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GUEST EDITORIAL:

CHORIOCARCINOMA — A REAPPRAISAL

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ONE in three hundred pregnant women in this country (Sivanesaratnam and Ng, 1977) may develop a molar pregnancy. A high number of these patients will develop choriocarcinoma. It used to be said that if one had choriocarcinoma and one survived, the diagnosis was wrong. Now, it is a potentially curable disease.

This, together with the easy availability of methotrexate, makes it tempting for specialists (and others) to attempt the management of these cases when they come across them. This is especially so in Malaysia where patients would otherwise have to travel long distances to get to specialist centres (who may not possess all that many extra facilities anyway) particularly as trophoblastic disease can be cured using agents like methotrexate in over 80% of cases (Lewis, 1976).

Unfortunately the truth is slightly different. In the presence of the full-blown, avillous, histologically proven metastatic disease seen so commonly in Malaysia, the survival rate is depressingly low. Though the unit in Singapore is very experienced in treating choriocarcinoma, and though it has modern facilities like radio-immunoassay of B-submit human chorionic gonadotrophin to monitor chemotherapy, Ratnam *et al.* (1976) found that if the patient came with metastatic avillous choriocarcinoma the survival rate was only 46.7%. His cases with early disease had over 80% survival rates. It is of course possible that the disease in this part of the world is biologically different from that in the West, but it is most unlikely that the fate of patients treated at random across the length and breadth of Malaysia is much better than of those in the highly specialised unit in Singapore.

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It is essential, therefore, for the sake of our patients, to examine how workers have been able to report cure rates around 80%, and determine how we, in this country, can achieve comparable results. Two aspects need close examination. The first is early diagnosis, and the second is management. Early diagnosis is very important. It is highly significant that patients diagnosed late are now grouped as high risk cases (Bagshawe, 1976) and require highly toxic combination chemotherapy, sterile rooms, and all the massive paraphernalia of specialised oncology units before they have any chance of cure.

This means that we can only hope to decrease the number of patients who die by catching the disease early. To do this one needs to have units which are capable of conducting the painstaking job of *close follow-up*, and which have facilities for assay of tumour markers to pick up early malignant change. Radio-immunoassay picks up the patient whose human chorionic gonadotrophin levels have dropped below the level of sensitivity of the usual immunological tests for pregnancy, *but have not reached zero, and who is therefore harbouring microscopic amounts of either malignant or potentially malignant trophoblast.*

It is when the disease is picked up at this early preclinical stage that 80% cure rates can be expected, as will be seen by inspecting the results of Ratnam *et al.* (1976).

It is also necessary to keep in mind that full-blown disease can be present even when human chorionic gonadotrophin levels are low, so that one cannot be complacent just because a pregnancy test is negative. It is necessary to be aware that recent work (Singh, J. and Sivanesaratnam, V., in preparation) has clearly shown that an x-ray chest may not reveal the presence of lung metastases, and other radiological monitoring techniques may be required. It is also necessary to be aware that choriocarcinoma invades the

myometrium, and may be present elsewhere than in the uterine cavity, so that *a negative D & C does not indicate absence of disease.*

For the woman who has had a molar pregnancy evacuated and nees to be followed up, there is evidence suggesting (Stone *et al.*, 1976) that the use of the contraceptive pill may lead to a slower removal of trophoblastic tissue from the system. If she unfortunately becomes amenorrhoeic during the period of observation, *it is essential to assume that she has choriocarcinoma until proved otherwise.*

There are few satisfactory ways one can find out whether this is a normal intrauterine pregnancy or choriocarcinoma. The first is the use of ultrasound: the gestation sac can be picked up on grey scale at six weeks' and fetal movements seen on real time at eight weeks' amenorrhoea, already rather late. The second is the use of radio-immunoassay; high human chorionic gonadotrophin and low human placental lactogen levels are rather suggestive of molar trophoblast (Lim *et al.*, 1976). The third is to evacuate the uterus and examine the contents. Finally one can wait, and see whether the patient lives, or dies.

The second problem is that of management. The drugs used in treating the disease are potentially lethal. It is therefore preferable that they are used only as long as necessary. However, if they are not used long enough, recurrence is certain. Incomplete therapy also renders the tumour resistant to chemotherapy and makes subsequent therapy difficult and ineffective.

Figure 1 shows that if one stops after an arbitrary number of courses after the immunologic test for human chorionic gonadotrophin is negative, the chemotherapy may be incomplete. It will be seen therefore that the *usually used immunological assay methods are adequate neither for the follow-up of molar pregnancies nor for monitoring chemotherapy in choriocarcinoma.*

If we review facilities available in this country, one will see that ultrasound is as yet available only in General Hospital, Kuala Lumpur, and radio-immumoassay for human chorionic gonadotrophin while until recently available in Institute of Medical Research, Universiti Kebangsaan and

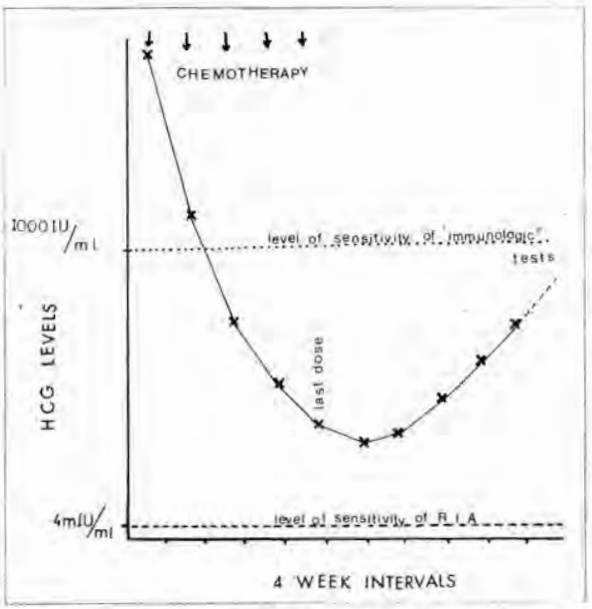

Fig. 1. Levels of human chorionic gonadotrophin (HCG) during course of chemotherapy showing inadequacy of latex agglutination test in monitoring; chemotherapy stopped too early while radio-immunoassays (R I A) would have shown the presence of viable, secreting tumour cells.

University of Malaya is not so far developed at any of these places that they can prepare their own B-submit antibody, and they were certainly *not being deluged by anything like the number of tests that should be asked for to cover all the patients in the country who have had molar pregnancy and should at this moment be on human chorionic gonadotrophin surveillance.* Also, serum for human chorionic gonadotrophin assay *does not travel well;* the hormone breaks down rapidly at room temperature. The facilities needed are beginning to be available. But they need to be developed, and used.

Finally it is essential to understand that follow-up does not just mean doing tests and clinical examinations on patients who come. Adequate follow-up implies tracing defaulters, persuading them to attend, understanding their difficulties, and assisting to overcome these, tracing results, and a general ability and willingness to spend time with and for each patient. This is obviously impossible for a busy specialist, and specialists throughout the country are very busy indeed.

The above is a fairly superficial review of the problem, as it stands. Countries like England long ago realised that adequate experience and care of cases like these can only be achieved by the use of regional centres. It is patently clear that we who have much more of this disease must similarly form and develop regional centres, and concentrate *at least* the serological follow-up of our patients there, NOT AFTER THEY HAVE DEVELOPED CHORIOCARCINOMA, BUT BEFORE.

Unless we do so, and make sure that these regional centres are not just centres in name but have the basic *functioning* facilities outlined above, and have people with enough skill, enthusiasm, and *available time* to cope with these patients we will have to admit, if we are at all honest with ourselves, that we are prepared (for whatever reason it may be) to let a proportion of our women who should have an 80% chance of survival have only a 40% chance to do so.

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THE EXTENSION OF MENTAL HEALTH CARE IN KELANTAN

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INTRODUCTION

THE CARE OF psychiatric patients in the community is an integral part of the treatment and rehabilitation process. Unlike other illnesses where the transition from ill health to health is well recognised and the period is short, this transition in psychiatric illnesses, except in some instances, is prolonged. Psychiatric patients face a crucial period of readjustment on discharge and this readjustment (rehabilitation) is more difficult if the period in an institution has been long. Without going into these secondary handicaps well documented by Russel Barton (1960) and Erving Goffman (1961) the problems faced by psychiatric patients on discharge include those of daily living. Often they have lost their jobs and their positions in the family or village are altered, some to the point of total rejection. They have to face the social stigma and prejudice which are still present in our society.

Another handicap is the medication they receive which if not reviewed periodically contributes to drowsiness, lethargy or muscular dystonia. Psychiatric illness in most cases needs relatively prolonged follow-up and this poses problems of continuing treatment in the community, least of which is the availability of trained staff to follow them up especially in areas not served by hospitals.

In this light, psychiatrists and others have been advocating the decentralisation of services and establishment of Psychiatric Departments in General Hospitals instead of big (often with thousands of patients) institutions as in the past. These Psychiatric Departments will function to bring prompt management of psychiatric illnesses in the community where it is needed. A step beyond the Psychiatric Departments in General Hospitals has been taken in some countries to render service in rural communities without hospitals by trained medical and paramedical staff. The W.H.O. is coordinating this effort in seven countries in its Collaborative Study on the Extension of Mental Health Care. This study extends from 1975 to 1980. The scope of this Study is to determine the feasibility of introducing basic metal health care in developing countries, to select priorities for interventions, to develop methods of task orientated training for health workers, to stimulte the community's understanding of and response to problems related to mental disorders and to research on alternative and low cost methods of mental health care (W.H.O. Protocol 1978).

The efforts of the Psychiatric Department in the General Hospital, Kota Bharu from March 1977 to May 1978 is reported here.

BACKGROUND

The Psychiatric Department in Kota Bharu is also the Regional Mental Health Centre for the east coast states. There are 116 beds staffed by medical officers, social workers, nursing staff and for the majority of the period under study there were three psychiatrists of whom one was the Consultant. The effective coverage was the whole of Kelantan and the northern part of Trengganu comprising of about one million people, the majority living in rural areas. There was a twenty-bed ward in Kuala Trengganu which was visited by the Consultant. The 116 bed wards in Kota Bharu were run as an acute unit with only a few long-stay patients and since 1975, no cases had been transferred to the long-stay institution at Hospital Permai, Johore.

Overcrowding in the psychiatric wards was a constant feature and at times in the male acute ward occupancy was over 200 per cent.

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Attempts had been continuously made to discharge patients but numerous difficulties were encountered. Relatives could not be contacted or did not come to fetch patients home. Motivation for relatives to take home patients and care for them was poor as they either felt the patients were still unwell or afraid of the patients at home. Patients discharged were readmitted within a short period for reasons often of a non-clinical nature. Hence there was a revolving door process of discharges and early readmissions. More discharges led to more readmissions.

The Psychiatric Department was conducting out-patient services in five peripheral centres at Health Centres in Tumpat, Pasir Mas, Pasir Putih, Macang and Tanah Merah. These clinics were twelve to thirty-five miles distant and were held monthly or fortnightly. These were only for follow-ups and conducted by a psychiatric trained hospital assistant. The staff at the Health Centres was not involved and no case finding or management of new cases were carried out.

The purpose of these clinics was multifold. It brought follow-up care closer to the patient and ease the burden of travelling and finance. It enabled patients or relatives to save time to continue follow-up. One reason for default was that they could not afford the time to travel as they had to work. It provided a link between the Psychiatric Department and the patient and was an attempt at continuing care in the community. On these sound principles the clinics should be well attended and readmissions reduced or more widely spaced. Yet this was not so. Default of follow-up was high and readmission was high as was shown by the annual increase of readmissions.

REAPPRAISAL

A reappraisal was made into the existing service in March 1977 with the view of enhancing the effectiveness of the service. This reappraisal was made on the ward service, peripheral clinic services and the inter-relation between the two.

One problem affecting both services was the lack of hospital transport for the Social Worker and peripheral clinic staff. A Social Worker's effectiveness is seriously curtailed if he is unable to visit patients' homes and relatives. The wards were overcrowded and put severe strain on physical and rehabilitative facilities and taxed the nursing capacity of the staff. Less obvious difficulties were staff morale and training and effective team-work. This was not due to lack of willingness to contribute and cooperate but due to overcrowded wards and frequent changes of staff.

The peripheral clinics were continuing medication for discharged patients but there was no attempt in meaningful involvement of the family in the patient's care or treatment of fresh cases. This was strongly felt in the area of the rapport established between staff in the hospital and relatives of patients. This rapport and trust in the staff could be established at the peripheral clinic but was not possible because of the widely-spaced visits of the hospital assistant.

The peripheral clinics were functioning as an extension of the Psychiatric Department deploying staff from the department. The Health Centre staff was not an integral part of the system. In this respect the attempt at decentralisation of service utlising local staff was ineffective. The advantages of local staff treating and managing cases are many. They live in and are part of the community. They are available to provide care daily instead of periodically. They could give immediate care for acute cases or relapses instead of the patients having to travel for miles. The establishment of rapport and trust in the ability of local staff will enhance the acceptance of mental health care locally.

INTERVENTIONS

A series of interventions were planned and carried out in stages. The interventions were closer cooperation of Department staff in patient care through weekly conjoint staff meetings, active occupational and recreational therapy as part of social rehabilitation, wider and more intensive utilisation of the social workers and involvement of them in patient care, closer initial supervision of peripheral clinics by the psychiatrists, to solve transport problem, staff training for the Department and peripheral clinics (Health Centre staff), the shift of discharged patient care from the Department to Health Centre doctors after training.

Conjoint staff meetings were initiated and held weekly to discuss all cases for discharge and

"problem cases". These were attended by doctors, nursing staff, occupational therapist, social workers and the peripheral clinic hospital assistant. A team approach was used towards patient care from contributions from all categories of staff. The social workers' reports were now available to all staff instead of the doctors only. The social workers in turn were able to share the experience of the nurses on patient behaviour and interaction in the wards. This team approach gave a clearer understanding of management procedures and of interdependent staff roles.

Simultaneously, a more active occupational and rehabilitative programme was instituted and the time the patient spent doing nothing was reduced. Auxillary staff was increased in this area.

The social workers were more extensively utilised as the transport problem was solved with the coooperation from the Medical Superintendent of the General Hospital. Home visits to contact relatives, to prepare social case reports, to send discharged patients home and to follow-up defaulting patients were intensified. There was more contact between doctors and relatives as a result. Doctors now had an opportunity to discuss with the relatives the patients' illnesses and plans for rehabilitation. A conscious attempt was made to impress on the relatives the continuity of care by the peripheral clinics. Particular attention was directed towards changing attitudes of relatives of patients towards mental health in general and attempts were made to clarify their doubts and fears.

Staff training was vital if they were to be involved more extensively. For some staff, the training was a refresher, for others it was a new experience. Lectures were held after office hours and attendence was voluntary. A systematic training programme for doctors from Health Centres was held to train them in community aspects of psychiatry and in early diagnosis, treatment and for follow-up. A two week course was held for doctors from the three East Coast States including Kelantan. This course was held twice within the year. In all fourteen doctors were trained.

In the beginning of this study period the psychiatrists started more frequent supervision of follow-up in the peripheral clinics. This frequency of supervision was reduced when the Department trained doctors took over in running these clinics. The scope of care was widened to include treatment of fresh cases in the clinics without referral to the Department. Towards the final stage of the study, the doctors at these Health Centres were operating independently in management of psychiatric cases but with opportunity for referral and discussion of difficult cases with the Department.

RESULTS

One outcome of these interventions was the reduced rate of daily occupancy of the wards (Figures 1 and 2). Readmissions which used to occur within weeks or even days of discharge were spaced out. Unlike past experience increased discharges did not bring about increased immediate readmissions after the interventions. The noisy and hectic environment in the wards was improved and the need for early quick discharges was eleviated. One pre-discharge ward could even be converted to a drug detoxification ward without any overcrowding in other wards. Working condition was improved with less patients.

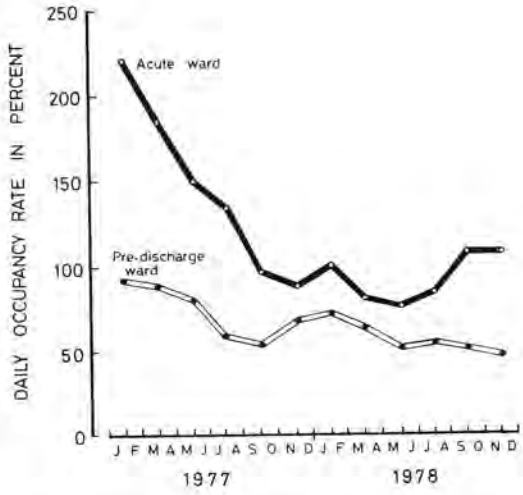

Fig. 1. Bi-monthly average daily occupancy rate of the acute and pre-discharge male wards from 1977 to 1978.

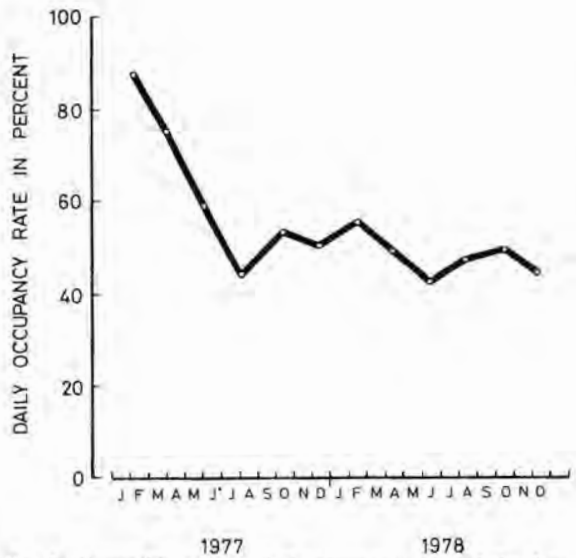

Fig. 2. Bi-monthly average daily occupancy rate of the female ward from 1977 to 1978.

The peripheral clinics took on an identity and function of their own in being independent units for early diagnosis, treatment and prevention. The number of patients treated and number of visits increased (Table I). Though no study was made of pre-intervention as against post-intervention morbidity, it could be expected that the districts covered by these clinics would eventually have reduced morbidity. More fresh cases which had previously remained untreated were detected.

Table 1
Number of cases treated at peripheral psychiatric clinics in Kelantan

	1976	1977	1978
Machang	592	795	829
Pasir Mas	565	757	871
Pasir Puteh	479	614	710
Tanah Merah	240	407	520
Tumpat	176	273	312
Total	2,052	2,846	3,242

DISCUSSION

This study was a planned course of extension of psychiatric care into the rural areas by utilising doctors in the Health Centres and with coordination with the Psychiatric Department in the General Hospital. It was also a study of social rehabilitation in the inpatient wards.

The Expert Committee on the Organisation of Mental Health Services in Developing Countries (W.H.O. 1975) had advocated the need for planned decentralisation of psychiatric services and the advocation of circumscribed training of paramedicals in the treatment of psychiatric illnesses. In India Murthy and Wig (1978) and in Columbia Climent *et al.* (1978) showed the feasibility of training paramedical staff in rural areas to treat psychiatric illness with a limited range of drugs. In this study the doctors were trained instead as it was felt that as under the present system of care they were already treating all illnesses, they should be managing psychiatric illnesses as well, as this would fit in line with their functions. The need for training of paramedical staff at sub-health centres, where there are no resident doctors, could be assessed.

This study attempts to show that with concerted efforts and a planned course of interventions, patients could be effectually maintained in the comunity with treatment continued by trained local medical staff with coordination from Psychiatric Department of a General Hospital. Discharges have to be planned and coordinated as unplanned discharges brought on increased readmissions and morbidity, not only to patients, but their relatives too. Social rehabilitation in the wards have been shown to increase staff morale and patients' motivation for discharges (Brown and Wing 1970). The increase of fresh cases coming for treatment could be interpreted as the acceptance of psychiatric care by the community which had previously depended on traditional healers. The extension of mental health care to the rural areas is feasible but needs coordinated planning with administrators, social scientists and other professionals if it is to be implemented on a large scale effectively.

SUMMARY

A series of systematic interventions in the Psychiatric Department, General Hospital, Kota Bharu and the extension and improvement of provision for mental health care in the Districts were carried out. As part of the extension programme, medical officers in the Districts were trained in the Department to provide care in the

Districts. These interventions and extension of care contributed to the maintenance of discharged psychiatric patients in the community, the reduction in the frequency of readmissions and the reduction in the daily occupancy rates of the psychiatric wards. Early detection and treatment of cases in the community resulted in the increase of new cases.

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ECOLOGICAL CHANGES AND HEALTH IN THE MUDA IRRIGATION SCHEME

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INTRODUCTION

ECOLOGICAL changes are continuously being effected in many parts of Malaysia. Perhaps one of the most significant is in the rice bowl of Malaysia, the Muda Irrigation Scheme, in Perlis-Kedah. This is one of Malaysia's largest agricultural development project and has been designed to enable double-cropping of more than one quarter of a million acres of padi land. Currently the Muda area produces about 45% of total padi production in Peninsular Malaysia.

The project area has had a long tradition of single crop padi cultivation which formed the main source of income and economic activity of more than 50,000 paid farming families. Indirectly the Muda Irrigation Scheme has provided income and employment opportunities for many thousands of others in the form of input supply industries, rural shop-keeping, rice-milling, and the maintenance of mechanical farm equipment. Currently the Muda area has a population of about 550,000.

More than $250 million has been spent on the engineering works alone. In addition, government investments in the form of agricultural research, extension, development of producers' organizations, marketing and artificial padi drying, amount to many millions of dollars more.

ENGINEERING ASPECTS

In order to supply irrigation water for double cropping, the Muda Irrigation Scheme called for the construction of 2 dams with a total surface area of 35 square miles, 61 miles of main canals, 564 miles of branch canals, 560 miles of drainage canals, a coastal bund 68 miles long, a tidal barrage across the Kedah River and 480 miles of farm roads.

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AGRICULTURAL ASPECTS

The principal crop grown is padi which accounts for almost 80% of land use. To be successful, double cropping requires the use of high yielding short term padi varieties, fertilizers, pesticides, the liming of acidic soils, a high degree of mechanization of farming operations and a strict adherence to a planting schedule. Double cropping was begun in 1970 and by 1973, 75% of the farms were being planted with high yielding varieties of padi, 97% of the farms applied fertilizers, 48% used pesticides and 85% had mechanised ploughing (Treasury Malaysia, 1975). However, these ecological changes naturally produced several major problems directly and indirectly related to health.

ECOLOGICAL CHANGES AND HEALTH

Padi cultivation in relation to pollution, fish, rats and the buffalo

The use of high yielding short term padi varieties makes a great deal of sense. Not only does it enable two crops to be planted but also ensures that each crop has a higher yield. During the single cropping period the average yields per acre were about 520 gantangs. In 1974 the yields had risen to about 630 gantangs per crop — an annual yield of about 1260 gantangs compared with 520 gantangs per year (Treasury Malaysia, 1975). The net incomes have increased. For example, in non-acidic soils income has more than doubled from $145 per acre during the earlier single cropping period to $312 during 1972-73 (Treasury Malaysia, 1975).

However, high yielding varieties are highly sensitive to cultivation practices, and fertilizers, pesticides and the liming of acidic soils must be carried out. This of course increases the overhead costs particularly since fertilizers are derived largely from petro-chemical products. For example the cost of fertilizers increased by 400% during the 2-year period 1972-1974, with inflation

rising by 45% during the 5-year period 1970-1975. To add to the problem the practice of modern agricultural methods and double cropping, with its consequent ecological changes, has resulted in several problems that have a direct bearing to the health and well-being of the people.

Due to the use of fertilizers and pesticides, a 90% reduction in the number of fishes breeding in padi fields has been reported, with the consequence that an important source of animal protein has been lost.

The number of rats have also increased. Where previously the fields were allowed to lie fallow for several months, agricultural activity is now an around-the-year feature and this seems to have removed one natural method of keeping the rat population down, with the consequence that much grain is destroyed and the danger from rat-borne diseases has increased.

Where previously the buffalo was able to graze on the fallow land, the use of agricultural lands all the year round, has severely reduced the amount of land available for grazing. Consequently, the farmer has had to replace the buffalo with the mechanical plough. Of course this process of mechanization has many advantages such as speed and thus the ability to adhere to the strict schedule of planting mentioned earlier. Thus by 1973, 85% of farms had changed to mechanized ploughing. However, unlike the buffalo, a mechanical plough must be maintained, it uses expensive gasoline, deteriorates and may break down, and most importantly it is unable to reproduce and beget baby ploughs. Further, buffalo dung is a natural fertilizer but the grease, smoke and oil of the mechanical plough are pollutants. Finally, the buffalo is an important source of protein and is an important cultural element in the festivals related to the cycle of life (birth, marriage, illness and death) and to the cycle of planting and the year (the harvest festival and the Muslim festivals). Presently, with the virtual disappearance of the buffalo numerous cultural and social events are being undermined.

The planting schedule in relation to labour supplies and the rains

Another set of ecological problems are related to the planting schedule. As mentioned earlier, double cropping demands that farmers adhere strictly to a planting schedule. However, such a simple system has several important repercussions.

Strict adherence to a planting schedule means that there will be a shortage of labour. Where previously, mutual cooperation by *gotong royong* over several weeks provided sufficient manpower for the cultivation of rice, the reduction of time available, particularly in relation to transplanting, has meant that there is now a shortage of labour, with the need to import labour from outside the Muda area and a consequent increase in the cost of production.

Further, the off season crop is usually harvested during the rainy season and artificial drying has had to be used. This has not only increased the cost of production but there is the added problem that the padi may be lightly contaminated with mud with the consequence that its selling price is reduced.

Roads and motor vehicular accidents

The addition of almost 500 miles of farm roads combined ith mechanization and the use of motorised transportation has shifted deaths due to motor vehicular accidents, among those below the age of 20 years, from 6th position in 1970 to become the 2nd leading cause of deaths in 1975 (Singh, 1978). On the other hand, probably due to raised income levels, better communications as well as a general rise in the standard of living, acute gastroenteritis as a leading cause of death in those below the age of 20 years has dropped from 4th position in 1970 to 7th position in 1975, while bronchopneumonia has dropped from 2nd position in 1970 to 4th position in 1975 (Table I).

Irrigation canals, drownings, enteric fever and filariasis

As noted earlier the Muda Irrigation Scheme has added to the rice bowl 61 miles of main canals, 564 miles of branch canals and 560 miles of drains. A total of almost 1200 miles of canals and drains.

Consequently, deaths from drowning among youths below the age of 20 years has consistently remained as the second or third leading cause of death during the period 1970-1976 (Table I).

Table I
The ten leading medically certified causes of death in the age group 0-19 years, 1970 — 1976, the Muda area.

Order	1970	1972	1974	1976
1	Prematurity	Prematurity	Prematurity	Prematurity
2	Bronchopneumonia	Drowning	M.V. Accidents	M.V. Accidents
3	Drowning	Bronchopneumonia	Drowning	Drowning
4	Acute Gastroenteritis	M.V. Accidents	Bronchopneumonia	Bronchopneumonia
5	Tetanus	Acute Gastroenteritis	Acute Gastroenteritis	Congenital Anamolies
6	M.V. Accidents	Meningitis	Meningitis	Meningitis
7	Anaemia & Malnutrition	Tetanus	P.U.O.	Acute Gastroenteritis
8	Congenital Anamolies	Congenital Anamolies	Congenital Anamolies	Tetanus
9	Meningitis	P.U.O.	Tetanus	P.U.O.
10	P.U.O.	Anaemia & Malnutrition	Anaemia & Malnutrition	—

Source: Singh, A. (1978) Lapuran Kesihatan Kawasan MADA, 1970-1975.

One of the most dramatic problems has been a sharp increase in the number of enteric fever cases notified in the Muda area. Enteric fever notifications in Peninsular Malaysia as a whole has remained at a steady 12 cases per 100,000 population since 1957. In the Muda area it rose sharply in 1970 and seems to be associated with the amount of rice produced (Fig. 1).

Further, there is a suggestion that filariasis may be an increasing problem in the Muda area but this has yet to be confirmed.

General mortality rates

Have death rates decreased substantially in the Muda area? The answer is yes, they have (Singh, 1978). The infant mortality rate, which was higher

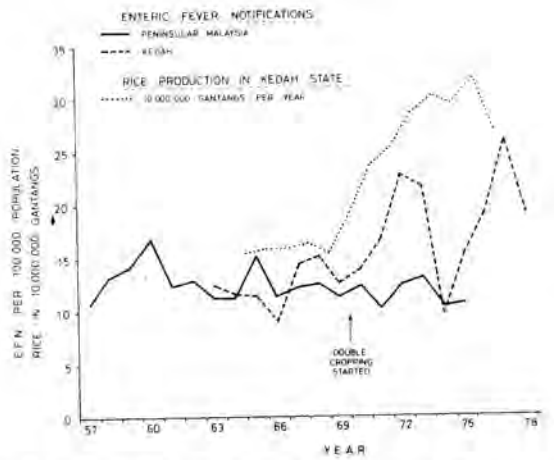

Fig. 1. Number of enteric fever notifications in Peninsular Malaysia and Kedah, and the amount of rice produced in Kedah.

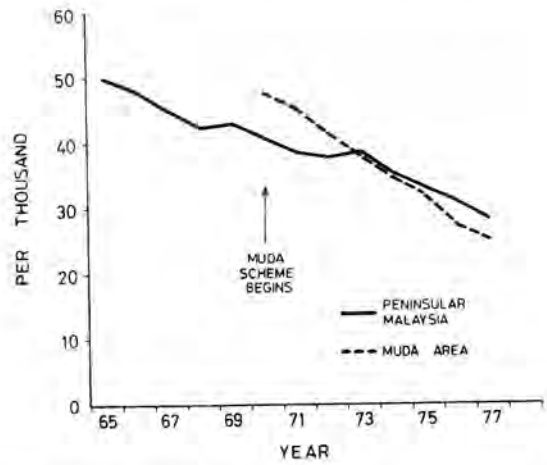

Fig. 2. Infant mortality rate in Peninsular Malaysia and the Muda Irrigation area.

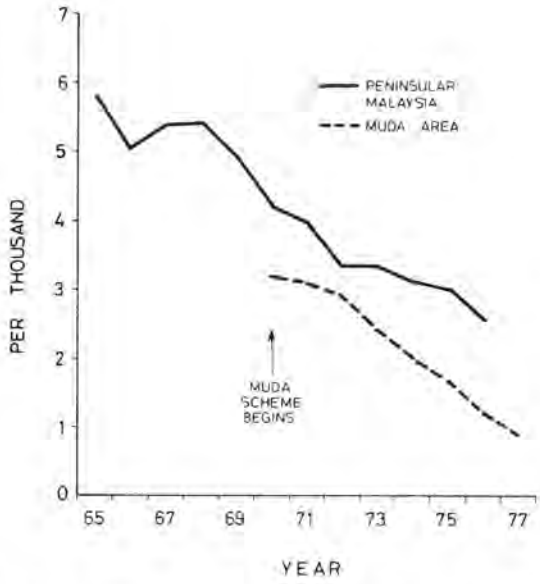

Fig. 3. Toddler mortality rate in Peninsular Malaysia and the Muda Irrigation area.

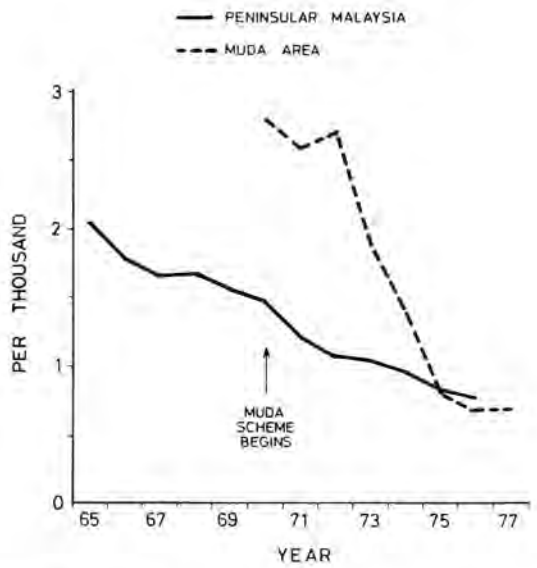

Fig. 4. Maternal mortality rate in Peninsular Malaysia and the Muda Irrigation area.

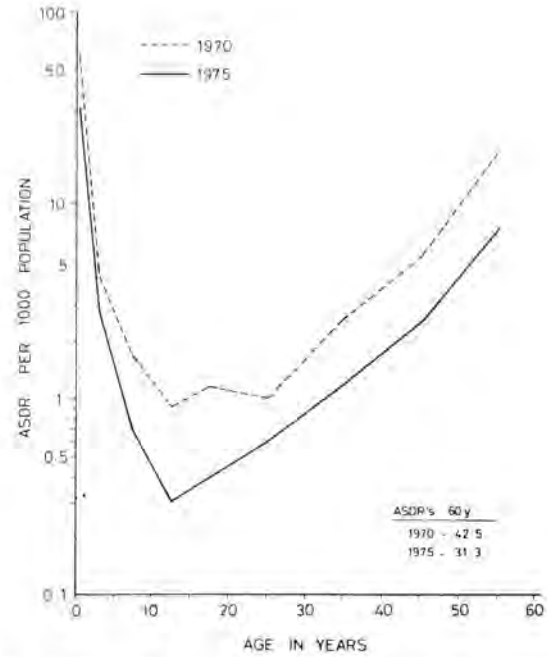

Fig. 5. Age-specific death rates in the Muda Irrigation area in 1970 and 1975.

than the national figure decreased to become lower than the national figure (Fig. 2). The toddler mortality rate decreased to half that of the national figure (Fig. 3). Maternal mortality took a sharp dive to the level of the national figure (Fig. 4). Age specific death rates for 1975 were lower, for all ages, than in 1970 (Fig. 5).

However, these decreases cannot be solely attributed to economic and other benefits brought about by irrigation and double cropping. Thus, (Table II) a comparison of health care facilities in 1970 and 1975 shows that there has been a 45% increase in the health care facilities of the Muda area (Singh, 1978). It would therefore seem that both a rise in the economic status of the people as well as an increase in health inputs have contributed to a decrease in mortality.

CONCLUSION

The Muda Irrigation Scheme illustrates that ecological changes can bring about both benefits as well as social, cultural and health problems consequent upon the destruction of traditional systems. Eisenstadt (1973) in his critical analysis of developing societies noted that "the mere

destruction of traditional forms did not necessarily assure the development of a new, viable, modern society, and very often the mere disruption of traditional settings — be they family, community, or even sometimes political settings — tended to lead to disorganization, delinquincy and chaos". Happily, the Muda shceme has not ended in chaos and so far as can be assessed the benefits outweigh the negative outcomes and the net result remains positive, at least from the point of view of mortality.

Table II
Health Facilities in the Muda Area, 1970 and 1975

Health Facilities	1970	1975
General Hospital	2	2
District Hospital	—	—
Main Health Centre	1	2
Health Sub-centre	8	11
Maternal & Child Health Clinic	2	2
Polyclinic	1	1
Community Nurse Clinic (Kelinik Desa)	—	7
Midwife Clinic	43	58
Total No. of Health Facilities	57	83

Source: Singh, A. (1978) Lapuran Kesihatan Kawasan MADA, 1970-1975.

SUMMARY

Major ecological changes have been introduced in the Muda Irrigation area. With double cropping and the associated use of fertilizers and pesticides, a 90% reduction in the number of fishes found in the padi fields has occurred. The rat population has increased while the buffalo, an important source of protein and an important cultural element in the cycle of life, has virtually been replaced by mechanised ploughs. The addition of 480 miles of farm roads has resulted in an increased number of deaths from motor vehicular accidents. The construction of about 1200 miles of canals has been associated with an increase in the number of enteric fever cases. However, general mortality at all ages has decreased. However, the decrease is most probably due to the combination of a 45% increase in health facilities in the Muda area and a rise in the economic status of the padi farmer in the Muda area.

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consecutive years, (Medical Research Council, 1965). Sixteen patients (19%) in the group did not have chronic bronchitis and were called Group I and 69 (81%) had chronic bronchitis as well (Group II).

Age: A breakdown of the age distribution of the patients showed 2 patients (2%) between 30-39 years, 11 (13%); between 40-49 years, 17 (20%); between 70-79 years and 1 patient (1%) over 80 years of age.

Sex: Eleven of the total (13%) were female, and the male to female ratio was 6.7:1 in the group.

Smoking: Eighty were smokers (94%) and the rest denied this habit. The former were mostly individuals with a long history of heavy smoking.

Race: The racial breakdown of the group is shown in Figure 1 and contrasted with that of the general hospital attendances during this period. There were 3.5 times as many Chinese as the other races within the group.

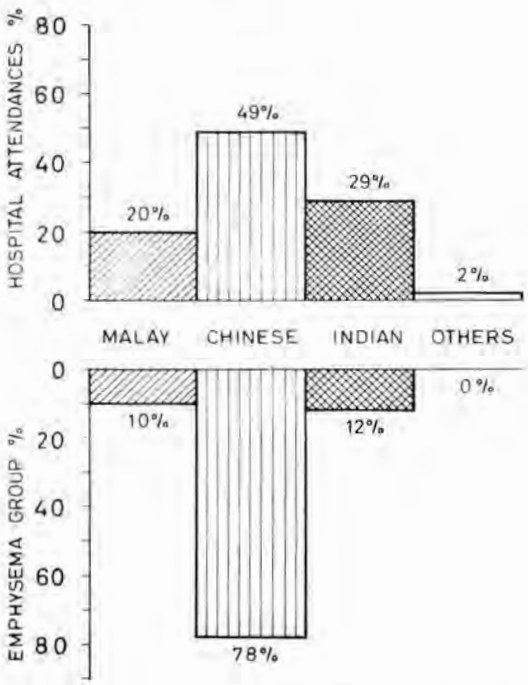

Fig. 1. Ethnic Distribution: in the study group and in the general hospital attendances.

Clinical features: Cough (88%) and dyspnoea (99%) were the most common symptoms experienced by the patients as a whole, the former being seen only in 6 patients (38%) in group I. Of these, 4 patients had a dry cough and 2 a productive one which did not however fulfill the criteria for chronic bronchitis. Wheeze was noticed or complained of by 20 of all 85 patients (24%). Only 2 of 16 patients (12.5%) in group I had wheeze, of whom one had bronchial asthma in addition, while in Group II, 18 patients (26%) had this feature. Of these 18, 3 patients had asthma in addition to chronic bronchitis. Wheeze therefore was seen almost exclusively in patients with coexistent chronic bronchitis and/or bronchial asthma. Seventy seven patients (91%) had diminished breath sounds on auscultation and 94% of patients had an increased antero-posterior diameter. Heart failure resulting from cor pulmonale had occurred at some time in 18 patients (21%) and all of these patients belonged to group II.

Radiological features: Eighty two patients (96%) had evidence of hyperinflation. In terms of the distribution of radiological changes, the commonest pattern was diffuse disease (42%). Thirty one per cent had predominantly upper zone disease and 27% lower zone disease. Bullae were visible in 26% and 22% had changes representing old tuberculous lesions. Pneumothorax had been sustained at some time by 9 patients including 4 with bullae, 3 with tuberculous scars, 1 with both bullae and scars and 1 with no other obvious cause.

Respiratory function data: Ninety per cent of all the patients studied had a RV/TLC value greater than 50%, and 86% a D_LCO below the predicted value. Elevation of TLC levels were seen in 37%. This is likely be an underestimate since this measurement was made by spirometry and not body plethysmography which also shows up the volume of poorly ventilated areas and bullae. A comparison was made between patients in Group I and II with respect to some important indices of lung function and the results are shown in Table I. A statistical analysis showed no significant differences at the 5% level in lung function as reflected by these variables between groups I and II. However, a greater proportion of patients in group II (71%) had a prolonged helium dilution time indicative of abnormal distribution

Table I

Lung Function indices in Group I & II Patients

	Mean	SD	Mean	SD
FeV_1 as % of predicted	48.2	+ 20.2	39.6	+ 14.3
TLC % predicted	116.3	+ 24.7	112.3	+ 23.4
RV/TLC %	60.1	+ 15.7	62.3	+ 9.4
D_LCO % predicted	64.6	+ 35.4	52.5	+ 32.6
Helium Dilution Time (mins.)	4.9	+ 1.5	5.2	+ 1.5

of ventilation, when compared to Group I (51%). Carbon dioxide retention was present at some time in 12 out of the 56 patients in whom this information was available and of these 10 were group II patients.

Polycythemia was considered to be present when the packed cell volume exceeded 55%, and was seen in four (5%), all of whom were group II patients. Elevated haemoglobin levels (taken as 15 Grams % and above) were seen in 25 patients, of whom 24 were from group II. Electrocardiographic changes indicative of right atrial hypertrophy, right ventribular hypertrophy and right bundle branch block were seen in 29 of 74 patients. The latter figure comprised 11 patients from group I and 63 from group II. Abnormal cardiograms were seen in 2 (18%) and 27 (43%) patients from the two groups respectively. However, the most severe changes were observed in patients in group II.

DISCUSSION

Emphysema is a morbid anatomical condition by definition, and is ubiquitous. Even where it exists during life, clinical expression in the form of respiratory disability, abnormal lung function or radiological changes may or may not be evident. Clinical emphysema generally represents severe disease of centrilobular or panlobular types which are believed to be distinct pathological entities (Anderson and Foraker, 1973). The centrilobular variety is more common but lungs with widespread emphysema often show the coexistence of various grades of centrilobular and panlobular emphysema (Thurlbeck, 1963). How often it causes clinical disease is unknown, and hence so is the prevalence of emphysema (Oldham, 1976).

The findings in our group of patients are generally in agreement with features found in patients with emphysema as described elsewhere. Forty four per cent were in their sixth decade of life. Hernandez *et al.*, (1966) found a rise in incidence and extent of involvement in adult lungs up to the sixth decade after which there was a levelling off as in our patients. The disease tends to predominantly affect men in whom it is found two to ten times (6.7 times in our group) as frequently as in women (Anderson and Foraker, 1976). The latter generally have milder disease, and an increase of frequency of emphysema with aging, whereas in men, this increase applies both to frequency and to severity (Thurlbeck *et al.*, 1974). The effect of age and smoking are difficult to separate as the total consumption of tobacco is related to the former, but emphysema seldom affects non-smokers, (6% of our group), in whom the prevalence of the condition is much lower (Dysinger *et al.*, 1963 and Dunnill, 1976). It appears that emphysema is more closely related to smoking than to age or sex (Anderson *et al.*, 1966); severe emphysema in smokers is almost always of the centrilobular variety whereas in non-smokers severe emphysema, though very uncommon, is invariably of the panlobular type (Dunnill, 1976).

The prevalence of emphysema has also been related to environmental factors like industrialisation (Isnikawa *et al.*, 1969) and to ethnic factors (Murphy *et al.*, 1962) and obviously the two factors may be inter-related. Though the total number of patients is not large, an impressive majority within the group (78%) were Chinese who also tend to be concentrated more in urban areas in this country.

The clinical diagnosis of emphysema is known to be unreliable and Fletcher *et al.*, (1963) cautioned against making a diagnosis clinically unsupported by physiological and radiological changes. However in severe and symptomatic emphysema, clinical findings may be helpful, and the most consistent findings are a hyperinflated chest with poor breath sounds, and prolonged expiration especially audible over the larynx (Hugh-Jones and Whimster, 1978). Hyperinflation and poor breath sounds were present in 94 and 91% respecitvely of our patients, while wheeze was uncommon in emphysema per se, indicating when present, coexistent chronic obstructive bronchitis or asthma. Radiology is a practical and useful

method of detecting emphysema though mild to moderate disease may be missed (Laws and Heard, 1962 and Reid & Millard, 1964). The presence of radiological emphysema on the other hand is always accompanied by changes at autopsy (Laws and Heard, 1962; Reid and Millard, 1964). Bullae, which have been cited as an additional important feature, (Simon, 1964) were seen in 26% of our patients. An interesting finding was the commonness of radiographic evidence of old tuberculous scars (22%). The increased frequency of emphysema in patients from tuberculosis Sanatoria has been noted and documented by several workers (Lancaster and Tomaschefski, 1963; Katz and Kunofski, 1964 and Gaensler & Lindgren, 1959). Of the lung function tests commonly used in assessing emphysema the following have came to be regarded as beign the most useful in practice, though not specific: a low FeV_1/FVC % (Burrows *et al.*, 1965), high RV/TLC % (Sweet *et al.*, 1960) and a low D CO (Thurlbeck *et al.*, 1970). While a low FeV_1 % was taken as a supportive diagnostic criterion in our patients, a high RV/TLC % and $D_L CO$ below the predicted value were found in the majority (90 and 86% respectively).

Our patients were grouped in an attempt to study the differential features of primary emphysema (Group I) as opposed to emphysema and chronic bronchitis (Group II). Burrows *et al.*, (1964, 1965 and 1966) classified their patients with chronic obstructive lung disease into two main groups A and B. Patients in Group A (corresponding to our group I) presented with radiological evidence of emphysema, increased total lung capacity, and a reduced diffusing capacity but without significant expectoration, cyanosis, polycythemia or cor pulmonale. In type B, chest films did not suggest emphysema and there was no significant change in the total lung capacity or diffusing capacity; these patients presented chiefly with evidence of obstructive bronchitis, with marked ventilation/perfusion mismatching as shown by hypoxia and carbon dioxide retention and a tendency to cyanosis, polycythemia, and cor pulmonale. There were also a number in whom there were mixed features (corresponding to our group II). Thurlbeck *et al.*, (1970) found a strong association between chronic bronchitis and emphysema which seldom occurred independantly without chronic bronchitis, and the two conditions have been thought to represent two ends of the spectrum of a single disorder. Hutchison and Menon (1975) analysed 46 British patients with emphysema and found that the presence of chronic bronchitis had no significant effect on a number of relevant lung function variables. They suggested the association merely indicated the simultaneous occurrence of two common conditions, both related to smoking.

Fletcher *et al.* (1976) have published an account of a detailed eight year follow-up of over a thousand individuals, and from their observations, it seems likely that there are three forms of lung disease resulting from cigarette smoking: mucous hypersecretion from the large bronchi (chronic simple bronchitis), changes in the small airways leading to diffuse airway obstruction (chronic obstructive bronchitis) and emphysema, affecting the acini. Coexistence of these conditions may occur without necessarily implying that one leads to the other, resulting in an overlap of features. Greater disturbances of ventilation perfusion matching have been found in emphysematous patients with chronic bronchitis than in those without (Fletcher *et al.*, 1963), and Millard and Reid (1974) and Semmens and Reid (1974) have shown tht cardiovascular changes are related to the presence of chronic bronchitis and not to emphysema.

In this study we have found results similar in several indices to those of Hutchison and Menon (1975) in a group of Malaysian patients of whom only 19% had emphysema without chronic bronchitis. However, there were some differences between groups I and II in that there was a higher incidence of ventilation/perfusion inequality (prolonged helium dilution time, CO_2 retention and polycythemia reflecting significant hypoxemia) and of cor pulmonale (E.C.G. changes and heart failure) in group II patients probably due to the effect of coexistent chronic bronchitis.

SUMMARY

A survey over five years of patients attending our Chest clinic revealed 85 patients with emphysema, of whom 66 (78%) were Chinese. The largest numbers (44%) were in their sixth decades of life, and the male to female ratio was 6.7:1. A history of smoking was obtained in 94%. The disease appeared diffuse radiologically in 42% and signs of old tuberculosis were seen in 22%. Only 19% presented solely with emphysema, while 81%

had chronic bronchitis, in which group there was more evidence of ventilation/perfusion abnormalities and of cor pulmonale.

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EMPHYSEMA II: THE ROLE OF ALPHA-1-ANTITRYPSIN DEFICIENCY IN MALAYSIAN PATIENTS

M. ASHOKA MENON, A. LYN VATERLAWS & THOMAS CHEOK

INTRODUCTION

FOLLOWING THE work of Laurell and Eriksson (1963, 1964 and 1965) it is known that individuals with severe alpha-1-antitrypsin deficiency (A-1-ATD) are more susceptible to emphysema. While the majority of others develop the disease in their fifth to seventh decades of life (Thurlbeck, 1963 and Talamo *et al.*, 1966) these individuals do so in their forties (Eriksson, 1965), often earlier and with less exposure to tobacco smoke (Hutchison *et al.*, 1972). The role in emphysema of the heterozygous deficiency state with its resultant intermediate deficiency of A-1-AT however remains unsettled. Present knowledge of its epidemiology suggests A-1-ATD is more common in populations of northern European origin and less so in other ethnic groups (Mittman & Lieberman, 1970). Eriksson (1964) reported finding a frequency of 0.06% for the homozygous (phenotype ZZ) and 4.7% for the heterozygous (MZ) deficiency state in Sweden. Subsequent reports have shown comparable incidences in Norway (Fagerhol, 1967) and the United States (Schwartz *et al.*, 1973), while two studies, one in American blacks (Kellerman and Walter, 1970) and the other in Japanese (Harada and Omoto, 1970), failed to detect any individuals with the deficiency genes in the groups studied. Janus *et al.*, (1965) compared the frequency of A-1-ATD in New Zealand whites with that in the Maoris and found however a higher incidence of both the ZZ and MZ phenotypes in the latter. In a group of 430 Indians, Kellerman and Walter (1970) found 0.23% and 0.69% incidence of the ZZ and MZ phenotypes respectively, and there are reports of the occurrence of A-1-ATD emphysema in Indians (Hobbs, 1971 and Viswanathan *et al.*, 1976). The incidence of A-1-ATD and related emphysema in South East Asia is unknown and we have been unable to fnd any documented evidence of its occurrence from this part of the world. We report the result of a study to assess the role of A-1-ATD in a selected multiracial group of Malaysian patients with emphysema seen at our Chest clinic.

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MATERIALS AND METHODS

Eighty five patients with radiological emphysema seen at the University Hospital, Kuala Lumpur between 1974 and 1978 were selected for this study. Patients with a history and clinical features suggestive of emphysema were screened, and the presence or otherwise of emphysema was assessed as in the previous paper.

For purposes of this study, patients selected had two additional investigations. Serum electrophoresis was performed on cellulose acetate paper and the strip examined for the presence of the alpha globulin band. A-1-AT levels were measured using a commercialy available kit (M Partigen, Hoechst). Venous blood was drawn from patients while in a basal state free of any detectable infection, allowed to clot, the serum separated and stored at -24°C. Alpha-1-antitrypsin was estimated by radial immunodiffusion on agarose plates containing antibody to A-1-AT. The values were expressed as milligrams per cent (normal value = 200-400 mg per 100 ml).

Controls: In order to obtain an indication of the normal levels in our population, A-1-AT levels were estimated in one hundred random blood specimens obtained from patients of comparable age free of lung or liver disease, and from detectable inflammatory or malignant conditions seen in the medical and surgical divisions of the hospital service.

RESULTS

The clinical characteristics of the group studied have been described in paper I.

Serum Electrophoresis. Severe flattening or absence of the alpha globulin band was not seen in any of the patients in the group.

A-1-AT levels in the groups studied are shown in Table I. There was no significant difference in the A-1-AT values in the two groups ($p => 0.1$).

Table I

A-1-AT values in the study group and in the controls

A-1-AT	Patients	Controls
Range of values (mg/100 ml)	190 — 396	172-380
Mean (mg/100 ml)	266	261
+ Standard Deviation	46	43

Table II

Frequency of Homozygous A-1-ATD in Emphysema

Author		% of patients
Kueppers *et al.*	1964	1
Lieberman	1969	10
Jones, Thomas	1971	18
Hutchison *et al.*	1972	28

DISCUSSION

Alpha-Antitrypsin deficiency has been quoted to account for 2-6% of all emphysema (Hobbs, 1971 and Litwin & Bearn, 1969). The estimated frequency of A-1-ATD in emphysema in some of the reported studies (all from American and British groups) is shown in Table II. Lieberman (1973) found that 26% of all patients with emphysema had either severe or intermediate deficiency of A-1-AT; the prevalence was 30% in patients aged 60 years of younger and it rose to almost 50% in patients aged 50 or less years. Hutchison (1973) states "nearly all of a narrowly defined group in whom severe lower zone emphysema has developed between the ages of 30 and 45 years are likely to have alpha-1-antitrypsin deficiency". It is apparent that successive reports have found a higher prevalence of A-1-ATD and given more prominence to its role in emphysema. The differences in the estimates of the frequency have been explained by different criteria for the selection of patients and the true frequency of the homozygous deficiency state amont patients with emphysema is uncertain even in western populations.

The criterion for selection and the functional data of the patients make it likely that only those with moderate to severe emphysema were included in our study. Despite this, we have not detected any patient over a five year period with severe deficiency wherein A-1-AT levels are reduced to around 10-15% of the normal, though we are unable to exclude the presence in our group of individuals with intermediate deficiency. In the group of patients with emphysema studied by Lieberman (1973) the age of individuals homozygous for the A-1-ATD gene averaged 45 ± 8 years and that of those with heterozygous deficiency 57 ± 8 years (Lieberman, 1969). Most of our patients were elderly, only 15% being below 50 years of age, and 27% had radiological changes preferentially affecting the lower zones. Only one male Chinese patient aged 37 had both of these features, in the presence of which the likelihood of A-1-ATD is high; however he had an A-1-AT level of 278 mg per 100 ml. It is known that the ZZ phenotype is uncommon, even in a group of emphysematous patients composed mainly of elderly males, and this may be taken to be the reason for the absence of cases with A-1-ATD in the group. However, considering the size of the hospital attendances per year (around 27,000), the fact that patients with clinical obstructive lung disease are referred to the Chest clinic, and that the criteria for selection were purely clinical, radiological and physiological without age limits, this is unlikely to be the case. Over this period we have not seen patients likely to have A-1-ATD on clinical and radiological grounds and we feel that it is very unlikely that such patients have been missed out from this study. We conclude that severe A-1-ATD is not likely to be a significant aetiological factor in emphysema in our Asian patients. Considering the commonness of the smoking habit and the fact that emphysema also occurs in non smokers and even children with the deficiency (Talamo *et al.*, 1971 and Kueppers and Black, 1974), the significance of this finding is obvious.

SUMMARY

Over a five year period, eighty five Malaysians of Chinese, Malay and Indian origin with emphysema seen at our Chest clinic were investigated for alpha-1-antitrypsin deficiency, using the radial immunodiffusion method. None of the patients studied had evidence of severe alpha-1-antitrypsin deficiency, and only one presented with lower zone emphysema of early onset. We conclude that severe alpha-1-antitrypsin deficiency is unlikely to be an etiological factor in emphysema among Malaysians of Asian origin.

ACKNOWLEDGEMENT

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ECHOCARDIOGRAPHY IN THE EVALUATION OF MITRAL VALVE DISORDERS

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INTRODUCTION

APPLICATION OF ultrasound for diagnosis in cardiology was initially reported by Edler and Hertz (1954). These studies were mainly on the recognition of mitral valve motion and the evaluation of mitral stenosis. Following this report development in this area of diagnostic cardiology has been rather slow and it is only in the last decade or so that significant advances have been made and its applications in clinical cardiology given adequate attention and recognition. Echocardiography as a diagnostic aid was introduced into this country at the University Hospital in May 1976. The purpose of this paper is to review its value with reference to evaluation of mitral valve disease in patients seen at the University Hospital.

MATERIALS AND METHODS

Six hundred and fifty examinations which yielded technically satisfactory echocardiograms recorded over the period 1st June 1976 to 30th July 1978 were reviewed.

Echocardiograms were obtained with a Smith-Kline Ekoline 20A ultrasonoscope using a 1.5 cm diameter 2.25 m Hz transducer focused at 10 cm and a repetition rate of 1000 per second prmitting an examination of up to 20 cm tissue depth with excellent resolution. Simultaneous electrocardiographic recordings were obtained in all patients. Echocardiograms were recorded on a polaroid photographic system and more recently on a Cambridge multi-channel photographic strip chart recorder. Patients were examined either supine or propped up. the transducer was positioned in the 3rd or 4th left intercostal space parasternally and a systematic examination of the heart was performed by the standard technique (Feigenbaum, 1977).

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RESULTS AND DISCUSSION

A large proportion of patients (37%) referred for screening had normal echocardiograms. Majority of these patients had borderline clinical abnormalities. A typical example of such a normal mitral valve echo is as illustrated (Fig. 1).

Rheumatic Mitral Stenosis: 63.8% of abnormal echocardiograms were performed for mitral stenosis. A review of the 261 echograms (40%) has shown that ultrasound is an excellent method of confirming the presence of mitral stenosis. The abnormalities noted are mainly those of the pathologic processes affecting the mitral valve and an assessment of the functional disturbances. In the diagnosis of mitral stenosis synchronous movement of the two leaflets (Duchak *et al.*, 1972) is an important sign and it distinguishes mitral stenosis (Fig. 2) from other disorders with a reduced EF slope and decreased C-E amplitude as seen in low cardiac output states. With respect to the pathological processes affecting the valve, fibrotic thickening is represented by thick lines instead of the fine lines of a normal mitral valve leaflet. The presence of very thick heavy irregular mutli-layered lines indicate the presence of calcification (Fig. 3). Nanda *et al.*, (1972) have shown ultrasound to be a sensitive method of assessing the presence of mitral valve calcification.

The severity of the mitral stenosis may be somewhat assessed by ultrasound. A slow anterior mitral valve leaftlet diastolic closure rate as manifested by a reduced E-F slope (Fig. 2) gives some idea of the severity of the stenosis. Several investigators have found this to be a useful parameter to assess severity (Edler, 1967 and Effert, 1967). It has been our experience that this is so. We have found it useful for the follow up of patients after mitral commissurotomy. An increase in the anterior mitral valve leaflet diastolic closure rate has been noted in our patients in the immediate and 6 month post-operative follow up. Its long term value in assessment of these patients is currently being evaluated at our centre. However,

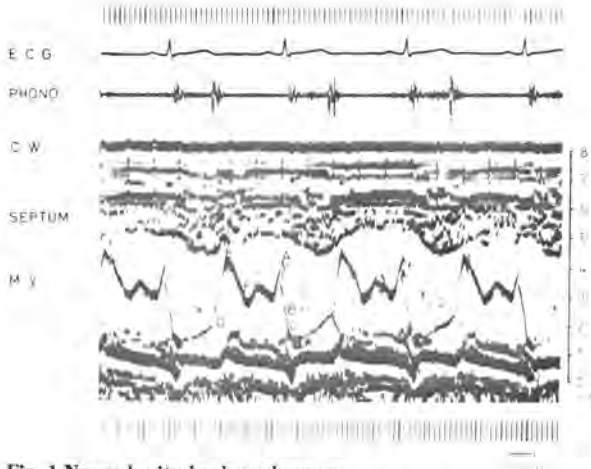

Fig. 1 Normal mitral valve echogram.
(C.W. = Chest Wall; M.V. = Mitral Valve)

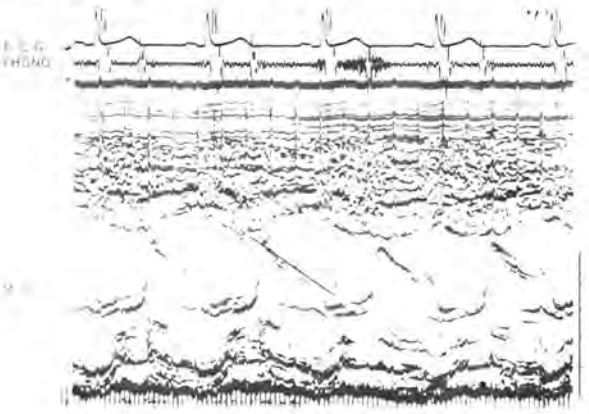

Fig. 2. Mild Mitral Stenosis (MV = Mitral Valve)

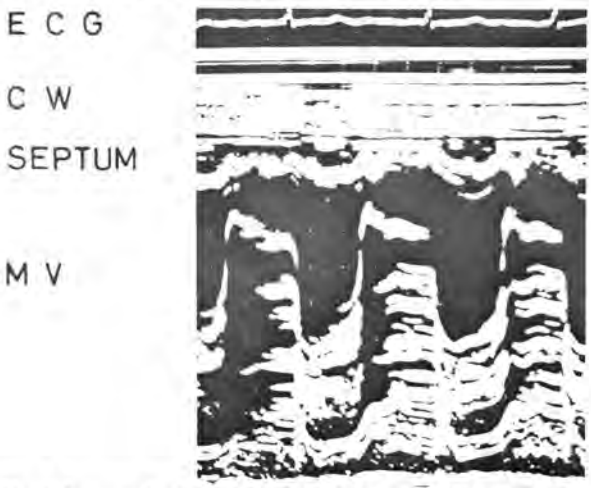

Fig. 3. Severe mitral stenosis with calcification of the posterior mitral leaflet.
(C.W. = Chest Wall; M.V. = Mitral Valve)

several authors (Mary *et al.*, 1973; Cope *et al.*, 1975 and Shiu, 1977) have refuted this and the accuracy of the E-F slope as an indicator of the severity of the mitral stenosis is doubted. A rough guide is that patients with synchronous movement of both leaflets and anterior mitral leaflet closing velocity (E-F slope) of under 35 mm/sec probably have mitral stenosis (Feigenbaum, 1977). Those with a velocity under 15 mm/sec have severe mitral stenosis (Feigenbaum, 1977). However any condition producing impaired left ventriculr filling such as low cardiac output states and hypertrophic cardiomyopathy should be excluded. It has been our experience that the mitral valve closure index as proposed by Shiu (1977) has been useful in assessing the severity in patients with mitral stenosis and following their progress after mitral commisurotomy. A reduced amplitude of motion (C-E) of the anterior mitral valve leaflet is related to the severity of obstruction but may also be seen in patients with heavily fibrotic or calcified and rigid valves (Fig. 4) which are therefore unsuitable for mitral commissurotomy and should be replaced.

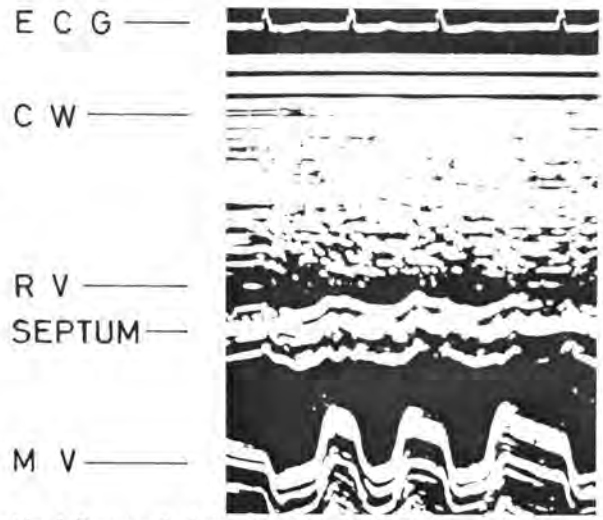

Fig. 4. Severe mitral stenosis with a rigid, fibrotic and calcified valve. (C.W. = Chest Wall; R.V. = Right Ventricle, M.V. = Mitral Valve).

Rheumatic Mitral Regurgitation: In mitral regurgitation uncomplicated by mitral stenosis a very rapid E-F slope is a common manifestation (Fig. 6). If mitral stenosis and incompetence co-exist the E-F slope is frequently reduced. The latter is probably the commoner manifestation. A frequent accompaniment is a very large left atrium. Sixteen

patients were examined for chronic rheumatic mitral regurgitation.

Non-Rheumatic Mitral Incompetence: In non-rheumatic mitral incompetence reflected ultrasound is useful in the diagnosis of a floppy mitral valve, ruptured chordae or papillary muscle dysfunction. Twenty seven patients had echocardiographic evidence of mitral valve prolapse (floppy mitral valve). A mid-systolic click in the phonocardiogram associated with a prominent mid- or late-systolic posterior displacement of the anterior and/or posterior leaflet(s) is of diagnostic value in patients with a floppy mitral valve (Fig. 5). Occasionally a holosystolic prolapse may be noted. A ruptured chordae will frequently show a prominent posterior prolapse of the posterior mitral leaflet in systole (fig. 6). Fine oscillation may be present and a rapid diastolic closure rate is a common accompaniment.

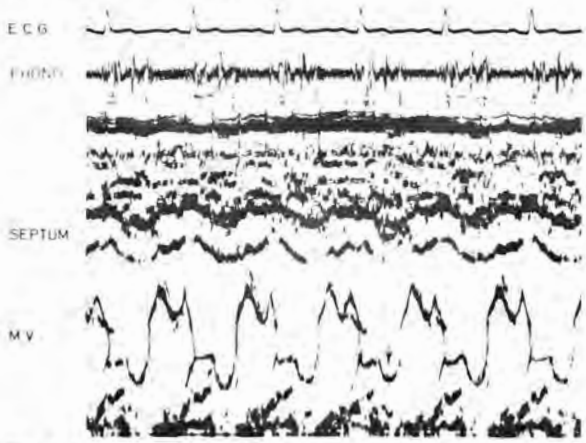

Fig. 5. Mitral valve prolapse (arrowed) [M.V. = Mitral Valve)

Changes in the mitral valve echogram in other disorders:

The mitral valve echogram has been found in our experience to be particularly valuable in the diagnosis of the following diseases of the heart: left atrial myxomas; demonstration of mitral valve vegetations; excluding the presence or organic mitral stenosis in patients who have a mitral diastolic murmur (Austin-flint) with aortic regurgitation; assessing the degree of premature closure of the mitral valve in acute aortic regurgitation; demonstration of aorto-mitral continuity in cyanotic congenital heart disease and thus excluding transposition of the great arteries or

Fig. 6. Posterior mitral valve chordae rupture.

double outlet right ventricle and the demonstration of systolic reopening of the anterior leaflet of the mitral valve in patients with hypertrophic obstructive cardiomyopathy.

CONCLUSION

Hence it appears that the echocardiographic study of the mitral valve is of value in the diagnosis of various disorders. It is of particular value in the evaluation of patients with mitral stenosis with specific reference to their suitability for mitral commissurotomy. Confirmation of mitral valve prolapse and mitral chordal rupture can be easily obtained. Apart from this, the mitral echogram can assist in the diagnosis of a variety of other disorders which indirectly affect the mitral valve. Its main advantage is that it is entirely non-invasive and offers total safety of the patient. It can supply information to the physician which can assist him in making an accurate analysis of the pathological processes that affect the mitral valve. In certain instances this information cannot be obtained by any other known examination of the heart, including invasive procedures.

SUMMARY

The clinical application of echocardiography in the evaluation of mitral valve disorders in Malaysian patients as seen in the study of 650 examinations performed during the period June 1976 to July 1978 at the University Hospital is reviewed. Diagnosis and evaluation of chronic rheumatic mitral stenosis appears to be its most valuable and frequent contribution. In addition it is useful in a variety of other disorders which directly or indirectly affect the mitral valve.

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AMNIOCENTESIS FOR ANTENATAL DIAGNOSIS OF CHROMOSOMAL ABNORMALITIES AND NEURAL TUBE DEFECTS

PRITAM SINGH

INTRODUCTION

AT SOME TIME during a pregnancy most women fear having a deformed or a mentally defective child. In most cases, sympathetic counselling by the obstetrician is sufficient to keep anxiety from developing to an abnormal extent. However, where a previous pregnancy has resulted in a chromosomally abnormal offspring or when there is a known genetic disease, a method has been available to demonstrate whether the fetus is normal or affected and a normal pregnancy allowed to continue or termination of pregnancy offered for an affected pregnancy. Midtrimester amniocentesis for antenatal diagnosis of a variety of genetic, developmental or metabolic diseases is now a practical procedure (Milunsky, 1973; Emery, 1973; and Goldman *et al.*, 1977).

Seventy-five cases undergoing amniocentesis for antenatal diagnosis of chromosomal disorders and neural tube defects are retrospectively and prospectively analysed.

MATERIALS AND METHOD

Clinical Methods

The patients were referred to the various consultant units at the Bradford Royal Infirmary and St. Lukes Hospital Maternity Services. Amniocentesis was offered whenever one of the indicators of increased risk was present. The procedure of amniocentesis and its related risks was explained to the patient. Trans-abdominal amniocentesis was performed under local anaesthesia whenever possible in the 14th to 16th week of pregnancy. An ultrasonic scan was performed prior to the procedure and towards the end of the study amniocentesis was performed under ultrasonic visualization. Under local anaesthesia and an aseptic technique a 19 gauge spinal needle was inserted at right angle to the uterine wall avoiding the placental site. The stylette was then withdrawn and the initial 1 to 2 ml. of amniotic fluid discarded, and then 20 to 30 ml. of fluid aspirated.

Selective abortion was performed when indicated by intra-or-extra-amniotic instillation of Prostaglandin F 2 alpha (PG F2α). The children who were ultimately delivered, however, were all examined by the paediatrician within 24 hours following delivery and again at the post-natal clinic.

Between 1972 and 1977, 76 patients had amniocentesis performed. Records of 72 patients were available for analysis. Three patients had amniocentesis performed in successive pregnancies, making a total of 75 pregnancies suitable for analysis.

Cell Culture Methods for Amniotic Fluid Cells

This involved centrifugation of the sample at full speed for 10 minutes and culture of cells in TC 199 medium enriched with AB+serum with added antibiotics (Penicillin and Streptomycin) in an environment of air enriched with 5% carbon dioxide at 37°C. After 10 to 14 days, cells were arrested in metaphase with colchicine. The chromosomes were stained with Giemsa and the karyotype decided after studying an average of 16 cells.

Determination of Alphafetoprotein in Amniotic Fluid

The supernatant was used to determine alphafetoprotein by the method of single radial immunodiffusion in 2% agarose gel containing 1.75% monospecific rabbit antiserum to human alphafetoprotein as previously described, (Stewart *et al.*, 1975).

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RESULTS

Ages of Patients and Indications for Amniocentesis

Table I shows the age distribution of the patients at the time of amniocentesis. Of the 75 patients, 26 were aged less than 35 years, and the majority, 49 patients, were aged 35 to 49 years. The highest proportion were in the 35-39 year age group and numbered 30 (40%)

Table I

Age distribution of patients undergoing amniocentesis

Age (years)	Number of Patients	%
20 — 24	8	(10.7)
25 — 29	14	(18.7)
30 — 34	4	(5.3)
35 — 39	30	(40.0)
40 — 44	16	(21.3)
45 — 49	3	(4.0)
Total	75	(100.0)

The amniocentesis was performed for the sole indication of maternal age of 30 years or more in 46 pregnancies (61.3%) and in 10 (13.3%) because of a history of a previous child affected by Down's Syndrome. Sixteen cases (21.3%) had it done because of a previous child affected by neural tube defect. In two (2.6%) there was a previous mentally retarded child where the precise diagnosis was not known and in another, because of a family history of Down's Syndrome and mental retardation. One patient requested the procedure because of anxiety of an abnormal fetus. In nine patients there was more than one indication for investigation.

Karyotype Results

The fetal karyotype was normal in 64 cases. In three cases it indicated a fetus affected by Trisomy 21 (Down's Syndrome) and these patients elected to have their pregnancy terminated. These patients were aged 39, 42 and 43 years respectively, in each the indication for the procedure was maternal age and the karyotype in all was 47 XXG+. The method of termination was by extra-amniotic Prostaglandin (PG F2α) in one case and by the intra-amniotic route in the other two cases.

In three cases anomalies of karyotype were reported. In none was the pregnancy terminated or a retap done. The first case had a karyotype reported as 46XX in 6 cells and 92XX in 2 cells, she delivered a normal male infant. The second case karyotype result was 46XX in 4 cells, 45XXB- in 2 cells and 45XXC- in 2 cells, a phenotypically normal female child resulted from the pregnancy. The third case had a karyotype of 46XX in 8 cells and 46XY in 12 cells and she was delivered of a normal male infant.

The sex of the child was unknown in 17 cases, 13 of which were undelivered at the time of writing and two cases where termination of pregnancy was performed. This included one case which was performed privately without the obstetrician's knowledge, and one in which the abortion was thought to be related to the amniocentesis.

Repeated Attempts at Amniocentesis

Repeated attempts at amniocentesis were necessary in 10 patients. Five repeat attempts were made because no fluid was obtained. In 7 cases there was failure of cell cultivation, of which in two cases a repeat attempt was not made. One patient had the pregnancy terminated privately and in the other the procedure was done specifically to exclude an open neural tube defect. There were dry taps in 5 (6.3%) and failure in cell cultivation in 7 (9.3%) cases.

Ultrasonic Scan in Midtrimester Amniocentesis

In 21 cases there was no scan done prior to amniocentesis, 13 were cases performed before ultrasound was available at the hospital, and a further 8 where no apparent reason was given. Of the 21 cases without a scan, one patient required two taps, and another had bloodstained fluid aspirated, hence multiple taps were necessary in one (0.5%) and a blood-stained fluid obtained in one (0.5%). Whereas in 54 cases who had a scan either before or simultaneously with amniocentesis, 8 (14.8%) required multiple attempts, in 4 (7.4%) because of a dry tap and in 4 because of a failure in cell cultivation. In two (3.7%) of the cases with scan done the fluid was blood-stained.

Alphafetoprotein Estimation for Detection of Open Neural Tube Defect

Alphafetoprotein estimation was done on 63 samples of amniotic fluid. Of the 12 samples not

assayed, 11 were collected before the value of this investigation was established. In the remaining case the result was not recorded and the pregnancy terminated for Trisomy 21. The levels of alphafetoprotein are shown on the plot below, (Figure I) and this shows that all the determined values fell below mean + 2 standard deviations, except one (Case 14) where the level was 34 ug/ml. at 21 weeks gestation. However, a normal male infant was delivered of this pregnancy, and the calculated period of gestation was in serious doubt. The fetus had no evidence of neural tube defect in 49 cases who had delivered or had termination of pregnancy performed. The remaining 13 cases were undelivered at the time of writing.

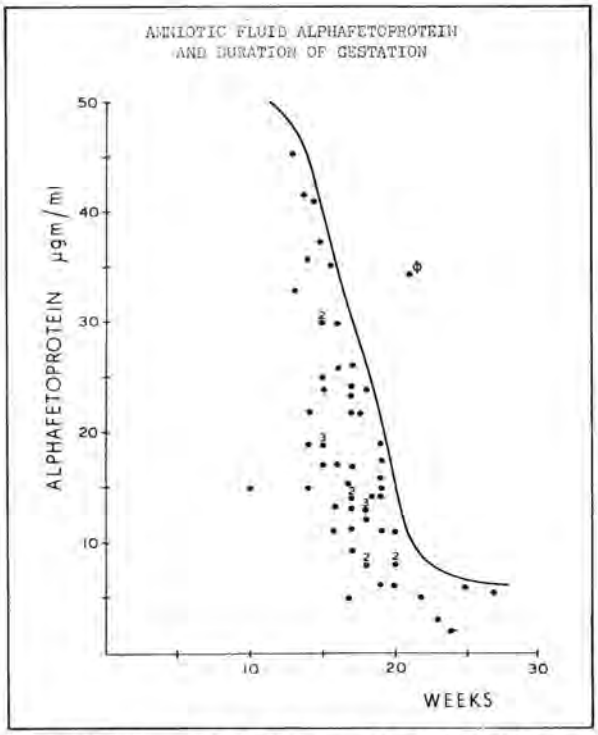

Fig. 1. Alphafetoprotein levels in amniotic fluid in 63 cases. Each symbol represents one case unless indicated by the numeral above it. The solid line represents the upper normal limit for alphafetoprotein in amniotic fluid (mean + 2 Standard Deviations).

1 Indicates Case 14, level of Alphafetoprotein, 34 /ml. However, the calculated gestation of 21 weeks was in doubt and she delivered a normal male infant.

Abortion Related to Amniocentesis

There was only one spontaneous abortion almost certainly related to the amniocentesis. This was a patient aged 36 years who had maternal age as the indication for the procedure. The patient started to lose amniotic fluid per vaginam the day after the procedure and this continued, in spite of bed rest in hospital. She aborted within a week of the procedure. This gives a risk of causally related abortion of at least 1/75 (1.3%).

Rhesus Negative Mothers Undergoing Amniocentesis

There were ten cases whose blood group was Rhesus D Negative. In five of these patients case notes, there was a specific mention made to the effect that Anti D Gammaglobulin had been administered after the procedure, in four no such mention was made, and in the other case there were already Rhesus D antibodies present.

Other Risks Associated with Amniocentesis

There were no cases of infection in this group, and no obvious injury (excepting the procedure-related abortion) sustained by the fetuses subjected to the procedure, though blood-stained fluid may be considered a feature of trauma to fetal vessels or fetal torso, and was noted in three cases, but since the Kleihauer test was not done on the red cells, maternal bleeding would be a possible cause of blood-staining of the fluid.

DISCUSSION

Antenatal diagnosis has become a practical procedure, and the area is rapidly evolving so that whereas the major indications were maternal age, previous Down's Syndome affected child, inborn errors of metabolism and X-linked recessive disorders, detection of neural tube defects is gaining in importance. Abnormal haemoglobin types and thalassaemias are the recent additions to conditions that can be diagnosed antenatally. A number of problems, however, are associated with midtrimester amniocentesis and diagnosis of chromosomal disorders and neural tube defects. Midtrimester amniocentesis is also not entirely free of risks and the problems, difficulties and precautions to be anticipated are as follows.

Problems in Antenatal Chromosomal Analysis

Three abnormal fetuses were detected out of 75

screened, a pick-up rate of 4% which is a reasonable discrimination in selection of patients (Scott, 1976). All these patients were above 35 years of age and older women are known to have a greater risk of having a child affected by Down's Syndrome than younger women. The risk to pregnant women 40 years and above is estimated to be about 2.6% and to women between 35-39 years of about 1.6% (Littlefield, 1974). Hence it is particularly important to screen women of advanced age of 40 years and above.

Anomalous karyotypes may be reported as in the three cases described, but in the first, a phenotypically normal male infant was delivered. Polypoidy is a significant problem in the interpretation of cytogenetic studies of cultivated amniotic fluid cells. Tetraploidy has been detected frequently in amniotic fluid cell cultures: 4% to 100% of cells (Milunsky *et al.*, 1971). In most cases the pregnancy has not been terminated and the infants born have had normal karyotypes. Possible explanations include an artifact of tissue culture or culture of cells derived from the amnion where tetraploidy occurs naturally. In the second case a phenotypically normal female infant was delivered whereas the result suggested that chromosomal mosaicism was present in the fetus. However, demonstration of mosaicism in a given individual may require study of more than one tissue. The finding of mosaicism in amniotic fluid cell cultures poses significant problems in terms of interpretation, for even if this finding was assumed to represent true mosaicism in the fetus it is often impossible to relate this to the phenotype of the child. There have been no documented reports so far of chromosomal mosaicism detected antenatally. In the third case the anomalous karyotype was due to maternal blood contamination, a normal male infant being delivered. A twin pregnancy was excluded by ultrasound scan. Nadler (1972) estimated that maternal cells would be growing on 0.5% of amniotic fluid cell cultures and this would lead to a number of false diagnoses. Phillip *et al.* (1974) reported two false sex predictions in 93 cases and they advocate the comparative study of Q-banded maternal and fetal chromosomes, since in most cases differences in fluorescent markers might enable a distinction to be made between mother and fetus. Mosaicism was considered highly unlikely for the reasons mentioned earlier. Regarding false sex predictions, therefore, there was a minimal error of 1/57 (1.8%) whereas Phillip *et al.* (1974) reported 2.2% in 93 cases.

Failures in Amniocentesis and Cell Cultivation

In this series there were repeated attempts in 6.3% whereas Niermeijer (1976) reported an incidence of 4% and Milunsky and Atkins (1974) in 10%. There was a 9.3% failure of cell cultivation whereas it was 1% and 10% respectively in the aforementioned series. Of the 7 cases of failure in cell cultivation, two were probably due to delay or contamination of the sample. In five cases there was no apparent reason and so a 6.3% incidence could be expected even with special care exercised to prevent delay and contamination before the sample reached the laboratory. This is in keeping with other reported series.

The length of time taken to obtain the karyotype following the dispatch of the sample to the genetic laboratory was on the average 4 weeks (Carter, 1978, Personal communication). This is an important criterion in evaluating antenatal diagnosis so that termination of pregnancy could be performed before fetal movements are felt (Ferguson Smith, 1971 and Golbus *et al.*, 1974).

Value of Ultraosonic Scan

The value of ultrasonic scan in midtrimester amniocentesis is the ability to localize the placenta and avoid trauma. Though its value is at present generally accepted, Gerbie and Vikolnik (1975) found the percentage of bloody taps to be the same whether a scan was done or omitted. Harrison *et al.* (1975), however, did note a decrease in blood-stained fluid with ultrasonic placental localization as did Crandon (1978, Personal communication). Though complications of midtrimester amniocentesis are few it seems logical to try and decrease even this small risk further by use of ultrasonic placental localization.

Alphafetoprotein Estimation for Detection of Open Neural Tube Defect

There was one case where the alphafetoprotein was falsely elevated due to an error in the calculated gestation as the date of the last menstrual period was in doubt. However, both false positive and false negative values are known to occur and Milunsky and Alpert (1976) reported their

experience of a 4.9% false positive rate. There were no false negative values in this group of cases. Accurate documentation of gestation is critical in interpretation of the result of alphafetoprotein.

Risks of Amniocentesis

The one causally related abortion following amniocentesis gives a risk of 1.3% in this series whereas it was 0.65% in Nadler and Gerbie (1970) and 1.47% in Milunsky and Atkins (1974) series. This is not significantly different from the risk of spontaneous abortion in the second trimester of approximately 1.2%.

No other fetal trauma resulted in this series whereas Lamb (1975) reported a case of fetal limb gangrene from needle puncture in midtrimester amniocentesis. The rhesus negative mother should have Kleihauer test done soon after the procedure and an extent of feto–maternal haemorrhage gauged and anti-D gammaglobulin given to those at risk.

CONCLUSION

In conclusion, antenatal diagnosis by midtrimester amniocentesis has been found to be a safe though not entirely risk-free procedure in this study as well as in a controlled study (Milunsky, 1975) and, when large numbers of cases are studied (Galjaard, 1976) and therefore it should be used more widely in appropriate cases for the benefit of the patient and perhaps her unborn child.

SUMMARY

Amniocentesis was performed in 75 patients for antenatal diagnosis of chromosomal abnormalities and neural tube defects. Three fetuses with Trisomy 21 were detected, and the pregnancy terminated. In three other cases there was an anomalous karyotype reported, in which all were delivered of phenotypically normal infants. There was one case where the sex prediction was in error. No case of neural tube defect was detected by alphafetoprotein estimation, whereas one case had a false positive value due to uncertain gestation. There was one causally related abortion. The use of ultrasonic placental localization was not associated with a decressed incidence of need for repeat attempts or blood-stained fluid. The value, risks, difficulties and precautions for midtrimester amniocentesis are discussed.

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AN EVALUATION OF THE BECKMAN GLUCOSE ANALYSER 2

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INTRODUCTION

THE Beckman Glucose Analyser 2 (Beckman Instruments, Inc. Fullerton, California) incorporates automatic pumps for filling and draining its reaction chamber, as against its earlier, less sophisticated version. This analyser offers a convenient and rapid means of processing routine glucose requests and also those that come in at odd times. The analyser is easy to operate, requiring only manual delivery of a sample into the reaction chamber, after initial calibration with an aqueous glucose standard. With the result obtained under 40 seconds after the introduction of a 10 ul sample, the analyser becomes very suitable for handling urgent requests and pediatric specimens.

The analyser utilises an oxygen-sensitive electrode to determine the rate of oxygen consumption, which is proportional to the glucose concentration in the sample, in the following reactions:

$$\beta\text{-D-Glucose} + 0_2 \xrightarrow{\text{glucose oxidase}} \text{Gluconic acid} + H_2O_2$$

$$H_2O_2 + \text{ethanol} \xrightarrow{\text{catalase}} \text{acetaldehyde} + H_2O_2$$

Iodide and molybdate are included in the glucose oxidase reagent to ensure destruction of H_2O_2, especially with diminished catalase activity on storage. The reactions are claimed to be free from interference from other reducing substances, and the usual blood anticoagulants and glucose preservative. Being a method independent of the optical properties of a solution, it is free from the effects of haemolysis, bilirubinemia and turbidity.

Acquisition of the Beckman Glucose Analyser 2 has removed the tedium of manual glucose assays from our laboratory. However, the o-toluidine method of Hyvarinen and Nikkila (1962), a reliable manual method which we have been using, is retained to serve as a back-up. Also, because our laboratory is the training and reference centre for the country, retention of the manual method is relevant as most peripheral laboratories will have to continue with manual glucose determination.

This paper presents the findings of our evaluation study of the Beckman Glucose Analyser 2. Comparisons were also made against a spectrophotometric hexokinase method carried out on the Kem-O-Mat autoanalyser (Coulter Electronics Ltd., England), and also against the o-toluidine method done manually. The superior modified glucose oxidase reagent of Fischl, *et al.* (1975) is recommended, and recycling of the reagent as proposed by Case and Phillips (1977) was adopted to cut costs.

MATERIALS AND METHODS

Glucose oxidase reagent (modified) by Fischl, et al. (1975)

Place about 1,500 ml deionised water in a 2-litre volumetric flask. Add 2.92 g of sodium chloride, AR, and dissolve. Add 5.68 ml of glacial acetic acid, and adjust the pH to 6.0 with sodium hydroxide. Add 25.0 g of glucose oxidase (EC 1.1.34) powder (Sigma Type II, Cat. No. G 6125) and dissolve. Add 0.5 ml of an aqueous solution of ammonium molybdate (10 g/litre), 2 ml of an ethanolic solution of iodine (10 g/litre), 200.0 ml of 96% ethanol and 4.0 mg of mercuric iodide powder. Shake vigorously for about 5 minutes (to prevent foaming, add a few drops of octanol at this stage). Pass the mixture through sintered glass

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filter, add 200.0 ml of glycerol, and 5.0 ml of 40% formaldehyde. Dilute to 2 litres with water.

After aging the reagent for about 4 to 5 days, during which time the insoluble matter will settle, carefully decant it into clean 250 ml polyethylene bottoles. At this stage, the reagent may be safely used for determination of glucose. The reagent is stable for over one year at 2 — 8 C, and at least 6 months at room temperature. Do not freeze.

Recyling glucose oxidase reagent according to Case and Phillips (1977)

Collect the used glucose oxidase reagent into a waste reservoir. Aerate by forcing air through the solution for about an hour. Filter through sintered glass filter before use.

According to Case and Phillips (1977), the glucose oxidase reagent can be recycled up to at least 12 times.

Glucose standard, 150 mg/dl

Dissolve 1.50 g D-glucose, AR, in 0.1% (w/v) benzoic acid, and make up to 1 litre with the benzoic acid solution. Keep at about 4°C.

Beckman Glucose Analyser 2 (Beckman Instruments Inc., Fullerton, California, U.S.A.), with the Beckman Blue-Tip Pipettor of 10 ul capacity iwth disposable tips

Plasma from patients' blood in fluoride-oxalate (2 mg sodium fluoride and 2 mg potassium oxalate per ml blood)

Lyophilised sera were reconstituted, and stood at room temperature for at least 1 hour to enable mutarotational equilibrium to be reached between the α and β forms of D-glucose.

(The Beckman Glucose Analyser 2 can also measure cerebrospinal fluid and urine glucose)

RESULTS

Each of 4 sera of glucose concentrations between 63 and 387 mg/dl was assayed 20 times in a single run. The "within-batch" coefficients of variation did not exceed 1.2% (Table I). For "between-batch" precision, duplicate analyses were performed for 10 consecutive days on 3 sera with 66, 200 and 397 mg glucose/dl. The coefficients of variation were not more than 1.7% (Table II).

Table I
Within-Batch Precision from replicate analyses, in a single run, of sera at 4 levels of glucose concentration

Serum	1	2	3	4
Number of analyses	20	20	20	20
Mean, mg glucose/dl	63	100	195	387
Standard deviation	0.74	0.74	2.00	4.47
Coefficient of variation	1.2%	0.7%	1.0%	1.2%

Table II
Between-Batch Precision from analyses in duplicate, over a period of 10 days, of sera at 3 levels of glucose concentration

Serum	1	2	3
Number of analyses	10 x 2 (10 days)	10 x 2 (10 days)	10 x 2 (10 days)
Mean, mg glucose/dl	66	200	397
Standard deviation	1.14	2.85	5.24
Coefficient of variation	1.7%	1.4%	1.3%

Several commercial control sera were assayed. The values obtained were compared, respectively, against the weighed-in glucose value in Versatol (General diagnostics, Warner-Lambert, U.S.A.), the glucose concentration quoted for Beckman Glucose Analyser in Monitrol (Dade, American Hospital Supply Corpn., U.S.A.) and Hyland (Travenol Laboratories Inc., U.S.A.), and the value stated for glucose oxidase methods in Wellcomtrol (Wellcome Reagents Ltd., England). The values specified for the control sera were returned to within limits of allowable error (Table III).

Table III
Results of analyses of commercial control sera with known glucose concentrations

Control Serum	Value Obtained mg glucose/dl	Value Quoted mg glucose/dl	% of the Quoted Value
Versatol	200	204	98
Hyland	88	90	98
Hyland	188	196	96
Wellcomtrol	60	61	99
Wellcomtrol	93	90	103
Monitrol	101	100	101

Three sera of known glucose concentrations were mixed to obtain samples with theoretical values from 114 to 324 mg/dl. Each sample was then analysed in triplicate, and the mean value obtained. Recoveries of the theoretical values closely averaged 99% (Table IV).

Table IV
Recovery Study using samples concocted from sera of known glucose values

Sample	Value Obtained (average of triplicates) mg glucose/dl	Theoretical Value mg glucose/dl	Recovery %
1.	135	136	99
2.	235	239	98
3.	303	305	99
4.	322	324	99
5.	181	183	99
6.	112	114	98

While it is recommended that a sample assayed should have a glucose concentration not exceeding 450 mg/dl, we favourably demonstrated linear response extending beyond 500 mg/dl. Also, no drift was recorded up to 50 tests after the initial calibration, although the manufacturer advises re-calibration of the analyser after every 10 samples in a test batch. Carry-over between sera of glucose concentrations 67 mg/dl (low), 200 mg/dl (medium) and 395 mg/dl (high) was negligible.

A comparative study of the Beckman Glucose Analyser 2 method against a spectrophotometric hexokinase method run on Coulter's Kem-O-Mat autoanalyser, involving 36 plasma samples of glucose concentrations up to 350 mg/dl, showed excellent correlation, with the coefficient of correlation, $r = 0.99$ ($p < 0.001$), and the line of regression, $y = 1.04x + 0.11$ indicating that the values from the glucose analyser are 104% that obtained by the hexokinase method. Good correlation was also noted when the manual o-toluidine method was compared against the Beckman analyser method. Based on analyses of 60 plasma samples, from 70 — 350 mg glucose/dl, the coefficient of correlation, $r = 0.96$ (p 0.001), and the line of regression $y = 0.9x + 4.42$.

We established a fasting glucose reference range of 70 — 115 mg/dl for plasma as against 70 — 110 mg/dl quoted by the manufacturer.

DISCUSSION

The Beckman Glucose Analyser 2, which is easy to operate with little maintenance required, was shown to be capable of precise and accurate glucose measurement. The "fast forward five" pipetting technique is easily mastered, and the user has only to recharge the electrode, which simply means changing the Teflon membrance of the oxygen electrode. Recharging is done once every fortnight, but may be of longer intervals if the daily workload is small. Little else is required in the maintenance of the analyser, which, for already more than 9 months since it was put to use, has remained trouble-free. Further, we have not yet had cause for replacing the tubings, although the manufacturer suggests replacement after 2 months.

The modified glucose oxidase reagent of Fischl, *et al.* (1975), which contains glycerol, is superior in that it also has the property of lubricating the tubing walls and the reaction chamber, and preventing rapid drying of the electrode gel. Its cost approximates to just one-fifth that of the Beckman reagent. Cost of running the Beckman analyser can even be further reduced by recycling the used reagent. Case an Phillips (1977) reported that the glucose oxidase reagent can be re-used up to at least 12 times by regeneration of the used reagent through a simple process of aeration. Owing to some loss during collection and recycling of the reagent, we have managed to re-use one batch of reagent 10 times, and have not found the capability of the reagent to be affected. Cost per test worked out to be less than 5 Malaysian cents.

Another glucose analyser currently in the market is the Yellow Springs Glucose Analyser (Yellow Springs Instrument Co., Yellow Springs, Ohio, U.S.A.). Like the Beckman analyser, it returns quick results, requires only microvolume samples for analysis, and is easy to operate; but differs in that it employs a hydrogen peroxide-sensitive electrode and uses "immobilised" glucose oxidase. While the enzyme-impregnated membrance for the Yellow Springs analyser and the free enzyme for the Beckman analyser cost about the same, adoption of the reagent of Fischl, *et al.* (1975) and recycling the used reagent have made it possible for the Beckman analyser to be operated far more economically. Chua and Tan (1978) reported no special advantage in the use of

immobilised enzyme (a relatively new concept) over free enzyme, and observed that the Yellow Springs analyser showed noticeable drift after only 10 consecutive analyses and that the recovery times and working life spans of different membrances vary.

Besides being burdened with urgent glucose requests which come in at odd times, many hospital laboratories have routine requests often exceeding the capacity of a manual method to cope with satisfactorily. A glucose analyser would be a definite asset to these laboratories. An existing manual method, however, need not be discarded as it can then serve as a back-up. The analyser could also be complementary where glucose assays are already automated, because of the convenience and rapidity with which the analyser can handle urgent requests.

SUMMARY

The Beckman Glucose Analyser 2, which employs the "glucose oxidase-oxygen rate" method, offers a convenient and rapid means of measuring glucose in microvolume samples with good precision and accuracy. Results from the Beckman analyser compare well with those from a hexokinase method run on Coulter's Kem-O-Mat autoanalyser, and also with the results from a manual o-toluidine method. The operating cost of the Beckman analyser can be made inexpensive by following the recommendations of Fischl, *et al.* (1975) and Case and Phillips (1977). The analyser should be appropriate for a busy hospital laboratory.

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RADIONUCLIDE IMAGING OF PERICARDIAL EFFUSION

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INTRODUCTION

THE DIAGNOSIS OF pericardial effusions can pose problems to the clinician. The differentiation between cardiomegaly and pericardial effusion is essential for appropriate and often life-saving therapy. Clinical findings may not be characteristic. Electrocardiographic findings are usually atypical and not diagnostic (Bailey *et al.*, 1968). The plain chest radiograph is frequently not useful. With large effusions no change of heart shape with posture is seen and fluoroscopy does not differentiate between gross cardiomegaly due to a large pericardial effusion from other causes. Right atrial contrast opacification is sensitive but is an invasive technique which is not without risks in ill patients. Echocardiography is currently the most effective method of detecting pericardial fluid (Feigenbaum, 1969). Rejali *et al.* (1958) first described radionuclide scintiscanning for the diagnosis of pericardial effusion. They used ^{131}I-HSA as a tracer and made the diagnosis of effusion on the basis of a significant difference between the size of the cardiac silhouette on PA chest film and the size of the cardiac blood pool on the scan. With improved scanners and iodipamide (cholegrafin) as a tracer subsequent workers described the "halo" sign, in which the body of the pericardial fluid is visualised as an incomplete ring of low radioactivity separating the cardiac tracer pool from pools in adjacent organs. Cardiovascular blood pool imaging received a further impetus from the development of commercial camera systems and short-life generator-produced radionuclides such as ^{99m}Tc and ^{113m}In. Various groups became interested in blood pool imaging and evolved the present day radionuclide angiocardiography. ^{113m}In bound to transferrin invivo, or ^{99m}Tc bound to serum albumin or sulfide or as ^{99m}TcO4 have been used as tracers. Radionuclide angiocardiography using the scintillation gamma camera now supersedes rectilinear scanning in accuracy, speed and practicality. The purpose of this paper is to illustrate radionuclide techniques using the scintillation rectilinear scanner and the scintillation gamma camera in the detection of pericardial effusion.

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CASE REPORTS

Case 1: Rectilinear Scintillation Scanning

This adult patient had an acute pericardial effusion with temponade. The instrumentation employed was a Magascanner V with a 5-inch diameter sodium iodide crystal detector and a 5-inch coarse focus lead collimator. 2 mCi of ^{113m}In bound to transferrin invivo was given intravenously and the patient was placed in the supine position and scanned from an anterior view. The entire procedure required about 40 minutes.

Rectilinear blood pool ^{113m}In scintiscan showed normal intracardiac blood pool and the characteristic crescent or "halo" sign, consisting a body of pericardial fluid visualised as an incomplete eccenteric ring of low radioactivity separating cardiac blood pool from tracer pools in adjacent organs (Fig. 1). Echocardiography performed using a Smith-Kline Ekoline 20A ultrasonoscope coupled to a fibre optic Cambridge strip chart recorder demonstrated the presence of a pericardial effusion (Fig. 2). Pericardiocentesis yielded one litre of blood stained fluid.

Case 2: Radionuclide Angiocardiography

This child developed post-operative cardiomegaly subsequent to a pulmonary valvotomy and

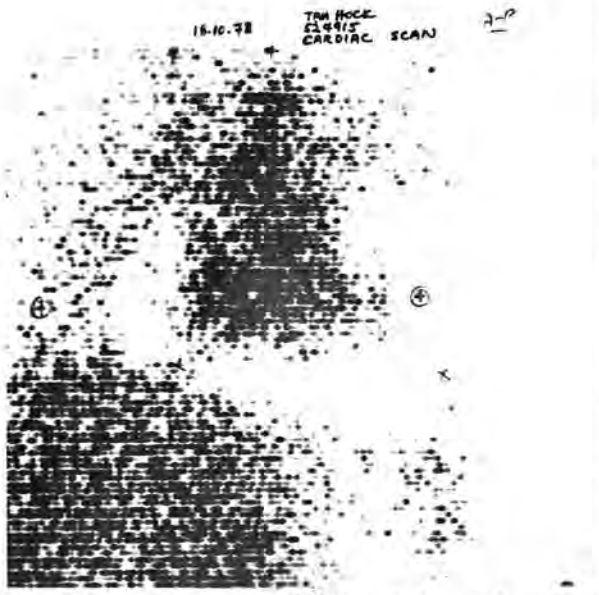

Fig. 1. Rectilinear blood pool ^{113m}In scintiscan. The normal intracardiac blood pool and the characteristic crescent or "halo" sign is clearly seen.

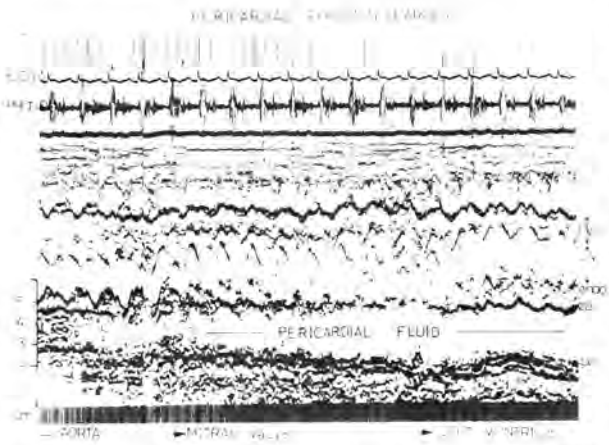

Fig. 2. Echocardiogram demonstrating large pericardial effusion.

closure of atrial septal defect under cardiopulmonary bypass. The instrumentation employed was an Ohio Nuclear Gamma scintillation Camera Sigma 400 with a 10-inch diameter crystal detector. For the dynamic studies a low energy (140 kev) medium resolution 16,000 hole parallel hole collimator and for static imaging a low energy (140 kev) high resolution 16,000 hole parallel hole collimator were used. The patient was placed in the supine position with the face of the detector over the precordium, so that a portion of the right side of the chest and the superior portion of the liver are included in the field of view. A rapid bolus injection of 1.0 mCi of ^{99m}Tc pertechnetate was administered through the right basilic vein, and serial 3-second scintiphotographs for a total period of 24 seconds were obtained by hand-pulled Polaroid films. A static (equilibration) blood pool scintiphotograph was taken 2 min. after injection. The entire procedure required about 10 minutes.

The radionuclide angiocardiogram showed the transit (Fig. 3 A, B, C) and the equilibration (Fig. 3D) phases. Progression of ^{99m}Tc bolus is visually monitored as it passes through the superior vena cava right atrium, right ventricle and pulmonary arteries. Arrow pointing to the narrowing of SVC at this level indicates the site of a temporary delay in flow where superior vena cava joins the right atrium, a finding present in about one-fourth of patients who have pericardial effusions (Fig. 3A). Later scintiphoto shows cardiac blood pool separate from pulmonary blood pools (arrows), a second early sign of pericardial effusion on transit sutdies (Fig. 3B). A crescent-shaped area of decreased radioactivity (arrows) surrounds a small cardiac blood pool with clear separation between the liver and heart (Fig. 3C). Equilibration (static) scintiphotograph made 2 min. after injection, demonstrates the crescent, or "halo" of low radioactivity surrounding the heart blood pool, and separating it from tracer pools in adjacent organs (Fig. 3D). In the normal patient there is no or very slight separation of the cardiac blood pool from the pulmonary and hepatic blood pools. A strip chart M-mode echocardiogram demonstrated the presence of both anterior and posterior pericardial effusion (Fig. 4). Pericardiocentesis yielded 320 mls of serous fluid.

DISCUSSION

The criteria for diagnosis of pericardial effusion by radioisotope scintigraphy are (1) Diameter of cardiac blood pool on the scan/ diameter of the cardiac silhouette on the radiograph is less than 0.80. (2) Separation of cardiac and hepatic blood pools. (3) Separation of cardiac and pulmonary blood pools produces a U-shaped clear zone around the heart. During radionuclide angiocardiography the physician observing the advancing tracer column in the persistence oscilloscope, may see a temporary delay in the flow

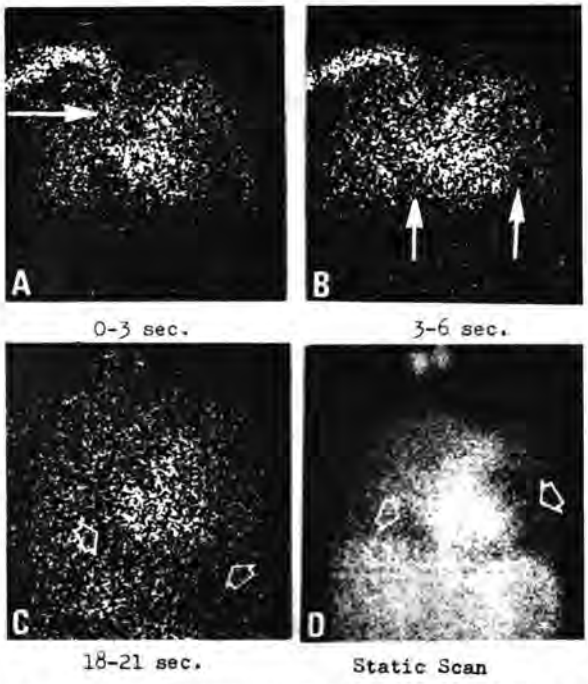

Fig. 3. Radionuclide angiocardiogram. Transit phases (A, B, C) and static (equilibration) phase (D).

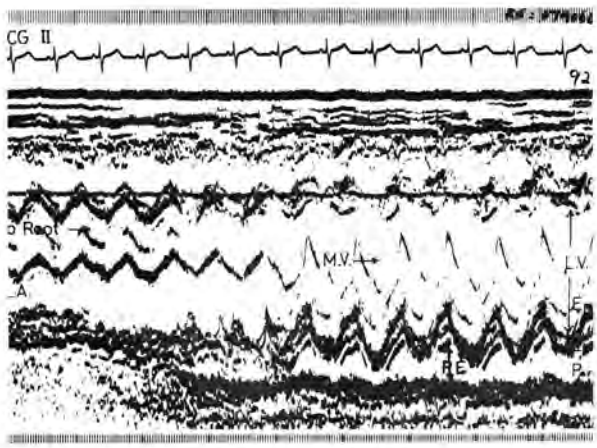

Fig. 4. Echocardiogram showing large anterior and posterior pericardial effusion.

in the superior vena cava. In a patient whose pericardial sac inserts upon the vena cava proximal to the atrial wall become distended with fluid produces compression and narrowing of the superior vena cava at this level. This finding is present in about one-fourth of patients who have pericardial effusions. The next visible sign of probable effusion is separation of the cardiac pool from the pulmonary pools. The conclusive finding, however, is the crescent, or "halo" of low activity. The equilibration scintiphotograph which can usually be made within 2 min. after injection of the pertechnetate bolus, has been used to demonstrate proved effusions of as little as 150 ml in volume.

Effusion which is asymmetrical in its disposition about the cardiac blood pool usually reflects the shape of the pericardial cavity, but may be due to the loculation which often develops if the effusion is of traumatic origin. The smallest detectable effusion is one forming a layer aroudn the heart approximately 1 cm. thick, and has been shown to represent effusions of 150 to 200 ml with relatively small normal hearts, but may be as much as 1000 ml in the presence of a large heart. With massive pericardial effusions, when the transverse diameter of cardiac blood pool plus fluid halo approaches twice the width of the cardiac pool, tamponade is either clinically present or is impending.

False positive interpretation may result from (1) apparent cardiac magnification resulting from the chest film obtained with the patient supine (the distance from patient to x-ray tube is less than 60 inches). (2) Excessive scan contrast enhancement and background suppression that decrease the apparent size of intracardiac blood pool. (3) Pleural fluid encapsulated along a pericardial border appearing as an incomplete crescent. A loculated pericardial effusion might give similar appearance. (4) Separation of hepatic from pulmonary and cardiac pools when the liver "floats" towards the abdominal midline in patients with voluminous ascites lying in the supine position. However, the even greater separation between hepatic and pulmonary pools, and the obviously medial location of the liver with respect to the right lung identifies it. (5) Thickened pericardium, or myocardium, or intramural clots and cardiac tumours like fibrosarcoma, myxomas, rhabdomyosarcomas, and metastatic neoplasms giving low activity or "filling" defects.

False negative interpretations may result from (1) fluid accumulation of less than 100 ml for normal-size hearts, and (2) rapid leakage of pertechnetate ion from the body vascular space

into the pericardial effusion. Leakage of pertechnetate ion into pericardial effusion as seen on 15-min delayed films may be a useful indicator of viral pericarditis in children (Conway and Sherman, 1970), but an unpredictable and unreliable diagnostic sign in adults.

Since the first description of pericardial scanning using ^{131}I-albumin by Rejali *et al.* (1958) experience has confirmed the usefulness of this procedure. However, rectilinear scanning are time consuming and may be difficult or impossible to do in very ill, dyspneic patients who cannot tolerate the supine position or the prolong scanning time required. The radionuclide angiocardiography using the gamma scintillation camera depend on the dynamic visualization of a radioisotope bolus as it ravels through the cardiac chambers and lungs after the intravenous injection, and both transit and equilibration scintiphotographs are taken. This test is an easy one both from the standpoint of the patient and of the nuclear physician. It requires study times of less than 10 minutes, occasions no discomfort, atraumatic, and reproducible and can be repeated daily if necessary. Chest roentgenograms are not required.

In our investigation we have not compared the several available radioisotope compounds presently in use. ^{99m}Tc pertechnetate is most commonly employed and has been used in dynamic vascular studies of the brain, heart and kidneys. ^{99m}Tc-DTPA or other chelating agents may be used for the study if serial studies are anticipated as their rapid renal clearance allows for repeating the study sooner than with pertechnetate. Weiss *et al.* (1972) preferred ^{99m}Tc sulfide due to its rapid clearance from the blood by reticuloendothelial system and its specific uptake by the liver aids in positioning of the patient and in the accuracy of diagnosis. The short half-life (6 hours) of ^{99m}Tc results in relatively little total body radiation and consequently large doses can be used to obtain good resolution with little risk to the patient. The dynamic study of cardiac output and ejection fraction could be combined with static gated images in order to detect wall motion abnormalities, and scintigraphic data is usually collected on videotape or computer disc. When such type of combined procedure is performed, then the blood pool radiopharmaceuticals ^{99m}Tc albumin or ^{99m}Tc labelled red blood cells would be used.

The various methods for detecting pericardial effusion have their obvious advantages each providing useful information. In many departments radionuclide procedure has supplanted the more cumbersome, morbid, and expensive gas or contrast agent roentgen angiocardiography. Its only serious competitor is the ultrasound M-mode scan and in many hospitals it has replaced radionuclide techniques for the diagnosis of pericardial effusion. The chief disadvantage of the radioisotopic technique is the lack of sensitivity of the method, i.e. approximately 150 ml of fluid is required for detection of the effusion, which more than is required by echocardiography. However, with echocardiography there are difficulties due to the great care necessary in the proper placement of the transducer, the number of confusing echoes from within the heart and the continuous echo-free area if a pleural effusion is present as well (Feigenbaum, 1969). In addition Klien and Segal (1968) pointed out that it tends to evaluate the dependent posterior parts of the pericardium most easily, since the fluid tend to be thicker here, but sometimes confusion can arise with a thickened hypertrophied myocardium.

The radioisotopic methodology described here represents an innocuous, highly reliable screening procedure that is easily performed on very ill patients with little risk. The studies are non-invasive, accurate and reproducible and they can be performed rapidly and repeatedly for evaluation of progress.

SUMMARY

Radionuclide imaging of pericardial effusion by rectilinear scintillation scanning and radionuclide angiography is discussed. The pitfalls in pericardial effusion evaluation is also discussed. Isotope imaging remains a valuable alternative to echocardiography in the differentiation between cardiomegaly and pericardial effusion.

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YEASTS IN SPUTUM

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INTRODUCTION

YEASTS are often implicated as primary, secondary or opportunistic pathogens in human infections (Conant *et al.*, 1971; Emmons *et al.*, 1971). They cause infections that can be life-threatening, particularly in debilitated individuals, and thus cause much concern in the management of such patients. Of greater concern, perhaps, is the noted increase in prevalence in such infections and their association with medical practices such as the use of antibiotics, corticosteroids, cytotoxic drugs, catheters (Keye & Magee, 1956; Seelig, 1966; Mazunder & Marks, 1975).

Yeasts are often isolated from clinical specimens of sputum and they present a diagnostic problem to the mycologist. Their isolations often confuse the diagnostic work-up on a patient because, while they may cause infections, they are more commonly present as commensal flora and contaminants in sputum. In this paper, results are presented on a study into the incidence of yeasts in sputum and the difficulties met in making a culturally based diagnosis of yeast infections. The relative prevalence of the different yeast types were also studied to offer some insight into the common yeast types that could be expected in the examination of clinical specimens of sputum. Particular interest was focussed on species of *Candida* other than *Candida albicans* because reports of their roles in human infections are increasing. In addition, the presence of factors that could predispose to the isolations of yeasts were sought.

MATERIALS AND METHODS

One hundred and twenty-five sputum specimens from 116 patients were examined over a period of 13 months and were subjected to investigation for yeasts microscopically and culturally.

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Microscopic examination for yeasts was carried out on Gram-stained smears and wet mounts in 20% potassium hydroxide. Each specimen was cultured for yeasts on 2 tubes each of Sabouraud's dextrose agar, sabouraud's dextrose agar with the incorporation of 0.036% potassium tellurite and mycobiotic agar (Difco). All culture tubes were kept for 3 weeks before discard.

Yeast colonies grown on culture tubes were identified according to methods in Mycology texts (Conant *et al.*, 1971; Emmons *et al.*, 1971 ; Hazen *et al.*, 1973; Lodder, 1974). Identification was carried out irregardless of the amount of growth on culture tubes.

RESULTS

Yeasts were isolated from 80 of the 125 specimens examined and these positive specimens were from 76 patients. A total of 82 yeast isolates were obtained from the positive specimens, with simultaneous occurrence of *Candida albicans* and *Candida tropicalis* in one specimen, and *Candida krusei* and *C. albicans* in another. Three genera of yeasts and 4 species of *Candida* were identified. The frequencies of their isolations are presented in Table I.

Table I
Yeast types and their frequencies of isolation

Yeast types	Numbe of isolates
Candida albicans	62
Candida tropicalis	11
Candida krusei	5
Candida parapsilosis	1
Cryptococcus neoformans	1
Trichosporon sp.	2

The amount of growth of yeast on culture tubes was recorded as follows:- sparse, where growth of colonies occurred only at the original site of inoculation, or were less than 20 in number otherwise; moderate, where colonies grew on subsequent streaks, were approximated to be greater than 20 in number and with predominantly isolated colonies; confluent, where the density of growth was so heavy that most colonies merged and counting was impossible. By these definitions, the growth of 34 isolates was confluent, 12 moderate and 36 sparse (Table II).

Table II
Growth density of yeast isolates

Yeast types	Growth density		
	confluent	moderate	sparse
Candida albicans	21	10	31
Candida tropicalis	9	1	1
Candida krusei	2	0	3
Candida parapsilosis	1	0	0
Cryptococcus neoformans	0	0	1
Trichosporon sp	1	1	0

Of the 46 specimens that yielded moderate to confluent growth of yeasts on culture tubes, 23 were specimens that were received for culture within a day from the collection of specimens and these were described as "acceptable" specimens (Table III). The other 23 specimens were "delayed" specimens that were received more than a day after the collection of specimen. The delay in the times of transport ranged from one to 7 days.

Table III
Acceptability of specimens with moderate and confluent growth of yeasts in terms of the time of transport to the laboratory.

Isolates	"ACCEPTABLE" specimens	"DELAYED" specimens
C.albicans	15	16
C.tropicalis	6	4
C.krusei	1	1
C.parapsilosis	0	1
Trichosporon sp.	1	1

Because of the high incidence of yeasts obtained in the study, a retrospective search for predisposing factors, such as underlying infections and antibiotic treatment, was carried out based on clinical histories submitted together with the positive specimens. Reasons for fungal investigation in these positive specimens included one or more of the following:- radiological evidences (30 cases), chronic cough (10), cough (4), hemoptysis (6), lung infection with no response to antibiotics (7), bronchopneumonia (4), pyrexia of unknown origin (5), bronchiectasis (1), dyspnea (2), chest pain (2), bronchial asthma (1) bronchoscopic evidence of a nodule (1). The underlying infections found that could perhaps predispose to the carriage of yeasts were carcinoma in 4 cases, pulmonary tuberculosis in 2 cases and bronchial asthma in one case. There were 4 old cases of pulmonary tuberculosis while 8 cases had antibiotic therapy specifically mentioned. Five cases had no histories submitted at all while the others had no mention of any underlying infections or predisposing factors. These figures are indicated in Table IV.

Table IV
Analysis of predisposing factors found in clinical histories of cases positive for yeasts

Clinical histories	Number of specimens	
	positive for yeasts	total examined
Antibiotic therapy	8	10
Bronchial asthma	1	5
Carcinoma	4	4
Previous pulmonary tuberculosis	4	11
Current pulmonary tuberculosis	2	4
Predisposing factors absent	50	72
No histories provided	11	19

DISCUSSION

In this study, 64% specimens were found positive for yeasts and 65.5% of patients had one or more positive specimens. Of the 82 isolates of yeasts, the predominating genus was *Candida*, accounting for 79 isolates. In earlier studies, Baum (1960) isolated *Candida* species from 55% of patients while Jen *et al.* (1967) found an incidence of 30.16% in pulmonary cases. The incidence obtained in normal healthy students in these two

studies were 10% and 20% respectively. Comparing these results, the high isolation rate obtained in this present study is not unexpected since all specimens investigated were from patients with presenting pulmonary complaints and who had reasons for investigation.

Among the isolates, members of the genus *Candida* were most frequently encountered (Table I). C. albicans was the specie most frequently isolated, accounting for 62 isolates. The other remaining isolates comprised 11 *C. tropicalis*, 5 *C.krusei* and 1 *Candida parapsilosis*. While the pathogenic role of *C.albicans* in human infections has been well documented and accepted, the same cannot be said of the other *Candida* species. In fact the view previously held by many that defined *C.albicans* as the only pathogenic specie in the genus has hampered the acceptance of etiological involvements of the other species in human infections. Although their degree of pathogenicity may be less than that of *C.albicans*, their ability to cause disease has nevertheless been proven by reports of species such as *C.tropicalis, Candida visvanathii, Candida pseudotropicalis, Candida stellatoidea, Candida guilliermondii, C.krusei, C.parapsilosis* as causes of bronchopulmonary candidiasis, endocarditis, meningitis, cutaneous and corneal candidiasis (Skinner, 1947; Conn *et al.*, 1959; Manchester & Georg, 1959; Winner & Hurley, 1964; Louria *et al.*, 1967; Painter & Isenberg, 1973; Sandhu & Sandhu, 1976; Mosur *et al.*, 1977). In face of this, laboratory tendencies towards the search and reporting of *C.albicans* only should be corrected and rightful attention be rendered to other *Candida* species during laboratory investigation of sputum specimens. In this present study, although no definite etiological significance could be ascribed to such isolates due to reasons to be discussed later, their presence in sputum could nevertheless be deemed significant on at least two counts. Where these organisms were present in abundance and collection and transport satisfactory, there is a possibility of etiological involvement (Winner & Hurley, 1964). Where they were present in insignificant amount, probably as commensals, then their importance lay in the threat they pose as sources for infections should conditions favour the transition from commensalism to parasitism (Winner, 1969). From table II and table III 22 isolates appear to satisfy the first count while 35 satisfy the second count.

No definite etiological involvement could be claimed in this study because species of *Candida* are known commensals in the oropharyngeal regions of many healthy individuals and contamination during sputum collection could not be ruled out. Indeed the isolation of *Candida* in sputum often confuses rather than enlightens a diagnostic work up. Critieria proposed to distinguish patients with *Candida* present as a respiratory pathogen from those with *Candida* as part of their normal flora have included chronicity of positive cultures, absence of other infective and non-infective causes, specific speciation, presence of mycelia as opposed to yeast alone, quantitative sputum culture, serology (Winner & Hurley, 1964; Drake & Maibach, 1973; Masur *et al.*, 1977), but none is completely satisfactory without the histologic demonstration of the fungus in lung tissue or a positive culture of a transthoracic biopsy specimen. A further drawback to a laboratory diagnosis of bronchopulmonary candidiasis is the delay and improper transport of specimens to the laboratory in this study. One criterion set by Winner & Hurley (1964) to ensure a reasonable certainty that organisms recovered from sputum were grown from organisms in the lung, was that specimens must be cultured within an hour or two after collection or they must be refrigerated. In the present study, of 46 specimens that yielded moderate to confluent growth, only 22 were isolated from "acceptable" specimens while another 22 were from specimens delayed for more than a day after collection and which were not refrigerated during transport (Table III). Therefore, although their significant amount of growth satisfies the criterion of quantity, these latter isolations have to be discounted so far as the diagnosis of bronchopulmonary candidiasis is concerned because of the delay in culture. Even among the "acceptable" specimens, it is probable that some specimens were received at the laboratory more than 2 hours after collection, but because the times of collection of specimens were not specified, these specimens could not be determined. The problem of delayed specimens is unfortunately here to remain until such times when mycological examination is readily available at or to each hospital. To minimize the problem, provisions for the refrigeration of specimens during transport must be catered for, and the consequences of the lack of refrigeration appreciated. In view of the problem of contamination by

commensals and delay in transport of specimens, it is urged that a diagnosis of bronchopulmonary candidiasis be made within the total framework of a clinical, roentgenological and laboratory picture; the mere presence of *Candida* in sputum should not lead to a halt in the search for a more likely pathogen, nor should its presence completely be ignored either.

Besides *Candida, Trichosporon sp* and *Cryptococcus neoformans* were the other yeasts isolated. *Trichosporon sp* is a common contaminant in clinical specimens, especially sputum (Conant *et al.*, 1971) and its importance in clinical specimens lies more in the differentiation of it from other yeast-like fungi. The one exception is in hair, where *Trichosporon cutaneum* is a known cause of infection. No member of the genus has been implicated in human bronchopulmonary infections. *C.neoformans*, on the other hand, is an important human pathogen known to cause infections that are inevitably fatal without treatment if the central nervous system is involved. Therefore a positive sputum culture had always been accepted as sufficient indication for anticryptococcal therapy, if not to treat the pulmonary infection, then to prevent widespread dissemination and cerebromeningeal cryptococcosis. However, the clinical significance of the one isolate of *C.neoformans* made in this study from a patient under investigation for tuberculoma or aspergilloma, was doubtful because culturally, very insignificant amount of *Cryptococcus* was isolated and histopathologically, the case was confirmed as one of tuberculoma. It was interesting then to note that Weidman (1949), still alive without therapy 15 years after *C.neoforman* was cultured from his sputum concluded that its presence had the same significance as that of *C.albicans*. More convincingly, Tynes *et al.* (1968) and Warr *et al.* (1968) reported patients in whom sputum were positive for *C.neoformans* for up to 6 months without dissemination, and subsequently became negative without any anticryptococcal therapy. Reiss and Szilagyi (1965) and Howard (1973) also reported isolations of *C.neoformans* in patients with no sign of cryptococcosis. These findings bear important implications to the treatment of cryptococcosis, especially when there are not many choices of effective and non-toxic drugs. But whatever the significance of a sputum culture, it is essential that the patient must be studied intensively to ensure that their disease is stable in the lungs and not disseminated.

The search for predisposing factors that could explain the high incidence of yeast isolations in this study was often hindered by inadequate information given in histories provided with the specimens. In 11 cases that were positive for yeasts, no histories were provided at all. From the histories provided, the largest number of specimens received for examination and the largest number positive for yeasts were from patients without any predisposing factors. However, it is believed that, although not stated, most, if not all, of these patients would have had some form of antibacterial therapy prior to fungal investigation. If so, then the high rate of yeast isolations in this group is not surprising since the use of antibiotics has been noted for its predisposing roles in opportunistic infections by yeasts (Keye & Magee, 1956; Seelig, 1966; Mazumder & Marks, 1975). Antibiotic therapy was specifically mentioned with 10 specimens and 8 of these were positive for yeasts. An underlying disease can also predispose to an increased incidence of yeasts isolations either through effects of the disease itself, such as general debilitation and lowered resistance, anatonomical abnormalities, and deficiencies in immune and defence mechanisms, or through effects of the treatment of the disease, such as the use of antibiotics, cytotoxic drugs and steroids. The underlying diseases mentioned in the histories of patients in this study that could perhaps have such effects were carcinoma, pulmonary tuberculosis and bronchial asthma. All 4 specimens with accompanying histories of carcinoma investigated were positive for yeasts. Four specimens which were positive for yeasts were from patients previously treated for pulmonary tuberculosis and 2 were from patients currently receiving treatment. In the one positive specimen with mention of bronchial asthma in the history, it is uncertain whether the condition predisposed the colonization of yeasts or whether the yeast (C.albicans) was the cause of the condition, as has been known to occur (Winner & Hurley, 1964). Although we have sought and attempted to define some factors that probably did play a contributory role towards the high isolation rate of yeasts in the study, the actual extent of their contribution could not be gauged because some of the yeast isolates might have been commensals in the oropharyngeal

region of the patients even prior to effects of predisposing factor.

In conclusion, the proper collection, transport and repeat of sputum specimens must be ensured, with total awareness of the high possibility of contamination, before any significance could be attached to any yeast isolation made since these organisms are such common occurrence in sputum. Any interpretation made on a laboratory isolation must also be done in the light of all clinical, roentgenological and other laboratory investigations.

SUMMARY

125 sputum specimens were examined for the presence of yeasts. A high percentage (64%) were positive. *C.albicans* was the most common isolate. Other species isolated included *C.tropicalis, C.krusei, C.parapsilosis, Trichosporon sp.* and *C.neoformans.* Their importance, the problems in laboratory diagnoses and the presence of predisposing factors were discussed.

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FATTY ACIDS AND POLYUNSATURATES IN SOME COMMON MALAYSIAN COOKING OILS

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INTRODUCTION

IN PENINSULAR MALAYSIA, about 42 grams of fat are available per head per day according to a Food Balance Sheet analysis for 1970. It was also estimated that about half of this amount is provided by separated oils and fats, principally in the form of cooking oils, with the remainder coming from the unseparated fats of animal sources (Nichol, 1975).

Fat availability in Malaysia thus seems to be low, accounting for only about 18% of the daily energy requirement. However with the recent widespread availability of cooking oils, it is conceivable that the daily per capita intake may be increasing and may well exceed the national average particularly for those living in the urban sector. Thus chemical analyses of hawker foods recently gave a mean value for fat of 30 grams in a single meal (Tee *et al.*, In Press) and analysis of defence rations revealed the daily availability of fat to be as high as 138 grams (Quah, 1977).

In addition, during the last decade or so, numerous brands of cooking oils have emerged in the Malaysian Market. Consequently, it is felt necessary to know more of the fatty acid composition of these products particularly in view of the fact that the only reported study on the same subject was made more than twelve years ago (Chong and Mills, 1966).

MATERIALS AND METHODS

The oils were obtained from various supermarkets in Kuala Lumpur and the homes of friends and laboratory staff. At least three separate samples were obtained for each type of oil to allow for batch variations.

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All samples were saponified by refluxing with alcoholic potassium hydroxide for one hour. The fatty acids were precipitated with 5N sulphuric acid and extracted into petroleum ether (b.p. 40-60 C). Methyl esters of fatty acids were prepared by refluxing with boron trifluoride methanol for 3 minutes, cooled and extracted into petroleum ether. The final extract was chromatographed on a Pye Unicam Series 104 Chromatograph equipped with an area integrator and using a column containing polyethylene glycol adipate.

RESULTS AND DISCUSSION

The fatty acid composition and polyunsaturated fatty acid (PUFA) content of a variety of common Malaysian cooking oils are presented in Table I and Fig. 1 respectively.

Of the samples analysed, vegetable oils such as soyabean, corn and sunflower have the highest content of linoleic acid which accounts for these oils being marketed with the label 'rich in polyunsaturates'.

Oils such as coconut, lard and palm which are popular with the Malaysian population have a high degree of saturation. Refined palm oil, which is now widely available and comparatively cheap, has the highest content of palmitic acid and is a common component in many varieties of blended oils. Hence it is not uncommon to find in these blended oils a high palmitic acid and a comparatively low PUFA content.

Since cooking oils are the main source of dietary fat and hence PUFA in Malaysia, the use of polyunsaturated vegetable oils are prefered in order to achieve the recommended PUFA intake of about one third the total fatty acide consumed (FAO, 1977). Thus among the more affluent urban groups who are now increasingly aware of the relationship between dietary fats and coronary heart disease, these oils are gaining increasing popularity.

Table 1

The fatty acid composition of some common Malaysian cooking oils

* Type of oil	No. of samples	% Total Fatty Acids									
		Lauric C_{12}	Myristic $C_{14:0}$	Palmitic $C_{16:0}$	Palmitoleic $C_{16:1}$	Stearic $C_{18:0}$	Oleic $C_{18:1}$	Linoleic $C_{18:2}$	Linolenic $C_{18:3}$	Arachidic $C_{20:0}$	Arachidonic $C_{20:4}$
Soyabean	3	0·5	**T	11·1	–	5·9	26·3	48·6	7·5	–	–
Sunflower / Sesame	3	–	–	9·0	–	8·6	31·0	51·4	–	–	–
Corn	5		–	11·8	–	5·1	33·7	49·3	–	–	–
Soyabean / Palm	3	0·1	0·3	16·2	T	6·2	28·3	43·5	5·3	–	–
Sesame	3	–	–	9·4	–	7·9	40·7	41·3	–	0·7	–
Rice	3	0·6	0·6	20·2	–	3·3	47·2	28·1	–	–	–
Groundnut	3	T	T	18·6	–	6·3	47·8	25·9	–	1·6	–
Corn / Palm / Soyabean	3	T	0·9	30·9	0·2	6·2	44·8	16·9	–	–	–
Groundnut / Palm	5	T	1·2	33·0	0·2	6·7	44·5	13·6	–	0·7	–
Palm / Groundnut / Sesame	5	0·3	1·1	32·7	0·3	6·6	45·4	13·2	–	0·3	–
Palm	5	T	1·1	34·8	T	7·2	45·3	11·5	–	–	–
Lard	3	–	2·1	26·1	3·0	13·9	42·5	10·9	–	1·4	–
Coconut / Palm	3	35·4	23·9	15·3	–	6·5	15·3	3·6	–	–	–
Coconut	4	40·9	23·5	14·1	–	5·3	13·4	2·7	–	–	–

*As purchased **Trace.

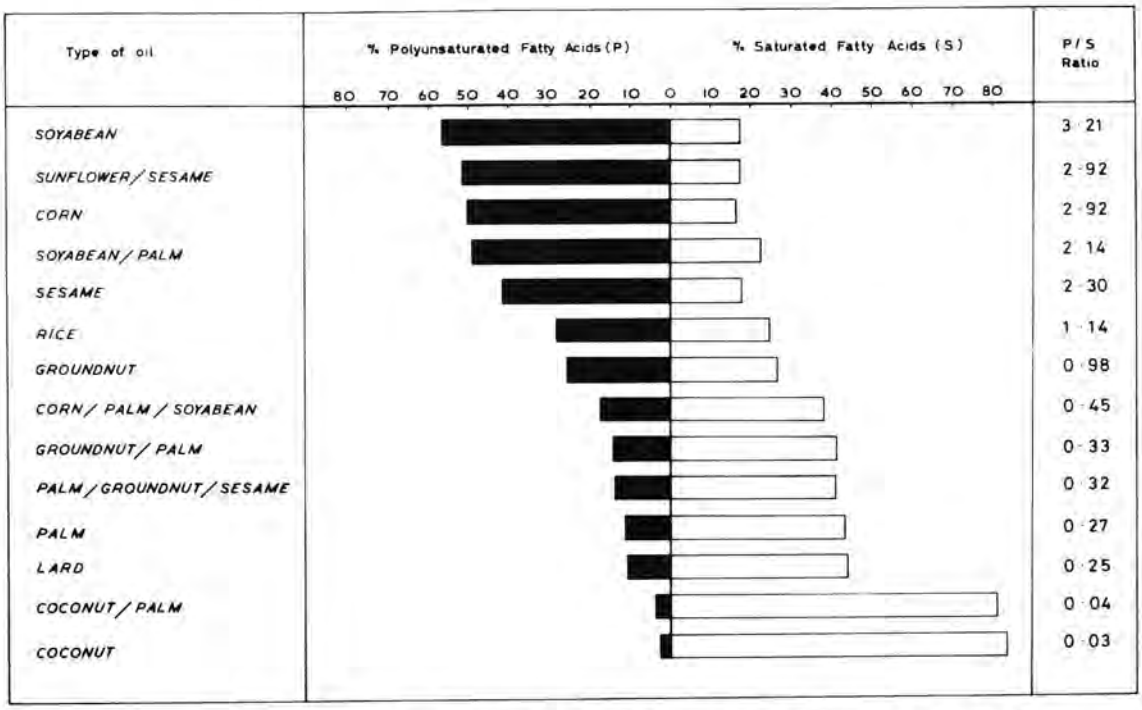

Fig. 1: The proportion of polyunsaturated and saturated fatty acids in some common Malaysian cooking oils.

Household food consumption studies in rurual, under-preveleged communities in Malaysia have revealed an inadequate daily calorie intake of which a low fat intake was contributory (Jackson, 1970; Kandiah and Lim, 1976). Consequently, from the viewpoint of satisfying energy requirements, the use of the more saturated varieties of cooking oils now widely available should be regarded as nutritionally desirable in such communities.

All varieties of blended oils examined did not declare the proportion of their component oils on their labels. One variety analysed had only about 17% PUFA when two of the three components cited were corn and soyabean oils. Another brand varied from 50% PUFA in one batch to about 35% in another. Thus the proportion of component oils in a blended oil may vary significantly from batch to batch and its fatty acid composition becomes unpredictable.

SUMMARY AND CONCLUSION

The fatty acid composition and polyunsaturated fatty acid content of some common Malaysian cooking oils were determined by technique of Gas Liquid Chromatography. PUFA the content was high in vegetable oils such as soyabean, corn and sunflower but low in coconut, lard and refined palm oils. Since cooking oils are still the main source of dietary fat in malaysia, the use of the more saturated oils with low PUFA content should not be discouraged particularly from the viewpoint of satisfying energy requirements.

The fatty acid composition of blended oils was unpredictable and may vary significantly from batch to batch. In view of such variability, oil millers should label appropriately the proportion of component oils in the blended varieties for the information of consumers.

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CHOLESTEROL CONTENT AND FATTY ACID COMPOSITION OF SOME MALAYSIAN FOODS

E.S. TEE, T.K.W. NG & Y.H. CHONG

INTRODUCTION

THERE IS NOW little doubt that dietary fats and exogenous cholesterol are major determinants of the level of serum cholesterol, which is positively correlated to the development of coronary atherosclerosis. Professor K.R. Norum of Oslo recently asked over 200 experts in antherosclerosis and lipid research from Europe, North America, England and Australia on their opinion concerning diet and the prevention of coronary heart disease. Almost all agreed that there is a connection between diet and the development of coronary heart disease, between diet and plasma lipoprotein levels and between plasma cholesterol and the development of coronary heart disease (Norum, 1978).

For those people at risk, and others who subscribe to taking a prudent diet as an early preventive measure, a knowledge of the fatty acid composition and the cholesterol content of local foods is thus absolutely essential. For this purpose, this paper reports on the fatty acid composition and cholesterol content of some Malaysian foodstuffs and commonly eaten cooked meals.

METHODS AND MATERIALS

Ready-to-eat meals were bought from eating places around Kuala Lumpur and Petaling Jaya. These foods were precooked, served in coffee shops or in adjoining stalls. Where possible, three samples were bought from three such different eating places to enable triplicate analyses of a food. No samples were taken from restaurants or restaurants in hotels as such samples would be quite different in portion size and price, and hence not comparable with the more widely consumed foods at the coffee shops and/or eating stalls. The raw foodstuffs studied were purchased from markets in the city.

Edible portions of all foods were well blended and aliquots taken for the various analyses. Analysis of proximate composition, using conventional methods, was carried out only for the cooked meals. Calorie values were calculated using the factors 4, 9, 4 for carbohydrate, fat and protein respectively.

The extracted fat was next used for the determination of cholesterol content and fatty acid composition. The fat was treated as described below (procedure modified from various methods given in Association of Official Analytical Chemists, 1970), prior to gas-liquid chromatography. After saponification using ethanolic potassium hydroxide, the saponified product was extracted with petroleum ether. The pooled petroleum ether extract was washed with water, dried (over anhydrous sodium sulphate) and evaporated to dryness. The cholesterol residue so obtained was made up to a suitable volume of ethyl acetate for injection into the gas-liquid chromatograph.

The aqueous fraction after saponification was acidified with sulphuric acid. The precipitated fatty acids were extracted into petroleum ether and after evaporation to dryness, were esterified with boron trifluoride-methanol (premixed, from Sigma). The methyl esters were then extracted into petroleum ether, evaporated to a suitable volume for chromatography.

Gas-liquid chromatography was carried out using a Pye Unicam Series 104 instrument, fitted with a hydrogen flame ionization detector. Trifluoro propyl methyl silicone and polyethylene glycol adipate columns were used for the chromatography of cholesterol and fatty acids respectively (prepacked from Pye Unicam). Quantitation of cholesterol in the foods was made by comparison

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of the peak areas obtained with that given by a cholesterol standard (chromatographic grade, from Sigma). The percentage of each fatty acid was obtained by comparing peak area of that acid to the total area for all peaks obtained for the particular food. For both lipids, peak areas were resolved with an integrator built into the recorder (Electronik 194, Honeywell).

RESULTS

Raw Foodstuffs

Table I gives, in descending order, the cholesterol content of some Malaysian foodstuffs (raw). It shows that brain and eggs are rich sources of cholesterol, as is well known. Prawns and other seafoods, such as cuttlefish and crab meat are moderately rich sources. At 383 mg per 100 g, the cholesterol content of whole *ikan bilis* appears unusually high, but it must be borne in mind that this is a dried product and therefore a very concentrated form of food. When calculated on a wet weight basis (assuming a moisture content of 70% in *ikan bilis*), the cholesterol content of the fresh *bilis* amounts to about 115 mg per 100 g, which is still about three times greater than that of a common marine fish, *ikan kembong*. However, when the heads and entrails of *ikan bilis* are removed the cholesterol content is reduced to 58 mg per 100 g of the dried *bilis*. Surprisingly cockles are not cholesterol-rich; neither are pork, mutton and beef. Fish have the lowest value for cholesterol and in *kurau* and *tenggiri*, the amounts present are minimal.

The fatty acid composition of the foodstuffs analysed is given in Table II. It may be seen here that certain foods, such as brain, liver and the sea-foods (like the cuttlefish), contain comparatively large amounts of arachidonic acid. Other investigators have observed a similar finding for organ foods and the marine oils (cod liver oil, herring oil and menhaden oil) (Anderson, 1969; Sober, 1970).

Ready-to-eat Meals

The mean cholesterol contents of cooked foods are given in Table III. It is seen that the foods richest in this lipid component are *rendang hati*, fried *mee* Indian style, *dosai* with egg, *sambal udang* and fried *kueh tiau* with cockles. This is to be expected since they contain ingredients that are rich in cholesterol (see appendix 1 for ingredients of foods analysed).

Table I

Cholesterol content of some Malaysian foodstuffs

	Foodstuff	Cholesterol (mg) in 100 g edible portion
1	Brain, pig	800
2	Egg, duck	650
3	Egg, hen	415
4	Egg, quail	415
5	Anchovies (whole) dried (ikan bilis)	383
6	Prawns, dried	353
7	Liver, pig	180
8	Prawns, fresh	130
9	Cuttlefish	120
10	Butter	120
11	Crab meat	100
12	Chicken meat	85
13	Pork fat	63
14	Anchovies (minus head and entrails), dried (ikan bilis)	58
15	Mutton	55
16	Pork, lean	50
17	Beef	45
18	Cockles (kerang)	45
19	Fish, kembong	35
20	Fish, kurau	4
21	Fish, tenggiri	3

The fatty acid composition of each food is given in Table IV, together with their content of polyunsaturated fatty acids and their ratios of polyunsaturated to saturated fatty acid (P/S). The highest P/S ratios are found in *satay, Lor Mai Kai*, big dumpling and chicken rice. This ratio is of course governed by the fatty acid composition of the ingredients and the type of cooking oil used in the preparation of the food.

Some variations in cholesterol content are observed for the same food bought from the different eating places (Table III). This is to be expected since portion size and amounts of ingredients vary. In spite of such variations, results expressed as a mean permit comparison with other foods. The difference in cholesterol content between, for example, big dumplings (with egg as one of the ingredients) and *char siew* dumplings is clearly evident. On the other hand, chicken rice and *char siew* rice, two similar foods, are shown to contain similar amounts of cholesterol.

Table II

Fatty acid composition of some Malaysian foodstuffs

	FOODSTUFF	Each Fatty Acid As A Percentage of Total Fatty Acids											* Percent Polyunsaturated fatty acid	** P/S ratio
		Lauric C12 0	Myristic C14 0	Myristoleic C14 1	Palmitic C16 0	Palmitoleic C16 1	Stearic C18 0	Oleic C18 1	Linoleic C18 2	Linolenic C18 3	Arachidic C20 0	Arachidonic C20 4		
1	Brain, pig	0	0 7	0	21 0	2 2	25 4	39 1	0	0	0	11 6	11 6	0 25
2	Egg, duck	0 3	0 6	0	26 8	4 3	5 9	60 9	1 2	0	0	0	1 2	0 04
3	Egg, hen	0	0	0	26 0	3 0	6 2	55 0	9 8	0	0	0	9 8	0 30
4	Egg, quail	0 5	1 0	0 5	26 2	7 1	9 5	40 9	14 3	0	0	0	14 3	0 38
5	Anchovies (whole) dried (ikan bilis)	0 3	12 9	1 3	37 6	13 9	12 4	13 2	3 2	0 4	2 2	2 8	6 4	0 10
6	Prawns, dried	1 5	5 1	1 9	24 5	11 3	18 6	14 9	3 5	0	0 6	18 0	21 5	0 43
7	Liver, pig	0	0	0	24 5	1 9	27 9	20 4	14 1	0	0	11 2	25 3	0 48
8	Prawns, fresh	3 2	2 8	0	33 1	3 4	9 3	29 8	18 4	0	0	0	18 4	0 38
9	Cuttlefish	0	5 1	0	40 8	2 5	20 2	10 4	0	0	0	21 0	21 0	0 32
10	Butter	8 5	9 4	0 4	33 5	0 4	12 4	31 8	3 6	0	0	0	3 6	0 06
11	Crab meat	2 0	6 8	0	32 7	11 7	16 2	19 4	3 7	0	0	7 5	11 2	0 19
12	Chicken meat	0	1 0	0	18 8	10 6	10 0	37 9	21 7	0	0	0	21 7	0 73
13	Pork, fat	0 5	1 4	0	23 8	3 0	16 0	48 4	6 0	0	0 6	0 2	6 2	0 15
14	Anchovies (minus head and entrails), dried (ikan bilis)	0	9 1	0 3	34 9	13 0	14 4	16 5	3 5	0	0 4	8 0	11 5	0 20
15	Mutton	0 5	2 9	0	20 8	3 9	19 3	47 8	3 9	0 9	0	0	4 8	0 11
16	Pork, lean	0 2	1 3	0	23 0	2 8	13 0	49 7	10 0	0	0	0	10 0	0 27
17	Beef	0 4	1 4	0	20 7	2 3	33 1	37 6	4 5	0	0	0	4 5	0 08
18	Cockles (kerang)	6 3	10 0	0	26 3	11 3	21 3	11 9	5 7	0	0	7 2	12 9	0 20
19	Fish, Kembong	3 1	9 7	1 2	29 3	14 4	12 3	12 5	4 7	3 9	3 3	5 6	14 2	0 25
20	Fish, Kurau	2 2	2 8	0 1	33 9	5 4	16 4	25 0	2 9	0 4	0 5	0 5	3 8	0 07
21	Fish, Tenggiri	0 6	6 0	0 3	40 0	7 4	15 1	29 1	1 3	0	0	0	1 3	0 02

* Polyunsaturated fatty acids = C18:2, C18:3 and C20:4

** P/S ratio = $\frac{\text{polyunsaturated fatty acids}}{\text{saturated fatty acids}}$

$= \frac{C18:2 + C18:3 + C20:4}{C12:0 + C14:0 + C16:0 + C18:0 + C20:0}$

Table III

Cholesterol content of some Malaysian ready-to-eat meals

	NAME OF FOOD	In 100 g edible portion (mg)	In each serving (edible portion) *** (mg)
1	Dumpling - big	46 3 * 20 2 - 84 8 **	86 7 39 4 - 146 7
2	Dumpling - char siew	13 0 8 2 - 17 4	8 9 5 7 - 17 4
3	Dumpling - sang yoke	17 3 11 5 - 28 3	13 3 7 8 - 21 2
4	Lor mai kai	10 5 7 9 - 12 8	16 3 13 4 - 23 0
5	Fried kueh liau with cockles	64 8 63 6 - 67 1	194 9 165 4 - 211 2
6	Chicken rice	13 7 9 5 - 18 0	47 0 29 8 - 55 3
7	Char siew rice	10 9 6 1 - 20 0	34 9 21 0 - 62 0
8	Fried rice (chinese style)	47 7	187 0
9	Fried kueh liau (kong foo chow - Cantonese style)	16 3 13 0 - 19 6	109 7 67 3 - 133 7
10	Fried mee (Fukien chow - Hokkien style)	16 9 11 8 - 26 9	128 1 74 3 - 209 8
11	Lup cheong (Chinese sausage)	55 8 49 8 - 63 8	-
12	Curry laksa	6 8 5 6 - 8 6	43 0 40 5 - 47 5
13	Nasi lemak	7 0 5 7 - 8 3	22 0 15 0 - 28 9
14	Satay	54 6	193 0
15	Nasi beriyani	11 0 10 5 - 11 5	50 6 40 2 - 61 0
16	Fried mee - Indian style	159 4 55 7 - 263 0	547 0 165 - 928
17	Rendang hati	215 208 0 - 221 0	-
18	Mutton curry	46 8 34 0 - 59 5	-
19	Sambal udang	79 0 49 0 - 109 0	-
20	Thairuvaddai	5 2 4 5 - 5 9	8 3 8 0 - 8 6
21	Boil	0 7	0 5
22	Dosai with egg	64 8	165 0
23	Dosai	0	0

* Mean

** Range

Where range not given single analysis was performed

*** Calculated from weight in each serving (see appendix 2)

Fatty acid composition appears to be the most variable for the same type of meal. Thus, the fatty acid composition of fried *mee* Indian style, appear quite different in two separate samples, though their proximate composition is similar. This would suggest that two different types of oils were used in the preparation of this food at the two different eating places. This is also true for the two samples of *rendang hati.* Nevertheless, most foods have their own characteristic fatty acid composition. For example, foods containing curry with coconut milk as an ingredient possess relatively high percentages of the short chain saturated fatty acids, such as capric, lauric and myristic acids, found in abundance in coconut oil.

The energy content and the proximate composition of the cooked foods, such as their moisture, protein, fat, carbohydrate and ash content are given in appendix 2.

DISCUSSION

There is continuing interest in the relationship between dietary fats, cholesterol and coronary heart disease. However little is known of the cholesterol content or the fatty acid composition of local foods. This report, although not wholly comprehensive, is a preliminary attempt to fill this gap of knowledge.

Most published reports on the cholesterol content of foods have been made using colour reactions, which are non-specific and hence may be misleading. This study used the gas-liquid chromatographic procedure which gives greater accuracy and is the method of choice (Sweeney and Weihranch, 1976).

The ready-to-eat meals are of particular interest. As far back as in 1940, Canton *et al.* in Singapore had described the proximate composition of 770 types of cooked foods. However, cholesterol and fatty acids were not given special attention in this monumental work which must be ranked as a nutritional classic. Standal *et al.* (1970) reported the fatty acids, cholesterol and proximate composition of 218 types of foods and prepared dishes. These however were "western" foods, unfamiliar to us in Southeast Asia. The present study is a somewhat similar study on Malaysian ready-to-eat meals.

It is hoped that the various tables in this report are of use to nutritionists, food scientists, dietitions and those conscious of their diet, like the enlightened executives or office workers in the highly urbanised Kuala Lumpur and Petaling Jaya who have to rely on part, if not all, of their daily meals on the away-from-home foods. For those who are at risk to coronary heart disease, it may well be remembered that there is no need to develop a pathological fear of all foods known to

Table IV

Fatty acid composition of some Malaysian ready-to-eat meals

	NAME OF FOOD	EACH FATTY ACID AS A PERCENTAGE OF TOTAL FATTY ACIDS DETECTED													* Per cent Polyunsaturated fatty acids	** P/S ratio
		Capric C10 0	Lauric C12 0	Myristic C14 0	Myristoleic C14 1	Palmitic C16 0	Palmitoleic C16 1	Stearic C18 0	Oleic C18 1	Linoleic C18 2	Linolenic C18 3	Arachidic C20 0	Arachidonic C20 4	Unconfirmed fatty acids		
1	Dumpling - big	0 1	0 5	2 1	0	23 6	4 2	10 8	43 0	14 2	0 6	0 2	0	0 7	14 8	0 40
2	Dumpling - char siew	0 1	0 9	3 4	0	27 2	3 0	13 4	41 1	7 8	0 6	0 2	0	2 2	8 4	0 19
3	Dumpling - sang yoke	0 1	0 4	2 0	0 1	25 3	3 3	11 9	44 1	10 7	0 4	0 2	0	1 5	11 1	0 28
4	Lor mai kai	0	0 8	2 0	0	24 7	3 8	9 9	43 7	14 5	0 7	0	0	0	15 2	0 41
5	Fried kueh tiau with cockle shells	0 1	0 4	1 8	0	26 3	2 8	10 8	43 2	12 8	0 3	0	0	1 6	13 1	0 33
6	Chicken rice	0	0 7	1 6	0 3	30 2	5 6	6 8	38 7	14 3	0 7	0	0	1 2	15 0	0 38
7	Char siew rice	0 1	1 3	2 1	0	32 3	2 8	10 8	37 8	7 9	0 1	0 2	0	4 6	8 0	0 17
8	Fried rice (Chinese style)	0	0 1	1 6	0	26 2	2 6	12 1	46 6	10 4	0 1	0 4	0	0	10 5	0 26
9	Fried kueh tiau (kong foo chow - Cantonese style)	0 2	0 5	1 9	0	26 7	3 2	11 2	42 9	12 6	0 2	0 1	0	0 5	12 8	0 32
10	Fried mee (Fukien chow - Hokkien style)	0 1	0 5	1 8	0	26 7	2 6	11 3	42 5	12 9	0 3	0	0	1 2	13 2	0 33
11	Lup cheong (Chinese sausage)	0	0 5	2 1	0	25 3	3 7	13 4	43 1	7 6	0 4	0 1	0	3 8	8 0	0 19
12	Curry laksa	4 3	29 5	12 3	0	18 2	1 0	5 1	20 4	8 9	0 2	0 1	0	0	9 1	0 13
13	Nasi lemak	1 5	13 0	5 6	0	30 8	0 9	6 0	29 1	13 1	0 1	0 1	0	0	13 1	0 23
14	Satay	0 4	2 4	1 6	0 1	22 0	3 2	6 1	38 5	23 5	0 6	1 1	0	0 6	24 1	0 72
15	Nasi beriyani	3 4	6 8	10 9	2 5	26 7	3 7	11 7	26 1	7 1	0 2	0	0	1 1	7 3	0 12
16	Fried mee - Indian style	2 7	12 8	11 6	0 3	22 8	6 2	10 2	17 8	7 9	0 4	0 4	3 1	4 0	11 3	0 19
17	Rendang hati	0	11 0	6 0	0 2	22 4	1 9	14 2	24 9	11 3	2 4	0 3	3 4	2 3	17 0	0 32
18	Mutton curry	4 0	16 9	13 2	0 3	16 9	1 7	13 0	25 5	6 8	0 9	0	0	1 1	7 6	0 12
19	Sambal udang	8 9	27 1	24 5	0	13 6	0 3	5 2	12 6	7 1	0 3	0 2	0	0 5	7 4	0 09
20	Thairuvaddai	7 1	16 4	18 6	0 6	19 2	1 4	10 0	19 6	3 4	0 6	0	0	3 4	4 0	0 06
21	Boli	15 7	18 8	23 0	0	13 7	0	4 1	12 4	10 8	0 5	0	0	1 1	11 3	0 15
22	Dosai with egg	8 8	20 7	23 6	0	15 7	1 4	4 3	18 7	5 4	0 5	0	0	0 9	5 9	0 08
23	Dosai	0	6 0	16 3	0 8	18 8	1 8	9 1	20 5	4 8	0 5	0	0	3 7	5 3	0 08

All values mean of three samples, except for numbers 8, 14 and 21 - 23.

* Polyunsaturated fatty acids = C18:2 + C18:3 + C20:4

** $P/S = \frac{\text{polyunsaturated (i.e. C18:2 + C18:3 + C20:4)}}{\text{saturated (i.e. C10:0 + C12:0 + C14:0 + C16:0 + C18:0 + C20:0)}}$

be rich in cholesterol or saturated fatty acids, or withdraw totally from them. It is important that the risk incurred in the occasional consumption of such foods be weighed against the valuable nutrients found in these foodstuffs. For instance, eating several eggs a day may well raise serum cholesterol level, but one egg a day may have no effect (Porter *et al.*, 1977). Cow's milk is well know to contain saturated fatty acids. Yet recently, a Cambridge study showed that consumption of 4 pints of whole milk daily for three weeks not only failed to raise serum cholesterol, but actually depressed the level (Howard *et al.*, 1977). These examples do not contradict the dietary fat and cholesterol hypothesis of atherosclerosis, but merely illustrates the complexities of food and serve to remind us that in some foods both hypercholesterolemic and hypocholesterolemic factors exist.

SUMMARY

This study has provided some data on the cholesterol content and fatty acid composition of some local foods, both raw as well as ready-to-eat meals. A gas-liquid chromatographic procedure has been used. The results obtained were discussed with reference to the contribution of cholesterol and fatty acids to the Malaysian diet.

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Appendix I

Description of ready-to-eat meals analysed

	Cost perserving (in MS)	Ingredients	Remark
1. Dumpling — big	0.60 — 0.70	wheat flour, pork, chicken, half-boiled egg	usually eaten by Chinese for breakfast or tea-break
2. Dumpling — *char siew*	0.30	wheat flour, roasted pork (lean)	as above
3. Dumpling — *sang yoke*	0.30	wheat flour, pork	as above. Size and ingredients similar to (2). Differ from (2) only in the way the pork is prepared
4. *Lor mai kai*	0.50	glutinous rice, roasted pork, chicken, sometimes mushroom	the Chinese usually consume this either for breakfast or tea. Usually served in the same stall selling dumplings
5. Fried *kueh tiau*	0.80	*kueh tiau* (rice flour noodles), egg, cockle-shells, *tau-geh* (bean sprout, pork lard	may be taken for lunch; usually consumed by the Chinese
6. Chicken rice	1.50	rice, chicken (leg meat), cucumber	taken for lunch/dinner by all races
7. *Char Siew* rice	1.00	rice, *char siew* (roasted pork-lean), cucumber	another popular quick lunch/dinner; only by non-Muslims, especially Chinese
8. Fried rice	1.50	rice, pork, shrimps, green-peas, egg, spring onion. (ingredients can vary considerably in different eating places)	served for lunch/dinner, taken by all races. For the Muslims, pork is replaced by other meat
9. Fried *kueh tiau* (*kong foo chow*-Cantonese style)	1.20	*kueh tiau*, pork, egg, prawns, vegetable	popular among the Chinese, taken for supper
10. Fried *mee* (*Fukien chow* — Hokkien style)	1.20	*mee* (noodles), pork, prawn, vegetables	supposedly introduced by the Hokkiens; popular among the Chinese; taken for supper. More non-Chinese (except Muslims) are taking such foods introduced by the Chinese
11. *Lup cheong* (Chinese sausage)	2.00 per 100 g (price vary according to type)	pork	taken by the Chinese together with rice (e.g. together with "char siew" in "char siew" rice)
12. *Curry laksa*	0.70 — 0.90	curry, *mee*, *tau-foo-pork* (soya bean curd), cockle-shells, bean sprout, chicken	a widely eaten food, taken for breakfast/lunch
13. *Nasi lemak*	0.60 — 0.80	rice (cooked with coconut milk), *ikan bilis* (small anchovies), egg, swamp-cabbage, cucumber, chilli, groundnuts	introduced by the Malays, now popular as a food for breakfast/tea-break for all races
14. *Satay*	0.20 per stick	chicken meat (also available beef); gravy of ground pea nuts and chilli. (analysis includes gravy)	originated from the Malays. Much liked by all races. As much as 10 sticks may be taken for supper
15. *Nasi beriyani*	2.50	rice, chicken, green-peas, carrot	served by Indian Muslims. Popular among the Indians and Malays. Usually for lunch/dinner
16. Fried *mee* — Indian style	0.80	*mee*, egg, *tau-kua* (soya bean curd), vegetable, tomato	also served by Indian Muslims. Usually taken for breakfast by Indians and Muslims. However, such Indian and Malay foods are now also popular with the Chinese
17. *Rendang hati*	1.00 per plate of 140 g	ox liver	served by Malays/Indians. Taken with rice (with other dishes, e.g. mutton curry, vegetables, etc.)
18. *Sambal udang*	1.00 per plate of 150 g	prawns in chilli	as above
19. Mutton curry	1.00 per plate of 200 g	mutton, cooked in curry (pungent gravy of coconut milk and chilli)	as above
20. *Thairuvaddai*	0.40 for two *vadai* in fermented milk (total 250 g)	black grams, grounded and then roasted in oil	the Indians like to take these for breakfast/tea-breaks
21. *Boli*	0.25 each	rice flour and green gram cooked in oil	as above
22. *Dosai* with egg	0.40 each	egg, rice flour and black grams fermented and then cooked with oil	as above
23. *Dosai*	0.20 each	ad above except without egg	as above

Appendix 2

Proximate composition of some Malaysian ready-to-eat meals

	NAME OF FOOD	In 100 g (edible portion)						In each serving (edible portion)		
		moisture (g)	fat (g)	protein (g)	carbohydrate (by difference) (g)	ash (g)	calories	weight (g)	fat (g)	calories
1	Dumpling - big	49 1* 46 1 - 51 2**	11 4 9 8 - 13 4	9 7 8 8 - 10 1	28 6 27 6 - 29 1	1 3 1 2 - 1 3	255 239 - 277	196 173 - 219	22 1 19 1 - 23 9	498 466 - 548
2	Dumpling - char siew	34 3 30 7 - 36 3	15 4 11 8 - 22 0	8 5 8 3 - 8 6	40 5 37 5 - 42 6	1 4 1 2 - 1 5	314 311 - 381	71 63 - 82	10 7 7 7 - 14 7	135 196 - 255
3	Dumpling - sang yoke	46 7 44 4 - 49 7	8 5 5 9 - 12 8	7 9 6 3 - 10 0	35 7 34 1 - 37 0	1 3 1 1 - 1 7	250 241 - 282	78 68 - 90	6 7 4 7 - 11 5	195 154 - 252
4	Lor mai kai	49 6 47 6 - 53 1	5 0 3 2 - 6 8	5 5 4 3 - 6 9	38 4 34 2 - 40 6	1 5 1 4 - 1 6	221 215 - 230	173 170 - 180	8 8 5 4 - 12 2	383 371 - 391
5	Fried kueh tiau with cockles	67 0 66 3 - 67 9	9 7 8 3 - 11 7	5 1 4 6 - 5 6	17 1 15 8 - 18 4	1 1 0 8 - 1 4	177 167 - 189	300 280 - 331	20 2 23 9 - 36 3	530 452 - 586
6	Chicken rice	66 9 64 6 - 68 1	4 6 2 7 - 6 2	6 4 6 0 - 6 7	21 1 19 4 - 22 2	1 0 0 4 - 1 8	151 140 - 169	315 307 - 325	14 3 8 8 - 19 0	476 454 - 518
7	Char siew rice	63 3 60 3 - 65 5	6 5 2 1 - 10 1	7 1 6 7 - 7 3	22 0 20 7 - 24 3	1 1 1 0 - 1 2	174 144 - 205	329 310 - 344	21 0 7 0 - 31 3	571 479 - 636
8	Fried rice (chinese style)	54 8	13 2	7 2	23 5	1 3	242	302	51 7	948
9	Fried kueh tiau (kong foo chow - Cantonese style)	74 8 68 4 - 79 7	5 5 2 3 - 9 3	3 8 3 0 - 4 8	15 1 14 1 - 16 8	0 9 0 7 - 1 0	125 89 - 170	652 518 - 785	34 1 15 7 - 48 2	800 607 - 911
10	Fried mee (Fukien chow - & Hokkien style)	68 9 66 5 - 70 1	6 6 5 1 - 7 5	4 6 4 3 - 5 0	18 8 17 4 - 19 9	1 1 1 1 - 1 2	153 140 - 167	751 624 - 848	48 5 43 2 - 55 4	1177 1042 - 1302
11	Lup cheong (Chinese sausage)	14 4 13 4 - 16 0	43 4 41 8 - 44 3	22 5 20 6 - 25 8	14 0 13 0 - 15 4	5 7 4 9 - 6 1	536 533 - 542	-	-	-
12	Curry laksa	77 3 75 7 - 78 2	6 4 5 4 - 7 6	3 5 3 2 - 3 8	11 3 11 1 - 11 6	1 5 1 3 - 1 7	117 109 - 128	650 552 - 734	40 9 39 6 - 42 0	752 707 - 800
13	Nasi lemak	62 4 57 9 - 66 8	3 6 1 5 - 5 7	4 8 4 2 - 5 3	28 3 26 6 - 30 0	1 0 0 9 - 1 1	165 137 - 193	306 263 - 348	10 1 5 2 - 15 0	492 477 - 506
14	Satay	66 7	10 8	8 8	12 4	1 3	182	353 (10 sticks)	38 0	642
15	Nasi beriyani	65 7 64 0 - 67 3	2 6 2 5 - 2 7	6 4 6 3 - 6 4	24 4 22 7 - 26 1	1 0 0 9 - 1 1	147 139 - 154	457 383 - 530	11 8 10 3 - 13 3	664 590 - 737
16	Fried mee - (Indian style)	63 4 62 6 - 64 1	9 0 8 8 - 9 2	6 6 6 5 - 6 6	19 1 18 0 - 20 1	2 1 1 6 - 2 5	184 178 - 189	328 297 - 353	31 6 31 1 - 32 5	595 561 - 628
17	Rendang hati	65 0 62 8 - 67 1	8 8 7 8 - 9 8	20 1 19 3 - 20 8	2 1 2 3 - 5 9	2 1 2 0 - 2 2	176 163 - 189	-	-	-
18	Mutton curry	68 7 67 1 - 70 2	14 1 8 7 - 19 4	11 1 5 1 - 17 0	4 3 3 8 - 4 8	2 0 1 5 - 2 4	188 166 - 210	-	-	-
19	Sambal udang	76 0 75 0 - 76 9	7 8 4 4 - 11 2	9 8 6 6 - 13 0	3 9 2 8 - 5 0	2 6 2 2 - 2 9	125 103 - 147	-	-	-
20	Thairuvädai	82 2 81 3 - 83 1	6 9 6 6 - 7 1	3 5 2 9 - 4 0	6 4 6 0 - 6 7	1 2 0 9 - 1 4	101 95 - 107	164 135 - 192	11 2 9 6 - 12 7	163 143 - 182
21	Boli	42 5	8 1	7 0	41 5	0 9	267	84	6 8	224
22	Dosai with egg	56 5	11 8	6 8	21 6	1 3	228	195	23 0	443
23	Dosai	70 1	0 7	3 5	24 2	1 5	117	132	0 9	154

* Mean
** Range
Where range not given single analysis was performed

MALIGNANT ORAL TUMOURS IN PENINSULAR MALAYSIA — A Preliminary Report on 2,263 cases

K. RAMANATHAN & NG KOK HAN

INTRODUCTION

MALIGNANT oral tumours kill more people than all the other serious oral conditions added together. It is indeed interesting to note from this preliminary study that the various histological types of malignant oral tumours have variations in the relative frequency, race, sex, peak age incidence, anatomical sites of involvement, morbidity and long-term survival of patients.

MATERIAL AND METHOD

This study was based on the records of the Department of Stomatology and for the years 1967 — 1978. Only histologically confirmed cases were included in this study. Malignant oral tumours formed about 22.5% of all specimens reported by the department. In all there were 2,263 patients. The male:female ratio was 1.2:1.

RESULTS AND DISCUSSION

Table I shows the frequency of malignant oral tumours by histological types. Squamous cell carcinoma (91%) was the commonest malignant oral tumour. Carcinoma was about 20 times more common than sarcoma. Sarcomas formed about 5%. Malignant minor salivary gland tumours formed about 4%. Malignant melanoma (Fig. 1) formed 0.3%. The peak age incidence for malignant melanoma was between 31-40 years (37.5%) and the commonest site of involvement was the lips (37.5%). The relatively low figure (0.2%) for metastatic carcinomas to the oral cavity could be due to cancer patients often seeking treatment very late and having a rather short survival period even following treatment.

Since the Department of Stomatology has already published several papers on the various aspects of oral squamous cell carcinoma, for economy of space the discussion will be limited to the other types of malignant tumours.

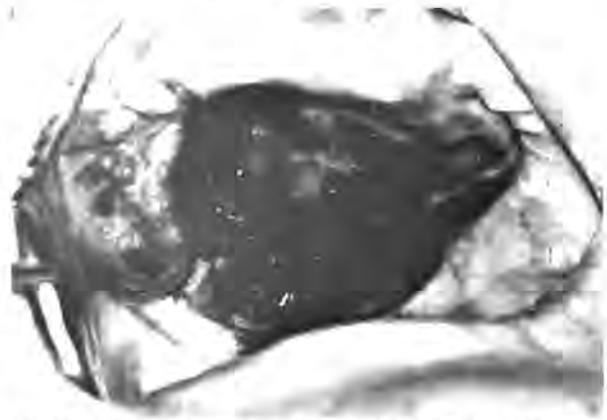

Fig. 1. shows a malignant melanoma of the hard palate presenting as a pigmented black lesion with evidence of haemorrhage.

TABLE I

Frequency of Malignant Oral Tumours (1967 — 1978)

TYPE	NUMBER	PERCENTAGE
Squamous Cell Carcinoma	2056	90.9%
Malignant Minor Salivary Gland Tumours	88	3.9%
Malignant Melanoma	8	0.3%
Metastatic Carcinomas	5	0.2%
Sarcomas	106	4.7%
	2263	100%

CARCINOMA: SARCOMA = 20.3 : 1

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MALIGNANT MINOR SALIVARY GLAND TUMOURS

Patients with malignant salivary gland tumours (Fig. 2) commonly presented as a firm swelling with evidence of ulceration and pain. In all there were 88 patients. Both sexes were equally affected. Mucoepidermoid tumour (Fig. 3) (40%) was the commonest followed secondly by adenoid cystic carcinoma (34%) Table 2. Eighty percent of the patients were between 31 — 70 years. About 7% of malignant minor salivary gland tumours occurred between 11 — 20 years. All of them were females with 83% of them being Chinese females. This would emphasize the need for clinicians to exclude malignant minor salivary gland tumours in Chinese female adolescents presenting with firm swellings in the mouth. Malignant minor salivary gland tumours most commonly involved the palate (40%), gingivae (25%) and the cheek (19%).

Fig. 2. shows a malignant minor salivary gland tumour of the hard palate presenting as a firm swelling with evidence of ulceration.

Table II

Distribution of Malignant Minor Salivary Gland Tumours by Historical Types (1967 — 1978)

	NUMBER	PERCENTAGE
1. Mucoepidermoid tumour	35	39.8%
2. Adenoid Cystic Carcinoma	30	34.1%
3. Adenocarcinoma	16	18.2%
4. Carcinoma in Pleomorphic Adenoma (malignant mixed tumour)	6	6.8%
5. Undifferentiated carcinoma	1	1.1%
Total:	88	100%

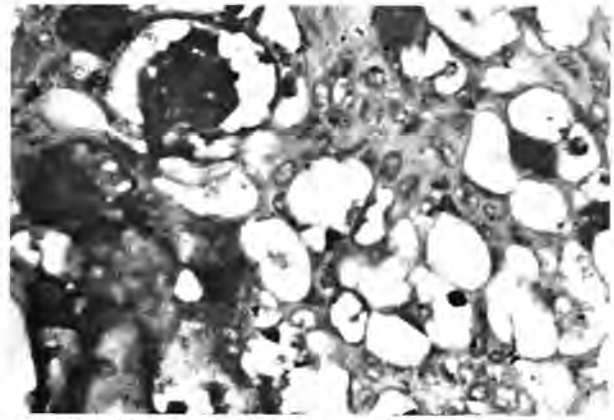

Fig. 3. A high-power (original magnification x 160) photomicrograph of a mucoepidermoid tumour showing (1) mucous cells (2) clear cells and (3) epidermoid cells. Mucicarmine stain.

MALIGNANT LYMPHOMAS

Malignant lymphomas formed about 3.0% of all malignant oral tumours. Reticulosarcoma (43%) (Fig. 4, 5) was the commonest malignant lymphoma, followed by Burkitt's lymphoma (30%) and lymphosarcoma (25%). Malignant lymphomas were more common in males. The peak age incidence for reticulosarcoma was between 51-60 years (35%). The male:female ratio for reticulosarcoma was 3.1:1. Burkitt's lymphoma (Fig. 6, 7) is the commonest malignant oral tumour in children in Peninsular Malaysia (Ramanathan and Tan Cheng Keat, 1972). The peak age incidence was between 0 — 10 years (70%) and almost 95% of the patients were between 0 — 20 years (Ramanathan, K. In Press). Ramanathan has emphasized that Burkitt's lymphoma is much more common than it has been reported so far. The male:female ratio for Burkitt's lymphoma was 2.3:1. Lymphosarcomas had two peak age incidences. Firstly between 0 — 10 years (35%) and a second peak between 31 — 40 years (29%). The male:female ratio for lymphosarcoma was 1.8:1.

OTHER SARCOMAS

There were 15 cases of fibrosarcoma forming 0.7% of all malignant oral tumours. Fibrosarcoma was three times more common in the male. The peak incidence was between 21 — 40 years (40%). There were five cases of osteosarcoma forming about 0.2% of all malignant oral tumours. Except for a Malay female all the other patients were males. The peak age incidence was between 21 —

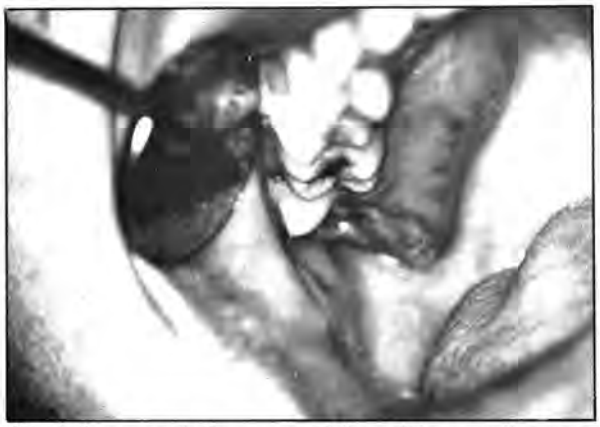

Fig. 4. shows a reticulosarcoma of the palate presenting as a soft tissue swelling.

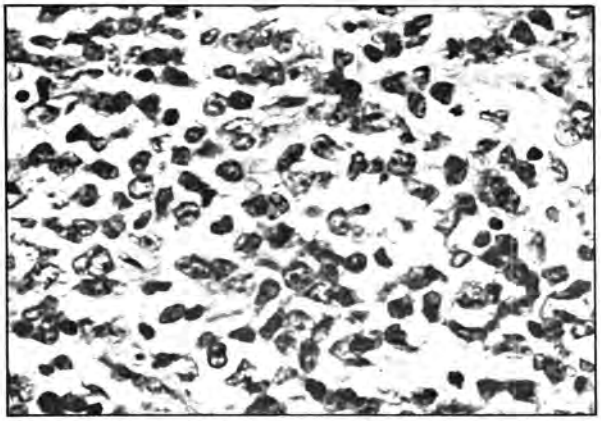

Fig. 5. A high-power photomicrograph (original magnification x 160) showing a sheet of reticulum cells with abundant pale-staining cytoplasm and indistinct cell borders. The nuclei are usually lobular or indented and have prominent nucleoli. H & E.

Fig. 6. A 2-year-old Chinese girl with Burkitt's lymphoma involving both quadrants of the maxillae and the right quadrant of the mandible.

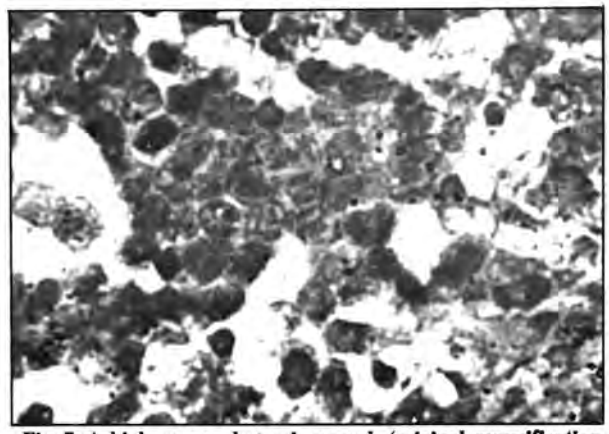

Fig. 7. A high-power photomicrograph (original magnification x 160) shows a monotonous distribution of undifferentiated lymphoreticular cells with little variation in size and shape. The non-neoplastic histiocytes with abundant clear cytoplasm contain tumour cells or cell debris. H & E.

30 years. (60%). There were four cases of malignant haemangioendothelioma, 3 cases of malignant haemangiopericytoma and 3 cases of Kaposi's sarcoma. Eighty-two percent of patients with angiosarcomas were between 0 — 30 years. Angiosarcomas were three times more common in the male. There was also one case each of alveolar soft-part sarcoma, rhabdomyosarcoma, plasma cell myeloma and neurofibrosarcoma.

SUMMARY

Malignant oral tumours formed about 23% of all oral pathology specimens. Squamous cell carcinoma (91%) was the commonest malignant oral tumour. Carcinoma was about 20 times more common than sarcoma. Malignant minor salivary gland tumours formed about 4%. There is a need for clinicians to exclude malignant minor salivary gland tumours in Chinese female adolescents presenting with firm swellings in the mouth. Reticulosarcoma was the commonest malignant lymphoma, followed by Burkitt's lymphoma and lymphosarcoma. Burkitt's lymphoma is the commonest malignant oral tumour in children in Peninsular Malaysia. Lymphosarcomas had two peak age incidences. Firstly between 0 — 10 years and a second peak between 31 — 40 years. Fibrosarcoma, osteosarcoma and angiosarcoma mostly occurred in the young adults.

ACKNOWLEDGEMENT

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RESPONSE TO RADIOACTIVE PHOSPHORUS TREATMENT OF POLYCYTHAEMIA RUBRA VERA IN MALAYSIANS: Analysis of 8 cases.

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INTRODUCTION

THE INCIDENCE OF Polycythaemia rubra vera in Malaysia is unknown. Between the years 1970 and 1977, only 8 cases of the disease were referred to the Radiotherapy Department, General Hospital, Kuala Lumpur for treatment with radioactive phosphorus. Although the use of radioactive phosphorus in the treatment of Polycythaemia rubra vera is established and documented for patients in the West (Szur *et al.*, 1959), these 8 patients are the first Malaysians to be treated with radioactive phosphorus. In this report we document the clinical and haematological response in these 8 Malaysian patients with Polycythaemia rubra vera who had been treated with radioactive phosphorus.

PATIENTS AND METHODS

Eight patients with Polycythaemia rubra vera were referred to the Radiotherapy Department, General Hospital, Kuala Lumpur, between 1970 and 1977. Of these, 6 were males and 2 were females. There were 6 Chinese and 2 Malays. Their average age was 53.3 years (range of 42 to 64 years).

All the patients satisfied the following laboratory criteria for the diagnosis of Polycythaemia rubra vera, namely, haemoglobin values greater than 16.5 g per 100 ml. for males and greater than 15.5 g per 100 ml. for females, red cell mass using radioactive chromium (51 Cr) greater than 35 ml per kg., total cell volume of greater than 85 ml per kg., hyperplastic bone marrow, and leucocytosis (greater than 10,000 per cu mm) and thrombocytosis (greater than 350,000 per cu mm) were not essential criteria. Secondary polycythaemia was excluded with arterial blood gases and intravenous pyelograms. Radioactive phosphorus was administered only when the patient's packed cell volume was 55 per cent or less. Patients with values greater than 55 per cent had venesection done to reach treatment levels. Three months after initial treatment another dose of radioactive phosphorus was administered in patients with no clinical or haematological remission and also in patients with clinical remission but with haematological relapse.

A full clinical examination and the relevant laboratory investigation were recorded at the initial visit. Following treatment with radioactive phosphorus, subsequent follow-ups were at monthly intervals for the first 3 months and then at 3 monthly intervals after that. At each visit, their response to treatment was recorded and a full clinical and haemotological assessment was performed.

RESULTS

The clinical features and response to treatment of the 8 patients is summarised in Table 1. Common presenting features were those of generalised pruritis, headache, vertigo and bleeding from peptic ulceration. Splenomegaly and hypertension were common signs. Thrombosis of the femoral vein was the presenting feature in one patient.

Seven out of our 8 patients achieved full remission. The average period of remission was 16 months. The haematological response to treatment is summarised in Table II. Although full haematological remission took effect after 3 to 6 months, the symptomatic improvement was felt much earlier. Pruritus, headache and vertigo

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Table I

Clinical Response in Patients with Polycythaemia Rubra Vera to Radioactive Phosphorus.

Symptoms/Signs	No. of Patients	No. of Patients with response.
Pruritus	3	3
Splenomegaly	6	3
Headache/Vertigo	4	4
Hypertension	2	2
Haemorrhage		
a) peptic ulcer	5	5
b) nasal	1	1
Thrombosis femoral vein	1	1

Table II

Response of Relevant Haematological Values in Patients with Polycythaemia Rubra Vera to Radioactive Phosphorus Treatment.

Laboratory test	Patients with elevated values	Patients with response
Haemoglobin	8	7
Platelet count	6	5
White cell count	4	3
Packed cell volume	8	7
Red cell count	8	7

responded well to treatment. The 2 patients with hypertension had normal blood pressures after treatment. Splenomegaly (in 6 patients) was evident in only 3 after treatment. All the 5 patients with peptic ulcer symptoms were relieved of pain after treatment with radioactive phosphorus. The single patient with thrombosis of the femoral vein had complete relieve of his signs and symptoms of the thrombosis. He was also treated with anticoagulants. The hyperuricaemia that occured in 4 patients (uric acid level more than 7 mg per ml.) responded well to radioactive phosphorus treatment as well as to allopurinol.

No side effects were noted in any of our patients on treatment. On one patient, the platelet count dropped to 90,000 but no evidence of bleeding was detected.

DISCUSSION

Polycythaemia rubra vera is characterised by an absolute increase in the number of red blood cells and the red cell volume, accompanied by leucocythosis, thrombosis and splenomegaly. As the etiology of the condition is unknown, the treatment is directed at the relief of the signs and symptoms and at the reduction of total blood volume. This consists of either venesection alone or venesection with chemotherapy or venesection with radioactive phosphorus.

Full remission in 7 out of 8 patients amongst Malaysian patients compares well with that achieved by Szur *et al.* (1959), who had full remission in 82 per cent. He also records good symptomatic response in his patients. In our patients, pruritus, headaches, vertigo and hypertension responded completely to the treatment. Lawrence *et al.* (1957) noted that only in one-third of his patients with hypertension, did the blood pressure return to normal after the successful treatment of polycythaemia.

We wish to document the good response that occurs with radioactive phosphorus treatment amongst Malaysian patients. The disease has a bad prognosis untreated; Chievltz (1962) found that 50 per cent of untreated patients died within 18 months of the onset of the first symptom or sign. With radioactive phosphorus treatment, Lawrence (1955) quotes a median survival of 13.3 years.

All Malaysian patients with a raised haemoglobin must be investigated for Polycythaemia rubra vera and the treatment started immediately. The small number of patients referred (8 in 7 years) for treatment perhaps shows that the diagnosis is either missed or is made very later. It is also possible that the doctor in charge of the case is unaware of the availability of radioactive phosphorus treatment in our country.

SUMMARY

The prognosis of untreated Polycythaemia rubra vera is bad. We document the clinical and haematological response in the first eight Malaysian patients with the disease treated with

radioactive phosphorus. Full remission occured in seven and there was excellent symptomatic response. We emphasise that the diagnosis amongst Malaysians must be made early and the treatment started soon. We feel that a through clinical and haematological search amongst Malaysian patients might reveal more cases requiring treatment with radioactive phosphorus.

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GROUP B STREPTOCOCCI IN A MATERNITY UNIT

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INTRODUCTION

STREPTOCOCCI of Lancefield's Group B also known as *Streptococcus agalactiae* were initially recognised in association with bovine mastitis (Ayers and Mudge, 1922). In the recent years, there have been reports from many parts of the world about their role in human infections (Anthony and Conception, 1975), (Mahlu, 1976) especially as causative organisms of neonatal meningitis. However, a retrospective study of cerebrospinal fluid culture results from neonatal wards in the General Hospital, Kuala Lumpur over a period of one and a half years showed that the majority of cases of pyogenic meningitis in the neonates were due to gram negative bacteria and *Staphylococcus aureus*, whereas, in some European countries and in the United States, Group B streptococci are often responsible for meningitis in the neonates, together with gram negative bacteria (Goldacre, 1977). The neonatal infections caused by Group B streptococci are described as "early onset" type if they occur within the first few days of life. The infection in most of these cases is thought to be acquired during passage through the birth canal (Baker and Barett, 1973) as these organisms are commonly present in the vagina. Therefore, a study was done to establish their presence in the vaginal flora of Malaysian women and to determine if a similar source of infection exists here.

MATERIALS AND METHODS

All vaginal swab specimens submitted to the routine diagnostic laboratory for culture and sensitivity over a period of six months were screened for the presence of group B streptococci. The swabs were sent to the laboratory in Stuart's Transport Medium and processed in the usual way, by streaking onto blood agar, chocolate agar, MacConkey's medium and Sabouraud's dextrose agar. All streptococci isolated were further identified by doing the following tests:

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Sensitivity to antibiotics:

Sensitivity to 0.1 unit of bacitracin (Oxoid) was determined for all beta-haemolytic streptococci on Ox blood agar plates. The organisms sensitive to bacitracin were provisionally reported as Lancefield's group A streptococci.

All alpha haemolytic streptococci were tested with optochin discs, 5 ug (Mast) in the same manner. Those strains which were sensitive to optochin were provisionally reported as *Streptococcus pneumoniae.*

Pigment production on colombia agar:

All strains were streaked onto columbia agar medium (Oxoid) and incubated for 18 — 24 hours, anaerobically using the Gas Pak system. Pigmentation was observed in comparison with a control pigment producing strain of group B streptococcus (Fallon, 1974).

Hydrolysis of aesculin and hippurate:

Aesculin hydrolysis was done to exclude group D streptococci, which produce blackening of the medium as they hydrolyse aesculin. Hydrolysis of hippurate was also done for a presumptive identification of group B streptococci which are positive for this test (Hwang, 1975).

CAMP test: (Christie, Atkins-Munch-Petersen, 1944) Strains of streptococci were inoculated on 4% sheep blood agar plates perpendicular to a single central streak of a beta-haemolysin producing *Staphylococcus aureus.* Plates were incu-

bated aerobically at 37 C overnight and inspected for the presence of complete haemolysis.

Growth on bile containing media:

All strains were streaked onto MacConkey's agar plates (Oxoid) to test for growth on medium containing bile salts.

Serological and Confirmatory test:

The identify of the strains was confirmed serologically by using a commercially prepared kit, the Phadebact (Pharmacia Diagnostics, Uppsala, Sweden).

RESULTS

18 strains of group B streptococci were isolated from a total of 83 vaginal swabs making these organisms the commonest streptococci present in the vaginal flora among streptococci which could be grouped by Lancefield's method. The specimens were from gynaecological and antenatal clinics, from cases presenting with various complaints, such as vaginal discharge, infertility, pruritis, etc. Most of the patients were under the age of forty and in the reproductive years of life. Anaerobic streptococci were excluded from this study.

Table I
Isolation of Streptococci from Vaginal Swabs

		No. of patients	No. of streptococci isolated				
			Group B	A	C	D	
Source of specimen:	ANC	16	4	0		1	
	Gynae	67	14	6	2	6	2
Total:		83	18	6	2	7	2

Total no. of specimens — 83
Streptococci which could be grouped by Lancefield's method isolated from 35.

These results show that the pick up rate of group B streptococci from vaginal swabs is about 21%, which is similar to that in other countries. Therefore, it can be concluded that a source of group B streptococci is present here, which may cause "early onset" type of infections in the newborn infants.

DISCUSSION

This is a preliminary report on the presence of group B streptococci and their rate of isolation from vaginal swabs. From this study, it appears that vaginal carriage of group B streptococci is not different here from elsewhere.

This study also shows that group B streptococci if present in clinical specimens can be recognised by the methods used in this laboratory.

Their role in producing neonatal infections, however, is not clear and group B streptococci have not been isolated from crebrospinal fluid from cases of neonatal meningitis, examined in UKM diagnostic laboratory so far. This may be due to an actual difference in the bacteria responsible for neonatal meningitis here and elsewhere. Results of cerebrospinal fluid cultures from other hospitals in the country, as well as examination of specimens from a greater number of cases would have to be taken into consideration before accepting this view.

Further studies are being done on the vaginal carriage of group B streptococci in the third trimester of pregnancy and during parturition with a follow up of babies born to such mothers. It is hoped that by these means, the role of group B streptococci in neonatal infections will be better understood.

Group B streptococci are present in the vaginal flora with an isolation rate of about 21%, as is shown by this study. Their role in producing neonatal infections is not clear and further studies are required before any conclusions can be drawn. The isolation of group B streptococci from vaginal swabs is being reported for the first time in this country.

SUMMARY

Eighteen strains of Lancefield's group B streptococci were isolated during a course of routine culture of eighty-three vaginal swabs in a clinical microbiology laboratory, over a period of six months. The identity of the isolates was confirmed by using a commercially prepared kit, the Phadebact.

From this study it appears that the rate of isolation of this organism from vaginal swabs in Malaysia is about 21% which is similar to that of other countries. But, from cases of neonatal meningitis, group B streptococci are rarely isolated.

A retrospective study of cerebrospinal fluid culture results from neonatal wards in the General Hospital, Kuala Lumpur over a period of one and half years, showed that the majority of cases of neonatal meningitis were due to gram negative bacteria and *Staphylococcus aureus.* Whereas in some European countries and in the United States, group B streptococci are often responsibile for meningitis in the neonates, together with gram negative bacteria. Therefore, the role of group B streptococci in producing neonatal infections here is not yet clear.

The isolation of group B streptococci from vaginal swabs is being reported for the first time in this country.

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USE-EFFECTIVENESS OF THE COPPER-7 INTRAUTERINE DEVICE IN A MALAYSIAN FAMILY PLANNING CLINIC

GOH TAI HENG

INTRODUCTION

THE PERFORMANCE OF an intrauterine device (IUD) is influenced by many complex factors including physician experience, clinic attitude as wellas the socio-cultural and demographic characteristics of the patient population (Mishell, 1975). Hence, although impressive results have been reported (Newton *et al.*, 1977; Simcock, 1976; Zipper *et al.*, 1976; Population Reports, 1973) with the Copper-7 IUD (Cu-7, Figure I) these results cannot be taken for granted in a purely service as opposed to a research-oriented clinic.

This study was initiated for two main reasons. Firstly, despite its importance there is little information available on the use-effectiveness of the Cu-7 in a service or public health clinic. Secondly this IUD was first used in our family planning clinic in 1972 in place of the Lippes loop and an evaluation of this innovation is long overdue.

MATERIALS AND METHODS

The study was carried out at the University Hospital, Kuala Lumpur. The case records of patients who had Cu-7 insertion at the family planning clinic during the years 1972-1975 were reviewed. The cut-off date for analysis was 31st December, 1977. The definitions and method of analysis used are those set out by Tietze and Lewit (1973).

The contraceptive service was only available to married women as a matter of policy. Insertions were carried out in the interval period using the withdrawal technique. Follow-up visits were scheduled at 6 weeks, 3 months, 6 months, 12 months and thence yearly. Defaulters were contacted by letter or telephone but home visits were not routinely carried out.

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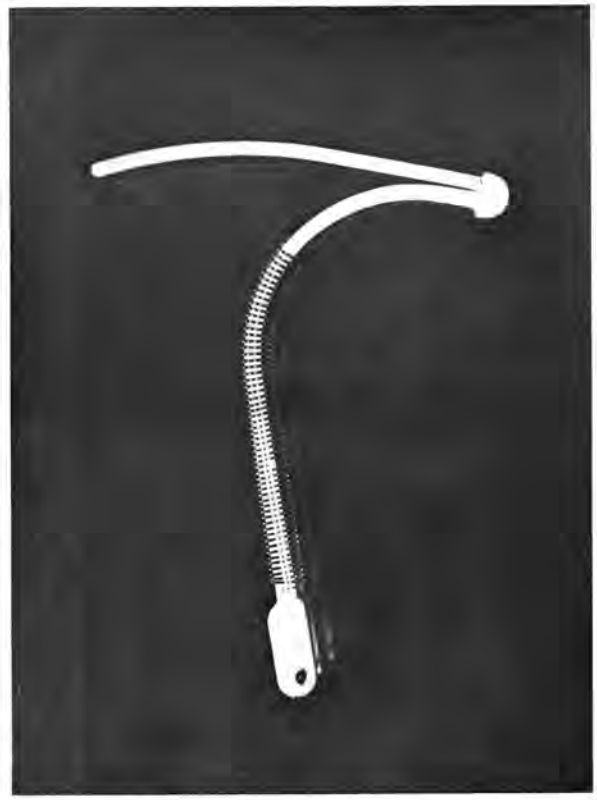

Fig. 1. Copper-7 intrauterine device (Gravigard)

RESULTS

A total of 497 insertions were carried out by 52 physicians, none of whom had previous experience of the Cu-7. Fifteen were academic staff members with previous experience of inserting the Lippes loop. The rest were trainee medical-officers or house-officers with little or no relevant experience. They carried out insertion of the Cu-7 under supervision of the academic staff members in charge of the clinic.

The age range of the study population was 18-45 years with 91% being under 35. The parity

range was 0-11. Seventy-nine percent were para 1-3 while 1.7% were nulliparous. The net cumulative termintion rates are shown in Table I. The annual rates of loss to follow-up were 18.3, 7.5 and 5.6 percent respectively in the first three years. Most of the IUDs were removed by the end of three years as recommended (Population Report, 1973).

Table I
Net cumulative termination rates per 100 women (1 SD) for 3 years of use of Copper-7

	MONTHS OF USE		
	12	24	36
Pregnancy	4.5 (1.0)	6.1 (1.1)	6.5 (1.2)
Explusion	3.7 (0.9)	4.9 (1.0)	5.1 (1.0)
Removal:			
Pain/Bleeding	4.2 (0.9)	5.4 (1.2)	6.9 (1.0)
Other Medical	0.3 (0.3)	0.7 (0.4)	0.5 (0.3)
Planning pregnancy	3.0 (0.8)	12.8 (1.5)	15.2 (1.4)
Other personal	3.6 (0.9)	3.9 (0.9)	7.6 (1.0)
Termination rate	19.3	33.8	41.8
Continuation rate	80.7	66.2	58.2
Woman-months	5,013	9,564	14,095

COMMENT

In the first year of use, the acceptability of the Cu-7 is high as indicated by the continuation rate. However the continuation rate in the second year is only comparable to that reported for the Lippes loop D (Tietze and Lewit, 1970). This poor performance is largely due to the high rate of removal for planning of pregnancy and reflects the low age and parity status of the study population. Evidently, the Cu-7 was used to space childbearing only.

The respective cumulative rates of accidental pregnancy are higher than those so far reported for the Cu-7. For example, in the first year a range of 1.4 — 3.2 pregnancies per 100 women is reported (Newton *et al.*, 1977; Simcock, 1976; Zipper *et al.*, 1976; Population Reports, 1973), whereas our rate is 4.5, even higher than the figure published for the Lippes loop D (Tietze and Lewit, 1970). Unrecognised downward displacement of the Cu-7 is commonly associated with pregnancy (Newton *et al.*, 1977); since this tends to occur in the first few months after insertion and is often asymptomatic, it is probable that our high pregnancy rate may be attributable, at least in part to the high default rate experienced in our clinic. Physician inexperience may also be relevant since correct fundal placement of the IUD demands practice.

The rates for explusion and for bleeding and/or pain are in the lower ranges of those reported. These favourable results may be due to the fact that over 98% of our patients were parous, in contrast to other series which include a sizeable proportion of nulliparous women. Reinsertion following expulsion of the Cu-7 is usually successful (Newton *et al.*, 1977) but our patients were often frightened and unwilling to have this done despite the most careful reassurance.

In the category of "other personal reasons" for IUD removal the majority were older, high parity women who elected to have sterilization. One translocated Cu-7 was detected in the 5th month of use and required laparotomy for removal. Significantly, no ectopic gestation and no IUD removal for pelvic infection was encountered in this study.

In conclusion, the use-effectiveness of the Cu-7 in our service clinic has been acceptable : use-related terminations were comparatively small in number and despite the relative inexperience and large number of inserting physicians, serious complications were few. This is fortunate as any adverse publicity may seriously hamper further acceptance of the IUD as had been the Singapore experience a decade earlier (Hu, 1970).

ACKNOWLEDGEMENTS

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INFLUENZA HI ANTIBODIES IN DENGUE-POSITIVE AND NEGATIVE SERA OF FEBRILE PATIENTS

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INTRODUCTION

INFLUENZA and dengue are very similar clinically in that they both cause sudden onset of fever, headache, muscle ache and prostration. Often they are mistaken for each other especially because outbreaks of these two diseases commonly occur at about the same time — during the rainy season. As a WHO National Influenza Centre, the Institute for Medical Research is duty-bound to keep a close surveillance of influenza outbreaks in the country and if influenza is not reported on time and the virus not isolated and identified early enough for precautionary measures to be taken by WHO, a serious pandemic due to a new strain of flu virus is likely to occur. Several cases of suspected dengue have already been found to be influenza during dengue outbreaks prior to this study.

The objective of this paper is to determine what proportion of dengue-suspected cases is, in fact, influenza and whether dual infection of dengue with influenza occurs.

MATERIALS AND METHODS

Paired, acute and convalescent, sera of febrile patients were examined for dengue haemagglutination-inhibition (HI) antibodies. Sera which showed significant rises in titre and those which were negative were subsequently tested for influenza HI antibodies.

The micro-HI test was used for both dengue and influenza. The dengue antigens types 1 to 4 were prepared by the sucrose-acetone method of Clarke and Casals. The sera was treated by the acetone-extraction method.

For influenza, the sera were inactivated at 56 C for 30 minutes prior to treatment with Receptor Destroying Enzyme (RDE) to remove non-specific inhibitors. The method adopted was that recommended by the WHO International Influenza Center for the Americas. The antigens tested used were A/Port Chalmers/1/73 and B/Hongkong/5/72.

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RESULTS

245 paired dengue-negative sera and 60 paired sera with significant rises in dengue antibody titre were tested for antibodies against A/Port Chalmers/1/73 and B/Hongkong/5/72. Of the dengue-negative sera, 74 pairs (30.2%) showed significant rises in titre, most of which were greater than 4-fold, against A/Port Chalmers antigen. None were positive against B/Hongkong/72 virus.

Only one (1.6%) pair of serum positive for dengue was also positive for influenza. The rise in titre was against A/Port Chalmers antigen and was from 1:20 to 1:80.

DISCUSSION

It may be noticed from this study that almost one-third of cases suspected of dengue turned out to be influenza instead. This is serious as the virus causing the influenza could have been a new strain with pandemic potentialities. Similar studies have been done in this laboratory (unpublished) which have shown also that many "dengue" cases were actually leptospirosis or rubella. Although overlooking leptospirosis may not be of much consequence, missing the diagnosis of rubella in a pregnant woman is definitely much more serious.

Physicians and clinicians are advised, especially in outbreaks of dengue fever, not to overlook the possibility that their PUO patients may in fact be suffering from influenza, leptospirosis or rubella. Any pregnant woman with fever and rash must be investigated not only for dengue but also for rubella. Likewise, influenza, being so similar to dengue fever in onset, should also be investigated

especially when upper respiratory symptoms are evident.

SUMMARY

30.2% of paired sera sent for dengue investigation turned out to be positive for A/Port Chalmers influenza and not for dengue. Dual infection of dengue with influenza was also observed but only rarely (1.6%).

The consequences of missing influenza in a dengue fever outbreak were discussed. Physicians were advised to keep in mind influenza, as well as leptospirosis and rubella, when investigating dengue fever outbreaks.

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PANCREATIC PSEUDOCYSTS: Clinical Features and Management

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INTRODUCTION

PANCREATIC PSEUDOCYSTS, a uncommon but not a rare condition, is a important complication of pancreatitis. At a recent clinical gastroenterology conference (Winship, 1977), it was concluded that the pseudocyst is "a serious condition with great morbidity, which constitutes a threat to life." Early recognition and careful management is essential if the serious complications of this condition are to be avoided.

We review the clinical features and management of six patients with pancreatic pseudocysts requiring surgical drainage, that we have seen in the past two years in the Medical and Surgical Units of the National University at the General Hospital, Kuala Lumpur.

RESULTS

Six cases of pancreatic pseudocysts occured between 1976 and 1978 amongst the admissions into the surgical and medical units of the National University at General Hospital, Kuala Lumpur. All patients were males; two were Malays, two were Punjabis, one was a South Indian and one was a Chinese. Their average age was 30.7 years (range of 20 to 41 years).

Etiology of pancreatitis and pseudocyst:

Abdominal trauma accounted for two patients (in one patient one week prior to admission and in another, four weeks prior to admission). One patient gave a definite history of heavy alcohol ingestion prior to onset of epigastric pain; one patient had proven gall-bladder disease with calculi. There was no etiology established in two patients (both Malays)

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Clinical Features:

The relevent clinical features in our six patients are summarised in Table I. Abdominal pain occured in all; five were epigastric in location and one was left hypochondrial. The duration of pain prior to admission ranged from three days to eight weeks. In three patients the pain was described as very severe and was associated with vomiting and nausea. Fever (average of 38 °C) was evident only in one of our patients. One patient had diarrhoea associated with epigastric pain and was admitted to the medical ward with the initial diagnosis of gastro-enteritis. A definite epigastric mass was palpable in three patients; in one patient, a vague epigastric mass was felt; the patient with the left hypochondrial pain had a mass in the epigastrium extending into the left hypochondrium. Only one patient complained on admission of progressive distension of upper abdomen. None of our patients were jaundiced at admission and there was no clinical evidence of ascites.

Table I
Clinical Features of Patients with Pancreatic Pseudocysts

Clinical Features	No. of patients with pseudocysts.
Epigastric pain	5
Left hypochondial pain	1
Nausea and vomiting	3
Fever	1
Diarrhrea	1
Palpable abdominal mass	5
Leucocytosis	2
Elevated serum amylase levels	6

The haemoglobin ranged from 9.8 gm percent to 14.2 gm percent. The white cell count averaged 8,600 cells per ml. (range of 7,000 to 10,800). Only 2 patients had leucocytosis (counts more than 10,000 cells per ml.). The serum amylase levels

were increased in all patients — the range being 300 to 2000 Somogyi unit/100 ml. (average being 914 Somogyi units/100 ml.). Of these, only two patients had values less than 800 Somogyi units/100 ml.

Five of the six patients had barium meal studies performed and all five had evidence of a large well defined smooth edged mass in the region of the pancreas causing displacement of the stomach, transverse colon and small bowel. The plain abdominal x-rays and the chest x-rays were not helpful in establishing the diagnosis.

Complications

No complication of pancreatic pseudocyst occured in our series.

Management

All six patients were surgically treated. Five patients had drainage via a cystogastrostomy and one patient had a cysto-jejunostomy and a Roux-en-Y procedure performed. There were no significant complications to the procedures. The follow-up period of these six patients has ranged from 6 months to 18 months and there has been no recurrence of the pseudocyst.

Size of pseudocyst:

The amount of fluid aspirated was measured in four patients in our series, and the average was 3.3 litres with a range of 1.7 litres to 4.5 litres.

DISCUSSION

The true incidence of pancreatic pseudocysts is difficult to estimate as some are too small to produce symptoms or enough symptoms to result in surgical exploration — and these are omitted in estimates of incidence. It is hoped that with the availability if newer radiographic (Eaton, 1973) and scanning techniques (Leopold and Asher, 1976), more information can be gathered about the true incidence. The occurrence of six cases over a period of two years compares well with the experience of Owens and Hamit (1977) who saw 19 patients with 21 pseudocysts in an American Hospital over six years.

Caravati *et al.*, (1966) records a peak age incidence of 30 to 50 years. Our patients were younger with an average age of 30.7 years.

In the West, alcohol abuse is the most common cause (Owens and Hamit, 1977) and up to 10 per cent of patients with alcoholic pancreatitis may develop a pseudocyst (Caravati *et al.*, 1966). Only one of our six patients had a history of alcohol abuse. The true incidence of traumatic pseudocysts has been increasing and two of our six patients had traumatic pancreatic pseudocysts. Owens and Hamit (1977) noted two patients out of 19 with proven biliary tract disease; we had one such patient.

The clinical features noted in our patients were fairly typical of pseudocysts. Clinical symptoms of abdominal pain, usually epigastric, nausea and vomiting, weight loss and some fever are most commonly noted, with diarrhoea and jaundice observed less frequently (Winship, 1977). One of our patients had fever; one had diarrhoea but none had jaundice. Although fever and leucocytosis are more common with pancreatic abscesses than with pseudocysts, they do occur with uncomplicated pseudocysts. In five of our six patients, the abdominal mass was palpable; experience elsewhere record palpable mass only in half the patients with the psedocysts (Winship, 1977). Although all our patients had elevated serum amylase, only 50 per cent of patients with pseudocysts show elevated serum amylase or lipase (Winship, 1977).

The radiographic techniques used in the diagnosis of pancreatic pseudocysts include chest radiograph (Komaki, 1974), supine radiograph of the abdomen, barium meal and hypotonic duodenography (Eaton, 1973). In our six patients, the chest x-rays and the plain abdomen x-rays were not useful; the barium meals were helpful in the diagnosis. Direct radiological and scanning techniques becoming useful are ultrasonography (Leopold, 1976), selective coeliac and superior mesenteric and subselective pancreatic angiography (Reuter, 1972). The use of isotopic pancreatic scanning has been disappointing and the role of computerized axial tomography (a new and primising technique) has not been fully established in the diagnosis of pancreatic disease. None of these techniques were employed in our six patients as the clinical diagnosis was clear.

Our present knowledge of the natural history of pancreatic pseudocyst is incomplete. There is evidence to show that some pseudocysts do resolve

spontaneously (Bradley, 1975). Conservative medical management may have a place in some selected patients with uncomplicated pseudocysts. This involves close serial observation for several weeks or until resolution occurs. The serial observation should include clinical means (e.g. size of abdominal mass), serial ultrasonography (as it is inexpensive and non-invasive) and serial creatinine-amylase clearance ratio determination (Vagerier, 1969). Surgical intervention earlier than 6 weeks of onset of acute pancreatitis has a mortality of 60 per cent; intervention after 6 weeks has a mortality of 9 per cent (Carilli, 1967). Surgical intervention however is indicated for enlarging cysts, symptomatic cysts, persistent cysts and complicated cysts. In all our 6 patients surgical drainage was only performed after 6 weeks of the acute episode.

Although we had no complication, the important ones include the pseudocyst as a space occupying lesion, conversion to an abscess, haemorhage into the pseudocysts or from the pseudocyst, perforation or rupture, jaundice and intestinal obstruction.

All our six patients with pancreatic pseudocysts had internal drainage of the cysts performed; five has cysto-gastrostomy, and one, a cysto-jejunostomy and a Roux-en-Y procedure. Although external drainage was satisfactory, Owens and Hamit (1977) felt that the preferred treatment for pancreatic pseudocysts was internal drainage particularly cystogastrostomy. In the surgical treatment of pseudocysts the device of operation depends on the location of the pseudocysts and the condition of the patient. A biopsy is often indicated to rule out cystadenocarcinoma, as five of the patients from the Mayo Clinic with cancer and pancreatitis developed a pancreatic pseudocyst (Gambill, 1971).

In conclusion we feel that it would be safe to observe (with serial evaluation) an uncomplicated acute pancreatic pseudocyst for 3 to 5 weeks. If the pseudocysts does not resolve by then, surgical treatment is the rational therapy.

SUMMARY

The clinical features and management of six patients with pancreatic pseudocysts occuring between 1976 and 1978 in the Medical and Surgical units of University Kebangsaan is reviewed. Epigastric pain, nausea and vomiting, a palpable abdominal mass and elevated serum amylase levels were common findings in the six patients. None of the patients had any serious complications of pseudocysts. All had surgical intervention and internal drainage of the pseudocysts; five had cystogastrostomy and one had cysto-jejunostomy and a Roux-en-Y procedure performed. The clinical features and management of pancreatic pseudocyst is briefly reviewed.

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CONGENITAL FACTOR VII DEFICIENCY PRESENTING AS IRON DEFICIENCY ANAEMIA — CASE REPORT

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INTRODUCTION

CONGENITAL Factor VII Deficiency was described by Alexander in 1951 (Wintrobe, 1974, Hardesty, 1974). By 1964, 40 more cases were added. Approximately 70 cases of Hereditary Factor VII Deficiency have now been reported (Wintrobe, 1974). The inheritence is autosomal, heterozygotes having a partial deficiency and homozygotes having more severe deficiency (Marder, 1964).

Both sexes are affected equally. While certain haemorrhagic manifestations in this condition are shared by both sexes, epistaxis and haemarthrosis have a male predilection while menorrhagia is severe enough to cause signs of iron deficiency (Owen, 1964). We report such a patient who was in cardiac failure as a result of iron deficiency due to menorrhagia.

CASE REPORT

Patient, an 18 year old student, admitted with a history of about week's duration of dyspnoea, swelling of legs and loss of appetite. She bled excessively during her periods in the last three years. Apart from mild haemarthrosis and epixtaxis, she had no history of bruising either spontaneously or after a trauma. Nor any history of prolonged bleeding after a cut or after dental extraction was elicited. She did not have any malaena or haematuria. Her diet seemed adequate. There was no history suggestive of diseases of the cardiovascular system, renal or liver.

She had an elder brother who had swelling of the knee which subsided spontaneously. She had three other brothers and sisters who do not give any history suggestive of haemostatic disorder.

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Examination revealed extreme pallor, angular stomatitis, loss of papillae of the tongue, and oedema without jaundice. There were no bruises or petechial haemorrhages. Both fundi showed haemorrhages. Lymphadenopathy, hepatosplenomegaly or sternal tenderness was absent. Hess's test was negative. There was evidence of congestive cardiac failure.

The provisional diagnosis made was of iron deficiency anaemia due to menorrhagia and confirmed by laboratory investigations. Laboratory investigations which confirm the diagnosis of iron deficiency anaemia were carried out. There include the haematological indices, blood film, serum iron, total iron binding capacity and bone marrow iron stores.

She was treated for her cardiac failure with frusemide and digitalis. Her iron deficiencies was corrected with packed cells, dose iron infusion followed by oral iron.

In the course of investigations for her menorrhagia, tests of haemostatic functions such as prothrombin time, partial thromboplastin time, clot retraction, clot stability test and thrombin time were done which revealed Factor VII Deficiency. Acquired causes of Factor VII Deficiency were looked into by carrying out liver function tests, the Euglobin clot lysis time, and by looking for LE cells and fibrin degradation products, but was not detected.

Family studies showed one brother had clinical signs of haemarthrosis and two out of five in the family had laboratory evidence of Factor VII Deficiency as indicated by a normal partial thromboplastin time and a prolonged prothrombin time.

DISCUSSION

Iron deficiency anaemia, the presenting feature in this case, was obviously due to menorrhagia. This had affected the patients for three years

without the cause being determined. Laboratory investigations concluded that the menorrhagia is the result of congenital Factor VII Deficiency. Although rare, it is mandatory on the part of the physician to investigate along these lines in patients with iron deficiency with menorrhagia; less cases of Factor VII Deficiency be missed. Thus more cases may come to light if we make this a routine procedure in the investigation of anaemias. Owen (1964) reported the following percentage of occurrence of the above findings, epistaxis (42%) haemarthrosis (26%) and haematuria (6%).

The patient did not have prolong bleeding after trauma which is in line with Hall's (1964) finding there is paucity of episodes excessive bleeding after trauma or surgical procedures other than dental extraction.

One brother had haemarthrosis. He was found on laboratory investigations to have Factor VII Deficiency. Owen (1964) considered Factor VII of 85% to be normal, 25% — 69% to be heterozygotes and less than 25% to be homozygotes.

Eliciting family history is often a neglected facet of clinical examination. This patient is a case in point to stress the significance of such history taking ritual. So much can be assessed even prior to laboratory investigation.

All the three patients seen by Owen (1964) had anaemia. In these cases, coagulation defects were not initially considered. Since patients may present with menorrhagia the tendency is to attribute the iron deficiency anaemia to menorrhagia. Treating the symptoms of iron deficiency anaemia per se without detecting the actual cause will be of no avail. Again any radical procedures, if contemplated for surgery can be beset with problems of severe bleeding. This can be channelled with care once we know the cause.

SUMMARY

An 18 year old girl who presented with cardiac failure as a result of Iron Deficiency anaemia due to menorrhagia. She was treated for iron deficiency anaemia until investigation of haemostatic functions revealed Factor VII Deficiency. This disorder is inherited as an autosomal recessive trait. Though clinical evidence of Factor VII Deficiency was found in one member of the family, laboratory investigations revealed deficiency in the other members of the family.

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CALCINOSIS OF HAND AND AXILLA IN POLYMYOSITIS/DERMATOMYOSITIS

A. ZULKIFLI

INTRODUCTION

POLYMYOSITIS is an autoimmune disease which may present in many ways (Bradley, 1977). As a result, various classifications have arisen over the years (Walton, 1958, Currie, 1971, Pearson, 1972). This reflects the variability in clinical and pathological findings. Classification provides a guide to prognosis and the response to therapy (Pearson, 1971). The first criteria for the diagnosis was by De Vere (1975). The clinical criteria were muscle weakness, usually proximal and symmetrical, as well as muscle pain and tenderness, while the laboratory criteria included a muscle biopsy showing perivascular inflammatory cell infiltration with or without muscle degeneration, electromyography findings, and raised serum creatinine.

Earlier on (Rose and Walton, 1966) the grading system used for disability was done. Unless the criteria are specified, many clinical studies may be contaminated with a wide spectrum of neuromuscular disorders, denervating disorders, metabolic and connective tissue disorders. We would like to report a patient who initially presented with what looked like a metabolic disorder.

CASE REPORT

Patient, 15 year old male, referred from the Orthopaedic Clinic with one year history of painless whitish lumps over the left hand and the right axilla which progressively increased in size. The swelling, sometimes, flakes off. He dis not have any joint pains, haematuria nor abdominal pain.

About the same time, he experienced difficulty in getting up from the squatting position. He had no difficulty in lifting his hands. With this he noticed wasting of the shoulder girdle and hip girdle muscles. Initially the muscles were painful but in the last six months this has improved. There was some weight loss. Bowel habits were normal, so was his swallowing.

His gait was unsteady for five years and he noticed that his feet were deformed. Examination revealed periorbital oedema without heliotropic rash. No oedema was detected. Patient was thin.

There were minute ulcers at the tips of the fingers, otherwise there was no deformity. A whitish, non-tender calcinosis of about two centimeters diameter was seen and felt at the first metacarpo-phalangeal joint of the left hand (Fig. 1). No wasting of the small muscles of the hand was detected. There was loss of crease on the dorsum of the fingers. The nails showed pitting and looked fragile. Calcinosis of similar size was detected in the right axilla (Fig. 2).

Fig. 1. Calcinosis of left hand.

Neck muscle was of normal power. There were bilateral symmetrical wasting, with tenderness, of the muscles around the shoulder and hip joints. No particular distribution of wasting was noted. No was there any fasiculation. The weak muscles were of grade 3. Reflexes were slightly diminish in the upper limbs but those in the lower limbs were more pronounced. The plantars were down going.

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Fig. 2. Calcinosis of right axilla and left thigh which is covered by dressings.

Sensations were intact. His gait was waddling. There was talipes equinus varus and pes cavus bilaterally.

Laboratory investigations revealed a raised serum creatinine phosphokinase, while the electromyography showed short polyphasity, fibrillations, and positive short waves. Biopsy of the deltoid muscle of the right arm showed chronic inflammatory changes. X-rays of the spine showed spina bifida occulta. Investigations for metabolic disorders such as serum calcium and phosphate, fasting lipids and serum uric acid and for connective tissue disorders such as antinuclear factor and L.E. cells revealed no abnormal findings.

He was put on high dose of Prednisolone initially and his muscle power improved from grade 3 to grade 4. He is now on a lower maintenance dose of Prednisolone. However, his calcinosis remained static. So were his talipes equinus varus and pes cavus.

DISCUSSION

Our patient was about 14 years old when he developed his first episode of polymyositis. The age distribution is a bimodal curve with peaks in the groups from 5 to 15 years and 50 to 60 years of age. (Bohan, 1975). The distribution of muscle weakness though proximal in two-thirds of patient, is diffuse in pattern and does not show the specific involvement in some groups of muscles and sparing of others as in muscular dystrophies (Bradley, 1977). This case showed similar features except that the lower limbs were also involved distally with talipes equinus varus and pes cavus. X-ray of the spine revealed the presence of spina bifida occulta. Because of his walking with a waddling gait and had difficulty in getting up from squatting (Grade 5 disability, Rose, 1966), he had proximal weakness. Probably his feet deformities were the result of the spina bifida occulta though there is tendency for polymyositis to develop atrophy and contractures in children (Pearson, 1972).

Raised serum creatinine phosphokinase is not confined to polymyositis but also occurs in muscle dystrophies (Bradley, 1977). However, it is important to think of polymyositis when faced with a problem of muscle weakness since its presentation need not always be classical.

The presence of calcinosis may imply a metabolic disorder such as gout or hyperlipidaemia. Gout, though often presenting with joint pains, is sometimes associated with muscular pains. Calcinosis occur in about 4% of cases of dermatomyositis and it is more common in children (De Vere, 1975). The patient showed some improvement in muscle weakness when treated. Children show good recovery and become asymptomatic three to five years later. By eight years, the disease burnt itself in 80% of the cases.

Hence polymyositis is a treatable condition and responds well to Prednisolone. Therefore the condition should be recognised early in order to avoid contractures. This is more so in children as the response is better and contractures occur more frequently.

SUMMARY

A fifteen year old boy presented with a year's history of weakness and wasting of hip and shoulder girdles with wasting of the distal muscles of the legs associated with talipes equinus varus and pes cavus. He had calcinosis of the left hand and right axilla. Clinical examination and laboratory investigations revealed that he had polymyositis with calcinosis and spina bifida occulta. His muscle weakness responsed to treatment with Prednisolone. This condition may be mistaken for muscular dystrophies or metabolic disorders.

ACKNOWLEDGEMENT

I am grateful to Prof. M. Kannan Kutty for the help and encouragement given and to Puan Baridah Abdullah for the secretarial help.

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CORRESPONDENCE

ARTHRITIS: A VITAMIN DEFICIENCY DISEASE

Dear Sir,

This is the title of a monograph written by the distinguished Biochemist, E.C. Barton-Wright, D.Sc., F.R.I.C., F.R.I.C., F.I.Biol., published in 1973 and reprinted in 1974 and in 1975.

The purpose of the monograph is to prove that arthritis, both osteoarthritis and rheumatoid arthritis, is due to a deficiency of pantothenic acid in the highly processed foods of modern diets. In the U.S.A. in 1965 there were known to be 10,000,000 arthritics, in 1973 there were 30,000,000. In Great Britain in 1963 there were 3,000,000 arthritics and in 1973 6,000,000.

In my experience the same is true of Malaysia. Nearly a quarter of my patients nowadays come to me complaining of rheumatism of various sorts.

The efficacy of calcium pantothenate is almost miraculous. It two tablets, 50 mgm size, are given in the morning, the same at midday and the same at night, i.e. six tablets per day, continued for weeks or months, the gratitude of one's patients is touching. The vitamin is non-toxic and has no side effects.

D. Reid Tweedie,
Estate medical Officer,
Sungei Siput N.
Perak.

COMPARATIVE STUDY OF THE BIOAVAILABILITY AND DISSOLUTION BEHAVIOUR OF FIVE BRANDS OF TETRACYCLINE CAPSULES

Dear Sir,

It is well to know that the various brands of tetracycline capsules in this country differ in bioavailability and hence in efficiency, but what practical value does such a study contribute unless the indentity of the makes of drugs is revealed to doctors who use them. Questions of ethics need not arise if the study (by Gan *et al.*, 1978) was done independently and scientifically, which presumably was the case.

Yours faithfully,

Neoh Choo Keong
M.B.,B.S.

Neoh Klinik,
Jalan Tunku Ibrahim,
Alor Star, Kedah.

REFERENCE

Gan, E.K., Lim, B.S. and Napsah bt. Mahmud (1978) Comparative Study of the Bioavailability and Dissolution Behaviour of Five Brands of Tetracycline Capsules, *Med. J. Malaysia*, 33, 72-75.

BOOK REVIEWS

CURRENT CONCEPTS IN THE DIAGNOSIS AND TREATMENT OF PARASITIC AND OTHER TROPICAL DISEASES IN SOUTH EAST ASIA

Proceedings of 18th SEAMEO-TROPMED Seminar, Kuala Lumpur, 2-5 Aug. 1977

A VERY successful regional seminar covering the above theme was held at the Institute for Medical Research. It was well attended by participants from SEAMEO and other neighbouring countries including Australia, Hong Kong, India, Indonesia, Japan, Malaysia, Philippines, Singapore, Sri Lanka, Taiwan and Thailand. Among the eminent scientists from outside this region, who participated, were Professors Beaver, Gilles, Gordon-Smith and Peters. A total of 66 papers were presented and were grouped in the following sessions: Helminthic diseases, Protozoan diseases, Microbial diseases, Nutritional disorders, blood disorders and Free papers. A stimulating keynote address was given by Professor Beaver, titled: "Communication in the Scientific Community". Of the 66 presentations, 41 are represented in full and 25 as abstracts, in the proceedings. The lively and highly pertinent discussion after each presentation is also recorded.

Due to space limitation, it is difficult in this review, to give the full titles and the names of all the authors, much less an abstract or critical review of each paper. A brief title is given and if there are more than 2 authors, the name of only the first author is given.

HELMINTHIC DISEASES

The session on Helminthic Diseases included the largest numbers of papers, e.g. 21; 9 on filariasis, 4 on drug trials of intestinal helminths, 3 on schistosomiasis and 5 other papers. Of the papers on filariasis, 5 deal with survey and control programmes; 1 in Province Wellesley, Peninsular Malaysia (Chee); the second in Java, Indonesia (Mahfudin *et al.*]; the third in South Sulawesi, Indonesia (Partono & Borahima); the fourth, a 16 year control programme in Thailand (Harinasuta & Smithasari) and the fifth, a trial of a DEC medicated salt in Taiwan (Fan *et al.*). The other 4 papers in filariasis are diagnostic in nature, two dealing with serological diagnostic techniques, the ELISA test (Kwa & Smyth) and the IFA technique (Ponnudurai); one differentiating the microfilariae of *B. malayi* from that of *B. pahangi* (Sucharit & Harinasuta); and the other comparing the thick smear with the nuclopore technique (Idris & Partono).

Clinical trails were reported, using Mebendazole against hookworm (Migasena *et al.*); against whipworm and hookworm (Bunnag *et al.*) and against *Taenia saginata* (Cabrera). A comparative trial using Oxantel/Pyrantel and Mebendazole was made against polyparasitic helminthic infections (Dissanaike).

Of the three papers on Schistosomiasis, one is a world-wide review (Gilles); the second on diagnosis (Sornmani & Vivathansesth); and the third, a drug trial using Ambihar against *S. japonicum* infection (Blas *et al.*).

Other papers in this session include a rural survey of soil-transmitted helminths (O'Holohan), a review of viseral larval migrans (Beaver); the value of radiology in the diagnosis of *Ascaris* infection (Singh); vaccination against taeniasis — cysticercosis in rats (Kwa & Liew); and a note on operculated eggs in stool (Vajrasthira).

PROTOZOA

In this section, 9 papers were presented on malaria and 4 on amoebiasis. The first paper (Peters) was a current review of drug treatment and the problems associated with it. Two papers dealt with field trials of drugs against chloroquine resistant *P. falciparum;* the first, a trial in Malaysia (Ponnampalam) using Doxycycline and the other in Thailand (Doberstyne *et al.*) using Mefloquine. The latter drug, a 4-quinoline

methanol, shows promixing results. There are two papers on the *in vitro* response of *P. falciparum* to anti-malarial drugs like chloroquine and quinine (Teerakiartkamjorn *et al.*) and to these two drugs plus amodiaquine (Sucharit & Eam-Sobhana). The sporonticidal effect of fansidar was tested in relation to quine and quinine pyrimethamine, and an increased viable gametocyte production was reported (Andre & Doberstyn), an important epidemiological consideration in areas where fansidar is used extensively. The other malaria papers included a presentation on the peripheral lymphocyte populations of Thai malaria patients (Wells *et al.*); a report on malaria in Malaysian army personnel (Natarajan & Singh) and a 15 year review of malaria research at the SEATO Medical Research Laboratory, Bangkok (Segal).

The presentations on amoebiasis were on drug trials, two of these using Timidazole, one against liver abscess (Kundu *et al.*) and the other against intestinal amoebiasis (Swami *et al.*). The third trial (Adjung *et al.*) used Tiberac against intestinal amoebiasis and the last, a short treatment with Ornidazole against both intestinal and liver abscesses (Lasserre).

MICROBIAL DISEASES

This session contains 11 presentations on the following infections: 3 fungal, 3 bacterial, 2 rickettsial and 3 viral. The presentations on the fungal and bacterial infections mostly pertain to the diagnosis, clinical pattern and treatment of the following: Chromomycosis (Kutty), Cryptococcus meningitis (Alora), vaginal candidiasis (Sjarifuddin *et al.*), typhoid fever (Zulkarnain), *Neisseria gonorrhoeae* resistance (Punsalang) and *Mycobacterium* ulcerans (Pettit). The papers on viruses include one on diagnosis (Gordon-Smith) and two on hepatitis B. virus infections, one concerning the incidence in Bangkok (Scott *et al.*) and the other on serological tests (Snitbhan *et al.*). Of the two papers on the Rickettsia, one pertains to the diagnosis of scrub typhus (Coolbaugh) and the other an immunological study on *rickettsia sennetsu* (Tachibana *et al.*).

NUTRITIONAL DISORDERS

There are 5 papers in this section and include: malnutrition and the immune response (Suskind); scrum protein fractions (Migasena & Schelp); proteinase inhibitors (Schelp & Migasena); protein calorie malnutrition (Balakrishnan) and hypovitaminosis A (Ng) the latter two reports from Malaysia.

BLOOD DISORDERS

The 5 papers in this session deal with: rarer tropical anaemias (Gunz); serum immunoglobulins (Yadav *et al.*); anti DNA activity in the diagnosis of immune complex disorders (Lopez *et al.*); lymphocyte transformation studies in leprosy (Smelt & Liew); and the house-dust mite and rhinitis (Tan & Thomas).

FREE PAPERS

This section contains 11 papers on a wide assortment of subjects to include: growth and development during the first three years of life (Guzman *et al.*); diptheria and tetanus antitoxin levels in Thai children (Petchclai *et al.*); integrated family planning and parasitic control (Harinasuta & Sornmani); chaemotherapy in viral infections (Lao *et al.*); the ELISA test (Cross & Chi); enteric fever (Singh); cobra bites (Sarvanathan); serological diagnosis of febrile illness (Brown *et al.*); toilet facilities and faecal borne disease (Roundy); management of febrile illness (Saunders *et al.*) and neonatal tetanus (Hasbullah & Balakrishnan). The last 6 studies were done in Malaysia.

There is an abundance of up-to-date review and original material within the main theme, which makes this publication a very useful source for research workers and for those interested in the diagnosis and management of parasitic and other tropical diseases. Copies of this publication are available, for US$8.00, from the Co-ordinator, TROPMED Central Office, SEAMEO-TROPMED Project, 420/6, Rajvithi Road, Bangkok 4, Thailand.

Shivaji Ramalingam

NOTICE TO CONTRIBUTORS

The Medical Journal of Malaysia welcomes articles on all aspects of medicine of interest in this Region in the form of original papers, research notes, communications and correspondence. The Journal also welcomes brief abstracts, of not more than 50 words, of original papers, published elsewhere, concerning medicine in Malaysia. Articles are accepted for publication on condition that they are contributed solely to the Medical Journal of Malaysia. Neither the editorial board nor the publishers accept responsibility for the views and statements of authors expressed in their contributions. The board further reserves the right to reject papers read before a society. To void delays in publication, authors are advised to adhere closely to the instructions given below.

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All manuscripts should be submitted in duplicate to Professor Paul C.Y. Chen, Hon. Editor, Medical Journal of Malaysia, c/o Faculty of Medicine, University of Malaya, Kuala Lumpur 22-11. Manuscripts should be typed on one side of quarto paper in double-spacing throughout (including tables, legends and references), with wide margins. The title page should include the title of the paper, initials and name(s) of the author(s), degrees and address. Introduction, materials and methods, results, discussion, summary, acknowledgements and references should follow. Scientific names and foreign words must be underlined. Papers may be submitted in Bahasa Malaysia but must be accompanied by a short summary in English.

Tables and Illustrations

Each table should be typed on a separate sheet of paper in double-spacing and should be fully labelled so as to be comprehensible without reference to the text. The contents of all tables should be carefully checked to ensure that all totals and subtotals tally. All measures should be reported using the metric system.

All illustrations and diagrams should be in Indian ink on separate sheets of thick, smooth white paper or Bristol board or in the form of photographs printed on glossy paper and should be larger than the finished block, to allow for reduction. They should bear on the reverse side the author's name, short title of the paper, the figure number and an arrow indicating the top of each illustration. All figures should be fully labelled so that each is comprehensible without reference to the text. Legends and captions should be typed on separate sheets and numbered correspondingly.

All illustrations and diagrams should be referred to as figures and given arabic numbers, while tables should be given roman numbers. Their approximate position in the text should be indicated. Illustrations and tables should be kept to a minimum.

References

References to the work of other authors should be cited in the text according to the following convention:

Peck and Lowman (1970) demonstrated .....
It was demonstrated (Peck and Lowman, 1970) that .....
The survey (Meyer *et al.*, 1971) showed .....

For works written by more than two authors, the first author only is named followed by the words *et al.* as shown above.

References should be listed only when cited in the text, in alphabetical order, in the following form: Surname of author(s), initials; year of publication; title of paper; title of journal (abbreviated according to the World List of Scientific Periodicals and underlined); volume number double-underlined; first and last page numbers of the work cited:

Peck, M. and Caster, V.A. (1965) Enterocolitis of infancy, *j. trop. Pediat.*, **28,** 155 — 160.

Up to four authors should be cited. If more, the first three authors are cited followed by *et al.* Book citations should include the author(s) name, date, title, edition, place of publication, publishers and pagination. Unpublished data or personal communications are not to be included in the list of References, but may be cited in the text.

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CORRIGENDA

Vol. XXXIII No. 2

p. 102, name of author
name of second author should be altered to
YEOH OON HOCK

p. 104, column 2, line 27
Ninety per cent should read Ninety-nine per cent

p. 146, heading
Trachael should read Tracheal

p. 162, title
Hysterical Muslim should read Hysterical Mutism

Vol. XXXIII No. 3

p. 201, 1st paragraph, line 1
Metal illness should read as Mental illness

pp. 202 and 204
p. 204 should appear as p. 202
p. 202 should appear as p. 204

p. 226, address
University Kebangsaan Malaysia shou'd read as University Kebangsaan Malaysia

Index to Vol. XXXIII — June 1979

SUBJECTS

AUTHORS