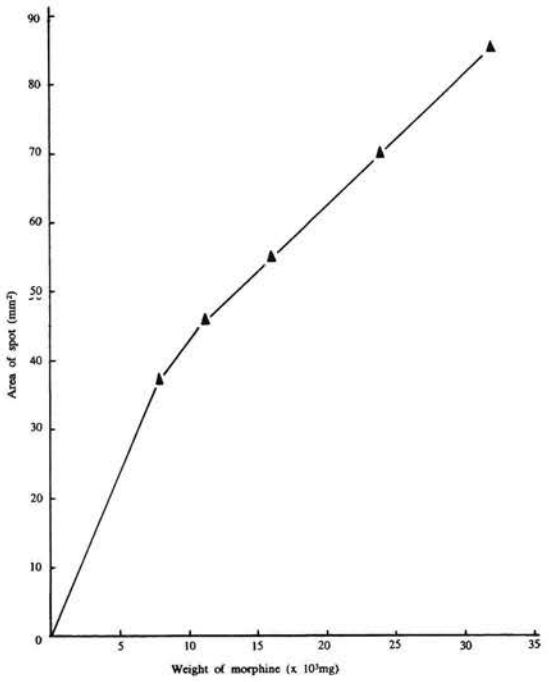

Figure 3
Calibration Curve of Spot Weight VS Area for Morphine on 0.1 mm thick Silical Gel TLC Plates. Spots were visualised with Dragendorf's Reagent.

was dissolved in 0.4 ml acetic anhydride and the mixture refluxed at 155° – 160°C for 5 hours. Excess acetic anhydride was removed under reduced pressure and the residue then taken up in 0.25 ml chloroform containing a trace of ammonia as described by Miller, 1972.

The original extract of brand E in chloroform (1.6 ml) was completely evaporated under reduced pressure. 0.4 ml acetic anhydride was added to the residue and refluxed at 155° – 160°C for 5 hours. Removal of the excess acetic anhydride as before and dissolution of the residue with 0.25 ml chloroform gave the product sample used directly for the gas chromatography.

Gas chromatographic analysis – This was carried out on a 5 feet × $\frac{1}{8}$″, 1.5% OV — 101 on chromosorb Y column at 225°C with nitrogen carrier gas flowing at 26 ml/min using a Varian 940 instrument equipped with a flame ionisation detector.

Results

Of the nine brands of preparation, only the extract of brand E showed an equivalent spot with identical characteristics as shown in figure 1.

In figure 2, trace A is the gas chromatogram of the sample E which does not show the morphine which was expected to be tenaciously retained by the column used. Trace B was obtained from sample E after acetylation; trace C was obtained from the products of the acetylation of morphine and finally trace D in a peak enhancement run with a combined aliquot of acetylated E and heroin. The enhancement of the new peak appearing in trace B confirms that it is heroin and therefore morphine was present in brand E. The TLC supports the conclusion reached with the gas chromatography results in that the morphine spots (Rf 0.20) ($CHCl_3$: IPA, 3:1) were replaced by diacetylmorphine (Rf 0.38).

From the calibration curve of figure 3, an estimate of 1.2 mg of morphine was obtained for a single dose of sample E which corresponded to a content of 0.1%.

Discussions

Both the TLC and gas chromatographic analyses confirmed the presence of opium alkaloids in brand E of the stomachache preparation. An estimate of 1.2 mg of morphine was obtained from the calibration curve with an authentic sample of morphine. It is likely that the actual content of morphine is higher than this as the best recovery of phenolic alkaloids by the procedure described had been shown to be no better than 80% and frequently much lower (Miller, 1972). The limit of detection of morphine by the present method is estimated to be 0.4 mg. The other 8 brands do not contain any morphine or if morphine is present in any, the concentrations do not exceed 0.4 mg/dose.

Conclusions

Nine commercial brands of herbal stomachache preparations were screened for the presence of morphine alkaloids by thin layer chromatography and by gas chromatographic analyses. One brand was found to contain morphine and the concentration present was estimated to be 1.2 mg/dose.

Acknowledgements

We wish to acknowledge the valuable assistance of Dr. Cyril S.F. Tang, School of Chemical Sciences, Universiti Sains Malaysia.

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Incidence of Otosclerosis in the Three Ethnic Groups in Malaysia

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Introduction

OTOSCLEROSIS is the primary focal disease of the labyrinthine capsule that may in some cases involve the oval window causing fixation of the stapes; in the other cases, it causes cochlear degeneration or a combination of both. In this study a diagnosis of otosclerosis was made if the patient complained of unilateral or bilateral hearing loss of insidius onset, progressive in nature and unaccompanied by earache or otorrhoea. The otological examination of these patients revealed a normal tympanic membrane and clinical conductive deafness. This was supported by an audiometric conductive deafness, and at operation the footplate was confirmed as being fixed.

Material & -ethods

In Peninsular Malaysia's multi-racial population of 9.4 million, the Malays form 50.7%, the Chinese 36.2% and the Indians 11% (Chander 1972). Up to date no study of otosclerosis has been made either in the whole country or in each of the three ethnic groups. The following study is an attempt to determine the relative incidence of otosclerosis in each of the 3 major ethnic groups, represented by the patient population of 15,700 new patients seen at the ENT clinic of the University Hospital over a period from August 1970 to August 1975.

Table I – Shows the distribution of otosclerosis in the ethnic groups in the total number of patients seen in this clinic.

Table II – Shows the number of cases of otosclerosis in the ethnic groups among the total number who presented with hearing loss between August 1970 – August 1975.

Table 1

	Malays	Chinese	Indian	Total
New Cases Attending ENT Clinic From August 1970-75	2574 (20%)	8909 (54%)	4218 (26%)	15700
No: Of Otosclerosis 1970 – 1975	4 (12%)	10 (30%)	19 (58%)	33
Incidence	1: 640	1: 890	1: 220	

Table 2

	Malays	Chinese	Indian	Total
Total No: Of Patients With Deafness 1970-75	308	997	448	1753
No: Otosclerosis	4	10	19	33
Incidence	1: 80	1: 100	1: 20	

Discussion

There is very little information available on the racial distribution of otosclerosis in South East Asia. Mawson (1963) states that the incidence in the general population in England is 1:200. Larsson (1952) found unilateral otosclerosis as high as 15% in his cases. Guild (1944) studied 1,161 temporal bones, equally divided between Whites and Negroes. He found the racial incidence of histological otosclerosis to be 1:12 for the Whites and 1:96 for Negroes. In Peninsular Malaysia the incidence as seen among the ethnic groups is Malay 1:640, Chinese 1:890 and Indians 1:200.

Kapur and Patt (1966) have found that the incidence of otosclerosis in South India is 30 – 31% of all patients with hearing loss. In our study the incidence among the Indians in Malaysia is only 5% of those with hearing loss. In the other ethnic groups it is even less, being 1.25% in Malays and 1% in the Chinese.

In the Indians in Malaysia the reason for the higher incidence would be explained by the fact that consanguineous marriages are very common among them, unlike in the other two ethnic groups. Morrison (1967) found a definite hereditory tendency in 70% of his patients.

Most of the above patients had been to several general practitioners before being diagnosed and operated on here. Many may as yet be undiagnosed since many general practitioners are still unaware of this form of deafness, and also of the possibility of its treatment by surgical intervention.

Summary

The incidence of otosclerosis in the different ethnic groups attending the University Hospital over the five year period 1970-1975 is outlined. It is noticed that there is a significant increase in the incidence of this condition among the Indian races.

Acknowledgement

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Complications in Cataract Surgery

by Keshmahinder Singh

CATARACT is one of the commonest ophthalmic conditions and every ophthalmic surgeon is interested in cataract surgery. Cataract surgery today has made considerable advancement and patients having this disability have excellent chance of regaining good vision following surgery. Most of us however do occasionally have problems and I hope these remarks which refer to senile cataracts would be of some assistance in coping with some of the problems.

The main objective in cataract surgery is to give the patient the best possible visual result, a comfortable post-operative period and the minimum of complications. A perfect anatomical result should be a secondary consideration, although one should try to achieve a good anatomical result with a central circular pupil.

1. Wound Closure

Adequate wound closure is essential and can be achieved by the placing radially three to five buried corneo-scleral sutures of eight 0 or ten 0 thickness. If the sutures are of ten '0' thickness, then five sutures should be placed as ten '0' sutures being very fine tend to cut out or break. One of these sutures, at least, must be preplaced. The anterior chamber should be reformed with Ringer's solution or saline and not air, as this is not only more physiological but also a good test of wound closure, for the anterior chamber is more difficult to reform with saline if the wound is not adequately closed. Early ambulation is then possible and desirable with the patient sitting up the same day and moving about the next day and if all is well, I discharge them 48 hours after surgery.

2. Haemorrhage

a. **Haemorrhage at Surgery:** In the tropics most eyes are pink and generally have a mild pannus so that the section usually tends to ooze blood. Therefore as a routine procedure light cautery of the superficial episcleral and scleral vessels running into the cornea is very helpful and is done after dissecting the conjunctival flap, before making the section.

Haemorrhage from the section can lead to the formation of fibrin clots adherent between the wound and the upper half of the iris. These fibrin clots tend to draw the pupil upwards into the section and this can be best prevented by cauterising the superficial scleral vessels at the limbus so that the bleeding is prevented.

Iris bleeding from one of the iris vessels, when its root is torn, can be troublesome. It is best to wait a few minutes for the bleeding to stop, then irrigate the AC and remove clots with Arruga's forceps before proceeding with the extraction of the lens.

b. **Post-Operative Haemorrhage:** Hyphaema is generally is due to excessive movement or direct trauma to the eye and occurs usually around the fifth day and is associated with pain. Fortunately most resolve well by keeping the patient in bed and padding both the eyes for 48 hours and one could also give Vitamins C and K. The intra-ocular pressure is rarely raised and settles well with diamox. One very rarely has to do a paracentesis and wash out the anterior chamber of blood clots but if the eye remains painful in spite of diamox and the blood

does not show a level in 48 hours it is best to do a paracentesis and evacuate some blood through keratome corneal incision, within the limbus and from the temporal side. Diabetes, hypertension and blood diseases must also be looked for and treated.

3. **Vitreous Loss**

Vitreous loss is a serious complication which must be avoided. It should be anticipated when there is evidence of positive pressure within the eye. One should be very careful if the wound tends to gape after making the section, especially if there is a horizontal corneal fold or the iris tends to prolapse into the wound or the lens moves forwards into the wound. This can often happen with patients who have prominent eyes and the appearance of slight proptosis or in tense patients.

The surgeon here must not rush but must be patient, gentle in all manoveours and make every attempt to reduce pressure within the eyeball. He should make certain that the akinesia is good with no squeezing of the eyelids. There is no tension on the superior rectus bridle suture and the eyeball does not tend to roll up and above all, the patient should not be tense and is relaxed. There should be a preplaced corneal suture which should be ready to be tied on extracting the lens. It is wise to do a sector iridectomy before proceeding to extract the lens.

When extracting the lens there should be no traction on the superior rectus suture. The right hand should hold the conjunctival flap with the forceps while the left hand with the cryopencil extracts the lens which is done by the sliding technique without any pressure on the eyeball.

However, if vitreous loss does occur, there is no reason to get depressed as these patients can have good visual results. One should relieve any pressure on the eyeball by releasing the superior rectus suture. The preplaced corneal scleral suture at 12 o'clock is quickly tied. The upper eyelid is brought down and the eye is closed for a few minutes to allow the vitreous to settle and time is taken to reassure the patient that all is well. When the patient is calm, the eyelid is retracted, the wound inspected and iridectomy and vitrectomy done if any vitreous or iris are found in the wound, and the wound sutured. The wound is washed cautiously with saline and any vitreous adherent to the wound washed back into the anterior chamber when forming the anterior chamber. This must be overdone as it can push vitreous out again. The cannula should not enter the anterior chamber.

b. **Vitreous in the Anterior Chamber**

This occurs when the iris and pupil suddenly sink after extraction of lens and the vitreous enters the anterior chamber through the pupil. Both the iris and the vitreous can become adherent to the wound resulting in the pupil riding upwards. A full iridectomy here is justified and any vitreous in the wound washed back in the anterior chamber by washing the wound with saline. This gives a much more satisfactory result with less traction on the vitreous, a more centrally placed pupil, the eye settling faster and a lower incidence of late uveitis.

4. **Sector Iridectomy**

There are certain situations when full or key-hole iridectomy would be preferable to a peripheral iridectomy as this gives rise to less post-operative complications, better visual results and a more central pupil.

a. When there is a vitreous loss or vitreous present in the anterior chamber.

b. In patients with very prominent eyes, having the appearance of slight proptosis who have a higher incidence of vitreous loss. They must be adequately sedated and relaxed and the eye massaged to lower the intra-ocular pressure. Plan doing an elective full iridectomy before intra-capsular extraction of the lens especially if there is tendency for the wound to gape.

c. When cataract extraction is done under local anaesthesia where sedation is not adequate, the patient being restless or there is still some eyelid movement, then an elective broad iridectomy should be done before extracting the lens. A neater and better cosmetic appearance is achieved.

d. When the pupil is small and does not dilate well, a sphincterotomy or an iridectomy could be done. Also when the iris tends to prolapse and there is difficulty in replacing it into the anterior chamber after closure of the wound.

e. In acute glaucoma, secondary to a mature or hypermature cataract, especially if the iris is atropic above and also in patients whose other eye is blind from a retinal detachment.

5. **Problems with Lens Delivery**

a. **Intumesent Cataract:** An intumesent cataract with a very tense capsule is often difficult to deliver especially when using an Arruga's forceps. If a cryopencil is not available a useful procedure is to puncture the capsule with a fine needle. This releases a bead of soft lens matter making the capsule less tense and easier to grasp enabling one to remove the lens within the capsule. One could also tumble the lens using the Old Smith's technique but it

would be wise to use alpha-chymotrysin when doing this, if the patient is under sixty five years of age.

b. **Rupture of Lens Capsule**

Cryo-extraction has greatly reduced the risk of capsule rupture which occurs when the capsule is either weak or if there is excessive traction on it. The capsule is generally degenerate and friable in the elderly patient with nuclear cataract or thin and stretched in intumescent cataracts. A defective tip of the intra-capsular forceps can the tear the capsule as also when the large area of the capsule is frozen when using cryopencil in a wet anterior chamber. When extracting the lens with a weak capsule the anterior chamber and the capsule should be dried with a sponge. It is best to apply the cryopencil close to the equator than at the centre of the lens. Only freeze the cryoprobe after it is in contact with the anterior capsule.

Traction on the capsule may be excessive if the section is small, the pupil has not dilated well, presence of post synechiae, a strong zonule or when the lens is large as in old patients with nuclear cataracts. A section of 160 circumference is adequate and if the pupil is not dilating a sphincterotomy at 6 o'clock is very useful unless one decides on a sector iridectomy.

It is also useful to use a little expression especially towards the end of delivery of the lens. If the capsule ruptures, then remove all capsule adherent to the cryopencil but at the same time do not release the pressure over the lower half of the cornea as the lens nucleus may fall back into the anterior chamber if pressure is not maintained.

The lens nucleus and soft lens matter is slowly eased out with an iris repositor. Remnants of the lens capsules lying in the wound and on the anterior surface of the iris are removed with an Arruga's forceps. The pre-placed corneo-scleral suture at 12 o'clock is tied and the soft lens matter in the anterior chamber is then gently washed out. Any capsule remnants floating in the anterior chamber can be picked with an Arruga's forceps and removed usually leaving a clear vitreous face and pupil.

6. **Subluxated Lens**

When dealing with a subluxated lens there should be at least one pre-placed corneo-scleral suture. The section should be larger, extending round 180 circumference and preferably made over the area where the zonule is still intact and the lens is lying on the surface of vitreous. A sector iridectomy is carried out exposing the subluxated lens. The anterior chamber is dried with a sponge including any presenting vitreous. The lens is then touched with the cryopencil, any iris or vitreous being pushed aside with the sponge. Lens is then lifted upwards and any remaining zonular fibres are gently broken by side to side movement, (the assistant holding the conjunctival flap and cornea with forceps) and no pressure is used to express the lens, the lens being delivered by the sliding technique. The vectis is used to remove the lens, when the lens is lying deeper in the anterior vitreous and covered by the vitreous, as it can be difficult to get the cryopencil to adhere to the lens. If the lens falls further back into the posterior vitreous and the capsule is intact make no attempt to extract the lens and close the wound for these eyes can have good vision for years. However, if the capsule has ruptured, try to remove the lens nucleaus. A retained lens with a ruptured capsule will cause chronic uveitis leading to an uncomfortable, irritable blind eye.

7. **Shallow Anterior Chamber**

The commonest causes of a shallow anterior chamber is a leaking wound, choroidal detachment or sudden emptying from trauma or straining. Adequate wound closure by multiple by carefully placed sutures has reduced the incidence of this complication considerably, choroidal detachment and trauma are now the major causes. There is also a strong psychological factor, as the majority of my patients who develop shallow anterior chambers are Indians and generally do well on tranquilisers. Reassurance, physical and mental well-being are important.

I prescribe diamox 500 mg statum and 250 mg thrice daily and dilate the pupil. Diamox is reduced to 250 mg twice daily after three days and once daily after six days. The action of diamox here is uncertain. It reduces the amount of the aqueous being secreted and it may thus dry the leaking fistula and also allowing time for the supra choroidal fluid to be absorbed.

It is necessary to operate if the anterior chamber does not reform after 14 days. Release the supra-choroidal fluid by a scleral puncture over the site of choroidal detachment and reform the anterior chamber with air (not saline) using $\frac{1}{2}$ cc of air. If there is a leaking wound this can be closed by the application of light diathermy or placing additional sutures at the site.

8. **Prolapse of Iris**

In these days with multiple sutures and careful closure of the wound, the incidence of prolapse iris is very low indeed. Prolapse of iris is generally due to a direct knock on the eye or severe jolt as from a fall. This must be stressed to every patient and he should be asked to have restrainers on his hands when sleeping. When it occurs, excision of the prolapse is done within 48 hours of discovery with suture of the gap, the patient prepared as for

cataract extraction. If the iris is just caught in the wound, then one could try for 48 hours a strong miotic (phospholine iodide or tosmillan) to pull the iris back into the anterior chamber but this treatment is very rarely successful.

9. **Secondary Cataract**

This is best prevented by washing out as much soft lens matter as possible at the time of surgery and removing as much of the capsule remnants as possible with an Arruga's capsule forceps or plane iris forceps. Any remaining posterior capsule should be observed and divided as soon as it is noticed to thicken.

Occasionally, one gets patients where there is dense pupillary membrane which has been present for some time, especially in monocular cataracts. This dense and strong membrane is best cut with a de Weckers acissors rather than dividing it with a Ziglers knife and this may have to be combined with an iridectomy.

10. **Enophthalmitis**

Endophthalmitis, in particular, bacterial endophthalmitis is one of the most serious and devastating complications of cataract extractions. Therefore early diagnosis and prompt intensive treatment is essential so that some good vision can be retained in the eye

Preventive measures must ensure the conjunctival sac clean and healthy Routine pre-operative culture for organisms in quiet eyes is of doubtful benefit and I do not culture as a routine Pre-operative antibiotics such as topical application of chloromycetin, soframycin or gentamycin eye drops could be very helpful and should be given routinely to all patients and the conjunctival sac irrigated before surgery. Sub-conjunctival soframycin or gentamycin injections may be given immediately after operation.

Post-operative infective endophthalmitis is suspected when there is severe anterior uveitis with pain and tenderness of the eye, swelling of the eyelids, chemosis, hazy cornea, cloudy anterior chamber or presence of hypopyon and this generally occurs on the second or third day. It is treated by conjunctival injections of gentamycin (garamycin) 25 mg and or soframycin 250 mg. This is repeated the next day when the patient in addition receives sub-conjunctival injection of prednisolone acetate 40 mg into the lower fornix and orbit. The sub-conjunctival anti-biotic injections are repeated at 24 – 48 hours intervals depending on the severity of the reactions until there is good response to treatment and the infection is resolving, (generally 4 – 6 injections are given). In addition to sub-conjunctival injections, the patients receives systemic therapy of either chloromycetin 250 mg four hourly or vibramycin 200 mg as initial doses and 100 mg daily. Sodium Fusidate (fucidin) is also reported to give good results. Prednisolone 20 mg daily is given for five days after which the dosage is reduced rapidly.

For topical therapy soframycin, gentamycin or chloromycetin drops are instilled every hour for the first two days after which in addition to antibiotic drops dexamethasone or prednisolone drops are instilled two hourly. The pupil is kept dilated by atropine drops twice daily. In order to achieve the best results it is essential to treat all cases with antibiotics and followed 24 hours later by addition of corticosteroids. With corticosteroids therapy the inflammation settles faster and the eye is more comfortable and the anti-inflammatory action of the steroids prevents or reduces formation of pupillary membranes.

Late uveitis usually beginning about the 7th – 10th day is generally less severe and may be due to a reaction to lens protein or to re-activation of endogenous uveitis. These patients are treated by dilating the pupil and the use of topical corticosteroids and sub-conjunctival prednisolone acetate.

11. **Anaesthesia**

A plea is made for more cataract surgery under local anaesthesia for adults. Local anaesthesia with adequate sedation is very suitable for cataract extraction in adults because:

a) It is safe as only 5 cc of 2% xylocaine solution is adequate for facial block, retrobulbar, superior rectus and eyelid injections, providing excellent anaesthetic effect.

b) Patients recover faster and are ambulent earlier.

c) It saves time, the time taken to operate under local anaesthesia is half of that taken under general anaesthesia.

d) During the present shortage of anaesthesiologists, the use of local anaesthesia in cataract surgery releases them for surgical procedures where their need is more essential.

e) It is cheaper in terms of cost of drugs, equipment needed and the staff required to administer it.

f) Retrobulbar haemorrhage is a rare complication and its incidence is reduced by the use of a round tipped or blunt needle.

12. **Astigmatism**

The resulting astigmatic error and the axis of astigmatism of the aphakic correction is greatly depended upon the care taken in suturing the corneo-scleral wound. If the track of the suture is deeper in the corneal lip and more superficial in the scleral lip then an astigmatic error with a horizontal acis results. So it is essential that the sutures should be well placed and the depth should be about equal in the cornea and the sclera to achieve the smallest astigmatic correction.

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Face Presentation

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FACE PRESENTATION is an uncommon presentation and due to its rarity, insufficient cases can be collected within any one obstetric period to permit proper critical evaluation of the various problems associated with its diagnosis and management. One has then to depend on cumulative data from various reports.

This paper reviews our experience with 16 cases of face presentation managed at the University Hospital, Kuala Lumpur from January 1968 to December 1975.

RESULTS AND DISCUSSION

1. Incidence

Sixteen cases of face presentation were managed between 1968 and 1975, out of a total of 20,903 hospital deliveries, making an incidence of 1: 1306 or 0.08%. Reported incidences vary from 0.09% to 0.55%. Cumulative series indicate a mean incidence of 1: 496 to 1: 458 or 0.20% to 0.21% respectively (2, 7).

Eight patients were Indians, five were Chinese, two were Malays and one was a Orang Asli.

2. Etiological Factors

As with brow presentation, much emphasis has been placed on the possible etiological factors. These can be divided into maternal, fetal and placental-membrane.

Maternal Factors

i) *Parity*

The majority of patients were multiparous i.e. 14 patients (87.5%). Six patients (37.5%) were para 5 and above. Although multiparity and grand-multiparity have been mentioned as factors, they are unlikely to be important predisposing factors.

ii) *Contracted Pelvis*

There was no case of pelvic contracture resulting in feto – pelvic disproportion. Feto – pelvic disproportion has been commented to be an important factor in the genesis of face presentation, its incidence varying from as low as 5.0% (1) to as high as 40.0% (4), with most reports from 10.0% to 15.0% (2, 5, 6, 7).

Fetal Factors

i) *Fetal size*

Two infants weighed less than 2500 g (12.5%) and one weighed over 4000 g (6.3%).

Prematurity (birth weight less than 2500 g) is one of the prominent predisposing factors and a clear cut relationship exists with face presentation. Reported rates vary from 8.0% to 50.0% (1, 2, 5, 6, 7).

Similarly, big babies (over 4000 g) have been claimed to be prominently associated with face presentation, with incidences varying from 10.0% to 15.0% (1, 2, 5, 6, 7).

ii) *Fetal abnormality*

One fetus was anencephalic (6.3%). Other studies indicate incidences of 2.5% to 11.0% (1, 2, 4, 5, 6). Other abnormalities of the fetus that have been associated with face presentation include tumours of the neck, goitres and hydrocephaly.

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There were no cases of multiple pregnancy in the present series.

Placental-membrane Factors

i) *Premature rupture of membranes*

This occurred in one patient at 29 weeks (6.3%), compared to reported incidences of 5.0% (1) and 22.7% (7). High incidences of premature rupture of membranes have been commented to be probably secondary to poor adaptation of the fetal presentation to the cervix uteri.

ii) *Cord round neck*

This was present in 4 patients (25.0%). A short cord or cord round neck have been claimed to be etiological factors with reported incidences of 2.5% to 19.2% (1, 2, 6, 7).

Unknown etiology

No predisposing factor was found in 6 patients (37.5%). Reported incidences vary from 20.0% to 50.0% (2, 5, 7).

3. **Position of Head before Diagnosis of Face**

In all patients, a diagnosis of face and brow (in 2 patients) was made at the first vaginal examination. There was therefore no data available on pre-existing occiput-posterior positions and deflexion attitudes.

An initial brow presentation was present in 2 patients (12.5%). Both corrected spontaneously to face, mento-transverse and while one delivered spontaneously, the other had a caesarean section for fetal distress. Initial brow presentation was found in 10.0% of patients (1).

Occiput-posterior positions with deflexion attitudes in labour no doubt play important roles in secondary face and brow presentations.

4. **Face Positions**

Of the 16 cases, 3 were mento-anterior (18.7%). 9 were mento-transverse (56.3%) and 4 were mento-posterior (25.0%). Of the mento-anterior cases, one delivered spontaneously, one by forceps and one by caesarean section. Spontaneous delivery occurred in 6 of the mento-transverse cases, one was delivered by forceps and 2 by caesarean section. Of the mento-posterior cases, 2 were delivered spontaneously and 2 by caesarean section.

Reports have indicated a higher incidence of mento-anterior positions, from 40.0% to 75.0% (1, 4, 5, 6), although high incidences of mento-posterior positions have also been reported, from 30.0% to 60.0% (4, 7).

Face positions are important factors in management as mento-anterior positions are consistent with natural spontaneous deliveries (2, 3, 6), while mento-posterior and mento-transverse positions are not so favourable and tend to be associated with higher rates of operative interference (2, 3, 6). Nevertheless, spontaneous rotation to mento-anterior positions can occur in 45.0% to 65.0% of mento-posterior positions (5).

5. **Time of Diagnosis**

Primary face presentation was diagnosed in one patient (6.3%) in the antenatal period. Even in this patient, X'ray was not taken for suspicion of face presentation but for suspicion of hydrocephalus.

Diagnosis of face presentation was made in early first stage labour (os less than 6 cm.) in 5 patients (31.2%), in late first stage labour (os more than 6 cm.) in 7 patients (43.7%), and only in second stage or at caesarean section delivery in 3 patients (18.8%).

It has been commented that in a large percentage of cases (over 50.0%), the diagnosis is not made until delivery is imminent (1, 5, 6, 7). Although there is this lack of accuracy in early detection, nevertheless most patients proceed in labour without incident and are delivered spontaneously or by low forceps.

6. **Labour**

i) *Incoordinate labour*

This occurred in 3 patients (18.8%). One patient had a brow presentation which spontaneously corrected to face presentation and delivered a live birth weighing 3030 g after a labour of 21 hours 45 minutes. The second patient laboured for 28 hours 10 minutes before she delivered spontaneously a live birth of 4080 g. The third patient was delivered of a live birth of 3330 g by manual rotation and forceps delivery under general anaesthesia after labouring for 24 hours 50 minutes.

ii) *Obstructed labour*

This was observed in one patient (6.3%) where a face, mento-posterior progressed to a brow posterior. At os 6 cm., the brow was still unengaged and a caesarean section was done for a 3830 g baby.

iii) *Duration of labour*

Of the 11 patients who delivered vaginally, labour was less than 12 hours in 8 patients (72.7%), between 18 – 24 hours in one patient (9.1%), and more than 24 hours in 2 patients (18.2%).

The mean duration of labour was 11 hours 20 minutes.

Dede and Friedman (2), in an excellent review of 88 cases, commented that face presentation did not appear to affect the course of labour in either nulliparous or multiparous patients to any significant degree, contradicting the previously held views that face presentations are associated with prolonged labours.

Nevertheless, there is a definite though not statistically significant trend in face presentation in babies weighing over 2500 g towards longer duration of labour with regards to the latent, active and deceleration phases and the second stage.

The relationship of feto-pelvic disproportion in face presentation to abnormal labour patterns is obvious.

In Cucco's series (1), 75% of patients delivered within 12 hours of labour and 7.5% after a labour of over 24 hours. The mean length of labour before delivery or caesarean section was 22 hours in primigravidas and 13.5 hours in multigravidas in Posner's series (6).

7. Mode of Delivery

Nine patients (56.3%) delivered spontaneously, 2 by forceps (12.5%) and 5 by caesarean section (31.2%). Of the 5 delivered by caesarean section, 3 were for clinical fetal distress, one for obstructed labour due to brow posterior and one for feto-pelvic disproportion (where postpartum X'ray pelvimetry showed the pelvis to be adequate and gynaecoid).

Caesarean section rate is high in face presentation with incidences varying from 7.5% to 53.0% (1, 2, 4, 6, 7, 8). This reflects the association of this form of malpresentation with dystocic labour and fetal distress.

Nevertheless, there are indications for good prognosis for vaginal delivery in face presentations, especially with mento-anterior positions (1, 5). Vaginal delivery in face presentation varies from 60.0% to 90.0% (1, 2, 5, 6, 8).

8. Maternal and Fetal Outcome

There was no maternal death and no maternal morbidity.

All 16 infants were live births. There was no stillbirth. Two of the infants died in the perinatal period, one because of anencephaly and the other of gross prematurity (birth weight of 900 g at 29 weeks gestation).

Six infants had an apgar score of 6 and below at one minute, while 10 infants had apgar scores of 7 to 10. At 5 minutes, only 2 infants had apgar scores of 6 and below and 14 infants had scores of 7 to 10. Of these two, one was the grossly premature infant and the other was a mature infant delivered by caesarean section. This latter infant had an uneventful neonatal progress.

Dede and Friedman (2) reported an increase in maternal morbidity but commented that this was related to the operative intervention rather than to the presence of face presentation per se.

In this paper, there was no fetal loss directly related to face presentation per se. Corrected perinatal loss have been reported at 37 to 47 per 1000 births (6, 7), although higher incidences of 100 per 1000 (3) and 130 per 1000 births (2) have been reported.

COMMENTS

One can make the following comments about face presentation:

1) there is a lack of accuracy in early detection and so obstetricians should have an acute sense of suspicion and recognise the malpresentation early

2) the important predisposing factors include disproportion, prematurity and large fetal size

3) once the diagnosis is made, the pelvis should be assessed to be adequate by X'ray pelvimetry and fetal abnormality excluded

4) in the presence of feto-pelvic disproportion and no fetal abnormality, delivery is best effected by caesarean section

5) early caesarean section should be practised more liberally in elderly primigravidas, mento-posterior positions, large babies and suspect pelvis

6) in the other cases, lack of fetal mortality and significant morbidity warrants a more conservative attitude. The maxim should be "if a *face* is making progress, leave it alone". This maxim should hold true even for mento-posterior positions because spontaneous rotation to mento-anterior occurs in a fairly large number of cases

7) conversion procedures have met with indifferent success and are best avoided in modern day obstetric practice. Internal podalic version and breech extraction should never be done

8) the Kielland's forceps may be employed in a few carefully selected cases after full dilatation

9) the freer use of caesarean section and the avoidance of complicated vaginal procedures will no doubt help towards an increased perinatal salvage.

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The Bacterial Causes of Diarrhoea in Malaysia

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DIARRHOEAL DISEASES are the cause of much morbidity and mortality in developing countries, particularly in the very young. In areas where health conditions are poor, acute gastro-intestinal infections account for a high proportion of deaths.

An idea of the problem in Peninsular Malaysia is obtained when returns of gastro-enteritis cases from government health facilities are examined (1). In 1972 there were altogether 123,422 cases of gastro-enteritis reported to the epidemiology unit at the Ministry of Health, Malaysia while in 1973 there was 131,552.

In this region, even in an urban society like Singapore, acute gastro-enteritis is the commonest condition seen in hospital paediatric practice (2).

Many agents have been held responsible for the causation of diarrhoea. Infective diarrhoea is caused by bacteria, parasites and viruses. Other causes of diarrhoea include the malabsorption syndromes, cystic fibrosis, gluten induced enteropathy, disaccharide intolerance, metabolic diseases, feeding mismanagement, parenteral infection, intolerance to drugs, milk allergy and surgical conditions (3).

Acute diarrhoeal disease is believed to have its basis in bacterial infections despite the observation that specific enteric pathogens may be isolated from only a relatively small percentage of individuals affected with diarrhoea (4).

In spite of this relatively small yield of enteric pathogens from clinical specimens it is necessary to carry out investigations of the etiology of diarrhoea for the purpose of epidemiologic studies as well as for the institution of the appropriate lines of treatment and clinical management.

In the present study, faeces from 3,809 patients (of all ages) with diarrhoea as the presenting symptom were investigated for the presence of recognised enteropathogenic bacteria. The purpose of the study was to see in what percentage of these cases could be recognised bacterial enteropathogen be isolated; the relative prevalence of the different bacteria found; and to see if there were any significant differences among the different age and racial groups and between males and females.

Materials and Methods

Specimens of faeces from cases of diarrhoea were sent to the bacteriology division, Institute for Medical Research, Kuala Lumpur. The study period commenced in September 1972 and was completed in August 1973. Specimens were sent from various parts of Malaysia including the towns of Seremban, Tampin, Bahau, Jelebu, Kuala Pilah, Port Dickson, Kajang, Pekan, Dungun, Kemaman, Kota Bharu, Kuala Lipis, Kuala Kubu Bharu, Kuantan, Mentakab, Bentong, Kuala Trengganu, Temerloh and the paediatric wards of the General Hospital, Kuala Lumpur. These contained a mixture of cases from both urban and rural areas.

Either fresh stool was sent (in cases where transport time was minimal) or stools were sent in Selenite medium, glycerine phosphate holding medium and alkaline peptone water.

Specimens arriving in transport and selective media were incubated overnight before being subcultured on to DCA and MacConkey and Blood Agar plates and on to Monsur's medium in the case of alkaline peptone water specimens. Fresh faeces were plated directly on to the above media and also into selenite F. which was subcultured after overnight incubation. Further identification was based on biochemical reactions and agglutination with polyvalent and specific antisera.

Salmonella, Shigella, Staphylococcus aureus, Vibrio cholerae, Vibrio parahaemolyticus and *Plesiomonas shigelloides* were looked for.

Enteropathogenic *E. coli* and *Staphylococcus aureus* were specifically looked for only in children under 10 years of age. For the isolation of *Staphylococcus aureus* specimens were inoculated into Robertson's cooked meat medium with 10% salt.

For purposes of discussion the cases were classified according to race, sex and the following age groups – 0-1 week, 1 week to less than a year, 1 to 5 years, 6 to 10 years and older than 10 years.

During the study period there was an outbreak of cholera in Malaysia and specimens sent from these cases, suspects and contacts were sent only in alkaline peptone water and thus were not suitable for examination of other pathogens. Because an outbreak of this nature would not reflect the true distribution of enteropathogens it was decided not to include in the study specimens sent only in alkaline peptone water for the specific isolation of cholera vibrios from contacts and cases.

Results

Table I shows the distribution of cases studied and the isolation rates of bacterial enteropathogens for the different age and ethnic groups, while Table II lists out the various isolates including those from mixed infections.

Isolation rates:

3,809 specimens of faeces were studied. In 605 of these recognised enteropathogens were isolated. This gives an overall isolation rate of 15.9%.

The isolation rates can be considered separately for the different age groups. Two isolates came from patients whose age group was not known. From these figures it appears that isolation rates for bacterial pathogens are progressively lower as the age of the patient increases.

Application of the X^2 test shows these figures to be significant ($p<0.05$) in all cases except for comparison between the 0 – 1 week and less than a year groups, the less than 1 year and the 6-10 years groups, the 1-5 and the 6-10 age groups.

Similarly the isolation rates may be compared for the different racial groups. Application of X^2 test shows significant difference ($p<0.05$) when the Chinese are compared with the Malays, and Indians. The difference seen between the Malays and Indians is not statistically significant.

Pathogens isolated:

605 isolates were found of which *Salmonella* constituted 51.0% (309 isolates); Enteropathogenic *E. coli,* 30.6% (185); *Shigella,* 9.3% (56); *Staphylococcus aureus,* 4.9% (30); mixed infections, 3.5% (21); *Vibrio parahemolyticus,* 0.5% (3) and *Plesiomonas shigelloides,* 0.2% (1). There were no isolates of *V. cholerae* from these cases.

Salmonella infections:

Salmonella infections formed the largest group of pathogens isolated (51.0%).

Including the *Salmonella* which featured in mixed infections there were altogether 327 isolates composed of 22 different serotypes (Table II). *S. typhimurium* was by far the most prevalent accounting for 189 isolates. Others which were relatively frequent were *S. weltevreden* (28 isolates), *S. typhi* (18 isolates) and *S. paratyphi* B (14 isolates).

S. typhimurium

The percentage of individuals in which this organism was isolated is shown in Table III.

From these figures it appears that the younger age groups are more commonly affected and also that Chinese patients seem to have a higher incidence. The differences seen between the Chinese and the other groups is found to be statistically highly significant ($p<0.01$). The difference seen between the Malays and Indians is also highly significant. When age groups are considered, the differences seen between those less than a year old and the older age groups is statistically significant.

Salmonella weltevreden:

The distribution pattern of isolates of *S. weltevreden* is seen in Table IV.

From the figures it appears that Indians and 'others' appear to be affected more than the other racial groups. However this difference was not found to be statistically significant. Similarly the higher incidence seen in the older age groups is not statistically significant except when the less than one year old group is compared with the older than 10 years age group.

Table I

Distribution of Cases Studied and Isolation Rates

AGE GROUPS

Race	0 – 1 week			1 week – 1 year			1 – 5 years			6 – 10 years			>10 years			Total	Isolation rates
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total		
Malays	11	15	26	251	170	421	121	77	198	37	31	68	406	240	646	1359	13.5%
Chinese	34	31	65	300	190	490	131	55	186	22	26	48	231	192	423	1212	21.2%
Indians	5	11	16	191	160	351	105	83	188	31	22	53	211	200	411	1019	14.0%
Others	0	0	0	13	7	20	13	8	21	11	7	18	87	73	160	219	9.1%
Total	50	57	107	755	527	1282	370	223	593	101	86	187	935	705	1640	3809	15.9%
Isolation rates			31.8%			23.8%			19.2%			18.7%			7.1%		

Table II DISTRIBUTION OF ISOLATES (this includes isolates from mixed infections)

RACE	MALAYS													CHINESE														INDIANS													OTHERS													GRAND TOTAL
AGE GROUPS (YRS)	<1/52		1/52-1		1-5		6-10		>10		TOTAL	<1/52		1/52-1		1-5		6-10		>10		TOTAL	<1/52		1/52-1		1-5		6-10		>10		TOTAL	<1/52		1/52-1		1-5		6-10		>10		TOTAL	
SEX	M	F	M	F	M	F	M	F	M	F		M	F	M	F	M	F	M	F	M	F		M	F	M	F	M	F	M	F	M	F		M	F	M	F	M	F	M	F	M	F		
SALMONELLA																																															
GROUP B																																															
S. paratyphi	-	-	1	1	3	-	-	1	1	-	7	-	-	2	-	-	-	-	1	1		4	-	-	-	-	-	-	-	-	2		2	-	-	-	1	-	-	-	-	-		1	14
S. typhimurium	2	3	13	11	1	-	-	-	-	2	32	4	-	37	33	12	3	3	1	4	7	104	-	2	12	11	12	3	1	1	4	3	49	-	-	1	1	-	-	1	-	1	-	4	189
S. stanley	-	-	-	1	-	-	-	-	-	1	2	-	-	1	-	1	-	-	-	-	1	3	-	-	-	-	-	1	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	6
S. heidelberg	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	1
S. derby	-	-	-	3	-	-	-	-	-	-	3	-	-	2	2	-	-	-	-	-	2	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1	-		2	11
GROUP C																																															
S. potsdam	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1	-	-	-	1	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	2
S. bareilly	-	-	-	2	-	-	-	-	-	-	2	-	-	-	1	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-		-	4
S. newport	-	-	-	1	-	-	-	-	2	-	3	-	-	2	-	-	-	-	-	-	-	2	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	6
S. bovismorficans	-	-	-	-	-	-	-	-	-	-	-	-	-	2	1	-	-	-	-	-	1	4	-	-	-	-	-	-	-	1	-	-	1	-	-	-	1	-	-	-	-	-		1	6
S. braenderup	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-
S. infantis	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		1	1
S. blockley	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	2
S. albany	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		1	3
GROUP D																																															
S. typhi	-	-	-	-	1	-	-	2	7	4	14	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	1	-	2	-	3	-	-	-	-	-	-	-	-	-		-	18
S. enteritidis	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	1
S. javiana	-	-	1	-	1	-	-	-	-	3	5	-	-	-	-	2	-	-	-	-	-	2	-	-	1	-	-	-	-	-	-	1	2	-	-	-	-	-	-	-	-	2	-	2	11
S. jamaica	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1	1
GROUP E																																															
S. anatum	-	-	-	-	-	-	1	-	-	-	1	-	-	2	2	-	-	1	1	-	1	7	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-	-	-		-	9
S. give	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	-	2	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-	-	-		-	3
S. lexington	-	-	-	-	-	-	-	-	2	-	2	-	-	1	-	-	-	-	-	-	1	2	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-		-	5
S. weltevreden	-	-	-	-	-	-	-	-	5	3	8	-	-	3	-	-	-	-	-	1	2	6	-	-	-	1	1	1	2	-	3	3	11	-	-	-	1	-	-	-	-	1	1	3	28
GROUP G																																															
S. havana	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	1
Salmonella group (unserotyped)	-	-	-	-	1	-	-	-	-	-	1	-	-	-	-	-	-	1	-	1	-	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		1	4
Staphylococcus aureus	-	-	5	4	2	2	-	-	1	-	14	-	-	6	4	2	-	1	-	1	-	14	-	1	3	-	1	-	1	-	-	-	6	-	-	-	-	-	1	-	-	-		1	35
Shigella flexner	-	-	-	-	-	2	-	1	3	7	13	-	-	-	1	3	1	-	-	1	-	6	-	-	2	-	1	-	-	-	3	1	7	-	-	-	-	-	-	-	-	1		1	27
Shigella sonne	-	-	-	-	6	-	-	-	2	2	10	-	-	4	1	2	2	-	-	-	-	9	-	-	2	-	3	1	1	-	-	3	10	-	-	-	-	-	-	-	-	-		-	29
Shigella (untyped)	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	1
ENTEROPATHOGENIC E. COLI																																															
026:K60 (B6)	-	-	-	2	-	1	-	-	-	-	3	-	-	1	2	1	-	-	-	-	-	4	-	-	-	3	-	1	-	-	-	-	4	-	-	1	-	-	-	-	-	-		1	12
055:K59 (B5)	-	-	-	2	1	-	-	-	-	-	3	-	1	1	-	-	-	-	-	-	-	2	-	-	2	-	-	1	-	-	-	-	3	-	-	-	-	-	-	-	-	-		-	8
086:K61 (B7)	3	2	1	4	3	-	-	-	-	-	13	5	-	17	10	2	-	-	-	-	-	34	1	-	5	2	1	3	-	1	-	-	13	-	-	-	-	-	-	-	-	-		-	60
0111:K58 (B4)	-	-	1	-	-	-	-	-	-	-	1	-	-	2	-	-	1	-	-	-	-	3	-	-	-	-	1	1	-	-	-	-	2	-	-	-	-	-	-	-	-	-		-	6
0112:K66 (B11)	-	-	-	-	-	-	1	-	-	-	1	-	-	-	-	-	1	-	1	-	-	2	-	-	-	-	1	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	4
0114:K90 (B)	-	-	2	1	-	1	-	-	-	-	4	-	-	2	1	-	-	-	-	-	-	3	-	-	1	2	-	1	-	-	-	-	4	-	-	-	-	-	-	-	-	-		-	11
0119:K69 (B14)	1	1	5	4	2	1	1	-	-	-	15	2	2	7	5	2	-	-	-	-	-	18	-	-	3	3	1	1	-	-	-	-	8	-	-	-	-	-	-	-	-	-		-	41
0125:K70 (B15)	-	-	2	1	1	-	-	-	-	-	4	1	-	-	1	1	-	-	-	-	-	3	-	-	2	1	2	-	-	-	-	-	5	-	-	-	-	-	-	-	-	-		-	12
0126:K71 (B16)	1	-	4	1	-	-	-	-	-	-	6	-	1	2	-	1	2	-	-	-	-	6	-	-	1	1	2	-	-	-	-	-	4	-	-	-	-	-	-	-	-	-		-	16
0127:K63 (B8)	-	-	-	2	3	-	-	-	-	-	5	1	-	1	1	-	-	-	1	-	-	4	-	-	-	2	-	-	-	-	-	-	2	-	-	-	-	-	-	-	-	-		-	11
0128:K67 (B12)	-	1	3	1	-	1	1	-	-	-	7	-	1	3	1	-	-	-	1	-	-	6	-	-	1	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	14
0142:K86 (B)	-	-	-	-	-	1	-	-	-	-	1	-	-	-	-	-	-	-	1	-	-	1	-	-	-	-	-	1	-	-	-	-	1	-	-	-	-	-	-	-	-	-		-	3
VIBRIO PARAHEMOLYTICUS	-	-	-	-	-	-	-	-	1	1	2	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	3
PLESIOMONAS SHIGELLOIDES	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	1

Table III

Distribution of *S. typhimurium* isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
0 – 1 week	19.2%	6.2%	12.8%	0%	10.3%
< 1 year	5.7%	14.3%	6.5%	10%	9.3%
1 – 5 years	0.5%	8.0%	8.0%	0%	5.3%
6 – 10 years	0%	8.3%	3.8%	5.6%	3.7%
> 10 years	0.4%	2.6%	1.7%	0.6%	1.3%
overall	2.4%	8.6%	4.6%	1.8%	

Table IV

Distribution of *S. weltevreden* isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
0 – 1/52	0%	0%	0%	0%	0%
< 1 year	0%	0.6%	0.3%	5.0%	0.4%
1 – 5 years	0%	0%	1.1%	0%	0.3%
6 – 10 years	0%	0%	3.8%	0%	1.1%
> 10 years	1.2%	0.7%	1.5%	1.3%	1.2%
overall	0.6%	0.5%	1.1%	1.4%	

Salmonella typhi:

The distribution pattern of *S. typhi* isolates is seen in Table V.

The impression that the Malays are more commonly affected is seen to be statistically significant when they are compared with the Chinese. Older patients appear to have a higher incidence of *S. typhi* infection with a peak at the 6-10 years age group.

Staphylococcus aureus:

Staph. aureus constituted 4.9% of all isolates. Its distribution is shown in Table VI.

There is no significant difference between incidence in the different racial groups.

The over 10 years old age group does appear to be less affected and this is found to be statistically significant when compared with all the other age groups except the less than a week old.

Shigella:

Shigella constituted 9.3% of all isolates.

The distribution of *Shigella flexner* is given in Table VII.

There is no statisticaliy significant difference between isolation rates in the different racial groups.

The 1-5 years old age group seems to be the most affected and when compared with the less than a year old the difference is found to be statistically significant.

The distribution of *Shigella sonnei* is given in Table VIII.

As in the case of *Shigella flexner* no significant racial differences are seen. Again the 1-5 years old age groups seems to be most commonly affected and this is found to be statistically significant when compared with the less than a year old group and the older than 10 years age group.

Table V

Distribution of *S. typhi* isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
0 – 1/52	0%	0%	0%	0%	0%
< 1 year	0%	0.2%	0%	0%	0.08%
1 – 5 years	0.5%	0%	0%	0%	0.2%
6 – 10 years	2.9%	0%	1.9%	0%	1.6%
> 10 years	1.7%	0%	0.5%	0%	0.8%
overall	1.0%	0.08%	0.3%	0%	

Table VI

Distribution of *S. aureus* isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
1 week	0%	0%	6.3%	0%	0.9%
< 1 year	2.1%	2.0%	0.9%	0%	1.7%
1 – 5 years	2.0%	1.1%	0.5%	0%	1.2%
6 – 10 years	0%	2.1%	1.9%	5.6%	1.6%
> 10 years	0.2%	0.2%	0%	0%	0.1%
overall	1.0%	1.2%	0.6%	0.5%	

Table VII

Distribution of *S. flexner* isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
0 – 1 week	0%	0%	0%	0%	0%
< 1 year	0%	0.2%	0.6%	0%	0.2%
1 – 5 years	1.0%	2.2%	0.5%	0%	1.2%
6 – 10 years	1.5%	0%	0%	0%	0.5%
> 10 years	1.6%	0.2%	1.0%	0.6%	0.9%
overall	1.0%	0.5%	0.7%	0.5%	

Table VIII

Distribution of *S. sonnei* isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
0 – 1 week	0%	0%	0%	0%	0%
< 1 year	0%	1.0%	0.6%	0%	0.5%
1 – 5 years	3.0%	2.2%	2.1%	0%	2.4%
6 – 10 years	0%	0%	1.9%	0%	0.5%
> 10 years	0.6%	0%	0.7%	0%	0.4%
overall	0.7%	0.8%	1.0%	0%	

Enteropathogenic E. coli:

Isolation of enteropathogenic *E. coli* was second only to *Salmonella* despite the fact that they were looked for only in children under 10 years of age. The commonest serotype isolated was 086:K61(B7) (60 isolates), followed by 0119:K69 (B14), 0126: K71(B16), 0128:K67(B12), 026:K60(B6) and 0125: K70(B15) in that order.

The distribution of *E. coli* serotype 086:B7 is analysed further and shown in Table IX.

The difference in isolation rates between the Chinese and the Indians and Malays is highly significant ($p<0.01$) whereas there is no significant difference between the Indians and the Malays.

The highest incidence is noted in the less than a week age group and this is found to be highly significant ($p<0.01$) when compared with the other age groups.

The distribution of *E. coli* serotype 0119/B14 is shown in Table X.

The differences seen among the different racial groups is not statistically significant. However again the less than a week age group shows the highest incidence and this is found to be statistically significant when compared with the other age groups.

Mixed Infections:

There were 21 cases of mixed infections accounting for 3.5% of positives. In twenty of these 2 organisms were isolated while there was one case from which *S. typhi, S. typhimurium* and *E. coli* 086/B7 were isolated.

Enteropathogenic *E. coli* constituted one of the organisms in 17 of these mixed infections, *Salmonella* serotypes in 16 and *Staph. aureus* in 6. Of the *Salmonella* serotypes, *S. typhimurium* occurred most frequently, being seen in 10 cases.

Table XI shows the detailed breakdown of the cases with mixed infections.

Table IX

Distribution of *E. coli* 086:B7 isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
1 week	19.2%	7.7%	6.3%	0%	10.0%
< 1 year	1.2%	5.5%	2.0%	0%	3.1%
1 – 5 years	1.5%	6.5%	2.1%	0%	3.4%
6 – 10 years	0%	0%	1.9%	0%	0.5%
overall	1.5%	5.6%	2.1%	0%	

Table X

Distribution of *E. coli* 0119/B14 isolates

Age group	Racial groups				
	Malays	Chinese	Indians	Others	Overall
0 – 1 week	7.7%	6.2%	0%	0%	5.0%
< 1 year	2.1%	2.5%	1.7%	0%	2.1%
1 – 5 years	1.5%	1.1%	1.1%	0%	1.2%
6 – 10 years	1.5%	0%	0%	0%	0.5%
overall	2.1%	2.3%	1.3%	0%	

Table XI

Cases of Mixed Infections

Patients Age	Sex	Race	Organisms		
6/52	F	Ch	*S. bareilly*	*E. coli* 0127/B8	
12/365	M	Ch		*E. coli* 086/B7	*Staph. aureus*
1/12	F	I	*S. javiana*	*E. coli* 026/B6	
34	M	Ch		*E. coli* 0128/B12	*Staph. aureus*
7	F	I	*S. typhimurium*	*E coli* 0125/B15	
1	F	Ch		*E coli* 0114/K90	*Sh. sonne*
9/12	M	I	*S. habana*	*E. coli* 0119/B14	
4/365	M	M	*S. typhimurium*	*E. coli* 0119/B14	
7	M	M	*S. anatum*	*E. coli* 0112/K66	
12/365	M	Ch		*E. coli* 086/B7	
1	F	I		*E. coli* 0114/K90	
				E. coli 026/B6	
3	M	Ch	*S. typhimurium*	*E. coli* 0119/B14	
1	M	Ch	*S. weltevreden*	*E. coli* 0127/B8	
10/12	M	I	*S. typhimurium*		*Staph. aureus*
3½/12	M	Ch	*S. typhimurium*		*Staph. aureus*
2/12	M	Ch	*S. typhimurium*	*E. coli* 086/B7	
2/12	M	Ch	*S. typhimurium*	*E. coli* 086/B7	
			S. typhi		
25	M	M	*S. typhi*		
			S. lexington		
B/0	F	M	*S. typhimurium*	*E. coli* 0128/B12	
6/12	M	Ch	*S. typhimurium*		*Staph. aureus*
14/365	F	Ch	*S. typhimurium*	*E. coli* 0119/B14	

Discussion

A reflection of the role of bacteria as causative agents of diarrhoea may be seen from a study of the isolation rates. In the 3,809 cases studied 15.9% showed the presence of enteropathogenic bacteria. However, it was proven that this isolation rate was age dependent, and was highest in the less than a week age group and decreased with increasing age. It appears therefore that bacteria play a bigger role in the causation of diarrhoea in infants and children while in adults other causes may be more important.

However one point to be considered in explaining this difference in isolation rates between newborns, infants and older age groups is that the younger patients tend to be admitted early to hospital, fresh stools are available and these are taken before antibiotic medication. This increases the chances of bacteria being isolated. In the case of older patients most are treated as outpatients and many have had some measure of treatment outside hospital which may have included antibiotic preparations.

Another point to consider of course is that perhaps in older patients agents other than bacteria themselves are more commonly encountered as causative agents of diarrhoea.

Isolation rates obtained in this study compared favourably with those by other workers (5,6,7,8) who studied diarrhoea in children. Pathogenic bacteria generally account for about 30% of diarrhoea in children (3). Methods employed were very similar and one is led to think that with present techniques only about one third of cases of diarrhoea in children can be attributed to bacteria. This percentage becomes even less when adults are considered and attention must be paid not only to looking for other causes of diarrhoea but also for improving techniques for isolation of a wider range of organisms. Some organisms have only recently been recognised to cause gastroenteritis and special effort must be made to look for them. Examples of this would be *Vibrio parahaemolyticus* (8), *Yersinia enterocolitica* (9), *Plesiomonas shigelloides* (10) and new serotypes of enteropathogenic *E. coli* which perhaps may need to be looked for in adults as well (11). A group of British soldiers flying from Britain to Aden developed diarrhoea and a new enteropathogenic *E. coli* serotype was incriminated. The etiological relationship was established when a technician working with the organism a year later developed diarrhoea and the pathogenic strain was isolated from his stool (12). This illustrates the possibility that organisms hitherto unrecognised or looked for as pathogens may in fact be responsible for some of the undiagnosed cases of diarrhoea.

The fact that enteropathogenic *E. coli* were only looked for in children in this study may also have contributed to the higher isolation rates in the lower age groups.

Chinese in general appear to have a higher isolation rate for bacterial enteropathogens than the other races. This could perhaps be due to the fact that a larger proportion of cases studied belonged to the younger age groups.

Salmonella species formed the largest group of isolates. It was observed after a 3 year study at this Institute in 1955 that the occurrence of *Salmonella* species in Malaya was quite common and apart from typhoid, members of group B were the ones most frequently found (13). In 1970 it was noted by workers in the Institute for Medical Research that salmonellosis due to serotypes other than *S. typhi* presented a growing problem second only to typhoid (14). The emergence of serotypes other than *S. typhi* is further illustrated in the present study where *S. typhimurium* was by far the predominant organism. Typhoid was only seen about one tenth as frequently as *S. typhimurium*. Data collected by the W.H.O. Salmonella Surveillance programme for the years 1969-1971 showed that in the European centres frequency of infections associated with other *Salmonella* serotypes tended to increase whereas those due to *S. typhi* and *S. paratyphi* B tended to decrease (15). This therefore appears to be a universal trend. *Salmonella* serotypes other than *S. typhi* and *S. paratyphi* are generally transmitted to man from an animal reservoir through foodstuffs in which a stage of multiplication at normal temperatures is necessary. Their progressive rise in recent years is linked with international traffic in animals and foodstuffs, which is conducive to the introduction of new serotypes, with large scale intensive stock breeding, with industrial food production methods and with communal restaurants which help the spread of *Salmonella* (16). Hospital cross infection also plays a part in the spread of salmonellosis, particularly in the case of *S. typhimurium* in paediatric wards. Whatever the organism involved, the infectivity rate is usually high and it is particularly so when infants of the same age group are grouped together.

In the present study racial and age predilections were noted for the commonly occurring *Salmonella* serotypes. For instance *S. typhimurium* was seen most commonly in Chinese and in the less than 1 year age group while *S. weltevreden* affected adults more commonly. *S. typhi* affected Malays most commonly and its peak of age incidence was the 6-10 year age group. In a review of *Salmonella typhi* infection in Singapore, it was noted that

S. typhi affected mainly the Malays although they formed a minority of the population. The authors attributed this tendency to socio-economic factors (17). The susceptible age group in the Singapore study was found to be between 5-20 year which again is compatible with our findings. Racial and age group differences such as seen in this study could be attributed to many causes including genuine difference in susceptibilities, socio-economic factors, food and cultural habits and the like.

Shigella infections constituted a surprisingly low percentage of isolates (9.3%). Improvement in environmental sanitation and standard of living probably explains this decrease and shigellosis in Malaysia today is probably a hand to mouth infection involving carriers connected with the preparation of food (14). A study in Iran showed however that in pre-school children, *Shigella* species were the commonest organisms isolated (6). The same situation was noted in an Indian study (8). These differences are therefore perhaps due to the variation in socio-economic factors.

Another reason that may be put forward for the low incidence of shigellosis in our study is that there is no suitable enrichment medium for *Shigella* and this may have resulted in some cases being missed.

Shigella flexner and *Shigella sonnei* were the two *Shigella* species commonly encountered in this study. Similar findings were obtained in a study in India (8) and a previous study at the IMR, Malaysia (14).

While there was no significant differences among the different racial groups with regard to frequency of isolation of *Shigella,* it was noted in the cases of both *flexner* and *sonnei* that the 1-5 year old age group was the most commonly affected while there were no isolates of *Shigella* from patients less than a week old.

Enteropathogenic *E. coli* were looked for in children under 10 years of age. They constituted a major part of the positive isolates in those age groups. Commonest occurring serotypes were 086/B7 and 0119/B14. In the previous study in the I.M.R. (14) the commonest serotypes found were 0128/B12 and 0119/B14. In that study 086/B7 were not looked for initially because the antiserum was not available but was found subsequently in aborigine children. This illustrates the possibility that new serotypes may continuously be found if looked for.

This is further illustrated by the outbreak of infective diarrhoea among babies in hospital at Winchester, England where after screening for the usual pathogens the outbreak was ultimately attributed to an *E. coli* showing resistance to several antibiotics. This strain was subsequently typed as 091 K? H7 (19).

Experimental work on rabbits suggest that disease producing strains may produce a toxic factor responsible for the clinical symptoms while other strains of the same serotype may not (20). This introduces a further problem in looking for incriminating strains of *E. coli* which are isolated from diarrhoea cases.

Enteropathogenic *E. coli* have traditionally been looked for in children but recently they have also been incriminated as possible agents of diarrhoea in adults (12).

In the present study, detailed observation of the distribution of *E. coli* 086/B7 and 0119/B14 shows that both are significantly common in the less than a week old age group and the incidence appears to decrease as the age increases. 086/B7 showed a significant predilection for Chinese patients and perhaps the same factors are involved as in the case of *S. typhimurium.* Diarrhoea due to *E. coli* most often occurs in newly born baby nurseries (3).

There were 21 cases of mixed infection. Mixed infections have also been reported in similar studies conducted by other workers (5,7,8). It is difficult to assess which one or all of the organisms are primarily responsible for the clinical symptoms.

Finding of two pathogens from the stools of diarrhoeal cases may suggest that cross-infection has been highly likely (18).

Summary

3,809 cases of diarrhoea were investigated. In 15.9% of these recognised bacterial enteropathogens were isolated from the faeces. Isolation rates were highest in the less than a week old age group and decreased progressively in the older age group. Isolation rates were highest in Chinese patients. There appeared to be no statistically significant difference in the isolation rates seen in males and females. *Salmonella* were the commonest encountered.

Significant racial and or age group differences in isolation rates were seen in the case of *S. typhimurium, S. weltevreden, S. typhi,* enteropathogenic *E. coli* and *Shigella.* Possible explanation for these differences are postulated.

Acknowledgements

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Tapeworm Infection in Perlis

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Introduction

HUMAN BEINGS are infected with tapeworms by consuming the larval stage of cysticerci present in infected meat and viscera of cattle (in the case of *Taenia saginata*) or of pigs (in the case of *Taenia solium*). In turn the cycle is perpetuated by the eggs in the human excreta which are the source of infection to the animals.

Very few reports of tapeworm infection have been made in the Malaysia/Singapore region in the last twenty years and various surveys on the incidence of intestinal parasites did not reveal the presence of tapeworms. Discussions with colleagues who had worked in hospitals in rural areas and with those working in the Institute of Medical Research confirmed the rarity of tapeworm infection in human beings in this country.

Three cases are reported from the border state of Perlis during the author's service there in 1972 and 1973.

Case Reports

1) A 23 year old Malay man from Kampong Tok Kayaman had been passing small segments of worms during the past year before seeking treatment at the Kangar General Hospital. He worked by leading cattle smuggled from Thailand to Perlis. He used to consume semi-cooked meat from these cattle. Stool examination showed the ova of the *Taenia* worms.

2) A 37 year old Malay man from Chuping district was seen in April 1973 with a history of passing flat worms. He worked in the sugar plantation as a labourer. He was very fond of eating "kerbau mentah", a local delicacy, one of its ingredients being raw beef. The specimens of the tapeworm were brought for inspection.

3) A nine-year old Malay boy from Kampong Sempering was brought with a history of passing small pieces of worms for the past three weeks. The family worked in the padi fields. There was a history of consuming semi-cooked "pickled beef".

All three patients described were well and of average nutrition. No anemia was detected on blood examination. There were no abnormal findings physically or in routine investigations.

Diagnosis

One of the patients brought the typical proglottids of *Taenia* species while the other two were confirmed to have tapeworms by stool examination. The adult worms which were expelled after treatment were sent to the Institute of Medical Research in Kuala Lumpur which confirmed the diagnosis of *Taenia saginata*.

Treatment

Mepacrine (Quinacrine) was used to treat the patients reported. All three were hospitalised during the course of treatment. Each patient was given a liquid diet and 15 ml of castor oil the day before. The next morning, on an empty stomach, each patient was given one mepacrine tablet (100 mg) every five minutes till a total of 1 gram (or 800 mg in the child) was reached. This was then followed by another 15 ml of magnesium sulphate.

Nausea and vomiting are common side effects of mepacrine. Toxic doses can lead to convulsions, especially in children. No side-effects were noted in the three patients reported.

The patients were instructed to save all the worms passed. These were examined for the scolex and then they were sent to the Institute of Medical Research for further identification.

Discussion

Reviewing the literature showed the rarity of *Taenia saginata* infection in humans in Malaysia/ Singapore even in the rural areas. Sandosham (1968) estimated that there were about a dozen cases identified per year and they were mainly found in immigrants from India and Indonesia. Local cattle were lightly infected. In a survey of 42,500 cattle slaughtered in local abbatoirs the cysticercus bovis count was only 15 out of 390 found infected.

T. solium is equally rare. Before the war it was more common as pigs were imported from Indochina and Indonesia (Sandosham 1968). In a survey of 744,400 pigs slaughtered in 1937, 1235 carcasses had cysticercus cellulosae and out of this number, only nine were locally bred pigs. Since the war Malaysia had been self-sufficient in pigs. A more recent survey (Griffiths, 1968) also did not show any tapeworm. *T. solium* does not occur in Muslims as they do not eat pork. It is rare in Chinese as they always cook their meat well. (Sandosham, 1956)

Several surveys on the local intestinal helminth infections including rural communities have been undertaken but none of the published reports mentioned the discovery of tapeworm. (Desowitz, 1961, Kleevens (1967), Kan (1970) and Siak (1969) in urban and rural communities in Singapore; Heyneman (1967) in Pulau Tioman; Balasingam (1969) in Pulau Perhentian and Bisseru (1971) in a survey on the rubber estate children. All these surveys did not isolate any case of tape-worm.

Similar surveys in other countries of South-east Asia failed to report tapeworm either: Colwell (1971) in Vietnam, Tantengco (1972) in Philippines, Clarke (1973) and Carney (1974) in Indonesia.

The likely source of infection in the three cases reported in this article is from smuggled cattle from across the border. This practice of smuggling cattle and beef from Southern Thailand is common in the border states of Perlis and Kedah. The villagers in Perlis like to prepare a sort of pickle called "kerabu mentah" in which is used raw or semi-cooked beef. Both these factors would explain the occurrance of *T. saginata* in Perlis.

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The Testicular Feminisation Syndrome

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Summary:
FOUR CASES OF testicular feminisation syndrome are reported with a discussion of the various peculiar features of this rare and interesting condition, in which an individual is genetically a male but is physically and mentally a female.

Introduction

One of the most interesting clinical curiosities in medicine is the condition of testicular feminisation syndrome in which the individual is essentially female in physical appearance and mental attitude but possesses gonadal testes. The following cases seen in the University Hospital, Kuala Lumpur are reported to illustrate the main features associated with this condition.

Case No. 1

Personal and family history:

TGT, a 21 year-old Chinese girl was referred from a district hospital in June 1974 with a history of primary amenorrhea. She was the sixth of a family of eight children, consisting of five girls and three boys. The eldest sister had seven children (four boys and three girls), the next sister had six children (all were girls), the third was 24 years old and had her menarche at the age of 14, and the younger sister was 17 years old and had her menarche at 15 years of age. The last two sisters and the patient were not married. There were two elder brothers and one younger brother. The mother had only one brother and no sister.

The patient had an apparently normal healthy childhood. There was no history of cyclical abdominal pain. Her breasts were noticed to develop at the age of 14 years. She had never felt any lump in her abdomen or her groins. She was average in her performance in school.

Physical examination:

She was generally thin-built and eunuchoid, 160 centimetres (five feet three inches) in height with normal proportions and weighed 39.7 kilograms (87.5 pounds).

She had an attractive feminine appearance with a fair complexion. There was no hirsuitism. She had long scalp hair but there was no axillary hair and only a few strands of hair in the pubic region. Her voice was high pitched. The breasts were fairly well-developed and the areolae and nipples were of normal size and pigmentation.

The thyroid gland was not palpable. Vision was normal. The heart and lungs were clinically normal. Examination of the abdomen and the groins did not reveal any lumps or tenderness.

The external genitalia were characteristically female with well-developed labia majora and minora and a normal-sized clitoris. The hymen was still intact. Examination per rectum did not reveal any cervix, uterus or palpable gonads. Further examination under anaesthesia showed a vagina of five centimetres in depth ending in a blind pouch.

Investigations

The routine blood and urine analysis, blood urea and serum electroloytes were normal. Radiographs of the chest and skull were unremarkable. The intravenous urogram showed both the kidneys

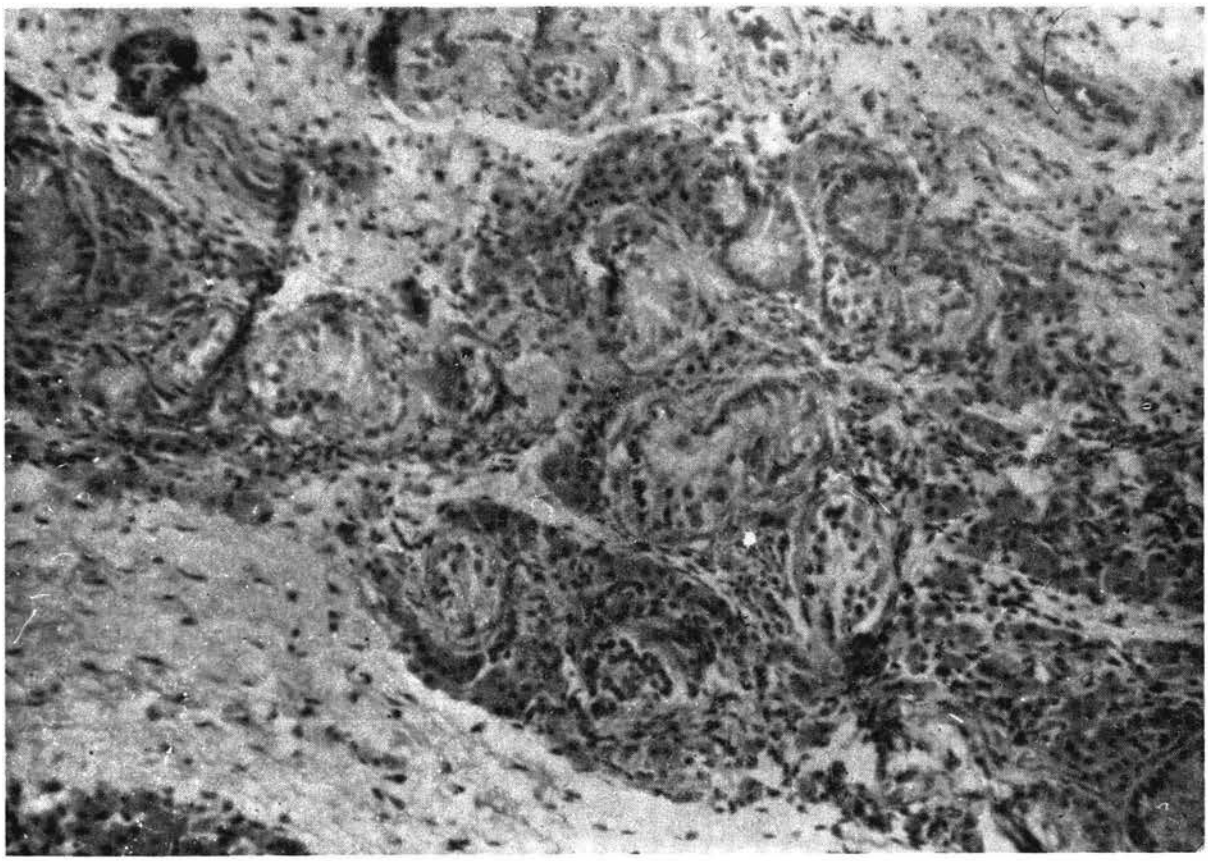

Photo 1.
(Low power) Dysgenetic testis with lobulated clumps of tubules lined by immature Sertoli cells separated by loose connective tissue stroma.

being normal in size, shape and position with no abnormalities seen in the pelvicalyceal system, ureters or the bladder. The total 24-hour urinary 17-ketosteroids was 14.4 milligrams and urinary cortisol was 730 micrograms (Normal limits).

The buccal smear did not show any Barr body and the blood leucocytes showed the drumstick in less than three per cent. Chromosome culture of peripheral leucocytes showed a 46 (XY) karyotype.

Psychosexual History

She was positively female-orientated. She used face powder and dressed in women's clothes. She mixed socially with both sexes but she had no special boyfriend as she felt that she was too young to get married. She admitted however that some boys had been interested in her but she did not reciprocate as she thought she was "abnormal". To quote her, "All I am interested is to have periods. All women have periods. I have no period. I am not normal."

Histopathology

A laparatomy with a small abdominal incision was done. No uterus or tubes were seen. A vestigeal ligament-like structure stretched from behind the bladder to end in small cysts, adjacent to the two gonadal swellings. Each gonad measured about two and a half by three by one centimetres and had a white capsule. A wedge biopsy of both gonads was made.

The histology of the biopsy specimens showed the structure of dysgenetic testes with Sertoli cell

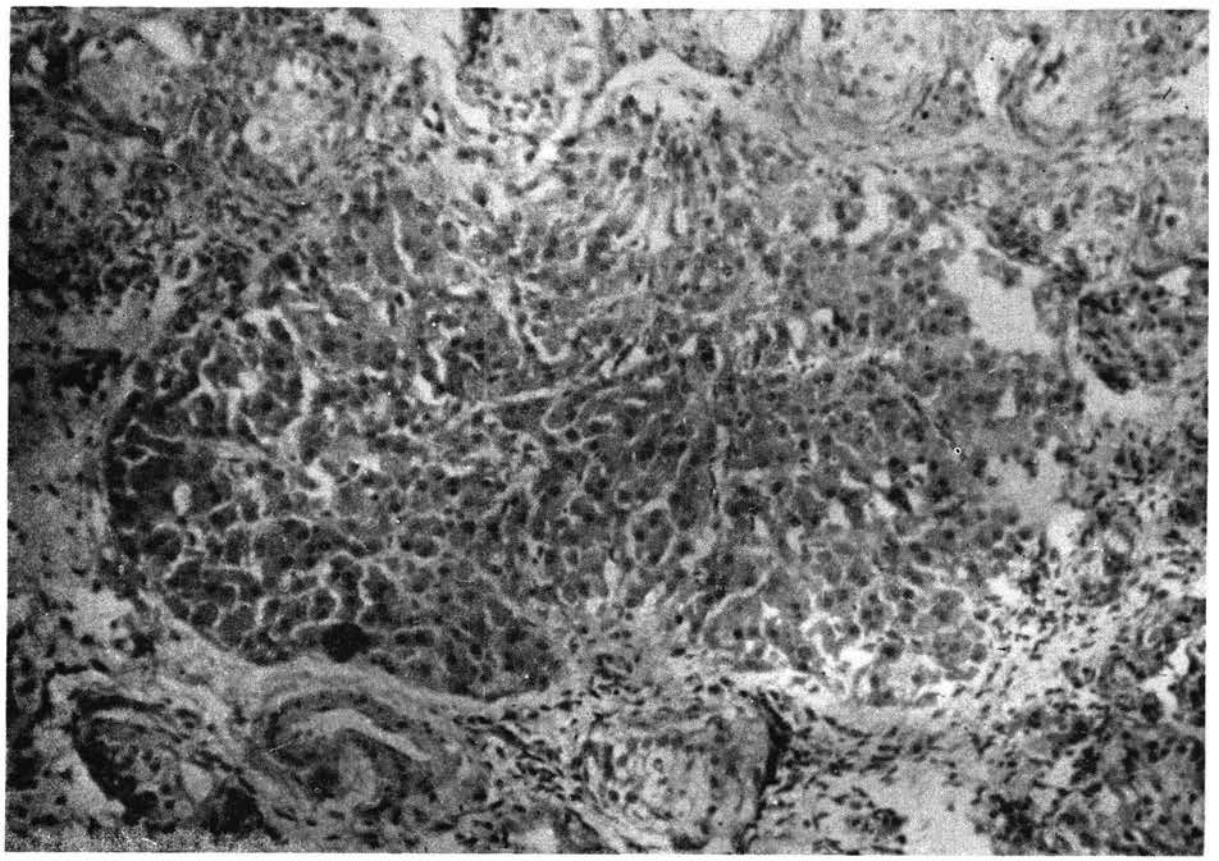

Photo 2.
(Low power) Dysgenetic testis showing hyperplastic Leydig cells.

adenoma. There was normal tunica albuginea. There were lobulated clumps of tubules lined by immature Sertoli cells separated by loose connective tissue stroma. Spermatogenesis was absent. Focal Leydig cell hyperplasia was evident. There was no evidence of any ovarian tissue or malignancy seen.

Management

When the patient was informed that there was no cure for her she became very depressed. However subsequent interviews with her managed to dispel her depressive mood. We convinced her that her amenorrhea had not affected her health or her feminity. She was told that her problem was not her fault or that of her parents. There were other women with amenorrhoea and infertility. She was reassured that she could lead a normal happy life as a wife as her sexual function would not be affected. She was encouraged to continue her usual activities. The decision whether to tell her future husband about her condition would be left to her. At NO time was she or her relatives ever told that she was a "male" and had testes. The ward staff were instructed to avoid discussing her condition in her presence.

She was advised gonadectomy but she only agreed to this after about six months. At the subsequent laparatomy, total excision of both gonads was done. Further histological examination did not reveal any malignancy. She was given stilboesterol one milligram daily as hormone maintenance therapy after gonadectomy.

Case No. 2

TML, a 14 year old Chinese girl who happened to be the niece of the first patient described was referred a year later as she had bilateral inguinal swellings and was suspected to have the same condition. She had not reached her menarche yet.

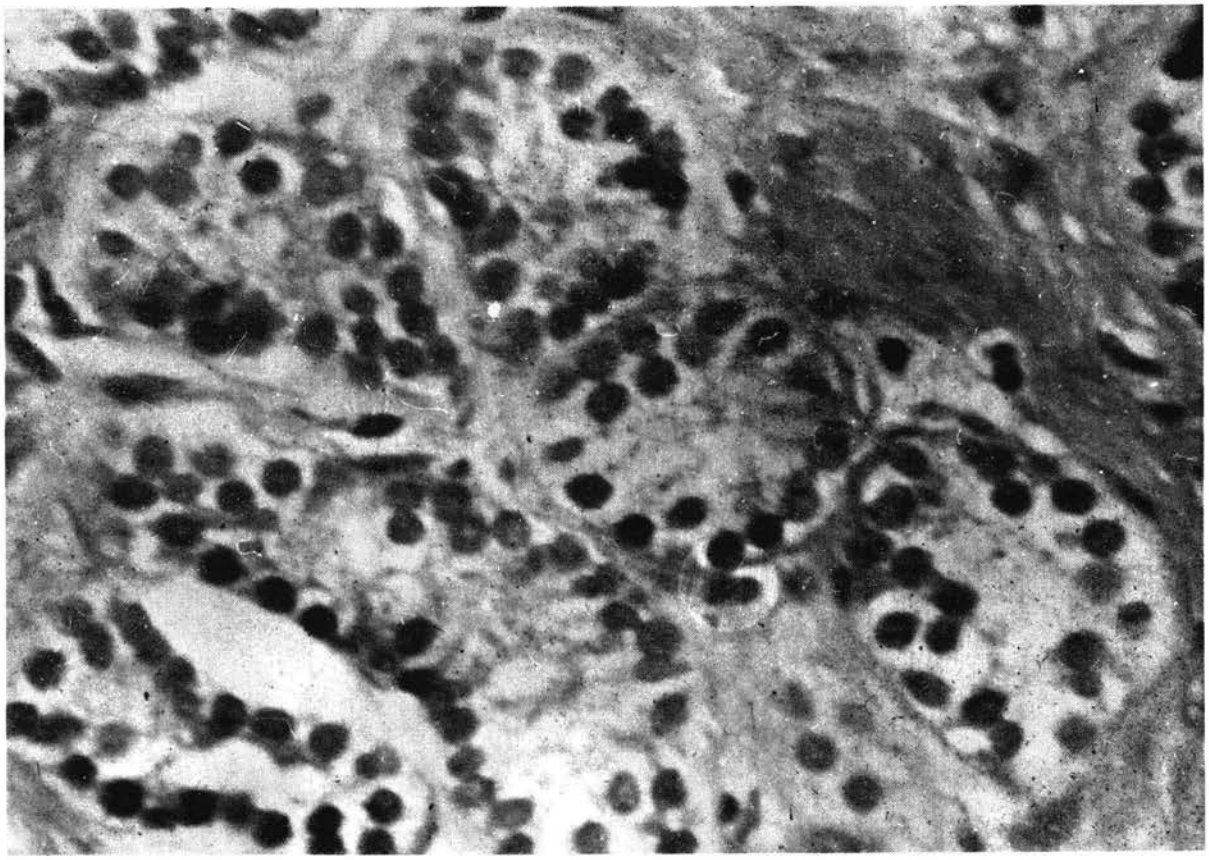

Photo 3.
(High power) Dysgenetic testis with Sertoli cell adenoma.

Otherwise she was feminine in other ways. Breast development was appropriate to her age. At the right inguinal region, there was a 3 by 2 cm soft, non-reducible swelling while on the left side, there was a similar swelling which was however reducible. The genitalia were female in appearance but the vagina which was about 8 cm deep, ended in a blind pouch. No cervix or uterus was felt. Neither the uterus nor the adnexal organs were present on laparascopic examination. Biopsy of the gonad showed infantile testicular tissue. Chromosome culture showed 46 XY karyotype.

Case No. 3

Z.I., a 16 year old Malay girl was referred for primary amenorrhoea. She was fair-complexioned with a typical female appearance. Her breasts were first noticed to develop at the age of 14 years. She also had bilateral inguinal swellings, which were tender on deep palpation. The right swelling was reducible while the left was not. Biopsy of the swellings showed hypoplastic testes and Leydig cell hyperplasia. The external genitalia were female although the vagina was only 4 cm deep and ended in a blind pouch. No uterus or ovaries was seen at laparascopy.

There were 4 other sisters in her family but all had normal menses.

Case No. 4

Z.B., a 22 year old Malay girl had been married for two years when she came to us with history of primary amenorrhoea and infertility. She was rather attractive with normal breast development and feminine voice. There was however no axillary or pubic hair. The labia and clitoris were normal and the depth of the vagina was about 6 cm. There was no cervix, uterus or tubes. She admitted to have occasional dyspareunia.

On laparascopy, the two gonads were seen within the abdominal cavity just at the internal inguinal ring. Chromosome culture showed 46 XY karyotype.

Discussion

These patients presented as a problem of intersex, a term which has replaced the old terms of pseudohermaphroditism. The sex of an individual is a composite of several factors: sex chromosomes, gonads, hormones, external genitalia, sex of rearing and sex of psychological orientation. Any anomaly in one or more factors will lead to a problem of intersex. Although the manifested sex is dependant on the dominating factor, the sex of rearing and the sex of psychological orientation are important for the individual's role in society. The other factors may be altered or ignored, if necessary, to suit this role.

The syndrome of testicular feminisation is diagnosed when an individual has all the external characteristics of a female, including psychological orientation, and yet has a male chromosomal and gonadal sex pattern.

This unusual condition was first reported in 1815 by Steglehner while performing an autopsy on a female, discovered, in his own words, "something wonderful and unheard of, the testes". However it was only in 1953 that Morris reviewed 82 cases in the literature and labelled the term "testicular feminisation syndrome". By 1963 there were 160 recorded in the literature with the incidence quoted as 1:60,000 (Morris 1963). However only 40 of these had complete chromosomal analysis (Pion 1965).

From the Malaysia/Singapore region, there has been only one family reported so far. (Wong and Salmon 1966)

Pathophysiology

Attempts to explain this syndrome on the hormonal status have been made in several experiments. Simmer et al (1965) have summarised their findings in their monograph:

1) the level of oestrogens in the urine is higher than that in the normal male and lower than that in the female (Wilkins 1957) but may fall to almost zero when the testes are removed,

2) the level of androgens have been found by most workers to be similar to most men,

3) the level of gonadotrophins is also of normal level but is sometimes increased especially after gonadectomy.

There have been several theories to explain the discrepancy between male gonads and female phenotype. One theory is that there was testicular insufficientcy in foetal life (Jost 1958) which is probably inherited as sex-linked recessive. Thus there is failure of the hormonal influence of the Mullerian system which is thus allowed to develop. A more acceptable theory is that there is failure of the end-organ response to the testicular hormones. This is supported by experimental evidence that showed that the level of androgens is normal with no increase in oestrogens. Even when exogenous androgens are given orally or percutaneously as an ointment, there is no response from the hair follicles or the clitoris. Thus Morris (1963) has also termed it the "androgen insensitivity" syndrome.

Recent work has shown that there is deficiency of 5-alpha steroid reductase which is necessary to convert testosterone in target cells to dihydrotestosterone which is the active compound (Wilson & Walker 1969). However, administration of dihydrotestosterone did not show any clinical response.

Other theories include those of Bardin (1970) who postulated that there was defective nuclear binding and uptake of the dihydrotestosterone; Dorfman who felt that there could be anti-androgenic substances in the peripheral tissues; and Wilkins who thought that there was rapid conversion of androgens into oestrogens in the end-organs.

The testes are found in the abdomen in 21 per cent of cases, in the inguinal region in 60 per cent, and in the labia majora in 19 per cent (Hauser 1963). There is rarely any evidence of spermatogenesis or the presence of normal Sertoli cells. The uterus and tubes are never present. However the vulva is essentially female. The pubic and axillary hair are usually absent. The breasts develop at the usual age and reach normal adult size. If the testes were removed, breast development would be affected (Hain & Schofield 1957). Jeffcoate (1968) however disagree with this.

The behaviour of these patients is undoubtedly feminine orientated and lead to normal sex lives complete with orgasm (Morris 1963, Wilkins 1957). Libido has been reported to be normal (Hauser 1963). Although they are sterile, they show normal instincts of motherhood.

The mode of inheritance has not been finally settled though most workers believe it to be sex-linked recessive manifesting in males.

Patients with this condition do not usually present problems at birth. Some may present with inguinal swellings and/or hernias in childhood.

Most of them present in adulthood with complaints of primary amenorrhea and sterility. Male nuclear sexing and chromosome karyotype of 46 XY from buccal smears and blood cultures in an otherwise normal female is characteristic and histology showing testicular tissue in the gonads is confirmatory. A few patients possess mosaicism of XY/XO and may manifest as incomplete testicular feminisation.

Some workers routinely perform gonadectomy after puberty for fear of the risks of malignancy in the intra-abdominal testes. Morris (1963) found that in a series of 50 patients who were more than 30 years, 22 per cent showed malignancy in the gonads. Other workers such as Jones and Scott (1958) found the incidence to be only five per cent. Hauser (1963) found ten cases of seminomas out of 128 cases of which eight were cured and only two died. Thus they advocate gonadectomy only if there is evidence of neoplasia. If gonadectomy is performed, it is necessary to treat these patients with small maintenance doses of oestrogens.

As there is no confusion in the sex identity, psychological workup is less indicated. It is stressed that it is not revealed to the patient or the relatives the existence of male gonads. They can be reassured of a normal sex life ahead and that amenorrhea and infertility are no bar to a happy married life.

Acknowledgements:

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Choroid Plexus Papilloma Five Years after Shunting for Hydrocephalus

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CHOROID PLEXUS PAPILLOMAS are rare tumors. They constitute 0.5% of all intracranial neoplasms.[3,5,6,11] Although usually located in the fourth ventricle in the adult, the lateral ventricle would appear to be the more common site in infants and children. Other locations include the third ventricle and cerebellopontine angles. They show a predilection for the younger age group with greatest incidence in the first and second decades of of life. Males seem to have a slightly greater incidence.

Raised intracranial pressure with hydrocephalus is the common presentation. Associated neurological findings will be dependent on the location and rate of growth of these tumors. Rarely malignant change may occur, when they can be multiple and show dissemination along the cerebrospinal fluid pathways. Diagnosis is established by contrast studies of which ventriculography is the more definitive.

We would like to report a case of choroid plexus papilloma that arose in a patient who had 5 years earlier undergone a ventriculo-atrial shunt for hydrocephalus. The bubble study done then documented the hydrocephalus but unfortunately the reason for it was not apparent. This particular case exemplifies the need for adequate contrast neuroradiological studies prior to shunting procedures.

Case Report

Y.M., a Malay male infant, was initially admitted to our Department at the General Hospital, Kuala Lumpur in January 1970 at the age of 5 months. He was a full term baby and had a normal delivery. The parents stated that the child had begun to have an increasing head size. He was unable to hold his head up. A week prior to admission, he had become apathetic and drowsy. There was no history of meningitis or trauma prior to his admission. On examination, the head circumference was 45 cm. The fontanelles were full and bulging. Head lag was present. Routine laboratory tests and chest x'rays were normal. Skull x'rays revealed a large head with wide separation of sutures. Bubble ventriculography confirmed the hydrocephalus. There was no evidence of tumor at that time. A ventriculo-peritoneal shunt was then concluded and the child discharged well.

Subsequently, three shunt revisions were necessary (all for blocked ventricular ends) over the next 5 years. In between episodes of re-operations for malfunctioning shunt, the patient was alert and well. No contrast studies were performed prior to any of these revisions.

On 17.4.75, the patient was readmitted for vomiting of some 5 days duration. The ventricular end of the shunt was again found to be blocked. A roentgenogram of the skull now revealed a large calcified mass near the midline in the (R) parietal area. This led to further investigation. A (R) brachial angiogram showed a shift (R) to (L) of the anterior cerebral artery with evidence of hydrocephalus. Air studies showed that the ventricular system was indeed generously dilated and the calcified mass was found protruding into the floor and body of the (R) lateral ventricle. CSF examination at this time showed protein of 48 mg%,

sugar 60 mg% with 55 polymorphs and 45 lymphocytes and few RBCs. Some few days prior to definitive craniotomy, the patient developed a (L) hemiparesis.

On 13.5.75, some 4 years and 4 months after his initial operation, a (R) parieto-occipital cranitomy was performed. The tumor was approached interhemispherically. By way of a transcallosal approach the (R) lateral ventricle was opened revealing the tumor. At this time, it was evident that the ventricle was the seat of recent hemorrhage. The tumor was attached to the lateral wall of the ventricle by a vascular pedicle. It appeared papilliferous, soft to gritty in consistency and was relatively avascular. It was totally removed.

The tumor weighed 28 grams and histopathological examination revealed this to be a choroid plexus papilloma with calcification. Villous fronds were numerous, lined by a single layer of cunoidal epithelium. Psammoma bodies and plaques of calcium were numerous.

Post operative recovery was satisfactory. He developed one generalised fit and was placed on Dilantin and Phenobarbitone. On discharge on 28.5.75, he was afebrile and generally well except for a residual (L) hemiparesis. There were no further fits.

A follow-up examination a month later (at the age of 6 years), revealed him to be in good general health with average mental functions and following a continued pattern of normal growth and development. The hemiparesis was hardly present and he was up and about to the satisfaction of all concerned.

Discussion

Progressively enlarging heads in children is often presumed to be due to congenital hydrocephalus. In this patient, it is highly probably that the tumor was present from the very beginning although it was not evident radiologically or felt during ventricular punctures for shunt placements. This may account for the ventricular end of the shunt being blocked on three separate occasions prior to definitive cranitomy to remove the tumor. The need for contrast radiological diagnostic studies prior to shunting cannot, therefore, be overemphasized.

Morbidity and mortality and neurological deficits depend on the size, situation and nature of a tumor. This patient, although had a significantly large tumor, was relatively asymptomatic following shunting as the tumor lay mainly within the lateral ventricle with little involvement of the surrounding areas. This would explain the insidious onset of lateralizing sign and the good post operative recovery. Following its removal, hydrocephalus can be expected to regress. Although rate of growth of these tumors is not known, there is evidence that at least in our case it took 5 years to become clinically manifest and significant. We are inclined to think that shunting may be all that is necessary in small tumors of the choroid plexus. However, in such small tumors, patients should be followed closely. Surgery should be carried out when focal neurological deficits develop, or when hydrocephalus is significant.

Summary

This is a case report of a patient now 6 years old with a calcified choroid plexus papilloma of the (R) lateral ventricle. He was first seen as an infant with the diagnosis of congenital hydrocephalus, aetiology unknown. He was then given a ventriculoperitoneal shunt. Subsequently, he came to require three revisions for blocked ventricular ends of the shunt. An intraventricular tumor was never suspected until radiological evidence was available some 5 years later. That ventricular hemorrhage can occur with these tumors is documented in our case as per our operative findings. The hemiparesis, which developed some 3 days previous to the craniotomy, was presumably the result of this intraventricular bleed.

This paper emphasizes the importance of investigating all forms of hydrocephalus before a decision not to shunt a patient is undertaken. Further, it shows the importance of regular follow-up care in these patients.

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Diagram I
Bubble ventriculography at the age of 5 months documenting hydrocephalus.

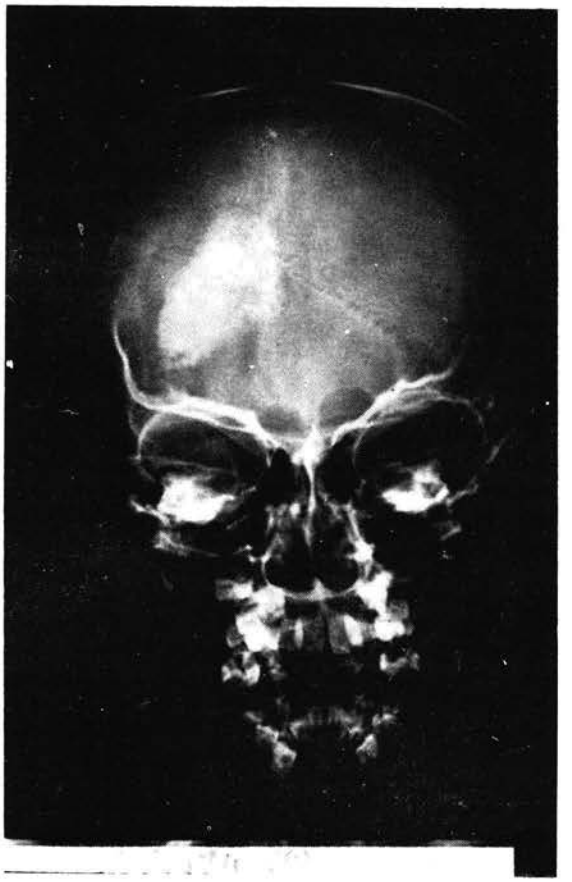

Diagram II
Skull radiograph at the age of about 5 years showed a large calcified tumor in the shape of the (R) ventricle.

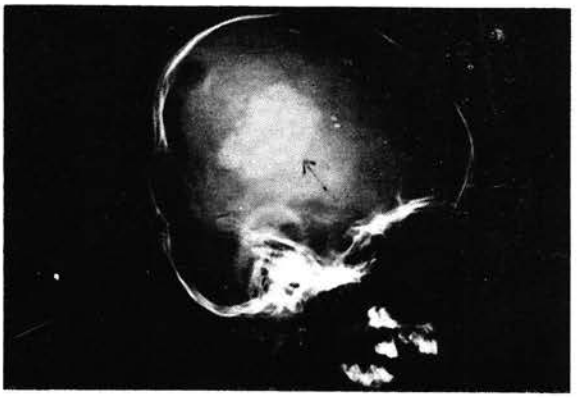

Diagram III
Roentgenogram lateral view illustrating the calcified tumor.

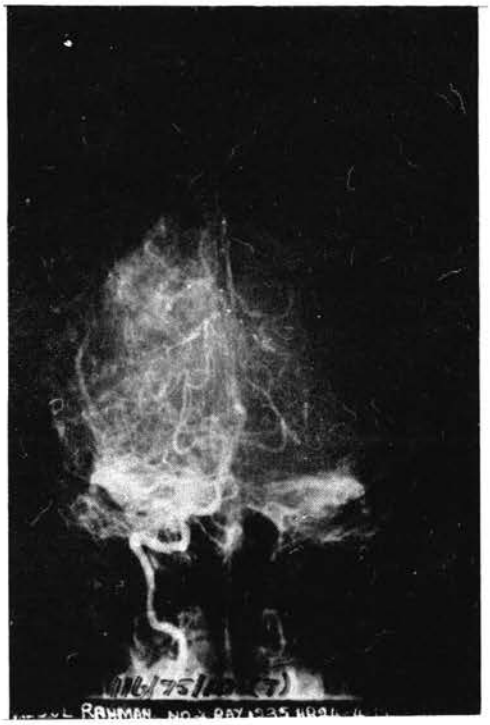

Diagram IV
(R) brachial angiogram showed a (R) to (L) shift of the anterior cerebral artery and lateral bowing of the middle cerebral artery.

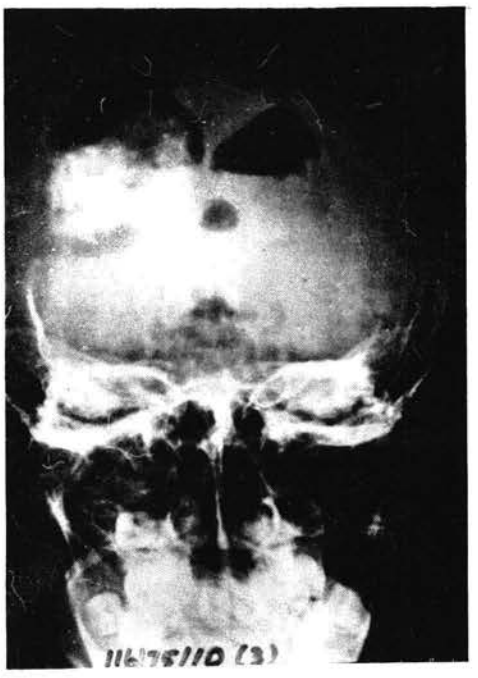

Diagram V
Air study revealed dilated (R) ventricle containing the calcified tumor and also an enlarged 3rd ventricle that was slightly shifted to the (L).

Diagram VI
Air study lateral view further delineated the extent of the tumor and hydrocephalus.

Diagram VII
Radiograph 5 months after operation showed the presence of shunt tip only.

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The Pterygium and Mitomycin-C Therapy

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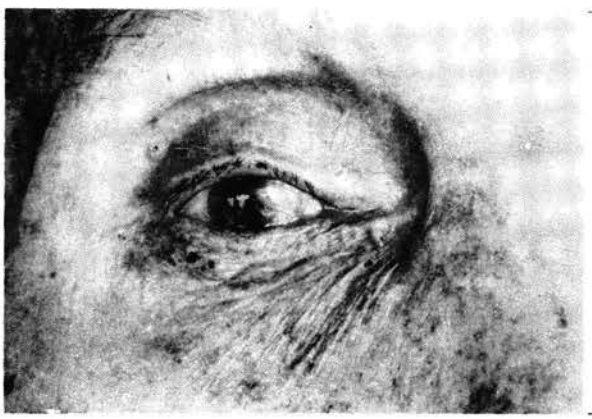
Introduction

THE PTERYGIUM (see photograph) is essentially a triangular tongue of conjunctiva overgrowing on to the surface of the cornea of the eye. It appears as a fleshy mass, its apex extending on to the cornea with its body drawn out from its base, which merges with the bulbar conjunctiva. When active it is vascular, the vessels running along its length. Though not malignant histologically, it possesses almost malignant characteristics as it spreads inexorably across the cornea which it may cover so extensively as to occlude vision.



Histologically, the pterygium is covered by a conjunctival type of epithelium, the cells being flattened on the surface and more cylindrical in the folds, with many goblet cells. The stroma is like that of the substantia propria of the conjunctiva, with many elastic fibres, some cellular infiltration, and areas of hyaline, amyloid or cystic degeneration. As the pterygium extends across the cornea, Bowman's membrane is destroyed and fibrous granulation tissue spreads across the superficial corneal stroma, lifting the epithelium into folds.

Symptoms are variable. There may be some discomfort, with recurrent redness, and occasional gritty sensation. The pterygium grows in "fits and starts", periods of congestion and turgescence alternating with periods of quiescence and whiteness of the eye. The vision becomes increasingly affected as the pupillary zone of the cornea is invaded; this occurs even before the pterygium itself has reached the area because of the irregular astigmatism produced by the corneal folds.

Its aetiology is still not fully understood. The pterygium is one of the oldest recorded eye conditions, being already studied and described by Susruta many years before Christ (Bidyadhar, 1941). Duke-Elder states that it is a degenerative and hyperplasic process. Ultraviolet rays in solar radiation appear to be the most significant aetiological factor (Duke-Elder, 1965). Hence it is more common in tropical than temperate climes. While it may be regarded as a minor ophthalmic disorder, it is a major ophthalmic problem, because of its growth across the cornea threatening vision and its tendency to recurrence after surgery. Trevor-Roper has aptly remarked of the pterygium: "At different times, this modest growth has been incised, removed, split, transplanted, cauterized, grafted, inverted, galvanized, heated, dissected, rotated, coagulated,

repositioned and irradiated. Pterygia continue to grow, and man's ingenuity is far from exhausted." (Trevor-Roper, 1974).

In the conservative treatment of the pterygium, topical corticosteroids have been used, with equivocal results. If the condition is quiescent, no treatment is necessary. If active, surgery is indicated. At present, surgical treatment is the only satisfactory approach to the problem, supplemented in case of recurrence by:-

(1) Radiational treatment, or

(2) Instillation of anti-mitotics.

No surgical technique is universally accepted as being perfect, as shown by a recurrence rate often as high as 30 to 50%. The recurrences are distressing, for the pterygium grows again at a rapid pace and many soon become as large or larger than the original growth. Although surgical treatment of the pterygium is a simple procedure, the high recurrence rate has stimulated the introduction of a multitude of operative techniques, such as: excision leaving an area of bare sclera, excision with plastic repair, transplantation into the lower fornix, cauterization, mucous membrane graft, lamellar corneal graft, and irradiation; while many ophthalmologists have been content to toe the line of "masterly inactivity" if the pterygium is early and not encroaching too far across the cornea to obstruct vision.

In recent times, anti-neoplastic drugs in the form of eye-drops had been advocated in the treatment of pterygium after surgery; these drugs had been claimed to reduce the recurrence rate of the pterygium after operation. In 1960, Langham reported on the use of topical triethylene thiophosphoramide (thio-tepa) to prevent alloxan-induced vascularization of rabbit cornea. In 1962, Meacham was the first to report on the use of a thio-tepa solution on the eye to prevent recurrence of pterygium after surgery. He used the drug on 19 cases of pterygium for eight weeks after surgery and found no recurrence, the follow-up in some being one year. In Japan, Mori (1962) used it on 31 cases after pterygium surgery for two weeks and had a 16% recurrence rate. In the United States of America, Liddy and Morgan (1966) used thio-tepa on 26 eyes after pterygium surgery for six weeks and found a 4% recurrence. Kleis and Pico (1973) of Puerto Rico used the drug on 48 cases of pterygium for six weeks post-operatively, and found a recurrence rate of 8%. On the local scene, one of us (Leong, 1969) used topical thio-tepa on 9 out of 18 cases of pterygium for a period of eight weeks post-operatively, and noted a recurrence rate of 11% compared to 44% in those not on thio-tepa. In Japan, Kunitomo and Mori (1963) announced the use of the anti-neoplastic antibiotic Mitomycin-C (MMC) as an eyedrop solution for the prevention of pterygium after surgery. They used it for two weeks post-operatively, and found no recurrence in the 17 cases operated on. They had also used topical thio-tepa on 31 cases and noted a 16% recurrence rate. Hence, they concluded that topical MMC was superior to thio-tepa in the prevention of pterygium recurrence after surgery.

The purpose of this paper is to report on a clinical trial of the drug Mitomycin-C used topically on the eye to test its degree of efficacy in the prevention of pterygium recurrence after surgery. Previously, one of us (Leong, 1969) had reported on the successful use of topical thio-tepa as a simple therapeutic procedure for both primary and recurrent pterygia, and had advocated its use as especially suitable for places where the pterygium was common but where elaborate and expensive facilities were not readily available. Mitomycin-C is a much cheaper preparation than thio-tepa and its comparative effectiveness would recommend its use in developing countries like Malaysia where the pterygium is a common occurrence.

Materials and Methods

Mitomycin-C is an anti-neoplastic antibiotic isolated from *streptomyces caespitosus*. Its crystal is a deep bluish-violet colour. It has a molecular weight of 1,120. Its molecular form is C54H69-N13019. It acts by inhibiting the synthesis of deoxyribonucleic acid (DNA), although the exact point of attachment to D.N.A. remains unknown. Used systemically, the drug is potentially toxic to the haemopoietic tissues. Used topically on the eye in its therapeutic dosage, it is not appreciably absorbed systematically, and is not apparently harmful to the eye. 2 mg. of Mitomycin-C is dissolved in 5 ml. of 5% glucose solution, forming a solution of 1:2,500 dilution, which had been found to be relatively stable when kept in the refrigerator for ten days (Kunitomo and Mori, 1963).

In this clinical trial, altogether 32 eyes with pterygium were operated on over a period from mid-June, 1974, to mid-October, 1974. The eyes belonged to 30 patients, 18 of whom were females and 12 males. Among these, there were 20 Chinese, 6 Malays and 4 Indians. All the pterygia were primary ones, except for 3 which were recurrent pterygia which had been operated upon previously. Most of the pterygia were advanced cases encroaching across much of the cornea.

All the patients were admitted into hospital one day before operation, when total white cell counts and differential white cell counts were done, and a 5-day course of prophylactic oral tetracycline was started. The method of pterygium operation was the same in all cases, and was performed by one of us (C.Y.F.) for uniformity. This was a combination of the bare sclera and transplantation techniques. Under local anaesthesia, the head of the pterygium was carefully dissected off from the cornea with a Bard-Parker blade. Two straight incisions were made in the conjunctiva radially upwards and downwards to the periphery. The subconjunctival tissues in the isolated body of the pterygium were excised up to the episclera, taking care not to involve the horizontal rectus muscle as well. The pterygial head was then transfixed by a needle and suture which transplanted it into the lower fornix, underlying the fornix conjunctiva to which it was tied. The suture was removed after four days. The sclera was left bare to be epithelialized later on. Atropine drops and antibiotic-corticosteroid ointment, with pad and bandage, were applied to the operated eye for 24 hours.

At the first dressing the next day, the pad and bandage were removed. Two drops of the special Mitomycin-C eyedrops were applied three-hourly to the operated eye, as well as antibiotic-corticosteroid eyedrops four times daily, for two weeks. Weekly total white cell counts and differential white cell counts were done for two successive weeks. The patients were discharged from hospital at the end of this two weeks' course of treatment, to continue antibiotic-corticosteroid eyedrops till the eye was white. They were instructed to return for regular outpatient checks for any signs of recurrence of the pterygium. Recurrence of the pterygium was judged on the appearance of revascularization of cornea previously covered by the pterygium.

Results

One of the operated eyes developed an allergic reaction with congestion, chemosis and swelling of eyelids three days after starting Mitomycin-C and antibiotic-corticosteroid eyedrops, and medication was stopped. With the remaining 31 eyes, no untoward reaction was noted. The operated eyes were not unduly congested, and patient tolerance was good.

Thus, excluding one allergic case, 31 eyes with pterygium were operated on between June and October, 1974; these were given a follow-up of more than one year to date to detect any recurrence. These eyes had post-operative Mitomycin-C eyedrops instilled for two weeks. Of the 31 eyes, 5 eyes showed recurrence of pterygium despite topical Mitomycin-C therapy. Of these 5 cases, 3 recurred among the 28 primary pterygium cases, and 2 recurred in the 3 recurrent pterygium cases which had re-operation in this series. This would indicate that Mitomycin-C is more effective in preventing recurrence in primary pterygium than in already recurrent pterygium. All the recurrences occurred within six months of surgery. Hence, our follow-up period of more than one year would justify a sufficient lapse of time to allow any recurrence to develop. The recurrent cases occurred in 2 Chinese females, 1 Chinese male, 1 Malay female and 1 Indian male. With 5 recurrences out of 31 cases, this works out to a recurrence rate of 16.13%.

Discussion

In the treatment of pterygium, the high recurrence rate after operation has always posed a serious problem. Not only does the pterygium recur after surgery, but the recurrent pterygium grows again at a more rapid and angrier pace, soon becoming as large or even larger than the original growth. In places where the pterygium is common, conservative treatment is generally preferred to radical excision: corticosteroid eye preparations being employed to relieve the congestion of an actively growing pterygium in the hope of slowing down its growth towards the centre of the cornea. This timidity in taking to surgery is rather paradoxical; the operation on a pterygium is a short, minor surgical procedure performed under local anaesthesia requiring only simple instruments and the patient can even be treated as an outpatient. Ultimately, conservative treatment has still to give way to surgery as soon as the pterygium has advanced far enough to threaten to involve the axial zone of the cornea and thereby obstruct vision. Out of a multitude of therapeutic devices, at present the only satisfactory procedures which ensure minimal recurrence rates are lamellae keratoplasty, surgery followed by irradiation, and surgery followed by the use of topical anti-mitotics. The latter procedure would appear to be the treatment of choice where elaborate and sophisticated equipment is not available.

Duke-Elder has stated that the recurrence rate of pterygium after surgery can often be as high as 30 to 50%. Any therapeutic procedure that could appreciably reduce this high recurrence rate would be a valuable adjunct to the surgery of pterygium. Topical thio-tepa therapy has been claimed by enthusiastic proponents to be able to reduce this high rate to one varying from zero to 16%. Now there is an equivalent therapeutic agent in the form of Mitomycin-C, which has been claimed by Kunitomo and Mori to reduce the recurrence rate to zero. However, in our clinical trial, a recurrence rate of

16% has been demonstrated. This would place topical Mitomycin-C therapy in the prevention of pterygium recurrence after surgery on a sound enough basis to recommend its use as a cheap adjunct to pterygium surgery, especially suitable for countries where the pterygium is common but where elaborate and expensive facilities are not available, as in many developing countries. Hence, topical Mitomycin-C therapy is advocated as a simple, cheap and effective means of preventing recurrence of pterygium after surgery.

Summary

The pterygium is essentially a triangular tongue of conjunctiva growing across the cornea. Though the pterygium may be regarded as a minor ophthalmic disorder, it is a major ophthalmic problem, because its growth across the cornea threatens vision, and it has a tendency to recur after surgery. A multitude of therapeutic measures has been proposed for this modest growth, with varying degrees of success. A simple but effective therapeutic procedure is a 2-weeks' course of an anti-neoplastic antibiotic drug, Mitomycin-C, in the form of eyedrops applied three-hourly to the operated eye, to reduce the high recurrence rate of pterygium after surgery. In a clinical trial of this drug involving 31 eyes, there were only 5 recurrences of the pterygium after surgery, giving a recurrence rate of 16%, which is comparable to the results of clinical trials of another antimitotic drug, Thio-tepa, used for the same purpose. Since Mitomycin-C is a much cheaper preparation, it would recommend itself as the treatment of choice in countries where the pterygium is common but where elaborate and sophisticated facilities are not readily available.

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Carotid Body Tumour – A Case Report

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Introduction

CAROTID BODY TUMOURS are rather rare. 500 cases have been reported in the literature (Westbrooke et. al., 1972). We are reporting here the only case seen in the Department of Otolaryngology since the hospital was founded.

Case Report:

T.S.S., a 45 year old Chinese male was admitted to the University Hospital on 23.6.75 with a history of a lump on the right side of the neck of 5 years duration. This lump had not increased in size during the five years since he first noticed it.

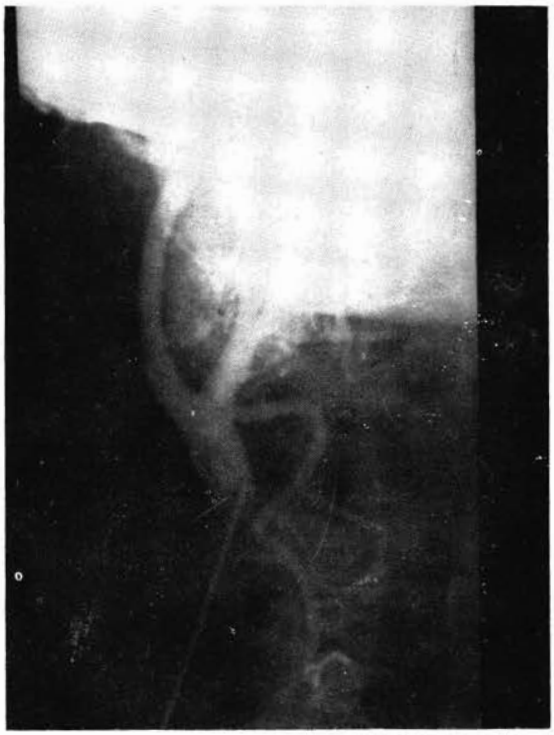
On examination, there was a lump on the lateral aspect of the right side of the neck, 7 x 5 x 3 cm at the level of the Thyroid and Hyoid cartilages deep to the Sternomastoid. The lump was firm and had a smooth surface. It was mobile in a horizontal but not in a vertical direction. Transmitted pulsations were present. No bruit was heard over it.

A provisional diagnosis of a carotid body tumour was made. A right carotid angiogram showed a large carotid body tumour (Figs. I & 2).

We decided against excision for the following reasons. The patient was symptomless, the tumour had not increased in size and the high risk of attempted excision. The patient is being followed up. The tumour will be excised only if it begins to press on adjacent structures or shows malignant change.

A right common carotid angiogram showed the presence of a carotid body tumour at the bifurcation of the right common carotid artery Fig. I and Fig. II

Lateral projection of right common carotid angiogram – Fig. I



Anteroposterior projection of right common carotid angiogram – Fig. II

NOTE:- The highly vascular soft tissue mass pushing apart the internal and external carotid arteries at the bifurcation of common carotid artery

Discussion

The carotid body is the largest of the paraganglia that make up the chemoreceptor system. Histologically it consists of nests of small uniform epithelioid cells surrounded by a vascular stroma. The only pathological change occurring in the carotid body is neoplasia. Microscopically the resulting tumours are well encapsulated, homogenous pinkish grey, or brown, firm masses. Histologically, carotid body tumours resemble normal carotid body tissue. Formerly all these tumours were thought to be non-functional and were called nonchromaffin paragangliomas, but this is not so as neurosecretory granules have been demonstrated in both normal chemoreceptor tissue and in carotid body tumours. (Grimsley et. al. 1967). Furthermore, elevated urinary catecholamines have been demonstrated in carotid body tumours. The percentage of these tumours that are functional is not known.

Carotid body tumours are symptomless when small. Symptoms are seen in patients with large tumours due to pressure on the Vagus, Hypoglossal nerves, the oesophagus and trachea. An early report (Harrington et. al. 1941) suggested that about 50% of these tumours were histologically malignant, but it is now believed that malignant change occurs only in about 5% (Javid et. al. 1967). Bilateral carotid body tumours occur in 3 – 4% of patients. Other chemodectomas such as glomus tumours can be associated with them as can medullary carcinomas of the thyroid.

Biopsy of these tumours can lead to severe haemorrhage and thus angiography is preferred to establish the diagnosis (Javid et. al. 1967). Stell and Maran (1972) point out that one of the worst mistakes in neck surgery is to biopsy a chemodectoma.

Management of these tumours could be by (1) Observation and follow up alone, (2) Surgery, and (3) Radiotherapy. In view of the supposed high incidence of malignancy surgical excision used to be advised in all cases. At present management tends to be more conservative in view of the high operative morbidity and mortality and the fact that malignancy is known to be rare. In Shamblins (1971) review, there was a mortality of 7% and hemiplegia in a further 22% in patients undergoing surgery. Therefore surgery should be carried out only when (1) Tumours show evidence of malignancy, (2) Cause pressure symptoms such as airway obstruction, and (3) Possibly in young patients with small tumours which are easier to excise without damaging the carotid system. Once surgery is decided upon it should be carried out under hypotensive hypothermic anaesthesia with facilities available for carotid grafting if necessary. Preoperative, catecholamine estimations and repeated blood pressure estimations are required, to exclude functioning tumour.

Radiotherapy does not cause marked regression of the tumour. However, it can cause temporary or even permanent cessation of tumour growth. Hence it is a palliative measure used only when a patient is deemed unsuitable for surgery.

Summary

A case of carotid body tumour is presented and the relevant literature reviewed. The dangers of biopsy and the value of angiography in diagnosis is stressed. Conservative management is advised in the majority of cases.

Acknowledgement

We wish to thank Miss A.M. Tan of the E.N.T. Department, University of Malaya for typing this paper.

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Case Report of Renal Tubular Acidosis Presenting with Periodic Paralysis

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Introduction:

PERIODIC PARALYSIS is usually the result of cellular potassium imbalance. Sometimes the cause of hypopotassemia can be diagnosed as in this patient.

Case Report:

P.W.T., a 22 year old Chinese Male, was admitted on 6th January 1975 with complaints of low backache on strenous work and weakness of limbs of sudden onset, and short duration followed by spontaneous recovery. He had another episode on 22nd January and 15th March.

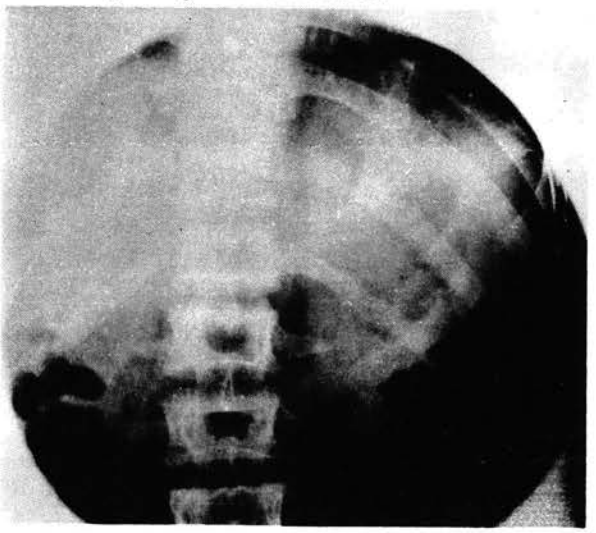

Fig. 1
Cone View of Renal Area Showing Bilateral Nephrocalcinosis and codfish vertebrae.

There were no significant findings on clinical examination except muscle weakness during the acute phase.

Investigations:

Blood

Bl. urea 28 mg%
Serum Uric Acid 5.5 mg%
Serum Calcium 9.6 mg%
Serum Phosphate 3.1 mg%
Serum alkaline phosphatase 9.5 K.A.U.
Serum Sodium 1.38 meq./litre
Serum Potassium 3.9 meq./litre when patient was well and 2.6 meq./litre during acute weakness
Serum Chloride 100 meq./litre
Haemoglobin 15 g%
T.W.D.C. = 7,400 (P = 75%, L = 23%, M = 1%, E = 1%)

Urine

1) PH = 6.5
2) Calcium excretion = 0.13 g/24 hours
3) Phosphate excretion = 4.0 g/24 hours
4) Pitressin test showed impaired concentration
5) S.G. = 1.005

Urine acidification tests were not performed since ammonium chloride could not be obtained.

X-rays – see illustrations

Treatment:

Sodium bicarbonate 10 gram nocte and mist. pot. cit. Patient improved with no recurrence of symptoms.

Fig. 2
"Cod fish" vertebrae clearly seen on lateral view of lumbar spine.

Discussion

Renal tubular acidosis was suspected as the cause of periodic paralysis (low serum potassium during acute weakness) from the abdominal X-rays – nephrocalcinosis in kidneys of normal size and cod-fish vertebrae with rarefaction of bone indicating osteomalacia. The other common causes of nephrocalcinosis are hypercalcaemia (e.g. hyperparathyroidum, sarcoidosis, milk alkali syndrome) and medullary sponge kidney. In the former the kidneys are small due to the long standing effects of hypercalcaemia and there are other sites of metastatic calcification. In the later, the kidneys are often large because of congenital dilatation in the collecting tubules and young patients are often asymtomatic (Lindvall, 1959)[3]

Renal tubular acidosis (R.T.A.) has been divided into 2 types (Rodriguez-Soriano J. and Edelmann, C.M. jr 1969)[6] – (1) proximal RTA caused by impaired bicarbonate reabsorption in the proximal tubule and (2) distal R.T.A. secondary to an inability of the distal tubule to normally reduce urine PH. Renal potassium wasting in the latter is probably due to reduction in the $H^+ - Na^+$ exchange; $K^+ - Na^+$ exchange thus increase reciprocally. Corrective alkali therapy by raising urinary pH to values equal to or greater than arterial pH, could remove the gradient restriction on renal H^+ secretion (Gill, J.R. Jr et. al. 1967). The shortage of base with which to excrete acid may lead to a local demand for calcium. The resultant hypercalciuria is probably responsible for the nephrocalinosis and the complication of osteomalacia (Albright and Reifenstein, 1948)[1]

Biochemically in R.T.A. the plasma Co2 combining power is low and the chlorides raised; the serum calcium normal or low and the plasma phosphorus low. If bone changes are marked, the alkaline phosphatase is usually raised. The serum potassium is frequently low. The urine is usually neutral or alkaline but is sometimes slightly acid in the presence of the more severe grades of acidosis. The titratable acidity and the ammonia content of the urine are low, the urine specific gravity is low since the kidneys cannot concentrate normally. Typically there is hypercalciuria (L.N. Pyrah 1960)[5]

For completeness I shall mention other causes of periodic weakness which include aldosteronism, hyperthyroidism, myophosphorylase deficiency, myasthenia gravis, hysteria, paramyotonia congenita, acute intermittent porphyria, idiopathic myoglobinuria, gastrointestinal and renal disease associated with excessive loss of potassium, exposure to exogenous toxins and familial idiopathic periodic paralysis. (Mark Dyen et. al. 1969)[4]

Acknowledgements

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Resistance of Insect Vectors of Diseases to Insecticides in Malaysia and other South East Asian Countries

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VECTOR BORNE DISEASES take pride of place as among the most important communicable diseases in various countries of South East Asia including Malaysia. The recent sporadic outbreaks of haemorrhagic fever which occurred repeatedly almost every year throughout the vast areas of Asia extending from Sri Lanka to the Philippines, the resurgence of malaria transmission in the sub-continent of India, Sri Lanka and fast increasing number of incidence in other countries in South East Asia have caused great concern among public health and vector-control authorities in this region. The effective control of vectors and insects of public importance, therefore, is a matter of utmost importance, to countries of this region.

During the past quarter of a century or more, persistent insecticides have proved so successful that they are still the main weapon used against vector-borne diseases. Many species have developed resistance to these compounds, and have been criticized time and again on the ground that they contribute to the pollution of the environment, but insecticides are still responsible for the control of vector-borne diseases in many areas of the world. They remain the most economical means of fighting insects and have saved millions of lives and have elevated the suffering of many more millions of people.

Many insect vectors, however, have developed resistance to insecticides. The problem of insecticide-resistance in vectors is like a ripple, ever increasing its spread among more species of insects to most types of insecticides over larger geographical areas. Insecticide-resistance in anopheline mosquitoes has created more concern than any other problem in applied medical entomology during the last two decades. This is especially so because of the serious challenge which the problem of resistance now poses to man's attempt to eradicate vector-borne disease like malaria on a world basis.

The areas covered in this review include countries like Malaysia, Singapore, Indonesia, Thailand, Philippines, Khmer Republic, South Vietnam, and Korea.

Among the anopheline mosquitoes, the following four malaria vectors have developed resistance to insecticides:

Anopheles sundaicus has developed DDT resistance in 1954 in Java, Indonesia (Chow & Seoparma, 1956). On the south coast, dieldrin resistance was detected in Jogjakarta Province in 1959. In south Sumatra this species was found to be refractory to DDT and dieldrin in 1961. Dieldrin resistance was reported in this species in 1961 in Sabah, East Malaysia (Chow, 1963, 1970a).

A. aconitus: Resistance to dieldrin first appeared near Suban in Central Java in 1958 after six half-yearly cycles of 0.5 gr/m. In the next three years it spread rapidly over large areas of Java necessitating the replacement of dieldrin with DDT in malaria eradication project (MEP). Double resistance to DDT and dieldrin was demonstrated in this species in 1962 in Jogjakarta Province. Further intensive testing revealed that this condition was widespread especially in Central Java. Tests done in 1973 at several sites in Central Java and Jogjakarta Province revealed high resistance to DDT. Intra-

domicillary application of DDT however, have reduced transmission of malaria by this species (Loekman, 1973).

A. minimus flavirostris which is the major vector in Philippines has developed resistance to dieldrin in 1959 (Chow, 1959). DDT is still effective against the species. This species is also a vector of filariasis.

A. sinensis which is the main vector in the Republic of Korea has developed strong resistance to dieldrin in Western plain and hill areas of Korea (Hong, 1971). It has also showed intermediate resistance in Korea to fenitrothion and fenthion (Self et al, 1974). These are the only indication of O.P. resistance in *Anopheles* in this part of the world.

A few other species have also developed dieldrin resistance in 1962 (Chow, 1963) in Sabah, East Malaysia:

A. philippinensis has developed dieldrin resistance (Chow, 1963) in Sabah, East Malaysia.

A. barbirostris has developed intermediate DDT resistance in Thailand.

A. barbirostris, A. annularis and *A. subpictus* have developed resistance to dieldrin in Java, Indonesia.

A. vagus vagus was found to be resistant to dieldrin in Peninsular Malaysia (Chow, 1963) and highly resistant to dieldrin in Java, Indonesia (Chow, 1958). This species is resistant to dieldrin and DDT in Saigon, Vietnam in 1965 (Chow, 1965).

A. vagus limosus has developed resistance to dieldrin in Philippines in 1959 (Chow, 1959).

Among the Culine mosquitoes, the following vectors have developed resistance to insecticides:

Culex pipiens fatigans – the most important vector of urban strain of *Wuchereria bancrofti* in addition to being naturally refracting to DDT in this region, has developed a high degree of resistance to DDT, dieldrin, BHC (Reid, 1955, Wharton, 1958a & b, Thomas 1970b) and strong resistance to fenthion (Thomas, 1970a). In Singapore, this species has been found to be resistant to malathion (Chan *et al,* 1972). Some degree of resistance is also reported in *Culex pipiens complex* to malathion and fenthion in South Vietnam.

Culex tritaeniorhynchus which is a major vector of Japanese encephalitis has developed resistance to dieldrin (Hwang *et al,* 1965) and DDT (Chow, 1973) in Korea. Larvae of *C. tritaeniorhynchus* was reported to be DDT and lindane resistant (Self *et al* 1974) in Korea.

Aedes aegypti vector of dengue and haemorrhagic dengue has developed resistance to DDT, fenthion and malathion in Malaysia and to DDT, dieldrin BHC and malathion in South Vietnam, and DDT, BHC, dieldrin and fenthion in Khmer Republic (Mouchet *et al,* 1972).

Aedes albopictus has developed resistance to DDT in Malaysia, Singapore, Philippines, Khmer Republic and South Vietnam; resistance to dieldrin in Malaysia and South Vietnam, Philippines and fenthion resistance in Malaysia. (Mouchet *et al,* 1972).

Musca domestica

Housefly *Musca domestica* has developed resistance to many insecticides in Cameron Highlands, Malaysia. It has developed very high heterogenous resistance to lindane and to DDT in about 80% of the population, high resistance to contact effect to trichlorfon, quite high resistance to dichlorvos (DDVP). In addition, this species has developed intermediate or moderate resistance to diazinon, dimethoate and fenthion (Keiding 1968).

Bedbugs

Bedbugs *Climex hemipterus* was found to be resistant to dieldrin and DDT in Malaysia (Reid, 1960; Cheong, 1964). Thevasagayam (unpublished data 1969) found DDT and dieldrin resistance in this species in houses sprayed during malaria eradication programme. *Climex lecturalius* was found to be resistant to DDT and dieldrin in Korea (Cha *et al,* 1970).

Lice

Body lice was found to be resistant to DDT in Korea in 1951 (Hurlbut *et al,* 1952).

Fleas

Strong resistance to DDT and dieldrin was noticed in *Xenopsylla cheopis* in South Vietnam (Chow, 1970b).

Implications of Resistance in Vector Control

The resistance problem of arthropods to insecticides have been thoroughly reviewed by the Expert Committee on Insecticides (1970) and later by Brown and Pal (1971). The implications of resistance in vectors have been reviewed by Hammon

Table I

Resistance of Insect Vectors to Insecticides in Malaysia and Other South East Asian Countries

Species	Resistance to DDT Group	Resistance to Dieldrin/BHC Group	Resistance to Organophosphorus Group
Anopheles aconitus	Indonesia	Indonesia Sabah	—
A. sundaicus	Indonesia	Indonesia	—
A. minimus flavirostris	—	Indonesia	—
A. sinensis	—	Korea	Korea
A. barbirostris	Thailand	Indonesia	—
A. annularis	—	Indonesia	—
A. subpictus	—	Indonesia	—
A. vagus vagus	S. Vietnam	Indonesia S. Vietnam Malaysia	—
A. vagus limosus	—	Philippines	—
A. filipinae	—	Philippines	—
Culex pipiens fatigans	Malaysia	Malaysia	Malaysia Singapore S. Vietnam
Culex tritaeniorhynchus	Korea	Korea	—
Aedes aegypti	Malaysia S. Vietnam Khmer Rep.	S. Vietnam Khmer Rep.	Malaysia S. Vietnam Khmer Rep.
Ae. albopictus	Malaysia Singapore Philippines S. Vietnam	Malaysia Philippines S. Vietnam	Malaysia
Musca domestica	Malaysia	Malaysia	—
Cimex hemipterus	Malaysia	Malaysia	—
Cimex lectularius	Korea	Korea	—
Pediculus humanus	Korea	—	—
Xenopsylla cheopis	S. Vietnam	S. Vietnam	—
Cockroaches – German	Malaysia	—	—

and Garrett-Jones (1963); Busvine and Pal (1969); and Pal (1974). The implications of insecticides resistance in vectors in Malaysia and other countries in Southeast Asia are very similar to that which has already been described by these authors.

Although resistance has been found in various vectors, it does not exist in all insects throughout the geographical range of the species, but the problem is limited to certain pockets only and their distribution is patchy. So far, none of the important vectors of malaria in Malaysia has been proven to have developed resistance to insecticides. As shown in the table, the majority of these have developed resistance to dieldrin and/or DDT only. Dieldrin resistance when it occurs, appears rapidly and reaches a high level, whereas DDT resistance appears more slowly and has not prevented malaria control and/or eradication programmes. Where there is double resistance to these compounds as present in the same major vectors of malaria in Java, the control of malaria becomes extremely difficult. It is then necessary to look for substitute insecticides among organophosphorous groups or carbamates. However, these are considerably more expensive and may be beyond the economic reach of many developing countries in South East Asia. It is calculated that malathion is at least 5 times the price of DDT and propoxur 20 times, making spraying operations with them at least 3 and 8 times more expensive, respectively (Pal, 1974).

Culex pipiens fatigans which is refactory to DDT and *Aedes aegypti* vector of haemorrhagic dengue as well as *Aedes albopictus* have developed high levels of resistance to chlorinated hydrocarbons. However, these species are still susceptible to many O.P. compounds although resistance to a few others has been reported. Its effect does not seem to be far reaching and the great majority of species are still susceptible to these compounds. However, in some insects, a low level resistance to the O.P. compounds is sufficient to prevent their effective use in the field. Moreover, they are more expensive.

In the Cameron Highlands, Malaysia, control of houseflies poses a real problem as the resistance in this species is multivalent. This probably is as in some other cases, due to the great number of insecticides used against agricultural pests in the farms where the houseflies breed. It is difficult however, to assess with accuracy the effect of pesticides/insecticides which are used in agriculture on the development of insecticide-resistance in vectors. Insecticides-resistance in other vectors also causes considerable difficulties in their effective control in S.E. Asia.

The extensive use of a wide range of chemically diverse pesticides in agriculture for crop protection most probably exerts a strong insecticidal selection pressure on many vectors. Therefore, a mutual consultation between agricultural and public health authorities in the use of various types of insecticides against agricultural pests and/or against insects of medical importance would be of immense benefit. An integrated method that includes appropriate combinations of control measures such as the introduction of new insecticides, mechanical, biological and genetical methods designed for local suitability and needs must be considered for use in vector control programmes. However, these involves financial educational, organizational and operational implications.

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Book Reviews

1974 EVALUATION OF SOME PESTICIDE RESIDUES IN FOOD. WHO PESTICIDE RESIDUES SERIES, NO. 4. PP. 545. WORLD HEALTH ORGANIZATION, GENEVA. 1975. Sw. fr. 48.

This is a very valuable reference monograph prepared by the joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues which met in Rome from 2-11 December 1974. It gives in details the hazards to the consumer from 34 pesticide residues in food and food-stuffs. It contains an excellent account of the general consideration, including the principles adopted for the evaluation and the summary of results of evaluation on a number of pesticide residues. It summarises conclusions reached and recommendations made by the Expert Committee members of the two U.N. Bodies. Recommendations on acceptable daily intake of these pesticides, maximum permitted concentrations of the residue known as "tolerance" for pesticide residues in food and information on the methods of analysis of pesticide residues are also given. Further it contains a wealth of relevant and valuable information on these pesticides obtained from published literature and other sources. Two annexes are included at the end of the monograph. ANNEX I gives the recommendations made on acceptible daily intakes and residues limits made at the 1974 meeting. ANNEX II gives an extensive bibiliography of all previous Reports, monographs and other publications of a general nature. This publication is a must for all those who are engaged in pest control and environmental health.

Vijayamma Thomas

ERRATA

RE: LUMBAR EPIDURAL ANAESTHESIA IN A SOLO

Med. J. Malaysia Vol. XXX No. 4 June 1976 pq. 316

The title of the article should have been "Lumbar Epidural Anaesthesia in a Solo Surgical Practice" instead of the above-mentioned.

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