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# GUEST EDITORIAL

# USING EPIDEMIOLOGY IN CLINICAL MEDICINE

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EPIDEMIOLOGY, the study of disease in population, is traditionally the concern of physicians doing public health and has been paid little attention by those caring for individual patients. Yet most of the facts we use as clinicians are drawn from populations, and the decisions we make concerning individuals depend on the groups into which we categorize them, often subconsciously. There is thus increasing interest in "clinical epidemiology" and in applying the logic of epidemiologic inquiry to general medical practice.

When a physician evaluates a patient presenting with fever, he typically considers such features as occupation, age, race, sex, and place of living or travel, along with the presence or absence of other symptoms, physical signs, and laboratory findings. This categorization places the patient in a series of overlapping subgroups of the population which have differential chances of having certain diseases and of benefiting from certain courses of action or therapy. In epidemiologic terms, he establishes the patient *characteristics* which influence the probability of having, or not having, certain *conditions*. If the febrile patient also has chills and headache and is a young male working on a new oil palm land scheme, the chances increase that he may have a rickettsial or malarial infection, and indeed might be cured by a single dose of doxycycline or pyrimethamine-sulfadoxine. One would then pay particular attention to lymph nodes and spleen on physical exam and probably seek a thick blood film and hemaglutination titer. What is transpiring in the course of such clinical judgment, often in only a few minutes time in a busy practice, is the estimation of a series of "conditional probabilities" — the likelihood of D given the existence of A and B but not C. The basis for making these quick decisions — for assigning the relative probabilities on which we must act — is a cumulative set of associations observed in previous patients, from our own practices and those reported by others, which suggest that people with certain characteristics are likely to have (or not have) a certain condition.

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Unfortunately, apparent relationships are often misleading. Epidemiologic experience suggests several questions worth asking when evaluating associations that seem clinically important. 1) Is there a problem with false labelling or *bias* in the observations used? 2) Are the data being compared with an appropriate *denominator group?* 3) Is it a *secondary association*, not a direct one? 4) Could the association be simply due to *chance* or sampling variation?

The pervasive problem of *bias* simply refers to the fact that the symptoms, signs, and tests we rely on clinically often do not represent what they purport to. There may be problems with *reliability* — patients recall selectively what they think is important, and observers in both the laboratory and the examining room tend to find what they expect to find and to have idiosyncratic preferences in the classifications they use. There are also problems with *validity* — we can rarely measure directly the phenomena of interest and must use tests and criteria that though *sensitive* may have frequent false positives, or though *specific* have frequent false negatives. The enlarged spleen is a sensitive criterion for malaria in that, at least by the second week of infection, it occurs in the great majority of patients. However, it may be falsely positive, i.e. enlarged due to prior infection unrelated to the current fever, or falsely negative early in the infection. If reliably performed the thick film will be positive only when malaria parasites are in the blood and is thus a

specific test; however it may be falsely negative if taken at a low point in the parasitemia cycle. Another bias problem, termed *selection*, refers to patients coming under study in ways that may give results unrepresentative of other populations. For example, the character of malaria as seen in a teaching hospital differs from that seen in an estate dispensary which in turn differs from an urban general practice. The critical physician must constantly evaluate the effects of these various biases on the data he uses — whether in a published report or in his own set of clinical impressions.

One of the most common fallacies in associations drawn from clinical work comes from examining only cases without an appropriate comparison or denominator group. One may be impressed that most babies with colic are being bottle-fed. But to draw an association between bottle-feeding and colic one must then examine what proportion of babies one sees without colic are also bottle-fed. It may be that one is simply seeing more bottle-fed babies. Simple as this sounds, this fallacy occurs often in subtle forms. For example, a distinguished clinical observer reported data from his practice showing that most men with chronic bronchitis were smokers whereas most female bronchitics were non-smokers. He concluded thus that something other than smoking underlay bronchitis in the female. What was lacking? The denominator data as to the proportion of non-bronchitic women who smoked, which would likely be smaller than that for those with bronchitis. One thus needs regularly to ask, when examining an interesting set of numbers, what is the relevant denominator with which the numerator data should be compared?

Another recurrent problem is that the association may be real but only a secondary one. For example, one might well find an association between refrigerators and coronary heart disease because both are associated with affluent, stressful modern life, not because cold drinks bring on heart attacks. The following is a more clinically important example of the same problem. Hookworm infection in Malaysia is common but usually does not involve enough worms to cause anemia. Yet one might find an association between the presence of hookworm eggs in the stool and anemia because the infection is a marker for living amidst poor sanitation and hence for lower economic status, which in turn is related to the poor nutritional status which likely produces the anemia. Thus one must ask if the characteristic studied (hookworm infection) is likely leading directly to the condition (anemia) or if it is simply a proxy indicator of some other characteristic (economic status and nutrition) which may be the direct (and actionable) association.

Finally there is the problem of whether the observed association could happen by chance alone. This determination of course is the main function of statistics, and there are many tests used. However, the $p < 0.05$ often seen in articles usually says simply that the observed difference in means between groups (most commonly using that t test) or in distribution of individuals among categories (with the chi squared test) would occur by chance with the numbers given less than one time in twenty. The most commonly useful do-it-yourself statistical assessment is to make a two by two ("contingency") table cross-tabulating the number of individuals with and without the characteristic and condition of interest. Looking at the association of bottle-feeding (BF) with colic (CL) as suggested above, we would tabulate:

| | | Colic YES | Colic NO | Total |
|---|---|---|---|---|
| Bottle-feeding | YES | a | b | $t_1$ |
| Bottle-feeding | NO | c | d | $t_2$ |
| | Total | $t_3$ | $t_4$ | T |

and calculate: $X^2 = \frac{(ad-bc)^2 T}{t_1 t_2 t_3 t_4}$

If the result is four or greater the chances are only 1 in 20 that the distribution would occur by chance. Often just putting the data in the tabular form will give a sense of likely significance, but the calculation is simple enough with the generally available pocket calculators. If any of the numbers a, b, c, or d are smaller than five statisticians prefer a more exact test, but still this one will give an approximate estimate. "Statistical significance" is largely dependent on the numbers studied and should not be confused with "clinical significance". If four out of five patients treated for a rare fatal disease with medicine A live, and four out of five treated with medicine B die, the clinical

significance may be quite impressive even though the statistical significance will be marginal due to the small sample size. Of more general importance, clinicians should not be cowed by the complexity of the mathematics in a report. The math will usually be done properly; what requires scrutiny is the logic of the data put into the computation.

Epidemiology is basically a disciplined way of asking questions, and most of its rules are simply an organized form of common sense. Unfortunately, like most common sense, it is anything but common. The physician thus needs to develop his own critical sense for assessing the logic of associations on which his clinical decisions are based.

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# INSTITUTIONAL NEUROSIS: FEATURES AND ASSOCIATED FACTORS*

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## INTRODUCTION

METAL ILLNESS is still regarded with fear and shame despite the many advances in science and technology in the world. In the interest of society, such people are segregated by keeping them in asylums for purposes of caring for them, as they are considered to be both incapable of looking after themselves and a "threat" to the community. Some professionals however, question whether the mental hospital has any beneficial effect whatsoever beyond human custody. They see the goal of the mental hospital as serving to isolate deviant members of society (August, 1968; Goffman, 1961; Gove, 1972).

As a result of the large patient population and the small inadequately-trained staff, it is inevitable that the restrictive measures adopted for the few aggressive or potentially dangerous patients are extended to the rest of the harmless majority. The smooth running of the hospital thus, depends upon the submission of the patient with a minimum of resistance. The encompassing or total character of such a set-up is symbolized by the barrier to social intercourse with the outside world, by locked doors, high walls and windows bars, thus completing the description of a *"total institution"* as described by Goffman (1961).

In a *"total institution"* there is a basic split between a large managed group, conveniently called inmates, and a small supervisory staff. Each grouping tends to conceive of the other in terms of narrow hostile stereotypes; staff often seeing inmates as bitter, secretive and untrustworthy, while inmates often see staff as condescending, high-handed and mean. In this kind of oppressive atmosphere, patients gradually learn to surrender their existence to the staff and are no longer able to feel the need to think for themselves. In other words, they become "institutionalised."

Barton (1976) describes the syndrome of "Institutional Neurosis" seen in chronic patients as characterised by apathy, lack of initiative, loss of interest, submissiveness, lack of interest in the future, deterioration in personal habits, toilets and standards generally, loss of individuality and resigned acceptance that things will go on as they are — unchangingly, inevitably and indefinitely. Rosenham (1973) on the other hand, described the process as of "depersonalization" where patients are gradually robbed of their human dignity, deprived of many of their legal rights, and shorn of credibility by being labelled as "psychiatric". With restricted freedom of movement, he cannot initiate contact with the staff and his personal hygiene and waste evacuation are also monitored. The geographical distance from the general community, the loss of contact with families and the lack of community resources to rehabilitate the mentally ill, also contribute to the problem. Wing and Brown (1970) enumerate various factors which may handicap the resettlement of a mentally-ill patient which can be classified into three large groups as follows:

a) Disabilities present before the onset of illness
b) "Primary" disabilities which are basically part of the illness, such as incoherent thought processes, delusional motivation, catatonic slowness or apathy and,
c) "Secondary" handicaps which have been accumulated during the illness because of his own and other people's reactions to the illness.

The primary disabilities may be influenced by an understimulating social environment (social withdrawal) or social over-stimulation (delusion, hallucinations). Thus, the social environment may influence the patient's illness and also produce a secondary handicap or institutional neurosis.

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on as before (F), 63% were apathetic (A), while thirty-one per cent were found to have deteriorated in personal habits, toilet and standards generally (D). Although some of the patients showed mild to moderate degree of characteristic posture and gait (G), none of them were rated as severe (Table II and III).

After determining the degree of severity of each feature, the next step was to determine the extent to which a patient had the syndrome of "institutional neurosis". Thus, each patient was rated on all the seven features of "institutional neurosis" in terms of the absence or presence of that feature. An arbitrary rating of 1 was given in the absence of a feature and 5 if that feature was present. The lowest score of 7 denotes absence of "institutional neurosis" and the highest score of 35 denotes the presence of all the features of "institutional neurosis". Patients with a range of 8 to 25 were grouped as less severe cases of "institutional neurosis" while those with scores of 26 to 35 were classified as severe cases of "institutional neurosis".

The above table shows the classification of the sample into "severe" and "less severe" degrees of "institutional neurosis". Sixty-four per cent of the males and 54% of the females were rated as severe cases of "institutional neurosis". However, the difference is not statistically significant.

**Table II**

**Degree of Severity for Female Patients (N=50) on each feature of Institutional Neurosis**

| Features | Degree of Severity (No. of Patients) | | | | | Total No. of Patients with severe rating of 4 and 5 |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | |
| A — Apathy, loss of interest | 7 | 4 | 9 | 1 | 29 | 30 |
| B — Submissiveness | 0 | 0 | 3 | 0 | 47 | 47 |
| C — Lack of interest in future | 0 | 0 | 14 | 3 | 33 | 36 |
| D — Deterioration in personal habits | 27 | 4 | 1 | 0 | 18 | 18 |
| E — Loss of individuality | 0 | 1 | 3 | 34 | 12 | 46 |
| F — Resigned acceptance of things | 0 | 0 | 2 | 0 | 48 | 48 |
| G — Posture and gait | 18 | 26 | 6 | 0 | 0 | 0 |

**Table III**

**Degree of Severity for Male Patients (N=50) on each feature of Institutional Neurosis**

| Features | Degree of Severity (No. of Patients) | | | | | Total No. of Patients with severe rating of 4 and 5 |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | |
| A — Apathy, loss of interest | 7 | 4 | 6 | 1 | 32 | 33 |
| B — Submissiveness | 3 | 3 | 0 | 0 | 44 | 44 |
| C — Lack of interest in future | 2 | 0 | 4 | 3 | 41 | 44 |
| D — Deterioration in personal habits | 28 | 6 | 3 | 3 | 10 | 13 |
| E — Loss of individuality | 1 | 0 | 2 | 28 | 19 | 47 |
| F — Resigned acceptance of things | 0 | 0 | 2 | 0 | 48 | 48 |
| G — Posture and gait | 20 | 24 | 6 | 0 | 0 | 0 |

For further analysis, the relationship between the sociodemographic factors and the severity of "institutional neurosis" was studied (with the use of statistics). However, the severity of illness was found to be related on only two variables, that is, age and education for male patients. For males, the relationship between age and severity of illness was statistically significant at the 0.05 level and education was also found to be related to severity of illness, and statistically significant at the 0.05 level.

### Factors associated with Institutional Neurosis

The eight factors found to be present in the patient's environment as postulated by Barton (1976) and associated with "institutional neurosis" were also examined in the present study.

### Loss of contact with the outside world

Fifteen female patients were visited at least once in the first six months of admission compared to six male patients. This figure dropped to two visitors each for male and female patients in the past six months prior to the study.

### Enforced Idleness

Enforced idleness was determined in terms of the number of activities a patient was involved in. As shown in Table IV, 29 per cent of the patients made their own beds and 34 per cent helped to clean the wards. Seventy-one per cent of the patients were engaged inactivities ranging from one to three and only 29% were involved in more than four number of activities in the hospital. There were significant differences between the "less severe" and "severe" category of both the sexes in the number of activities and this difference was found to be statistically significant ($p < .001$).

### Brutality, Browbeating and Teasing

As shown in Table V, there were 16 females and 14 males who had a history of abuse and assault. Fourteen females and twelve males were indeterminate as they could or would not give any indication of abuse.

### Bossiness of Staff

Fifty-four per cent of the females and forty-two per cent of the males denied that there were too many regulations. The rest of the patients gave no response when asked about the too many regulations.

### Loss of personal friends, possessions and personal events

All of them had lost their personal friends. Seventy per cent of the patients were unable to form a close relationship. Table VI lists the type of things that the patients had as their personal belongings. Only 20 females and 8 males were reported to have some form of personal belongings. As shown in Table VII, the degree of severity of institutionalisation was found to be related to the number of personal belongings. This difference is statistically significant ($p < .001$) for female patients. As regards to the personal events, only 3 females and 3 males could remember their birthdays, 12 females and 19 males did not even know their names.

**Table IV**

**Number of Patients who are Involved in Various Ward Activities**

| Description of Activity | Females | Males | Total |
|---|---|---|---|
| (1) Make own bed | 13 | 16 | 29 |
| (2) Bathe by own self | 35 | 38 | 73 |
| (3) Help to serve food | 12 | 8 | 20 |
| (4) Wash own dishes | 6 | 1 | 7 |
| (5) Prepare own food | 0 | 1 | 1 |
| (6) Engage in O.T. | 6 | 3 | 9 |
| (7) Help to clean ward | 16 | 18 | 34 |
| (8) Go for walks | 43 | 34 | 77 |
| (9) Do gardening | 1 | 4 | 5 |
| Total | 132 | 123 | 255 |

**Table V**

**History of Abuse in Relation to Severity of Institutional Neurosis**

| History of Abuse | Females | | Males | | |
|---|---|---|---|---|---|
| | Less Severe | Severe | Less Severe | Severe | Total |
| Absent | 12 | 9 | 9 | 15 | 45 |
| Present | 9 | 7 | 7 | 7 | 30 |
| Indeterminate | 2 | 11 | 2 | 10 | 25 |
| Total | 23 | 27 | 18 | 32 | 100 |

$X^2 = 0.9414$ N.S. $X^2 = 0.5638$ N.S.

The aetiology of institutional neurosis is uncertain, however, as it is associated with many factors in the environment of the institution. Barton (1976) postulates eight factors associated with institutional neurosis namely loss of contact with the outside world, enforced idleness, brutality, bossiness of staff, loss of personal friends, possessions and personal events, drugs, ward atmosphere and lastly loss of prospects outside the institution.

Though the syndrome of institutional neurosis has been generally known to be prevalent in our mental institutions, however there has been no previous study done in Malaysia. The present study therefore aims to investigate the features of institutional neurosis as well as to ascertain the factors associated with this syndrome as postulated by Barton (1976), in Hospital Bahagia, a large mental hospital in Malaysia.

## METHOD AND MATERIALS

There were 50 male and 50 female subjects selected on the basis of random sampling from the long-stay wards which were separate buildings located at quite a distance from the main hospital and therefore were often neglected. Data was collected by personal interviews on structured questionaires.

## RESULTS

### Sociodemographic data

#### Age:

With a mean age of 49.1 years, the female age range was 27 to 84 years while the male age range was 24 to 79 years with a mean of 49.7 years.

#### Ethnic Group

The sample population comprised of 66% Chinese, 21% Malays, 11% Indians and 2% others, which is comparable to the hospital population distribution of various ethnic groups.

#### Duration of Stay

The range of stay varies from 2 to 37 years for the females and 2 to 31 years for the males. Average duration of stay for the females was 18.9 years and 19.8 years for males (Table I).

#### Marital Status

Thirty-six per cent were married females, while only 4% of the males were married.

**Table I**

**Duration of Stay in the Hospital**

| No. of Years | Females | Males | Total |
|---|---|---|---|
| 0 — 5 | 5 | 6 | 11 |
| 6 — 10 | 5 | 1 | 6 |
| 11 — 15 | 6 | 8 | 14 |
| 16 — 20 | 8 | 7 | 15 |
| 21 — 25 | 17 | 14 | 31 |
| 26 — 30 | 8 | 13 | 21 |
| 31 — 35 | 0 | 1 | 1 |
| 36 — 40 | 1 | 0 | 1 |
| Total | 50 | 50 | 100 |

#### Occupation

There were only two females who were skilled workers. Seventy-two per cent of the females and 78% of the males were unemployed.

#### Education

There were 7 females and 11 males who had been to primary schools, 2 females and 1 male with a secondary school background and 41 females and 38 males had never been to any school.

#### Diagnosis

A large number of the sample population were diagnosed as schizophrenic (73%) while 10% of the sample were mentally-retarded patients.

#### Features of Institutional Neurosis

Features of institutional neurosis were classified into seven major groups and each feature was further defined in terms of the degree of severity. Tables II and III show the distribution of the sample population according to the degree of severity on each of the seven features. The patients were rated for each feature on a five point scale measuring the degree of severity. A rating of 4 and 5 was considered to be severe and denoting the presence of that feature. On this basis, it was found that 91% of the patients were submissive (B), 90% had lost interest in the future (C), 93% of patients had lost of individuality (E), 96% of them were resigned to accepting that things will go

**Table VI**

**Number of Patients in Possession of Personal Belongings**

| Description of Possession | Females | Males | Total |
|---|---|---|---|
| (1) Suitcase | 1 | 1 | 2 |
| (2) Locker | 0 | 1 | 1 |
| (3) Own Clothes | 2 | 1 | 3 |
| (4) Thermos/Mug | 0 | 2 | 2 |
| (5) Comb/Brush | 11 | 1 | 12 |
| (6) Toothbrush | 5 | 2 | 7 |
| (7) Cosmetic/Shaving set | 1 | 0 | 1 |
| (8) Photographs | 0 | 0 | 0 |
| Total | 20 | 8 | 28 |

**Table VII**

**Number of Patients in Possession of Personal Belongings in relation to severity of Institutional Neurosis.**

| No. of Items Possessed by Patients | Females | | Males | | Total |
|---|---|---|---|---|---|
| | Less Severe | Severe | Less Severe | Severe | |
| Nil | 12 | 26 | 16 | 32 | 86 |
| One or more | 11 | 1 | 2 | 0 | 14 |
| Total | 23 | 27 | 18 | 32 | 100 |
| | $X2 = 13.2561$ $p < 0.001$ | | | | |

**Table VIII**

**Attitude of Patients to Discharge**

| Attitude to Discharge | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | Yes | No | No Response | Yes | No | No Response |
| Contented to Stay | 22 | 17 | 11 | 23 | 10 | 17 |
| Fear of Leaving Security of Hospital | 23 | 16 | 11 | 16 | 17 | 17 |

### Drugs

A survey of patient's medication was made and it was found that only 17 females and 16 males were receiving neuroleptics.

### Ward Atmosphere

When asked to express their feelings about the ward atmosphere, 30 females and 26 males reported that they were happy, 6 females and 6 males reported being unhappy with the ward atmosphere, and 14 females and 18 males were indeterminate about their feelings.

### Loss of prospects outside the Institution

As shown in Table VIII, there were 23 females and 16 male patients who expressed their fear at the prospects of leaving the security of the hospital, 11 females and 17 males did not respond at all. When asked about their feelings of leaving the hospital, 45% of the patients were contented to stay in the hospital.

## DISCUSSION

### Patient Characteristics

This study was conducted on the patients of a long stay ward with an average length of stay being 18.9 and 19.8 years for females and males respectively. It has often been assumed that the long period of stay in the mental hospital would initiate the process of institutionalisation. However there was no such relationship found between the two as the statistical analysis was found to be insignificant.

The age seems to be related to the severity of institutionalisation for the male patients and this was found to be significant at the 0.05 level.

In order to assess the relationship between the severity of "institutional neurosis" and other socio-demographic variables, the data was statistically analysed and only two variables, that is, age and education were found to be significantly related to the severity of institutionalisation for male patients. However, this significance needs to be interpreted cautiously in the light of the fact that growing older is a natural process and growing older in a particular environment could bring about certain changes and it is the effect of that environment over a long period of time that may determine the severity.

Education, on the other hand has been considered an important variable as an indication of good pre-morbid functioning (McCabe, 1976). It is interesting to note that 79% of the patients were uneducated and of these, 51 of the uneducated patients were classified as severe cases of institutionalisation, whereas only 8 out of the 21 educated ones were severe cases of institutionalisation.

It has been stated that the long stay wards tended to have more schizophrenics that any other illness (Sommer and Witney, 1961) and the findings of the present study are not different as the majority of the patients were diagnosed as schizophrenics. The symptom of "institutional neurosis" has been shown to be prevalent in all types of patients irrespective of their diagnosis, which may suggest — that the symptoms of institutionalisation indicate a disorder separate from the one first responsible for bringing the patient into the hospital and the disease is produced by methods of looking after people in mental hospitals and is not part of the mental illness, preceding or existing with it. However, in our sample, it was difficult to verify this as the majority of the patients in our sample were schizophrenics. A further analysis of the clinical features of institutional neurosis as postulated by Barton (1976) showed that all the patients in the present study showed almost all of these features with varying degrees of severity.

A significant proportion of the patients accepted things without challenging and complaining about the system, with total submission expected of the inmates for the smooth running of an institution. This resigned acceptance of things also leads to lack of interest in the future and an inability to make any plans resulting in total apathy and a gradual loss of individuality and identity which started with the initial stripping off of his usual appearance on admission, his accustomed affirmations, satisfaction and defenses and a gradual mortification through restriction of free movement, diffuse authority and communal living. However, the characteristic posture and gait described by Barton, as one of the features was not so prevalent in the present sample. The low prevalence of this feature may relate to the fact that patients were involved in daily evening walks as a routine activity of the hospital. The presence of all these features marks the setting of the process of insitutional neurosis. It is necessary and important to recognise these sysmptoms which indicate a disorder separate from the one which brought the patients to the hospital in the first place.

The fact that these symptoms seen in the patients are different from the ones seen on admission raises an important issue as to what causes them. Though difficult it is to ascertain any direct causation of this illness, a number of studies have postulated and shown the significant importance of the environment in which the patient lives in and the factors associated with that environment. In viewing the hospital as a total system, the ward interaction is considered as a transactional phenomena, that directly affects the patients and permeates every aspect of ward life. Such interaction constitutes the environment which may range from the most impoverished form of custody to the most enlightened form of therapeutic process. Apart from the variables of patients' characteristics and staff characteristics, an important variable related to the hospital effectiveness, is the treatment environment ranging from the extremes of custodial to therapeutic effects.

**Factors associated with Institutional Neurosis**

Considering the factors associated with institutional neurosis, it was found that patients had very little contact with the outside world, and very few of them had been visited in the beginning and even these few gradually had no visitors at all. Being left to live in the same limited environment, they are further faced with enforced idleness, with the main activities being bathing and making their beds and going for a walk. It was found that the number of activities were significantly related to the severity of 'institutional neurosis' for both the sexes. A common occupational therapy unit in the long-stay wards with over 1,000 patients was able to cater for the needs of only about 10 males and 10 female patients. It would seem that a good therapeutic environment embodies more than just frequent interaction to dish out the medication, an active therapeutic day to day environment of the ward may produce the highest therapeutic potential.

Fear of being bullied, physically assaulted and browbeating may also lead to the submissiveness on the part of the patient. Cunningham Dax (1968) noted in his study of mental hospitals in Malaysia that more patients have died from assault than suicide over the past few years. Thirty per cent of the patients reported being abused. Brutality is unsanctioned and usually goes undetected through the misplaced loyalty of other staff and the intimidation of witnesses. Farleigh (1971), Whittingham (1972) and the South Ockendon (1974) reports established beyond reasonable doubt that brutality occurs and should always be watched for and investigated.

Another established feature is the possiness of the staff where the patients are subjected to the boring and dictatorial ways of the staff who decide everything for the patients assuming that they are superior and know more than a mentally ill person. This attitude consequently discourages independence and initiativeness, and results in apathy and lack of interest in the patients. The denial of too many regulations by the patients in the present study could be reflective of their submissiveness and lack of initiativeness, or lack of education and low I.Q.

Loss of personal friends after coming into a mental institution is not surprising. This however, coupled with loss of personal possessions and finally the loss of memory about the important events can be a very important factor which leads to isolation, lack of purpose and loneliness thus begetting apathy which further leads to isolation completing a vicious circle. Wing and Brown's (1970) study on institutionalism and schizophrenia found that patients with the fewest possessions tended to be occupied in the least interesting activities, least in touch with the outside world and spent most of their time doing absolutely nothing. Similar results were found to be statistically significant for the female subjects in the present study where the degree of severity of institutional neurosis was related to the number of possessions. The general impression a ward creates can produce a very substantial response in the chronic patients. Drab surroundings communicate to the patient the idea that 'nothing matters' which fosters the apathy. The walls, floors and ceilings were bleak and beds were cramped with poor ventilation and lighting with smell of urine being pervasive, conditions of the toilets were unsatisfactory without any doors, floors slimy, far from home-like atmosphere. The authorities may defend the poor ward atmosphere by declaring that chronic patient is oblivious to his surroundings, however, there were twelve patients who were dissatisfied with their ward surroundings.

Once in the institution, the patients adapt themselves to the life there, surrendering their responsibilities, losing their skills through disuse and finally they come to the stage of feeling insecure on the prospects of a discharge. They have been away from the outside world for so long that they lose confidence in their ability to adjust or work and have an irrational fear of re-entering the society.

## CONCLUSION

The implications of this study are important indeed, for they point most definitely to that aspect of the hospital which should receive primary attention particularly the ward atmosphere or the treatment milieu which is not only predictive of hospital effectiveness but it has a definite potential in preventing the symptoms of "institutional neurosis". Firstly, these symptoms represent a form of adjustment to the institution to which patients are committed to for an indetermined period. The loss of friends and outside world coupled with the ward atmosphere and its mundane routine leaves very little for the patient's initiative and involvment resulting in apathy, submission and other characteristics of 'institutional neurosis' as described above.

Secondly, while hospitalisation is an important facet of the treatment of a patient, high levels of effectiveness demand much more than just the custodial care for the patient. Since so much of the therapeutic process revolves around the staff-patient interaction process, an extensive effort must be made in the staff training process toward inculcating a realistic set of expectations with regards to patient problems and creating an appropriate ward atmosphere. Functional communication is an important variable which would restrain patients from withdrawing themselves and encouraging them towards a more meaningful participation and interest in the activities of the ward. While patient's symptoms are found to play an important role affecting treatment attempts, the manner in which the patient responds and interacts with his environment as well as his perceptions of such an environment are just as important.

Finally, the success with which the environment creates a therapeutic milieu rather than a custodial one determines the chances for the patient's successful return to the community, instead of developing 'institutional neurosis'.

## SUMMARY

The study was undertaken to examine the characteristics of patients in a long-stay ward and determine the features associated with institutional neurosis. Fifty females and males were selected with average age of 49.1 years for females and 49.7 years for males, who had been staying in

the hospital with an average duration of stay of 18.9 years for females and 19.8 years for males. With an exception of the characteristic posture and gait associated with institutional neurosis, the majority of the patients presented all the features of institutional neurosis as postulated by Barton. The various factors found in the patient's environment which have been associated with institutional neurosis are discussed.


## ACKNOWLEDGEMENTS

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# TREATMENT OF INSTITUTIONAL NEUROSIS*

TAN CHEE KHUAN

## INTRODUCTION

THE FEATURES and factors associated with institutional neurosis had been described in the preceding paper in this journal. This paper attempts to give an account of the treatment of institutional neurosis based on the therapeutic community model carried out over a nine weeks period at Hospital Bahagia, Ulu Kinta, Perak.

Ideally, the treatment of institutional neurosis should be by prevention. This means that mentally ill patients should be diagnosed early and treated promptly with all available therapies. The idea is to aim at early discharge or the avoidance of admission altogether in order to prevent the accumulation of long-stay institutionalized patients.

However, once a patient had already been institutionalized, then the emphasis should be on rehabilitation and resettlement, through the provision of meaningful domestic and industrial roles within an open hospital setting, leading through transitional communities of various kinds to full participation in community life for a certain proportion of patients (Barton, 1976).

## METHOD

In late 1977, the Department of Psychological Medicine, University of Malaya collaborated with the staff of Hospital Bahagia, Ulu Kinta to set up two "model" wards in that hospital. One was a male acute admission ward and the other was a female ward for rehabilitation of chronic patients. This study is based on work done in the latter ward.

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Two wards in the hospital were chosen and renovated. The staffing of the wards was favourable. In the female "model" ward, there was a part-time sister, two staff-nurses, two assistant nurses and several attendants as well as student-nurses who were there for their training.

Fifteen patients were selected from various chronic wards on the basis of, a duration of stay of at least two years, age of less than 50 years, and preferably, but not necessarily, from Perak, so that relatives are more readily contactable.

Those chosen were transferred to the new ward. The severity of institutional neurosis was scored at the time of transfer, according to the rating scale described in the preceding paper in this journal.

## TREATMENT

The ward was run along the lines of a therapeutic community. A simple definition of a therapeutic community is "one is which a conscious effort is made to employ all staff and patients' potentials in an overall treatment programme, according to the capacities and training of each individual member." (Sainsbury, 1974).

The aims of running the ward on the therapeutic community model are as follows. Firstly, opening up of communication between patients and staff and amongst staff of different grades and disciplines. This had rarely been possible in the tradition custodial setting. Secondly, the creation of an atmosphere of acceptance of disturbed behaviour with understanding, rather than attempting to control it by arbitary authority and rule. Thirdly, the development of independence and the ability of patients to make decisions to the maximum degree their illness will permit.

The rehabilitation programme may be conveniently described under the headings which

Barton (1976) used as a basis to discuss the correction of factors associated with institutional neurosis.

**Re-establishment of Patients' contacts with the outside world**

Re-establishment of patients' contact with the outside world starts in the ward. It is essential for the ward staff to talk with the patients for some minutes each day. As there were only 15 patients, they were given a lot of attention by the staff. The patients gradually came to be interested in the staff as people and often inquired about their family and personal life and vice-versa.

To prepare patients for contact with the outside world, their appearances had to be improved so that they would not appear repulsive or be stared at. All of them were given decent clothings donated by the hospital staff. Their hair was attended to by the ward staff. They were encouraged to brush their hair and make themselves neat. One patient was referred to Hospital Besar, Ipoh for dentures and another for a pair of spectacles.

On weekends, they went for walks in the hospital grounds or to Tanjong Rambutan, a town which is close to the hospital. They also went for outings in the hospital bus. Patients were encouraged to write home to their families. Those who could not write were helped by the staff who wrote on their behalf. Relatives were invited to come to the ward for visits.

**Provision of a daily sequence of useful occupations, recreations and social events**

Wing and Brown (1970) found that the only really important category distinguishing patients who improved clinically from those who did not, was work and occupational therapy. Ideally, each patient should have an individual programme tailored to her needs but this is not practical if it is intended to introduce to model ward for other wards to emulate, the main obstacle being the shortage of staff. Instead, a common ward programme was drawn up by the staff after discussion. Later, patients were invited to give suggestions. Table I shows the final programme agreed upon by the staff and patients.

The ward programme included three group therapy sessions a week, lasting about an hour each. Discussions were conducted in three languages, Bahasa Malaysia, Chinese and Indian language. Communication was not easy in the beginning. Patients were a little unsure of what they were supposed to say. A few patients expressed hostility at having to do so much work, comparing the idle existence in their previous wards. However, as time passes and the community spirit spread, ideas were shared and patients began to contribute suggestions about improving the ward social life. One patient volunteered to make pyjamas which were more comfortable to sleep in and shorts for working and gardening. The patients began to take a real pride in their ward and to form strong attachments to the staff.

The question of transfering a disturbed patient to another ward was a matter of community concern and was discussed at the group meetings. Destructive behaviour was discussed for its meaning and methods of handling it was suggested. Disciplinary action if deemed necessary, was decided upon by consensus of opinions of patients and staff, which carried equal weights.

Patients were encourages to socialize with the patients from the male "model" ward. As seen in Table I, they met on five occasions a week. As a result of these meetings, patients learned to take pride in their appearances and developed a healthy relationship with men.

To encourage the patients to participate in the programme, a system of "token economy" was instituted. This is essentially a simple reward system which is nevertheless effective in modifying behaviour. The system is characterised by the fact that the desired behaviour has to be specified, there must be a feedback of patients' feelings regarding the desired behaviour and the reward, and there must be a good back-up system in terms of rewards. It was pointed out to the patients that the ultimate reward was the return to the community as a useful member.

The staff worked out an arrangement whereby tokens were awarded for desired behaviour and participation in various ward activities. Each patient could earn tokens which could be exchanged for a total of 70 cents a week. If they

**Table I**

**Programme of Ward Activities (In 3 Languages)**

| TIME \ DAY | MONDAY | TUESDAY | WEDNESDAY | THURSDAY | FRIDAY | SATURDAY | SUNDRY |
|---|---|---|---|---|---|---|---|
| 7.00 — 8.30 | Wake up, Personal Hygiene, Bed making, Laundry, Breakfast and Medication | | | | | | |
| 8.30 — 9.30 | Ward Meeting | Occupational Therapy | Ward Meeting | Complete cleaning of ward and wash Linen, Bedsheet etc. | Ward Meeting | Outing to Tanjong Rambu tan Town (with male Patients). | Morning walk in Hospital (with Male patients |
| 9.30 — 10.30 | Gardening or Needlework | | Staff Meeting patients do Gardening. | | Psychodrama | Letter writing or reading. | Hair Care (Shampoo etc.; Beauty Culture |
| 10.30 — 12.30 | Bath, Prepare Lunch, Cooking and Wash up | | | | | | Male Patients come to ward to have lunch |
| 12.30 — 2.00 | Free Period — Relax, sleep, read newspaper, magazines, listen to music, discussions | | | | | | |
| 2.00 — 4.00 | Male Patients come to ward — singing — dancing — games | Tidying the Ward, Needlework, patchwork, ironing clothes. | | Patient meet male patients at Hospital Library for discussions | Tidying the ward (sweep floor etc), Needlework (including sewing dresses) patchwork and ironing clothes. | | |
| 4.00 — 7.00 | Prepare Dinner, cook and wash up, Bathe and Medication. | | | | | | |
| 7.00 — 9.00 | Card-games, reading, listen to music, brush teeth, wash hand and feet, then to bed | | | | | | |

earned a minimum of 40 cents a week, then they were allowed to go to town on weekends to buy whatever they wanted (usually food) with their money.

As patients continued to improve, they were given leadership training. They were divided into three teams of patients each. A team-leader was appointed from each team in rotation. She was responsible for ensuring that her team members did their work and took care of their personal hygiene properly. There was a sense of responsibility and friendly rivalry.

**Eradication of brutality, browbeating and teasing**

The staff were encouraged to complain about any patient's behaviour during the group meetings. There was no evidence of any ill-treatment during the period of this study, even though some patients could be rather provocative at times.

**Alteration of staff attitudes to amiability, acceptance and assistance**

Many full-scale mental hospitals in all parts of the world are completely open or have no more than two or three closed wards in the whole hospital and yet there are comparatively few serious problems (Dax, 1969). As a result, the hospital loses its traditional custodial function with the usual restraints, locks and bars. Consequently, the staff have to be reorientated from their previous roles as custodians. In our ward, the staff were able to quickly adjust to their new roles as teachers and friends, working together with the patients instead of merely supervising them as in the past.

Staff meetings were useful in establishing a closer relationship among the staff. Mutual confidence grew and the meetings became increasingly free and helpful. The needs of all staff members were looked into. Any difficulty in the ward, including interpersonal relationships was discussed and resolved.

**Encourage and make it possible for patients to have friends and personal possessions and to enjoy personal events**

By their constant contact with the staff and fellow-patients, patients gradually grew to feel for others, trust them and accept them as friends. Each patient had her own bed with a locker and a few sets of clothings, a toothbrush, a comb and a pair of slippers. Other facilities were provided such as a dressing table, and some cosmetic for common use. Patients were taught to read calenders and to remember their dates of births.

**Reduction of drugs**

It was found that several patients were on medication they no longer needed, others were on unsuitable dosages while still others were denied medications which were useful. After their transfer to the ward, patients' medications were reviewed and necessary adjustments were made. Where possible, patients were medicated on a twice daily basis or even on night doses only. The patient with manic-depressive psychosis was treated with lithium carbonate after she was presented at the weekly hospital case-conference.

**Provision of a friendly, homely, permissive atmosphere**

Before the patients were transferred into the ward, one of the female wards was selected for renovation. (Fig. I). Part of the wall was knocked down and a kitchen was built, equipped with a gas stove, sink and larder, with new melamine crockery. Another area of the ward was converted into a visitor's room, with nice comfortable furniture, and potted plants. The walls were repainted and bright curtains were hung on the windows. The number of beds was reduced from 40 to 15. Partitions were set up so as to enclose four beds together to provide a sense of privacy (Fig. 2). Beautiful pictures of sceneries and attractive ladies decorated the ward. A common dressing-table with a mirror was placed at one corner. The surrounding garden was planted with flower plants and vegetables.

**Fig. 1. A gloomy, depressing ward.**

**Fig. 2. The same ward after renovation. Note the bright and lively atmosphere.**

**Make the patients aware of prospects of accomodation, work and friends outside the hospital and assist them in realizing these prospects**

Although we tried to make the ward as home-like as possible in terms of aesthetic qualities of the interior and outside grounds, the way food is being prepared and served, and the social activities available, we did not intend to make the environment so pleasant that patients may be so contended as to not want to leave.

Right from the beginning, patients were informed that they were being trained for housework so that when they were discharged, they may be an asset to their families. Even if no relatives were available, the patients could still find employment as cooks, washerwomen, babysitters, domestic helps, etc. It was discussed and agreed upon that a registration book be kept by the social worker, so that prospective employers (initially hospital staff but later outsiders) could register and employ patients.

## ANALYSIS OF DATA AND RESULTS

There were 12 Chinese, two Malays and one Indian patient. Their mean age was 36 years with a range of 22 to 50 years. The mean duration of stay was 6.27 years with a range of 2 to 16 years. Eleven of the patients were married, one was widowed and the rest were single. The patients were diagnosed as schizophrenia (12), manic depressive psychosis (1), personality disorder (1) and epileptic psychosis (1).

The ratings of severity of institutional neurosis for the patients before and after transfer are as follows. Five patients were rated as severe, 9 patients as moderate and one patient as mild, before their transfer. However, 9 weeks after transfer, no patient was rated as severe, 7 patients were rated as moderate and 8 patients as mild.

The status of patients at the end of study are as follows. Seven patients remained in the ward, one patient was discharged home, 2 patients were transferred out to other wards, 2 patients were employed and 3 patients were expected to be employed soon. (These 3 patients already had prospective employers but they were unable to leave the ward yet, as the social worker was on leave and thus, was unable to register them at the time this study ended).

## DISCUSSION

If we consider discharge or employment as a criteria of success in rehabilitation, then six patients may be included, making a success rate of 40%. If clinical improvement is used as the criteria instead, then all patients may be said to have shown some degree of improvement. However, the ultimate criteria of success depends on how long the discharged patients can remain out of hospital and their ability to maintain a viable social adjustment. Brown *et al.* (1958) showed that 2 out of 3 long-stay patients who were discharged after a prolonged stay in hospital succeeded in remaining in the community for at least a year after discharge; and that 2 out of 3 of these successes were maintaining a viable social adjustments.

Those patients who did not show much improvement clinically might have needed more time to respond. Nine weeks of rehabilitation could only be considered as a "crash-course" and hardly adequate time for patients who had been ill for so long. It is therefore gratifying, that there was so much improvement.

The patient/staff ratio was much better than in other wards. However, an active rehabilitation programme obviously demands a greater proportion of staff to patients treated, than does custodial care. Although this may appear more expensive initially, it is in fact more economical as there is a good chance that some patients, who would never otherwise be discharged, may be usefully rehabilitated back into the community. This will save the hospital a great deal of money in terms of upkeep. Active treatment and rehabilitation of patients will enable society to avoid the heavy financial burden of life-long care.

**Table II**

**Result of treatment of 15 female patients in model ward**

| Ethnic Group | Age | Years of stay | Diagnosis | Ratings | | Status of patients at end of study |
|---|---|---|---|---|---|---|
| | | | | Before | 9/52 after | |
| Chinese | 39 | 9 | Schizophrenia | 20 M | 14 L | Remained in ward |
| Malay | 39 | 7 | Schizophrenia | 21 M | 19 M | Transferred out |
| Chinese | 42 | 2 | Schizophrenia | 18 M | 11 L | Employed (discharged) |
| Chinese | 37 | 3 | Epileptic Psychosis | 23 M | 19 M | Remained in ward |
| Chinese | 28 | 5 | Personality Disorder | 19 M | 8 L | For employment soon |
| Chinese | 32 | 5 | Schizophrenia | 15 L | 9 L | Remained in ward |
| Chinese | 35 | 5 | Manic-depressive | 26 S | 13 L | Remained in ward |
| Malay | 40 | 8 | Schizophrenia | 20 M | 15 L | Discharged home |
| Chinese | 26 | 3 | Schizophrenia | 20 M | 17 M | Employed (paroled) |
| Chinese | 49 | 14 | Schizophrenia | 22 M | 11 L | For employment soon |
| Chinese | 50 | 2 | Schizophrenia | 19 M | 11 L | For employment soon |
| Chinese | 29 | 16 | Schizophrenia | 26 S | 18 M | Remained in ward |
| Indian | 39 | 3 | Schizophrenia | 28 S | 21 M | Transferred out |
| Chinese | 22 | 6 | Schizophrenia | 27 S | 19 M | Remained in ward |
| Chinese | 33 | 6 | Schizophrenia | 26 S | 20 M | Remained in ward |

Note: L = Mild degree of Institutional Neurosis (rating score of 8 — 16)

M = Moderate degree of Institutional Neurosis (rating score of 17 — 25)

S = Severe degree of Institutional Neurosis (rating score of 26 — 35)

A striking observation is the effect of the ward on its staff. There was an almost universal excitement and intense dedication to their work. They were very proud to be associated and chosen for the ward. Even staff from other wards were pleased. As one hospital assistant put it, "The new wards are good for the hospital. We have worked here for so long without change and we feel stagnated. Now, we hope that the new wards signify the beginning of change in the hospital. At the moment, we can feel proud that at least part of the hospital is progressive."

Further improvement in the patients and the future of the wards will depend on the enthusiasm, ability and opportunity of the ward staff.

## SUMMARY

15 female patients, who were below the age of 50 years of age and who had stayed at least two years in the hospital were transferred to the "model" ward for rehabilitation, run on the lines of a therapeutic model. Factors associated with institutional neurosis were corrected on the lines suggested by Barton (1976) and consisted of the re-establishment of patient's contacts, the provision of a daily sequence of useful occupations, recreations and social events, the eradication of brutality, browbeating and teasing, the alteration of the attitude of professional staff, the encouragement of patients to have friends, possessions and to enjoy personal events, the reduction of drugs, the provision of a friendly, homely, permissive atmosphere, and the opportunity to make the patients aware of the prospects of accommodation, work and friends outside the hospital.

Before the rehabilitation programme, five

patients were rated as haivng a severe degree of institutional neurosis, nine as moderate and one as mild. After nine weeks of treatment, no patient was rated as severe, seven patients were rated as moderate and eight patients as mild.

Six patients were either discharged, employed or in the process of being employed, giving a success rate of 40%. However, it is most encouraging to see that there was not only clinical and social improvement of all patients but the staff participated with much enthusiasm and constructive ideas.


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# ORAL PRECANCEROUS CONDITIONS IN PENINSULAR MALAYSIA*

K. RAMANATHAN **

## INTRODUCTION

SOUTH-EAST ASIA has the highest frequency of oral carcinoma in the world because of the popularity of oral habits such as betel-quid chewing, smoking and the drinking of alcohol. Although the mouth is easily accessible for direct and detailed clinical examination and changes in the colour and or texture of the oral mucosa can be clinically and histologically diagnosed as precancerous conditions, nevertheless it is regrettable to note most of our oral cancer patients seek treatment at a very late stage. The size of the oral cancer and cervical lymph node metastasis at the time of diagnosis and treatment are two important factors that determine the long-term survival of oral cancer patients.

There is a high frequency of correlation of precancerous conditions with oral carcinoma. Ramanathan *et al.* (1975) in a study of 75 oral cancer patients reported that leukoplakia was present in 61% of Indian males, 47% of Indian females, 44% of the other males and 25% of the other females. Submucous fibrosis occurred exclusively in Indians in the above quoted study. It was reported in 32% of the Indian males and in 10% of the Indian females.

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* This paper was presented in the symposium on "DIAGNOSIS AND TREATMENT OF ORAL CARCINOMA" of the Plastic Surgery Section of the 51st General Scientific Meeting of the Royal Australian College of Surgeons and held in Kuala Lumpur on 10th May, 1978.

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Cancer prevention is better than cancer treatment. Oral carcinoma in a vast majority of patients is preventable (Ramanathan, 1977). The World Health Organization Expert Committee for the Histopathological Nomenclature and Classification of Oral Precancerous Consitions has spelt out histological gradings which will allow for the prompt treatment of oral precancerous conditions at the earliest phase of epithelial dysplasia. A programme aiming to diagnose oral precancerous conditions promptly and to treat them even before they develop into carcinoma can be regarded as a cancer prevention scheme. This plan can be regarded as a health programme of national importance if it could be extended to cover our entire population. As a first step towards this objective a National Registry of Oral Precancerous Conditions was established in December 1974 by a National Council and whose chairman is Dr. Abdul Rahman bin Awang, the Director of Dental Services of Malaysia.

## MATERIAL AND METHODS

This study was based on the records of the National Registry of Oral Precancerous Conditions and maintained by the Department of Stomatology, Institute for Medical Research, Kuala Lumpur. The period covered was from 1st April 1967 up to 31st October 1977. All patients diagnosed with (1) homogeneous leukoplakia (Fig. 1); (2) speckled leukoplakia (Fig. 2); (3) lichen planus; (4) submucous fibrosis (Fig. 3 and 4); (5) erythroplakia (Fig. 2) and (6) smoker's keratosis and with or without biopsies were registered in the National Registry. The definitions of the above mentioned oral precancerous conditions have been given elsewhere (Ramanathan *et al.*, 1973). They conform with the definitions outlined by the WHO Expert Committee on Oral Precancerous Conditions.

Where biopsies were available the premalignancy index (PMI) scores adopted by the WHO Expert Committee on Oral Precancerous Conditions were applied. The PMI scores are divided

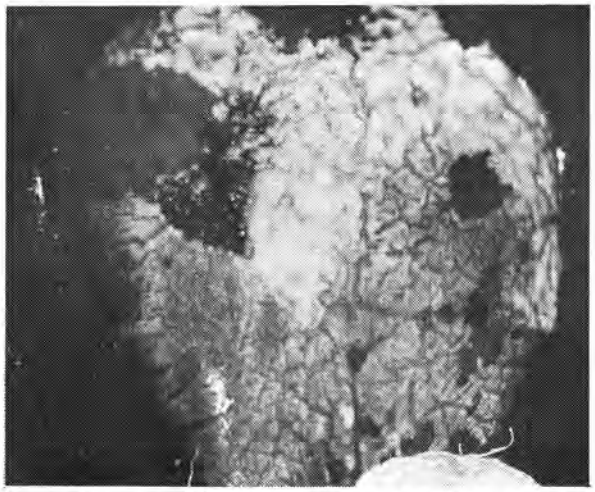


Fig. 1. Shows a homogeneous leukoplakia of the tongue having a uniform white appearance.

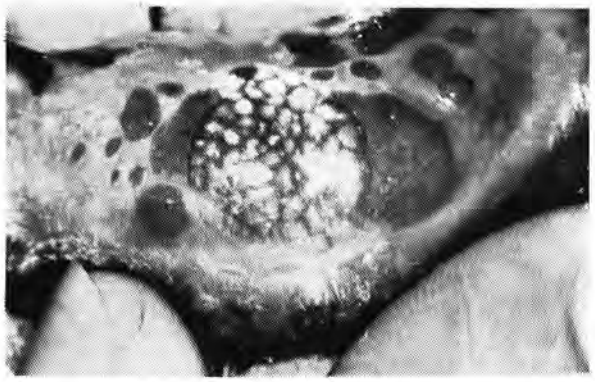
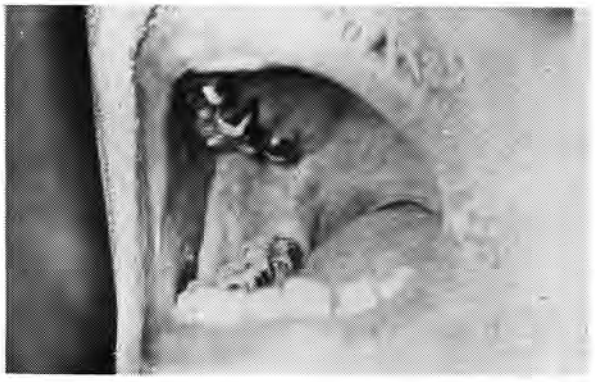


Fig. 2. Shows a Speckled leukoplakia in the centre of the lower lip. Red atrophic areas are interspersed with white hyperothokeratotic or hyperparakeratotic patches. Several erythroplakias of varying sizes and consisting of well-defined, fiery red patches can be seen at the periphery of the speckled leukoplakia.



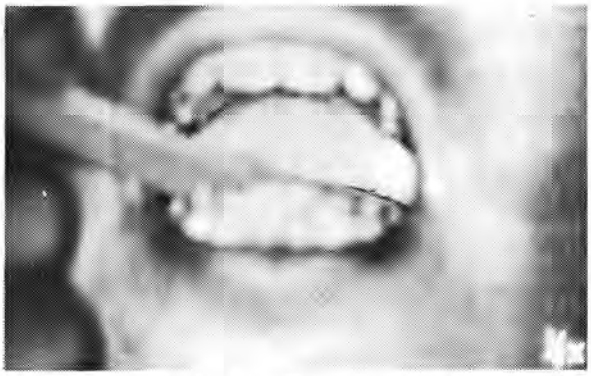


Fig. 3 & 4. Shows submucous fibrosis involving the lips, cheeks and soft palate and giving a blanched appearance of the oral mucosa. There is limited opening of the mouth. The fibrous bands are better palpated than seen.

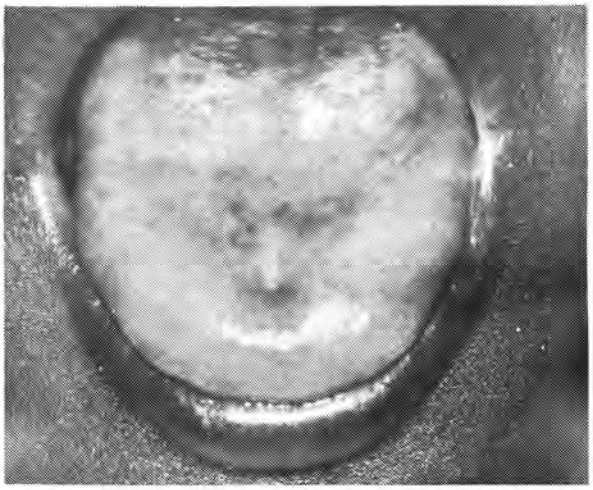


Fig. 5. Shows submucous fibrosis presenting as a bald, shiny tongue. A homogeneous leukoplakia is also present.

into the following four grades based on (1) changes in the individual cells and (2) in the interrelationship of one cell to another i.e. stratification, viz:

**(a)** — There is no evidence of future malignancy in the material examined.

**(b)** — There are some changes, such as mild atypia, but I do not think that malignancy is impending.

**(c)** — There is sufficient change (e.g. atypia) to make this lesion worrying. It should be eliminated if possible.

**(d)** — This is little short of carcinoma-in-situ.

A more detailed account of the operation of the National Registry of Oral Precancerous Conditions has been reported elsewhere (Ramanathan and Ng Kok Han, 1978). In all 194 patients were registered. PMI scores were recorded in 145 patients.

## FINDINGS AND DISCUSSION

Just like oral carcinoma (Ramanathan and Lakshimi, 1976) there is a predominance of Indian patients (72%) with oral precancerous conditions (Table 1). Like oral carcinoma precancerous conditions of the mouth would also seem to be closely related to oral habits. The peak age incidence was between 51 — 60 years (40%). The three patients below 20 years of age comprised of a 13-year-old Indian boy with lichen planus, a 15-year-old Indian boy and a 16-year-old Malay girl with submucous fibrosis.

The distribution of the oral precancerous conditions were (1) homogeneous leukoplakia (51.2%), (2) lichen planus (16.1%), (3) submucous fibrosis (15.2%), (4) speckled leukoplakia (11.9%), (5) erythroplakia (2.8%) and (6) smoker's keratosis (2.8%). Seventeen patients (8.8%) had two oral precancerous conditions. Of the patients with two oral precancerous conditions, the Indian female formed the largest group (59%). Of these 17 patients 76.5% had submucous fibrosis and leukoplakia (Fig. 5). In Malaysia so far no case of submucous fibrosis has been reported in the Chinese and Malay male. However, submucous fibrosis has been reported in Chinese living in Taiwan and Papua-New Guinea. (Su, 1954; Barnes, 1975).

Table II shows the distribution of oral precancerous conditions by race, sex and premalignancy index (PMI) scores. In 76 patients (47%) immediate surgical treatment was indicated because of their histological features of epithelial dysplasia. The peak age incidence of the PMI scores of (**c**) — 56% and (**d**) — 43% was also between the ages of 51 — 60 years. All the PMI scores of (**d**) and about 80% of the PMI scores of (**c**) occurred in the Indians.

The commonest sites for oral precanceous conditions were (1) buccal mucosa (65%), (2) tongue (13%) and (3) labial commissures (9%). The labial commissures (85%), tongue (47%) and the buccal mucosa (43%) had the most ominous precancerous histological features. Like-wise the most ominous precancerous histological features — PMI scores of (**c**) and (**d**) — seen in the various oral precan-

**Table I**

**Distribution of patients with oral precancerous conditions by race, sex, and age groups**

| AGE GROUP IN YEARS | MALAYS | | CHINESE | | INDIAN | | TOTAL | | TOTAL | PERCENTAGE |
|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | | |
| 0 — 10 | — | — | — | — | — | — | — | — | — | |
| 11 — 20 | — | 1 | — | — | 2 | — | 2 | 1 | 3 | 1.6% |
| 21 — 30 | 1 | — | 3 | 2 | 7 | 8 | 11 | 10 | 21 | 10.8% |
| 31 — 40 | 2 | 2 | 2 | 3 | 6 | 9 | 10 | 15 | 25 | 12.9% |
| 41 — 50 | 4 | 1 | 3 | 1 | 12 | 14 | 19 | 18 | 37 | 19.0% |
| 51 — 60 | 4 | 3 | 4 | 2 | 31 | 31 | 41 | 36 | 77 | 39.7% |
| 61 — 70 | 4 | — | 5 | 1 | 11 | 5 | 20 | 6 | 26 | 13.4% |
| 71 — 80 | — | 1 | 1 | — | 1 | — | 2 | 1 | 3 | 1.6% |
| 81 — 90 | — | — | — | — | 1 | — | 1 | — | 1 | 0.5% |
| UNKNOWN | — | — | — | — | 1 | — | 1 | — | 1 | 0.5% |
| TOTAL | 15 | 8 | 18 | 9 | 72 | 67 | 107* | 87** | 194 | 100% |
| PERCENTAGE | 7.7% | 4.2% | 9.3% | 4.6% | 37.1% | 34.5% | 55.1% | 44.9% | 100% | |

* — 2 males of other races; ** — 3 females of other races.

**Table II**

**Distribution of oral precancerous conditions by race, sex and premalignancy index (PMI) Scores**

| PRECANCEROUS CONDITIONS | MALE a b c d | FEMALE a b c d | MALE a b c d | FEMALE a b c d | MALE a b c d | FEMALE a b c d | TOTAL | PERCENTAGE |
|---|---|---|---|---|---|---|---|---|
| HOMOGENEOUS LEUKOPLAKIA | 2 4 6 — | — — 1 — | 1 3 1 — | 1 — 1 — | 6 14 18 5 | 3 12 8 3 | 90* | 56.6% |
| SUBMUCOUS FIBROSIS | — — — — | — — — — | — — — — | — — — — | 2 3 6 1 | 3 4 5 3 | 27 | 17.0% |
| SPECKLED LEUKOPLAKIA | — — — — | — — — — | — — 1 — | — — — — | — 4 5 2 | 3 1 6 1 | 23 | 14.5% |
| LICHEN PLANUS | 1 — — — | 1 1 — — | 3 — — — | 3 1 — — | 3 — — — | 1 — — — | 15** | 9.4% |
| ERYTHROPLAKIA | — — — — | — 1 — — | — — 1 — | — — — — | — — — — | — — 2 — | 4 | 2.5% |
| TOTAL | 3 4 6 — | 1 2 1 — | 4 3 3 — | 4 1 1 — | 11 21 29 8 | 10 17 21 7 | 159 | 100% |
| PERCENTAGE | 13 (8.2%) | 4 (2.5%) | 10 (6.3%) | 6 (3.7%) | 69 (43.4%) | 55 (34.6%) | 100% | |

* Others — Female — 1(b)

** Others — Female — 1(b)

cerous conditions were: (1) erythroplakia (75%), (2) speckled leukoplakia (65%), (3) submucous fibrosis (56%) and (4) homogeneous leukoplakia (48%).

Oral submucous fibrosis is an important precancerous condition in Indians. The cause of submucous fibrosis is unknown. There is also no known treatment for this condition. Submucous fibrosis is also challenging to manage for quite often leukoplakia supervenes and multiple oral carcinomas develop. Often there seems to be a wide field of cancerization in submucous fibrosis.

Submucous fibrosis seems to be the Asian version of sideropenic dysphagia (Plummer-Vinson syndrome; Paterson-Kelly syndrome) seen in Caucasians. In fact these two conditions are no more than two different spectra of one broad and common entity just like the obverse and reverse of one and the same coin. As suggested earlier (Ramanathan *et al.*, 1975) Behcet's syndrome, periadenitis mucosa necrotica recurrens (PMNR) and recurrent aphthous ulcers (RAU) again appear to be different spectra of this one broad and common entity. The latter conditions probably are progressively milder clinical expressions. Wray *et al.* (1975) and Sapiro (1977) have demonstrated iron, folic acid and vitamin B12 deficiencies in patients with recurrent aphthous ulcers. In all the above stated conditions iron deficiency and vitamin B complex deficiency appear to be important causative factors.

Submucous fibrosis appears to be an altered oral mucosa following a prolonged period of deficiency of iron and vitamin B complex. This altered oral mucosa appears to develop more easily a hypersensitivity to oral irritants such as spices, especially chillies and to the betel-quid, especially to the lime and tobacco components.

This rather limited study so far indicates that oral lichen planus, smoker's keratosis and keratosis in the floor of the mouth do not appear to be precancerous conditions in Malaysians as they have been reported in population studies elsewhere. This difference could be largely due to the different patterns of oral habits.

## SUMMARY

A programme aiming to diagnose oral precancerous conditions promptly and to treat them even before they develop into carcinoma can be regarded as a cancer prevention scheme. The pathologist by applying the WHO Premalignancy Index (PMI) scores to biopsies can be of great guidance and value to both the surgeon and the patient. In 76 patients (47%) with oral precancerous conditions immediate surgical treatment was indicated because of their histological features of epithelial dysplasia. The labial commissures (85%), tongue (47%) and the buccal mucosa (43%) had the most ominous precancerous histological features. Likewise the most ominous precancerous histological features seen in the various oral precancerous conditions were: (1) erythroplakia (75%), (2) speckled leukoplakia (65%), (3) submucous fibrosis (56%) and (4) homogeneous leukoplakia (48%). Oral submucous fibrosis is an important precancerous condition in Indians. The cause of submucous fibrosis is unknown. There is also no known treatment. The author has speculated that submucous fibrosis is the Asian version of sideropenic dysphagia seen in Caucasians.This rather limited study so far has indicated that oral lichen planus, smoker's keratosis and keratosis of the floor of the mouth do not appear to be precancerous conditions in Malaysians.

## ACKNOWLEDGEMENT

I wish to place on record my profound appreciation to Dr. Abdul Rahman bin Awang, the Director of Dental Services, Malaysia and Chairman of the National Council for the maintainence of the "National Registry of Oral Precancerous Conditions", all the National Council members, the Director, Institute for Medical Research, Kuala Lumpur and to the numerous colleagues throughout Peninsular Malaysia for their encouragement and valuable support in maintaining the National Registry of Oral Precancerous Conditions and in carrying out this preliminary study. I wish to also thank members of the WHO Expert Committee on Oral Precancerous Conditions for allowing me to apply the PMI scores in this study.

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# FOSSA OF ROSENMULLER AND NASOPHARYNGEAL CARCINOMA

U. PRASAD,

## INTRODUCTION

NASOPHARYNX is an area behind the nasal cavities between the base of skull above and soft palate below. In shape it is almost cuboidal and measures between 3 — 4 cm in height, breadth and antero-posterior dimensions. Due to its small size and difficult anatomical location it has, since long, been known to the clinicians as an obscure area and has been termed a "blind spot" (Cantril and Buschke, 1946), a hidden cavity (Davis, 1948) and an "unknown region" (Hickley, 1951).

Nasopharynx is bounded anteriorly by the posterior nasal apertures with the posterior edge of the nasal septum in the middle. The floor is formed by the dorsum of the soft palate, while the basisphenoid forms its roof. The posterior wall which is continuous with the roof is constituted by basiocciput and upper two cervical vertebrae. A prominent landmark along its lateral wall is the pharyngeal opening of the Eustachian tube (Fig. 1), which measures about 8 x 5 mm, and is roughly triangular in shape with apex pointing upwards. Along its superior and posterior margins there is a prominence called torus tubarius, formed by the medial end of the cartilaginous part of the tube. Behind this prominence lies a Fossa, or the lateral recess, first of all, described in 1808 by a German Anatomist, Johann Christian Rosenmuller (1771 — 1828). This Fossa of Rosenmuller has been said to be the site of predilection for the development of nasopharyngeal carcinoma (NPC) (Prasad, 1972, 1978; Oreskovic *et al.*, 1968). The gross pathological lesions in NPC are proliferative (exophytic) when the tumour bulges in the nasopharynx, and infiltrative, in which case the tumour grows submucosally without producing ulceration (Whiteleather, 1945) in early stages.

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The purpose of this paper is to establish that all the infiltrative types of NPC originate from the fossa of Rosenmuller. I shall put forward the anatomical, clinical and radiological evidences to prove this hypothesis.

## ANATOMICAL CONSIDERATION

The Fossa of Rosenmuller is a cone-shaped lateral extension of the nasopharynx, which is contracted dorsoventrally. This recess is hardly noticeable at birth, however with the growth of the person it increases more and more in depth, averaging about 10 mm when fully formed, probably in order to facilitate the movement of the Eustachian tube. The apex of this cone lies very close to the anterior margin of the lower opening of the carotid canal, while the base which opens into the nasopharyngeal space proper is related supriorly to the foramen lacerum (Fig. 2). This foramen is occupied, in the recent state, by fibrocartilage and no large structure either enters or leaves the skull through it. Thus the internal carotid artery and the sympathetic plexus of nerves which traverse forward and medially from the lower opening of the carotid canal to the cranial cavity are separated from the roof of the Fossa of Rosenmuller by thin bone which forms the floor of the carotid canal and the fibrocartilage which cover the foramen lacerum. This piece of bone is developed by a process of secondary fusion which is often incomplete. As such it is more convenient for the neoplastic process to enter the cranial cavity through the weak floor of the carotid canal and progress on to the cavernous sinus unhindered than to enter the foramen lacerum through its floor where the fibrocartilage is likely to offer tremendous resistance. However once the cavernous sinus is invaded, the maxillary, abducent, trochlear and oculomotor nerves are affected in that order (Fig. 2).

The anterior wall of the Fossa of Rosenmuller is related to thin mucosa covering the cartilaginous part of the Eustachian tube (Fig. 3)

superiorly and the fascia covering the levator palati muscle inferiorly. Again, the cartilage of the tube offers resistance to the spread of tumour to its lumen, as such it is very rare for the tumour to enter the middle ear and present as polyp in the external auditory meatus, however, it does compress the tube and cause conductive deafness. Deafness also occurs due to the involvement of the levator palati muscle which is responsible for the opening and closing of the tube. The fascial space surrounding the levator palati muscle is penetrated rather easily and thereby this muscle is infiltrated. This subsequently leads to the fixation of the soft palate.

The mandibular nerve, which is separated from the Fossa by the Eustachian tube and tensor palati, is fairly well protected (Fig. 4) and is affected only late, when the tumour invades the prestyloid compartment of the parapharyngeal space via the apex of the Fossa of Rosenmuller.

Laterally there is parapharyngeal space which can be divided into the following three compartments, by the styloid process, the muscles attached to it and the various fascial expansions (Fig. 5).

1. Retropharyngeal
2. Retrostyloid
3. Prestyloid

1. The retropharyngeal compartment contains the lymph node of Rouviere which is of importance, since this is most frequently and fairly early involved in nasopharyngeal carcinoma (NPC). This compartment separates the nasopharynx from the prevertebral muscles and upper two cervical vertebrae.

2. The retrostyloid compartment, which contain the internal carotid artery, internal juglar vein, the last 4 cranial nerves, the sympathetic trunk and few lymph nodes, is entered, either by way of direct spread from the lateral wall of the Fossa or indirectly after the node of Rouviere has been affected.

3. The prestyloid compartment, however is affected, only when the disease is fairly well advanced. In that case the structures affected are the mandibullar nerve, the parotid gland and pterygoid muscles and rarely the facial nerve. As

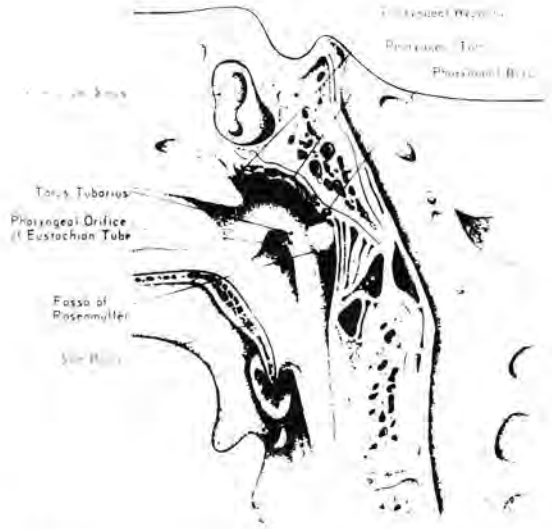


**Fig. 1. Section to show the normal boundaries of the nasopharynx.**

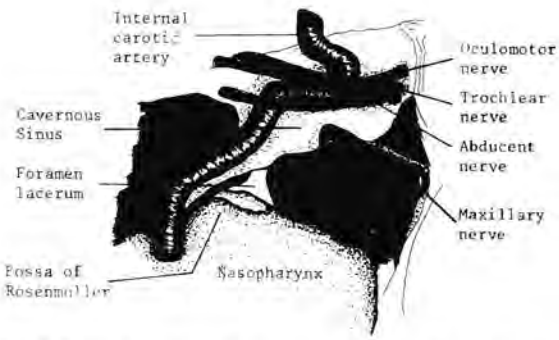


**Fig. 2. Coronal section of Cavernous Sinus and lateral wall of nasopharynx.**

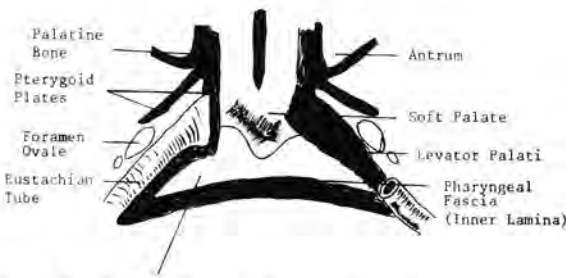


**Fig. 3. The Fossa of Rosenmuller seen from above.**

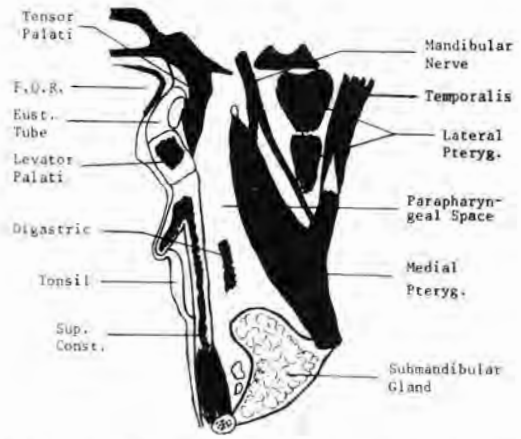


**Fig. 4. Coronal section through the prestyloid part of the Parapharyngeal space.**

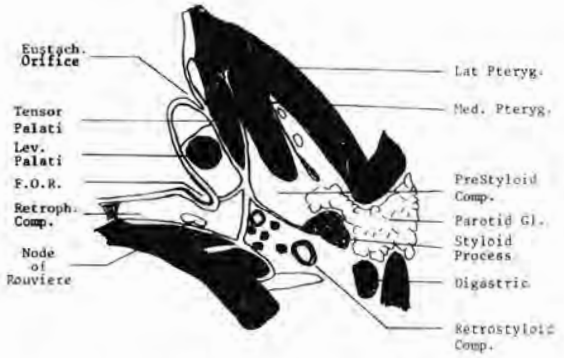


**Fig. 5. Horizontal section through the parapharyngeal space.**

the disease spread below in this compartment it pushes the tonsil and the lateral pharyngeal wall medially and may extend inferiorly to infiltrate the submandibular salivary gland which forms the floor of this compartment (Fig. 4).

The lymphatics from the Fossa of Rosenmuller first drain into the node of Rouviere and subsequently to the upper deep cervical lymph node situated below the tip of the mastoid process, deep to the upper attachment of the sternomastoid muscle.

## CLINICAL CONSIDERATION

Out of first 200 cases of NPC diagnosed at the ENT clinic of the University Hospital, Kuala Lumpur, it was possible to collect 60 cases where the tumour was localised to the region of the Fossa of Rosenmuller. It was interesting however to observe that, in 24 cases among these, either there was just fullness of this Fossa (18 cases) so that one could just differentiate between the depth of Fossa on one side as compared to the other side or no obvious lesion could be seen (6 cases) on posterior rhinoscopy. In all these 24 cases the mucosa was intact and histopathological examination of tissue taken from the Fossa through direct nasopharyngoscopy, revealed the diagnosis of NPC in each case.

On reviewing the clinical features of these 24 cases (Fig. 6) it was found that at the time of their first presentation to our clinic, 15 had mass of node in the neck, 14 had otological symptoms in the form of deafness and/or tinnitus, 9 had cranial nerve involvement, 5 had rhinological symptom of epistaxis and/or nasal obstruction and 3 even had distant bony metastasis.

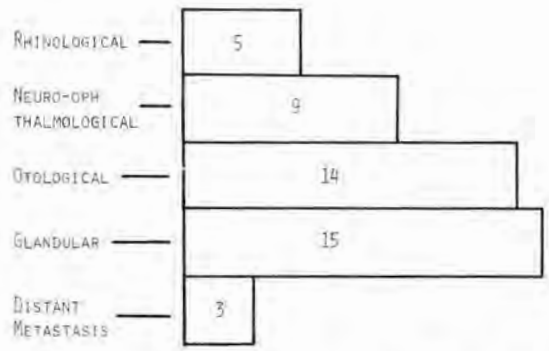


**Fig. 6. Symptomatology in 24 cases of NPC with fullness of Fossa of Rosenmuller.**

## RADIOLOGICAL CONSIDERATION

Routine X-ray examination of the nasopharynx, in nasopharyngeal carcinoma, reveal either thickness of the precervical fascia or soft tissue mass occupying the nasopharyngeal space or bony erosion. Out of these 24 cases, no abnormality could be detected in 17. In 7 cases there was only thickening of the precervical fascia and neither soft tissue mass nor evidence of bony erosion could be seen.

## DISCUSSION

Since Whiteleather's (1945) observation that initially nasopharyngeal carcinoma may grow sub-mucosally without causing ulceration, such infiltrative lesions have been reported time and again, however so far, there has been no mention of the behaviour of these tumours which are so very limited in their appearance in the nasopharynx, yet have spread far beyond the site of origin to the extent of producing distant metastasis. It seems obvious that these tumours arise in the Fossa of Rosenmuller and undergo such pattern of spread whereby instead of proliferating and producing tumour mass in the nasopharyngeal space, at least in the earlier stage of the disease, take other different routes of spread inwardly. The mucous membrance covering the tumour mass remain intact.

Extension anteriorly results in otological symptoms due to pressure over the Eustachian tube or infiltration of the levator palati muscle, as was the case in 14 of them. Superiorly the spread lead to involvement of the cranial nerves from 3rd to 6th (7 cases) and laterally those of 9th to 12th (2 cases). Largest number of cases (15) had cervical node involvement at the time of first presentation. Definitely these nodes were affected secondarily from the node of Rouviere which is very conveniently placed in the retropharyngeal compartment and drains lymphatics from the Fossa of Rosenmuller. Once these nodes are infiltrated distant metastasis is not highly unlikely. Radiological finding of thickening of the precervical fascia in those 7 cases further supports that these tumours had grown sub-mucosally and produced thickness of the posterior nasopharyngeal wall instead of giving shadow of soft tissue mass occupying the nasopharyngeal space. In the rest of the case, routine radiological examination of the nasopharynx did not reveal any tumour, although clinically there were evidences of growth extending from the Fossa of Rosenmuller inwardly.

## CONCLUSION

The anatomical consideration and the clinical and radiological evidences in histopathologically confirmed cases of nasopharyngeal carcinoma with suspected or very minimal lesion observed clinically and radiologically, suggest that the site of origin of, if not all, at least the infiltrative type of nasopharyngeal carcinoma, is the Fossa of Rosenmuller. As such I shall like to suggest that in all suspected cases of NPC, biopsy should be obtained from the Fossa and carefully studied for N.P.C.


## ACKNOWLEDGEMENT

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# RETROPERITONEAL TERATOMA

H.M. MOHD. BAHARI & ABDULLAH HARON

## INTRODUCTION

TERATOMAS are tumours composed of multiple tissues that are foreign to the area in which they arise. It is widely accepted that they originate from totipotential cells which had escaped the influence of the primary organiser during development (Willis, 1951). Rarely, teratomas occur in the retroperitoneal space, a large potential space extending from the thoracic to the pelvic diaphragms and bounded laterally by the iliac crests and the tips of the twelfth ribs. The first description of a retroperitoneal tumour was credited to Morgagni in 1761. Lobstein was the first to use the term retroperitoneal tumour in his description of a sarcoma in 1829, a tumour unrelated by origin to adjacent organs in the retroperitoneal space. Primary retroperitoneal teratomas was first described by Dickinson in 1871.

We are reporting three cases of primary retroperitoneal teratomas in adults seen in the General Hospital, Kuala Lumpur during the last five years. These tumours, which are allegedly rare in adults and thus infrequently thought of, presented a problem in diagnosis.

## CASE MATERIAL

### Case 1

The patient, a 28 year old housewife, complained of pain on the right side of the abdomen. There was no other significant history. On examination, her general condition was satisfactory. Pulse rate was 86/min. and blood pressure 110/70 mm Hg. On abdominal examination, a large painless, fixed mass was palpated in the right iliac fossa and suprapubic region.

Haematological investigations: haemoglobin 9 gm %, total white count 7,000/cu. mm. Plain X-ray abdomen showed a central soft tissue mass with presence of calcification, bone and a tooth (Fig. 1). Intravenous urogram showed lateral displacement of the lower pole of the right kidney (Fig. 2). A diagnosis of a retroperitoneal teratoma was made.

Exploratory laparatomy confirmed a retroperitoneal tumour 15 x 10 cm. below and medial to the right kidney, adherent to the right renal vein, the inferior vena cava and the aorta. Total excision was performed. Histological examination showed the tumour to be a mature cystic teratoma with presence of respiratory and cuboidal epithelia, cartilage, bone and fat cells.

Five months later, the patient was well and there was no evidence of tumour recurrence.

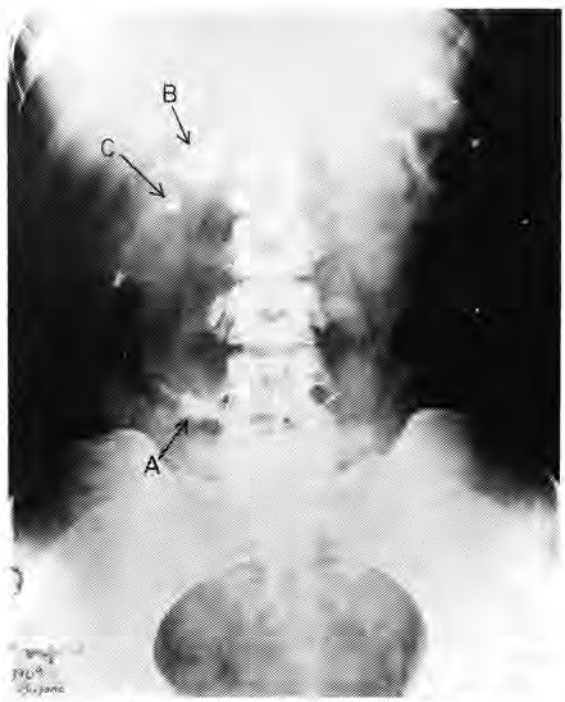


**Fig. 1. Plain X-ray of abdomen showing areas of calcification (A), bone (B) and a tooth (C).**

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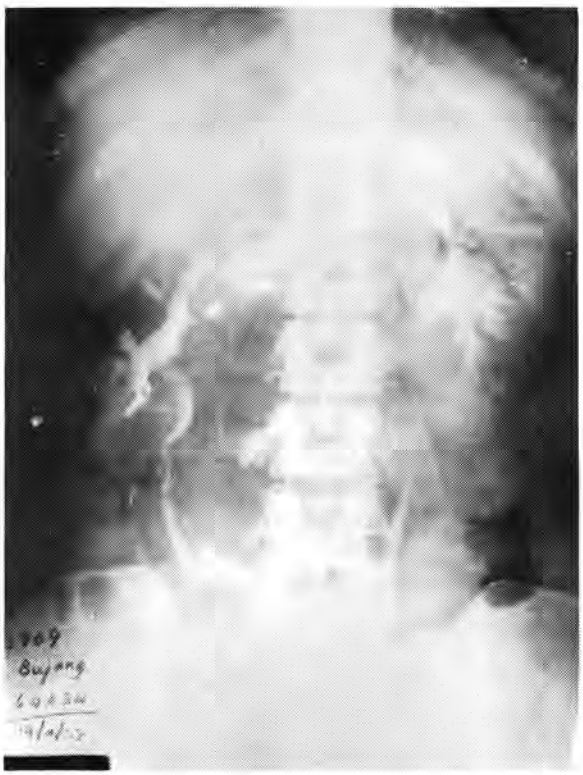

**Fig. 2. Intravenous urogram showig displacement of the right kidney.**

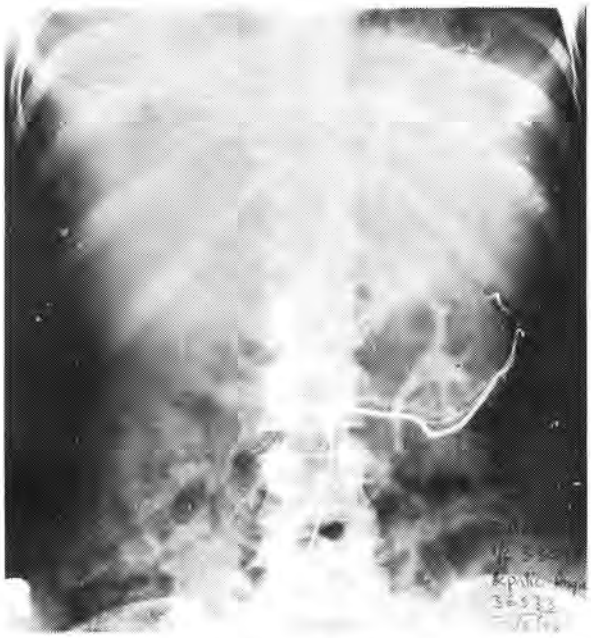

**Fig. 3. Hepatic angiogram showing non-vascular mass in right lobe of the liver.**

## Case 2

The patient, a 33 year old housewife, complained of loss of appetite, nausea and vomiting after meals and loss of weight for two months. Two weeks prior to admission she noticed a mass in the right hypochondrium. On physical examination, her general condition was satisfactory. Pulse rate was 84/min. and blood pressure 120/80 mm.Hg. A mass was palpated in the right hypochondrium. It had a smooth surface, sharply defined lower border and extended 5 cm. below the coastal margin.

Haematological investigations: haemoglobin 13.6 gm %, total white count 7,200/cu. mm. and erythrocyte sedimentation rate 67 mm/hr. Liver function tests were normal and alpha-fetoprotein was negative. Plain abdominal X-ray showed a radio-opaque density in the right hypochondrium. Liver scan showed a large cold area in the right lobe, suggesting a hepatoma. Hepatic angiogram showed a large, relatively non-vascular mass in the right lobe of the liver displacing the vessels medially (Fig. 3). Preoperative diagnosis of a hepatic cyst was made.

At laparotomy, a well encapsulated retroperitoneal tumour was found. It measured about 15 cm. in diameter and was situated between the upper pole of the right kidney and the inferior surface of the liver. It was adherent to the inferior vena cava and the aorta. The tumour was excised in toto. Histoligical examination showed a benign mature teratoma comprising smooth and striate muscles, bone, cartilage, lymphoid tissue, skin and intestinal epithelium.

Convalescence was uneventful. On the last follow-up one year later, the patient was well and there was no sign of tumour recurrence.

## Case 3

The patient was a 20 year old female factory worker. She complained of fever, pain in the right hypochondrium and jaundice for two weeks. Three years previously, she was treated in another hospital for a liver abscess which was drained by open operation. Three litres of purulent anchovy sauce-like material thought to be of amoebic origin was removed. Post-operatively the patient

was well, except for a persistently discharging sinus at the old drain site. Three years later, she was readmitted for recurrence of fever and pain and referred to the General Hospital, Kuala Lumpur. On examination, her general condition was satisfactory. Pulse rate was 80/min. and blood pressure was 120/80 mm. Hg. She had low grade fever of 37.5 C. There was a mass in the right hypochondrium. It was firm and slightly tender, and extended 10 cm. below the coastal margin. A sinus, discharging purulent fluid was present in the right lumbar region.

Haematological investigations: haemoglobin 12.4 gm %, total white count 12,000/cu. mm. and erythrocyte sedimentation rate 32 mm/hr. Liver function tests were normal. Plain abdominal X-ray showed a soft tissue shadow in the right hypochondrium with a small area of calcification. The stomach was displaced downward. Liver scan showed negligible uptake of dye on the right side. Splenic uptake was increased (Fig. 4). This suggested severe parenchymal damage of the liver. The patient was put on a course of tetracycline and flagyl with no improvement. The diagnosis of a hepatic cyst or tumour was made.

Exploratory laparotomy was performed. A large mass 15 x 20 cm. was found occupying the retroperitoneal space between the liver and the right kidney. It extended across the midline and was adherent to the inferior vena cava and the aorta. The right lobe of the liver to which the tumour was adherent was compressed and atrophied forming a thin capsule to the tumour. Near total excision of the tumour was performed. A part of the capsule adherent to the aorta and inferior vena cava could not be removed. Microscopically, the tumour contained hair, cartilage and bone. Histologically, it was a mature teratoma with various type of epithelia, smooth muscle, cartilage and lymphoid tissue. There was no evidence of malignancy.

Convalescence was uneventful and at the last follow-up four months after surgery, the patient was well. There was no evidence of recurrence.

## DISCUSSION

Tumours occuring in the retroperitoneal space account for 0.3 to 3 percent of all tumours (Wirbatz *et al.*, 1963). Of these, liposarcoma is the commonest and teratoma is the rarest. Palumbo *et al.* (1949), reported an incidence of 11 percent in a series of 55 cases of retroperitoneal tumours. Donnelly (1946) reported two teratomas in 95 consecutive retroperitoneal tumours, while Braasch and Mon (1967) did not report a single one in a review of 101 cases of retroperitoneal tumours. In our limited experience, we have seen three teratomas out of seven consecutive primary retroperitoneal tumours in adults over a five year period. Perhaps teratomas of the retroperitoneal space may not be as rare in Malaysia. There is only one report of a retroperitoneal teratoma in local literature (Hussein 1973).

**Fig. 4. Liver scan showing decreased uptake in the right lobe and increased uptake in the left lobe and the spleen.**

Our three cases were all females whose ages ranged from 20 to 33 years. Palumbo *et al.* (1949) reported that the average age at diagnosis was 13 years with only 10 percent occuring above the age 30 years, with a slight predominence of females. Engel *et al.* (1968), in his analysis of 29 cases whose ages ranged from 2 hours to 55 years, reported about equal incidence in the sexes.

Pantoja *et al.* (1976) reported that the commoner site of retroperitoneal teratomas was on the left but in these three instances, the tumours were on the right.

Symptoms in retroperitoneal tumours occur late and are usually vague and non-specific. The first two patients presented with pain, anorexia and loss of weight. The third had fever and pain in the right hypochondrium which initially led to a diagnosis of an amoebic liver abscess. These tumours have usually grown to a large size and are palpable before the patients have constitutional symptoms. All three patients had a palpable mass in the right side of the abdomen, leading us to suspect a hepatoma in two cases as hepatomas occur commonly in Malaysia. Teratomas are subject to infection and suppuration. This was probably the cause of the persistently discharging sinus in the third patient. Diagnosis then was difficult and an amoebic liver abscess was considered. They can also undergo malignant change.

Retrospectively, we feel that the diagnosis of a retroperitoneal teratoma should be considered when a patient presents with an abdominal mass and whose abdominal x-rays show presence of calcification or bone. Intravenous urogram is useful only in defining the site of the tumour to be retroperitoneal. Liver scan studies were not helpful in our cases. Angiography indicates the vascularity of a retroperitoneal tumour and would aid the surgeon in anticipating the extent of haemorrhage which may occur during surgical excision but is not an essential investigation for the diagnosis of a retroperitoneal tumour.

Teratomas may be cystic, solid or partially solid and partially cystic. The solid portion consists of fatty tissue, cartilage, bone, teeth and other differentiated structures such as digits or segments of intestines. In our cases there was no evidence of malignancy.

The treatment for retroperitoneal teratomas, as for any other retroperitoneal tumour, is total excision as this offers the only hope of cure. Adherence to structures such as major blood vessels is not a contraindication to excision. In cases of malignant teratomas, post-operative radiotherapy is indicated but response is usually poor. The prognosis for a benign teratoma is very good provided complete resection is accomplished, but malignant teratomas carry a poor prognosis even after apparently complete excision (Arnheim, 1951).

## SUMMARY

Three cases of retroperitoneal teratomas are reported. This constituted 42 percent of all retroperitoneal tumours treated at the General Hospital over a period of five years. This is a higher incidence than reported elsewhere. The patients were all adult females and the tumours were all on the right side. It is probable that the incidence of retroperitoneal teratomas is higher in Malaysia than in other countries and should be considered in the differential diagnosis in the presence of a palpable abdominal mass which shows areas of calcification on X-ray. These tumours are usually benign and the prognosis is good.

## ACKNOWLEDGEMENT

We would like to thank Professor M. Balasegaran under whose care the first case was admitted and Professor Q.M. Iqbal for suggestion in the preparation of the manuscript.

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# LUNG CANCER:
# I. PRESENTING CLINICAL FEATURES

M. ASHOKA MENON & SAW HUAT SEONG

## INTRODUCTION

LUNG CANCER as a disease entity has changed dramatically over the last five decades; from being an unusual form of pulmonary disease it is now one of the most common and lethal forms of malignancy. Diagnosis usually follows symptoms which are seen relatively late in the natural history of the disease, and the prognosis of the individual patient often hinges on the symptoms, signs and radiological features seen at the time of presentation and diagnosis. We report our experience with regards to the presenting clinical features of lung cancer together with a review of the relevant literature on their significance. The overall features of lung cancer as a problem in Malaysia are being published separately.

## MATERIAL AND METHODS

Data was obtained by analysis of the case records of patients diagnosed to have lung cancer at the University Hospital, Kuala Lumpur. Three hundred and eighty eight cases were seen during the years 1967 — 1976 and the diagnosis was based on two criteria: (i) clinical and radiological in 110 cases (28% of the total) and (ii) histological confirmation in addition in 278 cases (72%).

Symptoms encountered were classified into three clinical symptomatic groups as described by Feinstein (1966, 1968): (i) primary symptoms due to the local effects of the tumour e.g. cough, haemoptysis (ii) systemic symptoms, remote from the primary site and unrelated to metastases e.g. aesthenia, weight loss and (iii) metastatic symptoms, including those representing spread beyond the primary site e.g. dysphagia, cutaneous nodules, cord compression etc.

The anatomic extent of the disease was classified as described by the American Joint Committee for Cancer Staging and End Results Reporting (1974) into stages I, II and III.

## RESULTS

Figure 1 shows the incidence of the classes of symptoms in the patients. Twenty seven per cent presented solely with primary symptoms and 37% with symptoms both primary and systemic in origin. Features related to metastases were seen in a total of 34% and 10% had all three classes of symptoms. Four per cent presented solely with features attributable to metastasis and 2% with those due to systemic effects without metastasis.

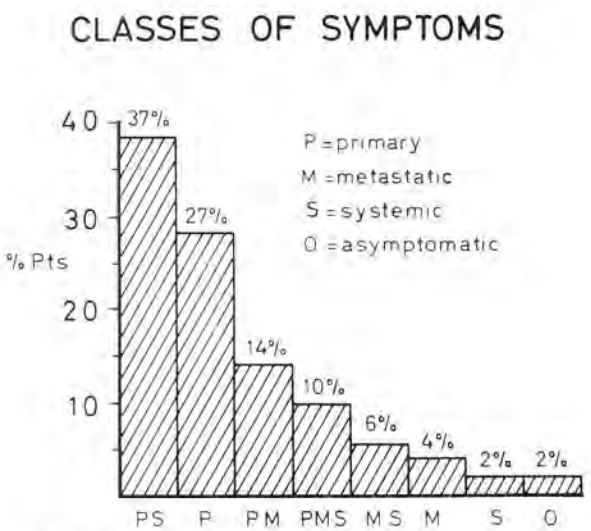


**Fig. 1. Each column represents that percentage of patients presenting solely with the class or classes as indicated, to the exclusion of others.**

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The individual clinical features and their frequency are shown in Table I. Two per cent were asymptomatic at presentation. The commoner primary symptoms were cough (68%) weight loss (47%), haemoptysis (35%) dyspnoea (30%) and chest pain (19%). Evidence of local and regional lymphatic spread was seen chiefly as mediastinal involvement in the form of hoarseness and evidence of vocal cord palsy (10%), SVC obstruction (9%) and dysphagia (5%). Two per cent presented as a Pancoast tumour. Of the metastatic features representative of distant spread, bone pain suggesting metastasis was the commonest, being seen in 8% at the time of presentation. Secondaries were sometimes noticed by patients in the form of swellings or lumps (6%); these were seen in the chest wall, along bones, in the supraclavicular, cervical, and axillary nodes and in the skin. Metastatic neurological involvement occurred chiefly as intracranial lesions in 7% including 5% with hemi or monoplegia and in the form of cord compression (2%).

**Table I**

**Presenting Clinical Features**

| | Features | % Patients |
|---|---|---|
| I | No symptoms | 2 |
| II | Primary symptoms | 88 |
| | Cough | 68 |
| | Haemoptysis | 35 |
| | Dyspnoea | 30 |
| | Chest pain | 19 |
| III | Systemic symptoms | 55 |
| | Weight loss | 47 |
| | General: anorexia, malaise, lethargy | 9 |
| | Fever | 5 |
| | Osteoarthropathy | 1 |
| | Neuropathy/myopathy | 1 |
| IV | Metastatic symptoms | 34 |
| | (a) Features of local and regional lymphatic spread | |
| | Hoarseness, huskiness | 10 |
| | SVC | 9 |
| | Dysphagia | 5 |
| | Dysphagia | 5 |
| | Pancoast tumour | 2 |
| | (b) Metastatic features | |
| | Bone pains | 8 |
| | Intracranial space occupying lesions (including hemiplegia, monoplegia) | 7 |
| | Swellings/lumps | 6 |
| | Hemiplegia or monoplegia | 5 |
| | Cord compression | 2 |
| | Cerebellar | 0.5 |

Systemic manifestations occurred in 55% of patients, weight loss being the most common feature seen in 47%. The other significant features in this group were general manifestations unrelated directly to metastases like anorexia, malaise and lethargy seen in 9% and fever (5%). Endocrine manifestations were not specially investigated for in most patients.

The duration of symptoms is set out in Figure 2. Thirty nine per cent had symptoms lasting under three months, 71% under six months and 86% under twelve months. The mean duration of symptoms in the total groups of patient was 5.1 months.

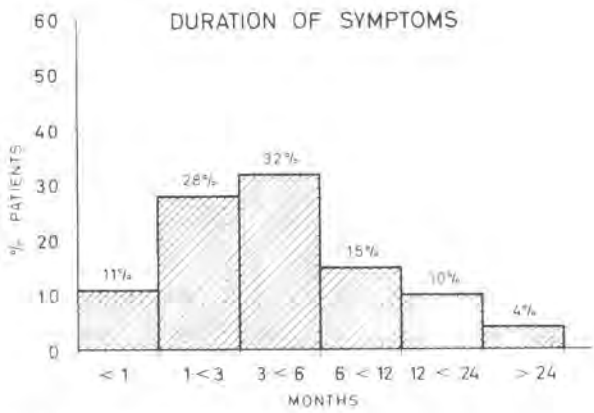


**Fig. 2. Duration of Symptoms**

Figure 3 shows the anatomic staging of the disease in the patients. Eighty seven per cent had stage III (generally non-resectable disease). There was no obvious correlation between the duration of symptoms and the anatomical staging and the mean duration of symptoms in the three anatomically staged groups were as follows: Stage I: 6.4 months, Stage II: 3.9 months and Stage III: 5.1 months.

At least 19% of the patients were initially clinically considered to have terminal disease as judged by severe weight loss and cachexia, weakness and poor performance status. Ten per cent were too ill to be discharged from hospital and died during their initial admission here within periods ranging from less than 24 hours to a few weeks. Of the non-histologically proven group 27% were either too ill for invasive investi-

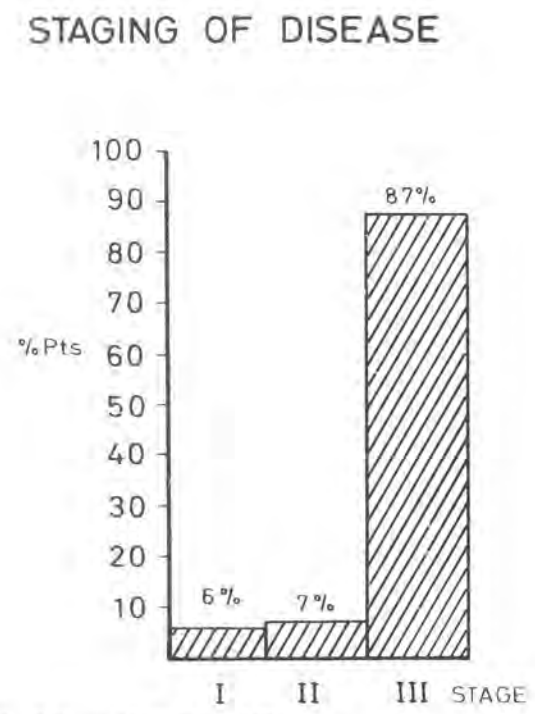


**Fig. 3. Anatomic Staging of Disease**

gations or died before investigations could be completed.

**Radiological features:** Details of the radiological abnormalities seen are shown in Table II. The commonest radiological abnormalities were a mass lesion/consolidation with or without atelectasis (56%) followed by hilar mass (36%) and pleural effusion (30%). Associated changes in addition to the lesions in the lung fields indicative of disease spread where most commonly in the form of bony lesions (13%), mediastinal involvement (9%) and diaphragmatic palsy (3%). The right lung was more commonly the site of the lesion (60%) and in 2% the lesion could not be lateralised. In both sides the upper lobes were the more commonly involved sites.

**Table II**

**Radiological Features**

| Features | % Patients |
|---|---|
| No change | 1 |
| Collapse/mass/consolidation | 56 |
| Hilar mass | 36 |
| Pleural effusion | 30 |
| Associated bone lesions | 13 |
| Mediastinal changes | 9 |
| Non-specific infiltration | 7 |
| Diffuse/bilateral shadows | 5 |
| Cavitating lesions | 3 |
| Coin lesions | 2 |
| Elevation of diaphragm (with other lesion | 2 |
| Side of lesion: Right | 60 |
| Left | 38 |
| Indeterminable | 2 |

## DISCUSSION

The prognosis of lung cancer has tended to be based solely on its anatomic extent and cell type. Assessments based on the anatomic extent of the disease do not take into account its effects on systems that have not been actively invaded. Tumours are often erroneously labelled "early" and "late" based on their anatomic extents and morphological characteristics whereas by the time a tumour is visible radiologically it has already passed through 80% of its life span, is not curable by resection in over 90% of the cases, and is therefore actually detected late in its course (Rhodes *et al.*, 1973). Feinstein (1966, 1968) pointed out the significance of the symptomatology as the function of the cancer and its effects on the patient. He grouped patients into the three clinical (symptomatic) classes as opposed to their anatomic groups (I, II and III based on the extent of disease) and found good correlation between their clinical group and survival rates. For each anatomic group the survival rates were best for asymptomatic patients followed by those with primary symptoms, and worst for those with symptoms representative of metastasis. Also, patients with primary symptoms of longer duration survived longer than those in the "early discovery group" with a short history. This was explained by the fact that while primary symptoms of short duration were of doubtful significance, those of long duration indicated a slow growing tumour with little systemic or metastatic effects. He concluded that data supplying information about both the anatomic and clinical groups would be more meaningful in general and especially so in studies involving cancer therapy involving survival periods.

These findings have been supported by the work of others (Johnson and Smith, 1971; Green *et al.*, 1971; Hyde *et al.*, 1973 and Lanzotti *et al.*, 1977). Asymptomatic patients have the best prognosis (Johnson and Smith, 1971; Green *et al.*, 1971 and Senior and Adamson, 1970). Johnson and Smith (1971) observed in addition that marked weight loss was a very important factor even in the absence of metastasis. Green *et al.*, (1971) found the presence of primary and general features to be more favourable in terms of survival than those attributable to metastasis. The most significant prognostic findings within each stage of tumour spread in their series were age, histology, dyspnoea, acute pneumonia, anorexia, aesthenia and weight loss. Duration did not appear to exert any significant influence on the prognosis. Lanzotti *et al.* (1977) graded the symptom status of their patients with inoperable lung cancer into five classes ranging from asymptomatic to totally bed ridden. In their patients with limited disease, weight loss was the major prognosticator followed by symptom status, presence of supraclavicular metastasis and age. In patients with extensive disease, symptom status and age were the dominant factors followed by weight loss and metastasis. Histological type appeared relatively unimportant in their groups. Hyde *et al.* (1973) thought the "performance status" (general condition) to be of importance along with the extent of disease and cell type in influencing the survival. The clinical features and symptomatology as shown by the above studies provide some direct evidence of the duration of disease and prognostic information relating to survival, and to staging of disease especially with regard to operability.

The clinical features manifested are determined by the biological behaviour of the tumour and this often varies with the histological type. Squamous carcinoma tends to have a slow growth rate, and this is reflected in the symptomatology. These patients have symptoms chiefly referable to local growth and to regional extension, distant metastasis being late. Radiologically 40 — 60% have a perihilar mass, 25 — 30% a single peripheral nodule often large (66% more than 4 cm and 30% more than 8 cm in size) and 8 — 10% show cavitation (Byrd *et al.* 1978). Large cell carcinoma tends to resemble the squamous type in its behaviour (Byrd *et al.* 1968). The natural history of small cell carcinoma on the other hand is compressed into a shorter clinical phase with early metastasis and early extensive involvement of the mediastinal nodes. At presentation, there is involvement of the bone marrow and liver in 45% and 50% respectively (Hansen *et al.*, 1972) and of the brain in 8% (Newman *et al.*, 1973). It presents most often as a perihilar mass in 60 — 75% and even when seen as a peripheral lesion there is hilar lymphadenopathy in 33% (Byrd *et al.*, 1968). Adenocarcinoma is frequently asymptomatic at the time of discovery but in the symptomatic cases, features of local extension especially involving the pleura are prominent and dissemination occurs early. Sixty to seventh per cent are located peripherally and pleural effusion occurs in about 10% (Byrd *et al.*, 1969).

Our patients have been seen at advanced stages of their disease with a relatively poor prognosis as judged by clinical presentation and symptomatology, radiology, anatomic staging and low operability rates (11%). In the 2% who were asymptomatic half were operable cases, a finding in keeping with the relatively favourable prognosis in asymptomatic patients. As in most series (Hyde and Hyde, 1974) cough, weight loss, haemoptysis, dyspnoea and chest pain have been the most prominent symptoms. There was however a high incidence of SVC obstruction, hoarseness, dysphagia, intracranial involvement and other metastatic lesions. Cord compression was also probably relatively more common being seen in 2% at presentation, often as the main problem.

One per cent of patients had a normal chest radiograph at presentation and only 2% presented with coin lesions which are generally associated with a higher resectability rate (Hyde *et al.*, 1973). This may be on account of later presentation in our patients and because small lesions had been missed or overlooked earlier as was evident in some cases. Tala (1967) found in resected surgical specimens that only an extremely small number of peripheral lesions one centimetre or less in diameter were detected radiologically. A hilar mass and pleural effusion were common findings in our series as were large mass lesions. Patients with these radiological features usually have a poorer prognosis than those with smaller lesions and lesions in the mid lung (Brewer, 1977).

Follow up information on our patients has been very poor and we are unable to correlate the presenting symptomatology and findings with survival. It is clear in our experience however that most patients are being seen at advanced stages of their disease even by clinical standards.

## SUMMARY

The presenting features of 388 patients with lung cancer seen over a ten year period at the University Hospital are discussed together with the implication of the different classes of symptoms and features. The influence of the symptomatology on the prognosis and survival is re-emphasised and the relevant literature reviewed. From our experience, we feel that: (i) earlier and more aggressive investigation appears warranted in suspicious lung lesions. Some patients had been treated on radiological grounds alone as tuberculosis or other infection. (ii) Where facilities for proper investigations and management are unavailable, patients with suspected lung cancer ought to be referred to appropriate centres as early as possible. Many of our patients were already in terminal states when first seen at this centre.

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# LUNG CANCER: II. DIAGNOSTIC METHODS

SAW HUAT SEONG & M. ASHOKA MENON

## INTRODUCTION

ALTHOUGH bronchogenic carcinoma was first described in the nineteenth century, it did not assume its present day significance till the early part of this century. Today, it ranks as one of the commonest visceral cancers in man. (Schneiderman & Levin, 1972; Crofton & Douglas, 1975; Carnow & Meier, 1973).

The diagnosis of lung cancer and its assessments for operability are especially important since Evarts Graham's epoch-making first pneumonectomy for cancer in 1933 — an event which heralded surgery as one of the therapeutic modalities in the management of lung cancer. Inspite of the increasing popularity that pulmonary resection enjoys, carcinoma of the lung is still looked upon as an incurable disease by some clinicians and as such, too much emphasis and reliance are placed on the plain chest x'ray in making a diagnosis. While this practice may be partially justifiable in far-advanced malignancy, when the clinical diagnosis may be fairly accurate every endeavour should be made to obtain tissue diagnosis in the more favourable patient.

This paper reviews our experience with the various methods of obtaining a histological diagnosis and analyses the yields obtained therefrom.

## PATIENTS AND RESULTS

The case protocols of all 278 patients with histologically provened lung carcinoma admitted to the University Hospital, Kuala Lumpur between the years 1967 and 1977, were studied and analysed retrospectively.

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Table I illustrates the diagnostic methods employed and lists the frequency of utilization of each method. It also shows the proportion of positive yields obtained from each diagnostic procedure.

Table I

**Method of Obtaining Histological Diagnosis and its Efficacy**

| METHOD | FREQUENCY OF UTILIZATION (%) | POSITIVE YIELD (%) |
|---|---|---|
| Sputum Cytology | 30 | 64 |
| Bronchoscopy | 44 | 41 |
| Lymph Node Biopsy | 21 | 74 |
| Effusion Cytology | 11 | 61 |
| Open Biopsy (Mediastinotomy & Thoracotomy) | 7 | 100 |
| Needle Pleural Biopsy | 10 | 55 |
| Biopsies from secondaries | 9 | 100 |
| Mediastinoscopy and Biopsy | 5 | 29 |
| Percutaneous Needle Lung Biopsy | 1 | 33 |

As can be anticipated, the highest yields (100%) were obtained from open biopsies and biopsies from secondaries.

It was disappointing to note that sputum cytology was requested for in only 30% of the patients inspite of the fact that it provided tissue diagnosis in 64% of the specimens examined.

The frequency of the various cell types are shown in Table II.

## DISCUSSION

The suspicion that a patient may be suffering from lung carcinoma is based on clinical features and radiological appearances of the chest. In a good number of patients, the chest x'ray (Figs. 1 and 2) may be so classical that, coupled with the clinical features suggestive of far-advanced

**Table II**

**Cell Types of Lung Carcinoma**

| CELL TYPES | FREQENCY (%) |
|---|---|
| Squamous | 34 |
| Adenocarcinoma | 25 |
| Oat (Small) Cell | 12 |
| Large Cell | 12 |
| Anaplastic | 15 |
| Others | 2 |

malignancy, further work-up beyond some relatively non-invasive procedures may appear to be an academic exercise. Also radiological features suggestive of an infectious process (Fig. 3) may make invasive investigations unjustifiable. Notwithstanding these remarks, errors in the diagnosis of malignancy, based purely on clinical and radiological grounds do occasionally occur. (Figures 4, 5 & 6) Likewise, the apparently benign lesion is occasionally subsequently proven to be malignant. In view of this, every attempt should be made to obtain a histological diagnosis and to determine the extent of the disease.

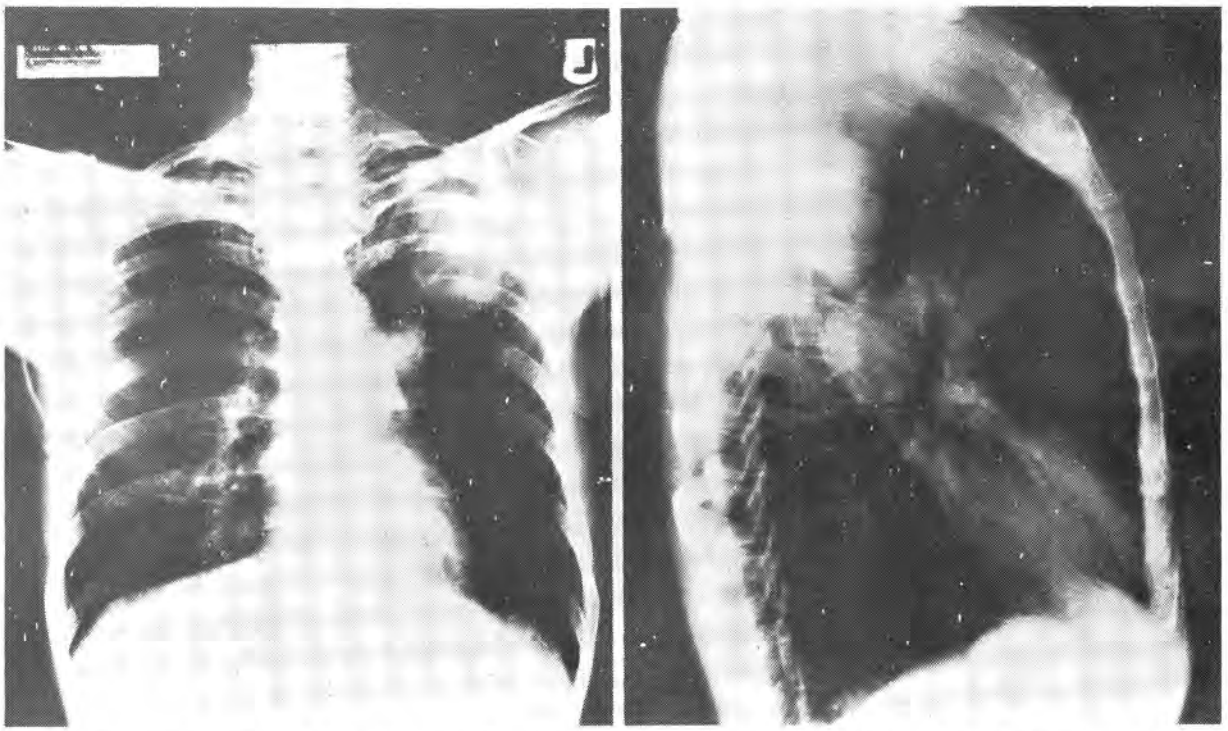

**Fig. 1. Posteroanterior and lateral chest x'ray of a 37 year old Malay male showing a mass shadow in the left upper zone with associated prominence of the left hilum indicative of lymphadenopathy.**

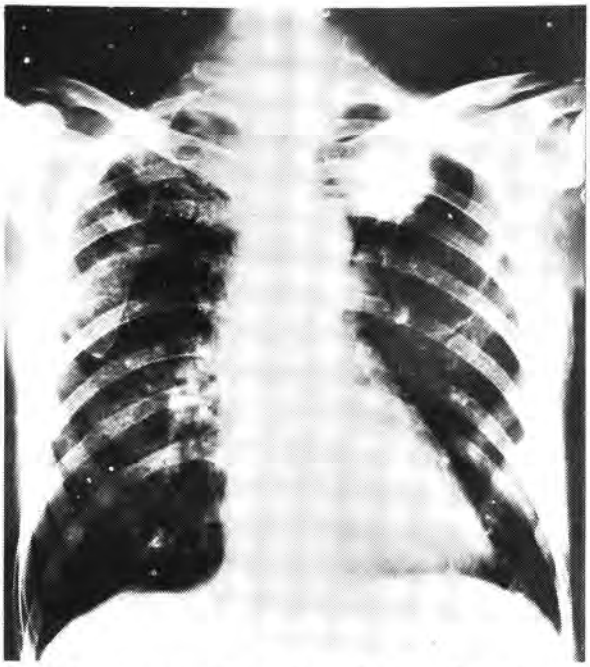

Fig. 2. Posteroanterior chest radiograph of a cachetic 65 year old female who complained of dyspnoea and haemoptysis.

## SPUTUM CYTOLOGY

In this series, sputum cytology was requested for in only 30% of patients. Inspite of the inadequate attention paid to obtaining a good specimen, the yield was surprisingly good (64%). Ideally, post-tussive morning specimens should be submitted, although specimens obtained after vigorous physiotherapy will do just as well. In patients with minimal or dry cough, sputum production may be induced with the aid of aerosol sprays.

The examination of multiple specimens of sputum will also increase the yield. It has been stated that the positive rate is slightly less than 50% with single specimen examinations, improving to over 75% when multiple specimens are examined (Koss, 1967; Nasiell, 1967; Frable, 1968).

As expected, and further supported by Srivastava's (1973) study, centrally placed tumours, even when small, tended to give a higher yield than peripherally positioned ones. This is a useful observation to bear in mind since centrally placed

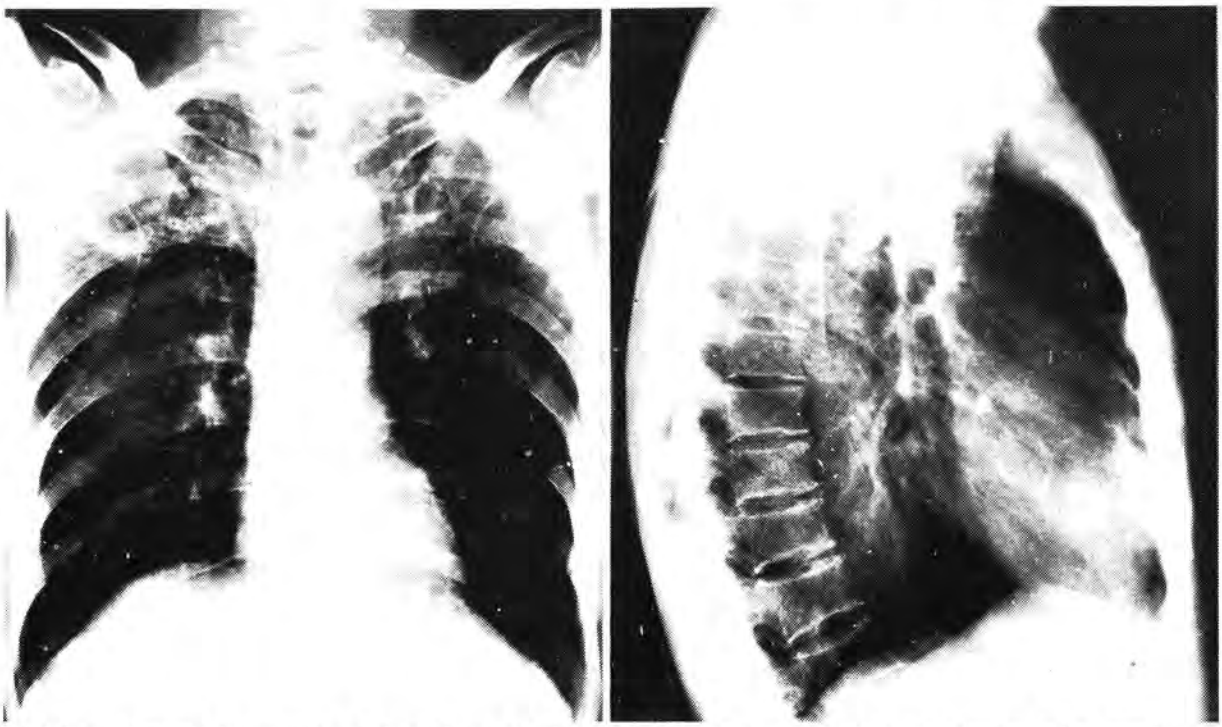

Fig. 3. Chest x'rays of a 60-year old man with a history of night sweats and chronic cough. Note the bilateral apical scarring typical of chronic pulmonary tuberculosis.

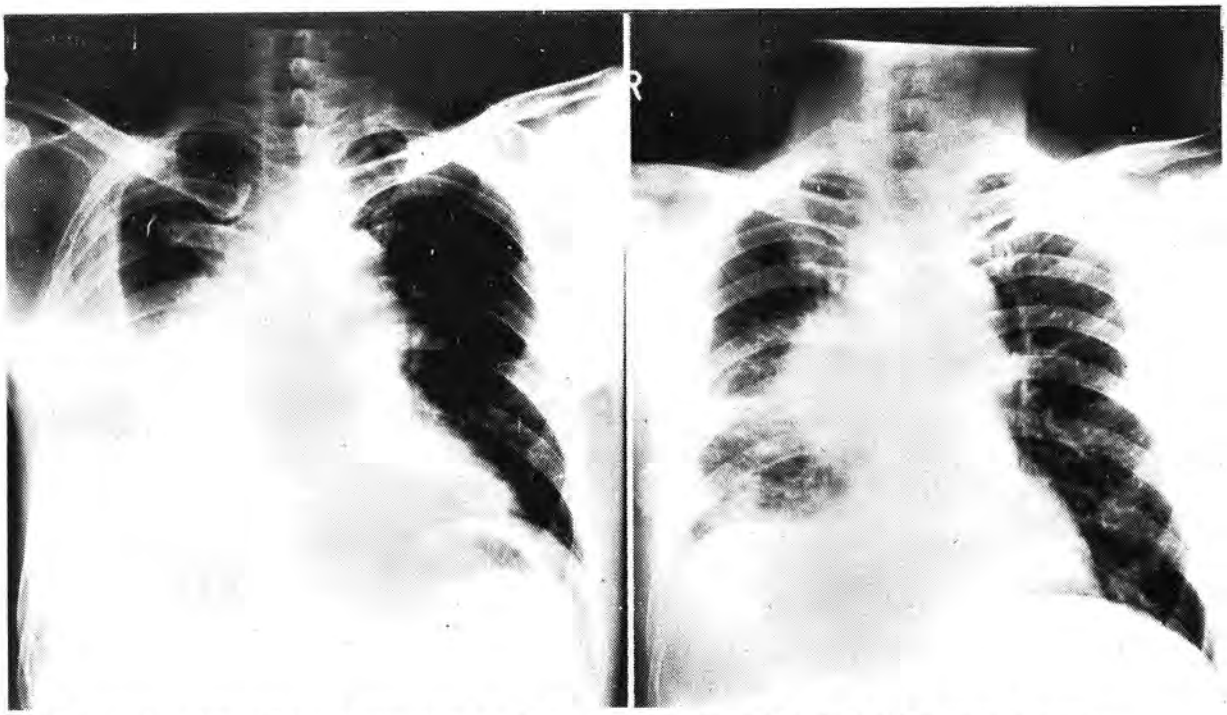

Fig. 4. These x'rays belonged to a 63-year old man with very strong circumstantial evidence of lung cancer. However, all investigations short of open biopsy did not reveal any malignancy. He was finally proved at exploratory thoracotomy and direct biopsy to have primary amyloidosis.

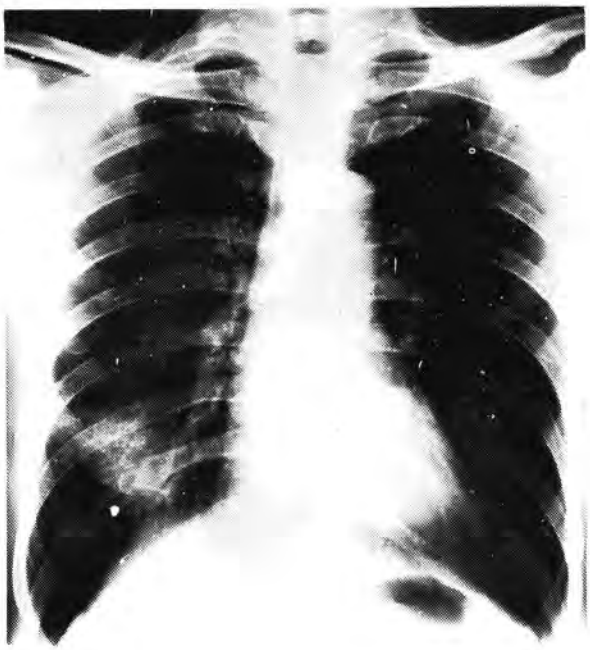

Fig. 5. When non-invasive investigations did not confirm malignancy in the patient who presented with this chest x'ray, he was given a therapeutic trial with various antibiotics. These too, did not produce any resolution. Exploratory thoracotomy with wedge resection and frozen section subsequently confirmed the lesion to be suppurative pneumonia.

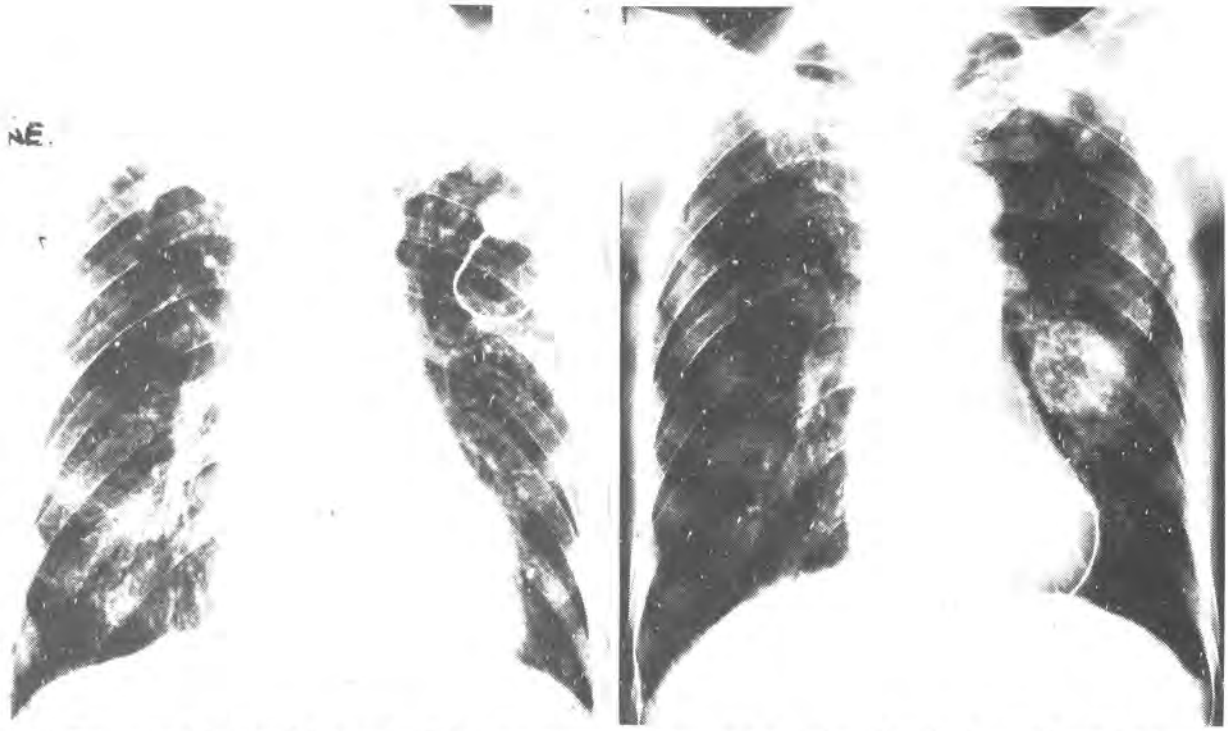

Fig. 6. The routine chest x'ray (left) taken in 1974 when a permanent pacemaker was implanted in this 60 year old man was typical of tuberculosis. In 1977, he returned for a change of pacemaker at which time the preoperative chest x'ray (right) done showed a mass lesion in the left midzone. Investigations for malignancy were negative. When subsequently subjected to exploratory thoracotomy and open biopsy, this mass proved to be a benign granuloma.

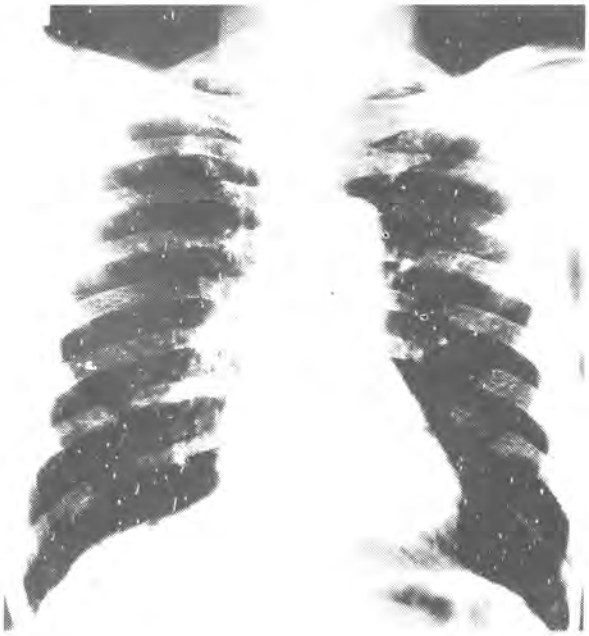

Fig. 7. This 70 year old male presented to the National T.B. Centre with complaints of haemoptysis and weight loss. The chest x'ray done (above) showed some scarring in the right apex and the Mantoux Test was positive. He was therefore started on antituberculous treatment. Five weeks after initiation of therapy, a right scalene node was palpable. This was biopsied and reported as being infiltrated with a well-differentiated squamous cell carcinoma. Subsequent bronchoscopy showed a similar tumour in the left main bronchus. (Note that his chest x'ray appeared essentially normal).

tumours may be difficult to detect radiologically (Fig. 7) so that sputum cytology and bronchoscopy may provide the key to diagnosis in these patients.

## BRONCHIAL WASHINGS AND BRUSHINGS

Examination of bronchial brushings for malignant cells has been advocated by some workers (Fry & Manalo-Estrella, 1970; Saltzstein *et al.*, 1977). In the initial technique described, a catheter is percutaneously introduced into the cervical trachea and advanced under fluoroscopic control, to the area of density. A thin wire with a brush at its tip is then advanced through the catheter to obtain specimens for microscopic examination. Using such a technique, a 75% diagnosis rate has been reported (Fry & Manalo-Estrella, 1970).

This rather laborious procedure has not gained popularity. However, during bronchoscopy with a rigid bronchoscope, many endoscopists have found it useful to instill about 10ml. of normal saline down the bronchoscope and to examine these aspirated washings cytologically.

With the introduction of the fiberoptic bronchoscope, bronchial brushings and washings have been most encouraging (Saltzstein, *et al.*, 1977) and should be routinely carried out when no tumour is visualised.

## PLEURAL EFFUSION CYTOLOGY

In patients with obvious pleural effusions and those where the costophrenic angles are obliterated, suggesting the presence of an effusion, diagnostic aspirations should be carried out and the fluid so obtained examined. Irrespective of the nature of the fluid malignant cells should be looked for because blood-stained effusions in association with bronchial carcinoma is not necessarily equated with pleural secondaries (Le Roux 1968). In our series, out of a total of 30 cases wherein the fluid was submitted for cytology, 61% were positive. Repeated aspirations and examination of the sanguinous fluid obtained from one patient did not reveal any tumour cells — this patient was subsequently provened to have primary amyloidosis.

## BRONCHOSCOPY

Today bronchoscopy continues to provide an important method of investigating for pulmonary carcinoma. It is not without risks, so that it should be performed only in patients assessed as operable or in patients in whom a diagnosis by less invasive procedures has not been obtained.

To date, all bronchoscopies performed in this institution has been with the rigid bronchoscope. Although it has the disadvantage of limiting examination to the more central portions of the tracheobronchial tree, the rigid instrument allows for better assessment of the fixity of the carina and the displacement of the main stem bronchus. In addition, bronchial washings and biopsies are more easily obtained through its larger lumen.

The flexible fiberoptic bronchoscope has several advantages over the rigid bronchoscope (Table III) but it should not be used to the exclusion of the latter. Used in conjunction with rigid bronchoscopy, positive histological results and assessment of operability will be enhanced.

**Table III**

**Advantages of Fiberoptic Bronchoscopes**

1. Better patient tolerance under local anaesthesia.
2. May be passed beyond constricted and distorted segments of bronchi.
3. Allows for brushing biopsies of lesions in distal bronchi.
4. May reveal occult lung cancer situated peripherally.

## LYMPH NODE BIOPSY

Scalene node biopsies were undertaken only when they were clinically palpable. We do not believe that a routine scalene fat pad biopsy should be undertaken. This policy is in keeping with the general observation that there is less than a 10% pick-up rate in patients with peripheral lesions which do not show radiological evidence of mediastinal lymphadenopathy Mulder, 1977).

## MEDIASTINOSCOPY, MEDIASTINOTOMY AND OPEN BIOPSY

Mediastinoscopy has not been done as a routine diagnostic procedure in our set-up because the lack of operating time and personnel forces us to embark upon procedures which are

more likely to give a positive result. Hence exploratory thoracotomy and open biopsies are resorted to more frequently (7%) than we would have otherwise preferred.

Mulder (1977) feels that if scalene node biopsies are positive, mediastinoscopy can be dispensed with. Apart from it being superfluous under such a circumstance, mediastinoscopy should not be considered as a minor surgical procedure since serious complications like large vessel injury, tension pneumothorax and cerebrovascular accidents caused by temporary occlusion of the innominate artery (Trinkle *et al.*, 1970; Stanford *et al.*, 1975) though infrequently reported my assume major proportions if this procedure was performed with impunity.

These potential complications have led McNeill and Chamberlain (1966) to suggest mediastinotomy as an alternative to mediastinoscopy. Here, these authors feel that an extra-pleural approach through the bed of the second or third costal cartilage provide a safer access to the mediastinum especially in lesions of the left lung and hilum. We have also preferred this approach and have had no hesitation to extend the incision intrapleurally to enable us to obtain a direct biopsy of the tumour. This technique was used in 7% of our patients with a 100% positive result.

## NEEDLE BIOPSY

Needle biopsy of the lung and pleura although providing a high positive yield, was done in only 11% of patients since this simple procedure is not without risks. It is usually performed in patients with pleural effusions and in the elderly or ill patients in whom a thoracotomy is contraindicated on account of high risk — the very group of patients who would tolerate the not insignificant incidence of pneumothorax and bleeding poorly. Presently, we have tended to limit this procedure to poor risk patients in whom the tumour is up against or invading the chest wall and where a diagnosis is required for radiotherapy or chemotherapy.

## EXPLORATORY THORACOTOMY

In the final analysis, the diagnosis and extent of the tumour are most accurately established by exploratory thoracotomy. This does not mean that all patients should be exposed to this most invasive investigatory procedure. In fact, exploratory thoracotomy should be reserved only for patients in whom there is a good chance of accomplishing curative resection.

## CONCLUDING REMARKS

From the foregoing discussions it can be appreciated that there are numerous investigatory procedures that a patient suspected of harbouring lung cancer can be subjected to — some are quite innocuous while others carry a substantial risk. It is important, therefore, to have a practical and safe approach to these patients (Fig. 8).

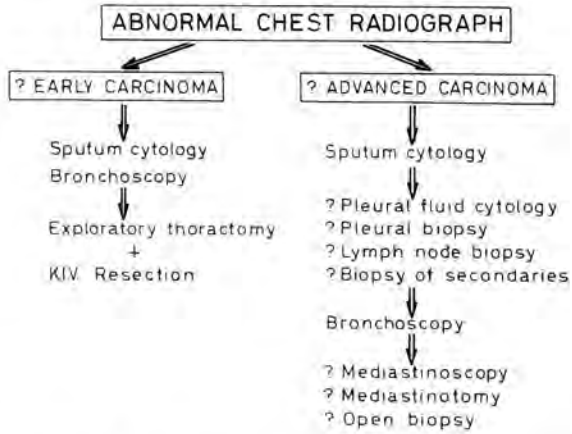


**Fig. 8. Suggested Flow-chart for patients suspected to have pulmonary carcinoma.**

When early carcinoma is suspected, too much time should not be unnecessarily spent on non-invasive investigations. Exploratory thoracotomy with a view to curative resective surgery should be embarked upon with little time loss.

The patient with suspected advanced carcinoma is a different problem altogether. Here sputum cytology should be repeatedly performed in the first instance. If a pleural effusion is present, diagnostic aspirations should be done. Where secondaries and lymph node involvement are suspected they should be biopsied. If these investigations prove negative, bronchoscopy and the other procedures outlined in Fig. 8 may be justified.

## SUMMARY

The rising incidence of lung cancer in Malaysia warrants a reappraisal of the approach to patients suspected of having pulmonary carcinoma. This paper reviews our experience with the disease at the University Hospital, Kuala Lumpur, over a 10-year period. The various diagnostic methods utilized are critically analysed and a recommendation is made as to the diagnostic work up of these patients.

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# HUMAN T- AND B-LYMPHOCYTE POPULATIONS IN BLOOD: LOCAL POPULATION STUDIES

T. PANG, N. PARASAKTHI & S.F. YAP *

## INTRODUCTION

THE RAPID increase in immunological knowledge in the past 10 — 15 years has been accompanied by an increasing demand for laboratory services in clinical immunology. Such laboratories, especially in the developing countries, restrict themselves to tests concerned mainly with the humoral aspects of immunity i.e. detection of antibodies in a variety of infections (serology) or the measurement of serum protein components (e.g. complement, immunoglobulins). However, and as pointed out recently (see reference 7), there is also a need to have available tests on *cellular* immunity. This communication reports the introduction of one of these tests, the enumeration of T and B lymphocytes in the University Hospital. Local population values, of which little is known, are reported together with the methods used and the application of the test in clinical conditions.

## MATERIALS AND METHODS

### Donors and patients

Healthy adult donors were selected from the Blood Bank, University Hospital, Kuala Lumpur or from students of the Faculty of Medicine, University of Malaya. ALL (acute lymphoblastic leukaemia) patients were selected according to the criteria of Brouet *et al.* (1976) and the diagnosis confirmed by standard cytological procedures.

### Specimens

4 — 5 ml blood collected into glass containers containing EDTA or heparin.

### Lymphocyte isolation

Lymphocytes were isolated using Ficoll-Paque density gradients by a technique modified from Boyum (1968). Diluted blood (3.5 mls blood and 3.5 mls balanced salt solution, BSS) was layered on 3 mls of Ficoll-Paque (Pharmacia Fine Chemicals, Uppsala, Sweden) in siliconized glass tubes. Tubes were then centrifuged at 400g for 30 mins, the lymphocyte layer recovered and the cells washed 3 times with BSS. Lymphocytes were then counted in a haemocytometer and viability determined by trypan blue dye exclusion.

### T cell enumeration

T cells were enumerated by formation of rosettes with sheep erythrocytes (erythrocyte-rosette-forming cells, E-RFC) using a technique extensively modified from Winchester & Ross (1976). Sheep red blood cells (SRBC) were first washed 3 times with phosphate-buffered saline (PBS). 100 µl of packed SRBC were then treated with 400 µl AET (2-aminoethyl isothiouranium bromide, Sigma Chem. Co., St. Louis, MO., U.S.A.; 0.402 gm AET made up with 10 mls distilled water, adjust to pH 9.0 with 4N NaOH) for 15 mins at 37° C. AET treatment of SRBC has been shown to improve the stability and speed of binding of rosettes (Pellegrino *et al.*, 1975). SRBC were then washed 5 times with PBS and 50 ul packed SRBC added to 10 mls BSS to give a final concentration of 0.5% SRBC. Rosette formation was carried out by mixing 0.5 ml of 0.5% SRBC suspension with 0.5 ml lymphocytes (conc. = 2 x $10^6$ cells/ml), incubating for 15 mins at 37° C and then centrifuging for 10 mins at lowest speed on the bench centrifuge (MSE bench top centrifuge). The tubes were then allowed to stand at 0 — 4° C (on ice) for 15 mins and the cell pellets resuspended by *gentle* shaking in a small volume of BSS. The proportion of rosetting cells was then counted under the light microscope. A lymphocyte is counted as rosette-forming if three or more erythrocytes adhere (Winchester & Ross, 1976).

### B cell enumeration

B cells were enumerated by direct immunofluorescence to detect the presence of surface

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membrane immunoglobulin (SmIg). Lymphocytes were suspended in PBS at a concentration of 2 x $10^7$ cells/ml. 20 µl of this suspension was then mixed with 20 µl of fluorescein-conjugated, heterologous anti-human immunoglobulin (antiserum to human IgG + IgA + IgM, fluorescein-conjugated, Behringwerke, W. Germany). Final dilution of antiserum was 1 in 2 or 1 in 4. The mixture was incubated for 30 mins at room temperature and then washed 3 times with PBS-albumin (2% bovine albumin in PBS). Pellets were finally resuspended in 0.1 ml PBS plus 1 drop PBS-glycerol (10% PBS in glycerol) and examined under a fluorescent microscope (Leitz ortholux II).

## RESULTS

The method used for isolation of lymphocytes (Ficoll-Paque density gradients) regularly gave > 35% recovery of input lymphocytes (mean recovery = 45%) with a viability of > 95% for the isolated lymphocyte population.

As shown in Table I, a value of 70% T lymphocytes (E-RFC) and 9% B lymphocytes (SmIg-positive cells) in peripheral blood was obtained in a study of the local population. The range of values was 55 — 86% for T cells and 3 — 20% for B cells (Table I). Further analysis of the data showed no significant differences between the various racial groups tested i.e. Chinese, Malays and Indians (Table II). Similarly, the values obtained did not seem to be influenced by the sex of the donors (Table II). In addition, the test was also used to analyze peripheral blood lymphocytes from 3 cases of ALL (Table III). According to the classification of Brouet *et al.* (1976) two patients had a T-derived ALL and one had a non-T non-B (null) ALL (Table III).

**Table I**

**Percentage of T and B cells in normal peripheral blood**

| Donors* | % T cells (E-RFC) | % B cells (SmIg) |
|---|---|---|
| Normal | 70.5 ± 8 (Range: 55 — 86) | 9.4 ± 4 (Range: 3 — 20) |

* Total no. of donors = 33

**Table II**

**Percentage of T and B cells in normal peripheral blood: Effect of race and sex of donors.**

| Parameter* | % T cells (E-RFC) | % B Cells (SmIg) |
|---|---|---|
| Race | | |
| Chinese (13) | 71.5 ± 8 | 7.8 ± 4 |
| Malay (10) | 71.9 ± 7 | 11.5 ± 5 |
| Indian (10) | 67.6 ± 8 | 10.1 ± 5 |
| Sex | | |
| Male (21) | 71.0 ± 8 | 10.5 ± 5 |
| Female (12) | 67.9 ± 8 | 6.6 ± 2 |

* No. in brackets indicate number of donors in each group

**Table III**

**Percentage of T and B cells in peripheral blood of ALL patients**

| Patient | % T cells (E-RFC) | % B Cells (SmIg) | Classification |
|---|---|---|---|
| P | 82 | 8 | T-derived ALL |
| Z.Y. | 44 | 22 | T-derived ALL |
| T.S.P. | 7 | 1 | Non-T non-B ALL |

## DISCUSSION

The detection of E-RFC and SmIg-positive cells are the most commonly used techniques for the identification of human T and B lymphocytes respectively (Strober & Bobrove, 1975; Winchester & Ross, 1976; Hayward & Greaves, 1977). Conclusive evidence has also been obtained that E-RFC's are in fact T cells and that SmIg-positive cells are B cells (Hayward & Greaves, 1977; Chess & Schlossmann, 1977). In the present report, these two methods were used to obtain values for T and B lymphocytes in peripheral blood in a local, Asian population. These values are of obvious importance if the test is to be used in a local context. The values obtained in the present study appear to be in agreement with those obtained for Caucasians where the following values have been reported for T and B lymphocytes respectively: 85% and 9% (Winchester & Ross, 1976), 77% and 21% (Strober & Bobrove, 1975), 75% and 10% (Hayward & Greaves, 1977), 70 — 80% and 5 —

15% (Waller & MacLennan, 1977). The results also indicated that approximately 10 — 20% of peripheral blood lymphocytes appeared to possess neither T- nor B-lymphocyte characteristics. These cells have been referred to as 'unclassified" cells (Hayward & Greaves, 1977) and probably include K cells and null cells (Winchester & Ross, 1976; Hayward & Greaves, 1977; Chess & Schlossmann, 1977).

It is important to note, however, that several factors may influence the tests. Firstly, monocytes are found together with lymphocytes isolated by the Ficoll-Paque technique (Winchester & Ross, 1976). The monocyte shares several cell surface markers with the B lymphocyte so that in disease states where monocytes are significantly increased (e.g. Hodgkins disease) they could be erroneously counted as B lymphocytes (Strober & Bobrove, 1975; Winchester & Ross, 1976). In the present study, the degree of monocyte contamination was about 10%. Secondly, antilymphocyte antibodies which adhere to the lymphocyte surface can confer positive surface staining to an otherwise SmIg-negative cell. These antibodies are often found in diseases such as rheumatoid arthritis and systemic lupus erythematosus (Strober & Bobrove, 1975; Winchester & Ross, 1976). Other factors which may influence the tests include physiological variations (Hayward & Greaves, 1977), antiserum specificity and technical factors (e.g. mechanical or thermal disruption of erythrocyte rosettes) (Winchester & Ross, 1976).

There are several areas in which the above tests could be used as clinical diagnostic aids. Firstly, the diagnosis of immunodeficiency disorders during infancy and early childhood can be supported by the above tests (Strober & Bobrove, 1975; Hayward & Greaves, 1977; Cooper & Seligmann, 1977). For example, infants with DiGeorge syndrome (thymic hypoplasia) have significantly decreased T cells (Strober & Bobrove, 1975) and, at the other extreme, the absence of peripheral blood B lymphocytes is characteristic of X-linked hypogammaglobulinaemia (Cooper & Seligmann, 1977). Secondly, these tests are also of use in the immunological categorization of leukaemic cells and lymphomas (Brouet *et al.*, 1976; Hayward & Greaves, 1977; Barrett *et al.*, 1977). These studies indicate that ALL patients, for example, could be classified into three groups: (i) non-T non-B ALL (ii) T-derived ALL (iii) B-derived ALL (Brouet *et al.*, 1976). Of the three patients studied in the present report, two seemed to have T-derived ALL and one a non-T non-B (null) ALL. A more extensive study involving more ALL cases is under way. In contrast, CLL (chronic lymphocytic leukaemia) appears to have predominantly B cell features (Cooper & Seligmann, 1977). Whether or not immunological typing of a patient's cells possesses any prognostic significance remains to be seen (Hayward & Greaves, 1977). Other areas in which these tests may be of use include sarcoidosis, hepatitis, various infections and certain non-lymphoid malignancies (Hayward & Greaves, 1977).

## SUMMARY

The relative percentages of T and B lymphocytes in peripheral blood in a local, Asian population was determined. The values obtained were 70.5% T cells (by sheep erythrocyte-rosetting test) and 9.4% B cells (by immunofluorescence to detect surface membrane immunoglobulin). There appeared to be no significant differences between males and females and between the various racial groups tested (Chinese, Malays, Indians). The test was also used to type leukaemic cells from 3 ALL patients.

## ACKNOWLEDGEMENTS

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# NORMAL SERUM IMMUNOGLOBULIN G, A AND M LEVELS IN FULL TERM MALAYSIAN NEWBORNS*

M. YADAV & F.H. SHAH.

## INTRODUCTION

NEWBORNS, have large amounts of IgG antibody almost all of which is passively derived from the mother via the placenta; sometimes IgM and IgA is also present in low concentration in the cord sera but these immunoglobulins are synthesised by the fetus (Solomon, 1971). The other immunoglobulins, i.e. IgD and IgE, appear in the circulation after birth. The level of the immunoglobulins in the newborn varies with several factors which may include gestation age, mother's health and congenital infections (Alford *et al.*, 1969; Hardy *et al.*, 1969). The IgG levels in the fetal circulation increase slowly initially and more rapidly in the third semester or pregnancy, and at term the IgG level in the cord serum may, in some instances, exceed the levels in the mother (Dancis *et al.* 1960, 1961, Gitlin *et al.*, 1964). The immune protection provided by maternal antibody lasts in the infants for over six months but this protection is directed against organisms to which the mother is immune and there is no protection to microorganisms which chiefly evoke IgM antibody (Vahlquist, 1958).

There are few studies on the cord serum immunoglobulins of tropical populations outside the African region (Michaux *et al.*, 1966; Edozein et al., 1962; McFarlane & Udeozo, 1968). Since Malaysia is situated in the tropical zone and the population is subject to regular incidence of protozoal and helminth infections it was desirable to conduct this study in order to obtain basic information on the immunoglobulins of newborns in the four Malaysian races.

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## MATERIALS AND METHODS

### Maternal and cord sera

Blood samples from the three Malaysian races (Malays, Chinese and Indians) were obtained from the Department of Obstetrics and Gynaecology at the University Hospital and the Orang Asli (Malaysia aborigines) samples from the Gombak Orang Asli Hospital. Maternal blood was taken by antecurbital venepuncture one to two weeks prior to delivery and cord serum was withdrawn from the placental side of the umblical cord within a few minutes of delivery. Blood samples were taken only from healthy mothers and newborns who under went an uneventful gestation and normal birth. The gestation age range from 35 to 43 weeks. The blood samples were kept at 4 C overnight after which the serum was separated by centrifugation and stored at -20 C until assayed for immunoglobulins.

### Quantitative determination of immunoglobulins

Immunoglobulin A, G and M and specific antisera to them were prepared according to previously described methods (Vaerman *et al.*, 1963; Fahey and McLaughlin, 1963). The anti-IgA and anti-IgM rabbit sera was made specific for the heavy chain by removing contaminants with pooled cord serum immunoabsorbents (Avrameas and Ternynck, 1969) low in IgM and IgA.

The antibody-agar diffusion plates were prepared and the immunoglobulins quantitated by the radial agar-immunodiffusion technique of Mancini *et al.* (1965). The anti-IgG agar plates were incubated for 3 days while the anti-IgM and anti-IgA agar plates were incubated for 5 days before measurement of the diameters of the precipitin rings. Immunoglobulin standards from World Health Organisation were used. Observations for standard immunoglobulin were plotted on semi-logarithmic scale and the concentration of immunoglobulins in test serum were determined from standard curves and expressed in mg/100 ml

and also in International Units per ml. The accuracy of the method in our hands using different batches of antisera was tested by incorporating a control serum in each plate made. The coefficient of variation for the assay of IgG, IgA and IgM were 3.5, 6 and 6.8 per cent, respectively. Thus, the day to day variation in our tests was small.

## RESULTS

### Immunoglobulin G, A and M levels

Table 1 summarises the data on the immunoglobulin levels in cord sera of full term newborns and maternal sera. Cord serum mean IgG levels of Indians, Malays and Orang Asli newborn are of similar magnitude and these levels are significantly higher ($p < 0.01$) than the cord serum IgG levels of the Chinese newborns. The Indian and Malay mothers have serum IgG of comparable magnitude but the levels in the Chinese mothers are significantly lower than those observed in the Indians ($p < 0.01$) and Malays ($p < 0.05 > 0.01$). The IgG levels in the Orang Asli mothers are similar in magnitude to those in the other three races.

The serum mean IgM levels of cord sera are of equivalent magnitude in the Chinese, Malays and Indians and these levels are significantly lower ($p < 0.01$) than those observed in the Orang Asli. Similarly, the maternal mean IgM level of the 3 races are of similar magnitude but these levels are significantly lower ($p < 0.01$) than those recorded for the Orang Asli. Cord sera IgA was detected in 34.6 percent of Chinese, 40.5 percent of Indians, 31.6 percent of Malays and 62.5 percent of Orang Asli. The mean cord serum IgA levels in infants who possessed IgA ranged from 2.9 to 3.7 mg/100 ml in the four races. The maternal IgA level was of equal magnitude in the four races.

**Table 1**

**Paired maternal and cord sera of full term infants of urban-dwelling Chinese, Indians and Malays, and forest-dwelling Orang Asli.**

| Race | Immunoglobulin levels mg/100 ml | | | | | |
|---|---|---|---|---|---|---|
| | G | | A | | M | |
| | Cord serum | Maternal serum | Cord serum | Maternal serum | Cord serum | Maternal serum |
| Malay | 1169 ± 286 (165) | 1257 ± 321 (165) F/M = 0.92 | 3.7 1.35 - 12 (25/79) | 270 + 84 (154) | 10.9 ± 5.8 (161) | 160 ± 65 (161) |
| Chinese | 1092 ± 270 (168) | 1181 ± 293 (168) F/M = 0.93 | 2.9 1.35 - 10 (27/79) | 286 ± 105 (175) | 11.6 ± 6.3 183) | 177 ± 60 (183) |
| Indian | 1211 ± 282 (210) | 1310 ± 270 (210) F/M = 092 | 3.1 1.35 - 17 (32/79) | 230 ± 73 (196) | 12.5 ± 7.3 (202) | 168 ± 61 (202) |
| Orang Asli | 1254 ± 441 (44) | 1256 ± 321 (44) F/M = 1.0 | 3.1 1.35 - 17 (30/48) | 263 ± 114 (40) | 16.7 ± 6.9 (43) | 268 ± 137 (43) |

a mean ± standard deviation in mg/100 ml; to convert to I.U./ml multiply value by 0.12 for IgG, 1.43 for IgM and 0.66 for IgA. Parenthesis indicates number of observations.

b mean and range; parenthesis indicates the ratio of samples with detectable IgA levels over number tested.

F/M Fetal-maternal ratio of IgG level in cord serum and maternal serum.

Since most of the IgG in the newborn is derived from the mother the fetal-maternal ratio are of interest. In the Orang Asli the ratio was 1 and in the other three races it was just less than 1 (Table 1).

**Correlation between immunoglobulin levels and birth weight and getation**

Table II summarises the multiple regression analysis of the cord serum IgG on the birthweight and gestation age of the newborns and the maternal serum IgG concentration. The statistical analysis indicates a significant dependence of cord serum IgG level on maternal serum IgG level in the Chinese, Indians and Malays. In addition, in Indians the cord serum IgG was significantly dependent at 5 per cent level on the gestation age.

## DISCUSSION

In the four Malaysian races, and also the Taiwanese (Yang *et al.*, 1971) and the Africans Edozien *et al.*, 1962, Michaux, 1966; McFarlane & Udeozo, 1968) the mean feto-maternal ratio was equal to one or lower than one but in contrast, the feto-maternal ratio was greater than one in normal deliveries of Caucasians from the temperate regions (McCracken & Shinefield 1965, Gusdon 1969, Kohlar & Farr 1966, Cockran and Good 1974). The biological reasons for the wide variations in the IgG level of the newborn relative to the maternal serum level is not known. There is a suggestion that in the tropics maternal IgG in the foetus may be catabolically removed at an accelerated rate (Schultze & Heremens, 1966; McFarlane, 1973) but, there is as yet no experimental evidence for this proposal. We feel other factors, such as nutritional status, rate of infections and health, may be important in interferring in the transmission of IgG from mother to foetus. Although, high IgG levels in the newborns provide immune protection for long periods, they also have a suppressive effect on the normal development of the antibody-producing capacity (Graf & Uhr, 1969, Osborn *et al.*, 1952; Perkins, 1959). Maternally derived IgG in the newborn declines at an exponential rate suggesting the absence of new synthesis to replace the catabolised IgG; the half-life of maternally derived IgG is 20 to 30 days (Orlandini *et al.* 1955).

There are two postulates which help to explain the mechanism of transmission of IgG across the placenta. In Caucasian cord serum IgG levels are significantly raised relative to maternal serum levels in normal vaginal delivery as opposed to elective Caesarian birth (Jones & Payne, 1967; Cochran, 1972; Cochran & Good, 1974). Thus, these observations led to the suggestion that con-

**Table II**

**Multiple Regression analysis of cord serum IgG concentration on the birthweight, gestation age and maternal serum IgG level of newborns of Chinese, Indian & Malay origin**

| | Chinese | | | | Indians | | | | Malays | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Y | $X_1$ | $X_2$ | $X_3$ | Y | $X_1$ | $X_2$ | $X_3$ | Y | $X_1$ | $X_2$ | $X_3$ |
| Mean | 1072.3 | 3021.9 | 39.5 | 1193.8 | 1189.6 | 3089.9 | 39.7 | 1299.6 | 1164.0 | 3135.4 | 39.6 | 1264.0 |
| Standard deviation | 272.9 | 335.4 | 3.3 | 299.0 | 288.9 | 356.5 | 1.6 | 316.7 | 289.1 | 313.0 | 1.4 | 320.0 |
| Standard error of mean | 20.1 | 25.2 | 0.25 | 22.5 | 18.5 | 16.4 | 0.1 | 20.3 | 21.65 | 23.54 | 0.11 | 50.03 |
| Correlation $X_i$ vs Y(r) | - | 0.074 | 0.097 | 0.388** | - | 0.079 | 0.176 | 0.380** | - | 0.080 | 0.108 | 0.234 |
| Regression coefficient | - | 0.068 | 9.04 | 0.37 | - | 0.075 | 26.88 | 0.372 | - | 0.079 | 15.86 | 0.1016 |
| Standard error of reg. coeff | - | 0.056 | 5.722 | 0.062 | - | 0.049 | 10.926 | 0.053 | - | 0.069 | 15.17 | 0.032 |
| T value | - | 1.218 | 1.579 | 5.882 | - | 1.535 | 2.463 | 6.96 | - | 1.152 | 1.045 | 3.170 |

Y = cord IgG level in newborns in mg%  X1 = weight of newborns in grams  T = t-test value

X2 = gestation age in weeks  X3 = IgG levels of maternal serum in mg%

tractions of labour at parturition are physiologically instrumental in causing increased maternofetal transmission of IgG which then cause an elevation of the immunoglobulin in cord over maternal levels. Brambell (1966) has proposed that maternal transmission of IgG is an active process mediated by IgG-specific Fc receptors on the trophoblast membrane of the placenta. Both these mechanisms however do not help in providing a satisfactory explanation for the variable transmission of maternal IgG to foetus particularly in the lower-than-one feto-maternal IgG ratios observed in Afroasian populations.

Since cord serum IgG is chiefly of maternal origin, a correlation between the serum IgG concentration of mother and newborn would be expected. We confirm in three Malaysian races the observations made in Americans (Allansmith *et al.*, 1968) and Europeans (Berg and Nilson, 1969) that a correlation which was independant of the birthweight and gestation, was present between maternal and fetal serum IgG levels. In full term Caucasian newborns there was no correlation between cord serum IgG level and other parameters like birthweight and gestation age (Berg and Nilsson, 1969, Thom *et al.*, 1967) and our data supports these observations. Cord serum IgA and IgM levels show no correlation to birthweight, gestation age or maternal immunoglobulin level.

In Hawaii (Wang *et al.*, 1973) Taiwan (Yang *et al.*, 1971) and America (Van Furth *et al.*, 1965) the cord serum IgM values range from 5 to 15 per cent of the adult serum levels, and in the Malaysian samples the Igm values are well within this range (6.3 to 7.4 per cent). The cord serum IgM levels in the three urban races are of equal magnitude and similar findings have been made for the Caucasians. In contrast, the relatively higher cord serum IgM and IgA levels in the Orang Asli, is suggestive of greater antigen stimulation of the fetus and this may be as a consequence of high infection rate prevalent in this community (Bolton, 1968). Furthermore, a high per cent of the newborns have IgA present in the serum; we find 34.6, 40.6, 31.6 and 62.5 per cent of the Chinese, Indian, Malays and Orang Asli, respectively, have demonstrable IgA in the cord serum. The absence of IgA in some cord sera may be due to absence of IgA synthesis by fetus because of inadequate antigen stimulation or transient IgA deficiency. Similarly, the low level of IgA level (2 to 10 mg/100 ml) in normal cord sera has been reported for several populations (de Muralt and Roulet 1962, Haworth *et al.*, 1965; Steihm & Fudenberg, 1966; Hobbs & Davies, 1967; Chandra *et al.*, 1970, Yang *et al.*, 1971, Corrodi & Hitzig, 1973, Maroulis *et al.*, 1971).

## SUMMARY

Immunoglobulin G, A and M were assayed using the Mancini's radial agar-immunodiffusion technique, in paired maternal and cord sera of full-term infants of urban-dwelling Chinese, Indians and Malays, and forest-dwelling aborigines (Orang Asli). The mean serum IgG level of newborns in Orang Asli (1254 $\pm$ 441 mg/100 ml), Indian (1211 $\pm$ 282 mg/100 ml) and Malays (1169 $\pm$ 286 mg/100 ml) were of comparable magnitude but these levels were higher than the levels in the chinese (1092 $\pm$ 270 mg/100 ml). In Malaysians, as reported for other races, there was a significant dependence of cord serum IgG level on maternal serum IgG levels. The mean feto–maternal serum IgG level ratio at term was equal to one or just less. The cord sera IgG was not correlated to the birthweight and gestation age. The cord serum IgM levels in Chinese, Indian, Malay and Orang Asli newborn at term were 11.6 $\pm$ 6.5, 12.5 $\pm$ 7.3, 10.9 $\pm$ 5.8 and 16.7 $\pm$ 6.9 mg/100 ml, respectively. Furthermore, IgA was present in 34.6%, 40.5%, 31.6% and 62.5% in Chinese, Indian, Malay and Orang Asli, respectively. Cord serum IgA and IgM levels show no correlation to birthweight, gestation age or maternal serum immunoglobulin levels. In general, cord serum immunoglobulin A, G & M levels in Malaysians are significantly elevated as compared to levels noted in Caucasians from temperate regions.

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# PENINCILLIN-RESISTANT GONORRHOEA
# A Report from University Hospital, Kuala Lumpur.

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## INTRODUCTION

WHEN PENICILLIN was first introduced in 1943, it provided an easy cure for gonorrhoea. However, soon after it came into regular clinical use, treatment failures began to appear and minimum inhibitory concentration (M.I.C.) determinations showed increasing levels of resistance to penicillin among gonococcal isolates (Reyn, 1969). This type of low level or partial resistance is chromosomally-determined and is apparently related to a decreased permeability of the cell envelope (Sparling, 1972), and diminished binding of penicillin to the cell membrane (Rodriguez and Saz, 1975). To maintain effective therapy, increasingly high doses of penicillin had to be used with the addition of probenicid (Center for Disease Control, 1974).

Since early 1976, strains of gonococci totally resistant to penicillin have been reported from many countries (Ashford *et al.*, 1976; Phillips, 1976; WHO, 1977). These strains produce an enzyme, B-lactamase (penicillinase), which destroys the penicillin nucleus. This new type of resistance is mediated by plasmids (extrachromosomal loops of DNA) which can be transferred between gonococci and into other bacteria by transformation or by conjugation. These plasmids are genetically very similar to B-lactamase (TEM) plasmids of ampicillin resistant *Haemophilus influenzae* and a number of enteric bacteria (Percival *et al.*, 1976; Elwell *et al.*, 1977). The prevalence of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) among gonococcal isolates appears to be very low (0-2%) in Europe and the United States (WHO, 1977; Siegel *et al.*, 1978). In the Philippines, however, the reported prevalence of PPNG among gonococcal isolates in certain areas was 20-40% (Sparling *et al.*, 1977).

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The PPNG infections found in Singapore have increased significantly in 1978 as they comprised 4.8% of total isolates up till the end of July 1978 as compared to 0.24% for the whole of 1977 (WHO, 1978a).

The Sexually-Transmitted Diseases Laboratory, University Hospital, Kuala Lumpur, initiated surveillance for cases of PPNG infections in February 1977. We report here some clinical and laboratory findings of 43 such cases diagnosed between February 1977 and November 1978.

## MATERIALS AND METHODS

### Isolation of Neisseria gonorrhoeae

Specimens were obtained from patients seen in the University Hospital, Kuala Lumpur (UHKL), general practitioners' clinics (GP clinics) and two sexually-transmitted diseases clinics (STD clinics). The specimens were collected on charcoal-impregnated cotton wool swabs and sent to the laboratory in Stuart's transport medium. In the laboratory, the swabs were examined microscopically for pus cells and intracellular Gram-negative diplococci and cultured on Modified Thayer Martin medium (BBL), which is selective for gonococci, as well as on chocolate agar (prepared using 10% ox blood in Oxoid Blood Agar Base). The culture plates were incubated in a candle jar at 36°C for 1 to 2 days. Colonies of *N. gonorrhoeae* were identified based on the Gram-stain, oxidase reaction and direct fluorescent antibody test, as well as sugar utilization tests. The gonococcal isolates were routinely tested for penicillin susceptibility on chocolate agar using discs containing 10 units of penicillin. If the zone of inhibition was less than 20 mm in diameter, a $\beta$-lactamase test was done using the rapid iodometric method (WHO, 1976). Strains were preserved for further tests by freezing nutrient broth suspensions at -70°C.

The first 10 strains of PPNG were sent to Dr. Clyde Thornsberry at the Center for Disease Control, Atlanta, U.S.A., who confirmed the $\beta$-lactamase

production and reported on their susceptibilities to several antibiotics.

### Antibiotic susceptibility testing

The agar plate dilution method (Jaffe *et al.*, 1976) was used to test the susceptibilities of the first 19 penicillinase positive strains and 60 penicillinase negative strains to 9 antibiotics. A multiple inoculator was used to test 25 strains simultaneously.

## RESULTS

A total of 2509 specimens were received in the 22-months study period. 71% of the specimens were high vaginal or endocervical swabs, 16% were urethral swabs, 7% were conjunctival swabs and 6% consisted of miscellaneous specimens like throat swabs, rectal swabs, swabs of genital ulcers, urine, bubo or joint aspirates and prostatic fluid. From these specimens, 211 cases of gonococcal infections were diagnosed out of which 43 were by penicillinase producers.

Figure 1 shows the temporal distribution of all cases of gonococcal infections and Fig. 2 shows the temporal distribution of cases seen in UHKL only. The first two cases of infection by PPNG were diagnosed in October 1977 in UHKL (Ngeow and Chong, 1978). A 5-month interval lapsed before the next 2 cases were detected in April 1978. Since then, there has been a continuous isolation of PPNG strains. From August 1978 special efforts were made to obtain specimens from private clinics and the increase in number of specimens received resulted in a larger number of isolations of penicillinase negative and positive strains over the last 4 months of the study. As shown in Fig. 2, there were 43 cases of gonococcal infections from UHKL in the 11 months of 1977 with only 2 cases due to PPNG while 9 out of the 62 cases in the 11 months of 1978 were due to PPNG i.e. an increase in the proportion of PPNG cases from 4.7% in 1977 to 14.5% in 1978. A similar analysis is not made for cases from GP clinics and STD clinics because GP clinics contributed a rather small number of cases and most of the cases from STD clinics were seen after July 1978.

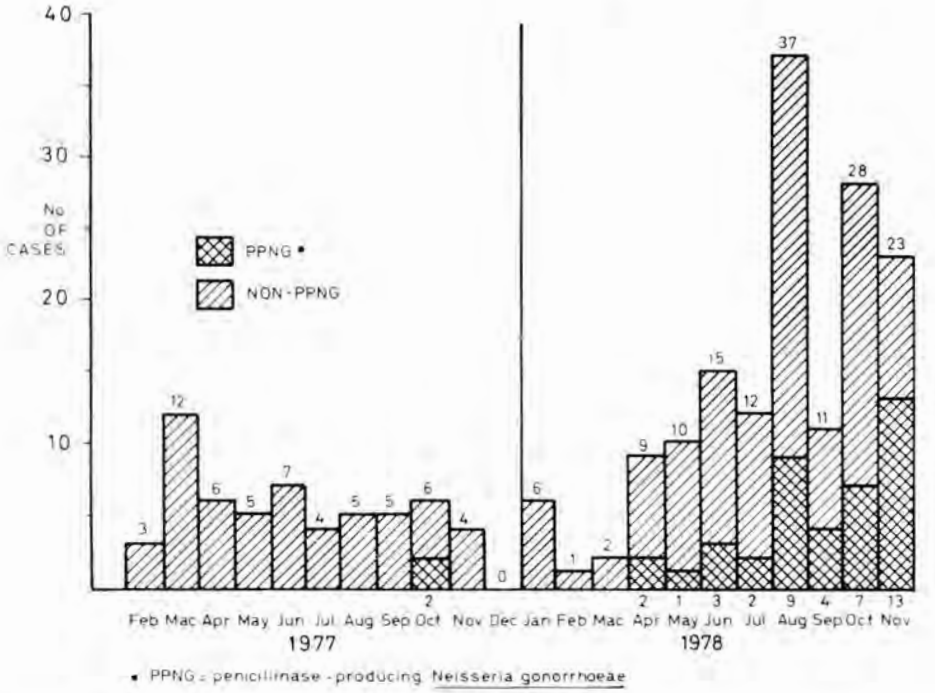


**Fig. 1. Total number of cases of Gonococcal Infection by month from UHKL, GP Clinics and STD Clinics.**

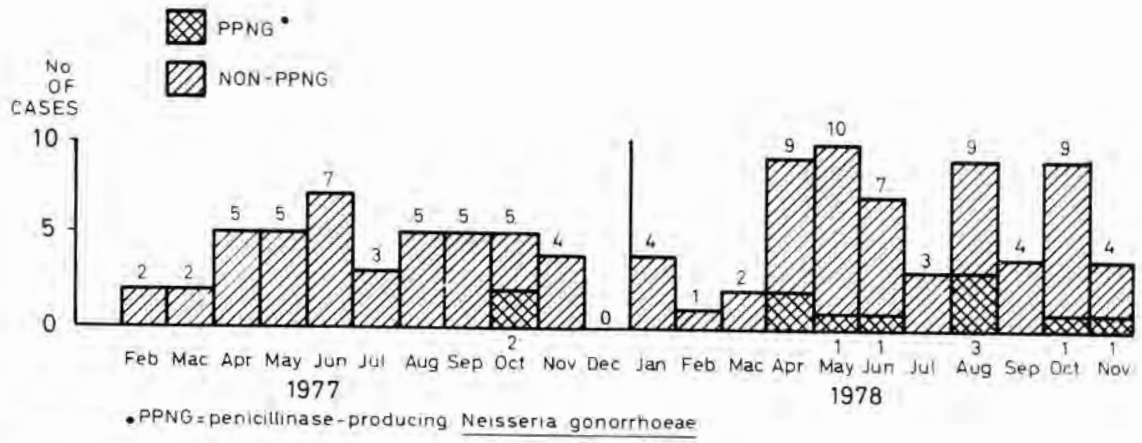


**Fig. 2. Number of cases of Gonococcal Infection by month from UHKL**

**TABLE I**

**Distribution of PPNG infections from 3 sources**

| Sources | February 1977 - November 1978 (22 months) | | August 1978 - November 1978 (4 months) | |
|---|---|---|---|---|
| | Total number of gonococcal infections | Total number of PPNG infections | Number of gonococcal infections | Number of PPNG infections |
| UHKL | 105 | 11 (11%) | 26 | 5 (19%) |
| GP clinics | 14 | 2 (14%) | 3 | 1 (33%) |
| STD clinics | 92 | 30 (33%) | 70 | 27 (39%) |
| Total | 211 | 43 (20%) | 99 | 33 (33%) |

Table I shows the distribution of gonococcal infections in the 3 sources. Out of 211 cases of gonorrhoea, 105 (49.8%) were from UHKL while various GP clinics contributed 14 (6.6%) and the remaining 92 (43.6%) came from 2 STD clinics in Kuala Lumpur. For UHKL, an overall 11% of gonococcal infections were by penicillinase positive strains while the corresponding figures for GP clinics and STD clinics were 14% and 33% respectively. Because of the increase in number of specimens received from August 1978 onwards with most of the specimens coming from STD clinics, a separate analysis was made for the 4-month period August to November 1978. During this period about a year after the first appearance of PPNG, the percentage of gonococcal infections by PPNG was 19% for UHKL, 33% for GP clinics and 39% for STD clinics.

Some clinical features associated with infections by penicillinase-producing gonococci were gathered from culture request forms (Table II). Most of the cases appeared to be uncomplicated genital tract infections occuring in young males in the 20-29 years age group.

Table III shows the distribution of MICs of 9 antibiotics for both penicillinase positive and penicillinase negative strains. The positive strains were much more resistant to penicillin and ampicillin compared to the negative strains. For penicillin, the positive strains had MICs ranging from 4 to 64 mg/L with a median between 8-16 mg/L while the negative strains were all inhibited by 2 mg/L or less with a median MIC between 0.25 — 0.5 mg/L. Among the negative strains, 36% were fully sensitive to pencillin (MIC 0.06 mg/L or less) while the remaining 64% were less sensitive to penicillin. Similarly for ampicillin, the MICs for the positive strains were much higher than those for the negative strains. For tetracycline, 90% of the positive strains and 40% of the negative strains were considered less sensitive (MIC more than 1 mg/L). Although all strains were inhibited by 8 mg/L of tetracycline, the median MIC for the positive strains was 4-fold higher than that for the negative strains. Hence the PPNG strains were more resistant to tetracycline than the non-PPNG strains. For the other 6 antibiotics, however, both types of strains were not markedly different in their susceptibilities. The median MICs for kanamycin, gentamicin and spectinomycin were the same, and those for erythromycin, chloramphenicol and cotrimoxazole were two-fold higher for the positive strains.

## DISCUSSION

In July 1977 the Ministry of Health, Malaysia reported the appearance of PPNG for the first time in this country. The source of the infection was believed to be from Thailand. From our surveillance, it is apparent that following their introduction into the country around the middle of 1977, these strains have spread rapidly and have become firmly established in our population.

The different isolation rates of PPNG among gonococci from UHKL, GP clinics and STD clinics may be a reflection of different populations at risk, and other problems associated with the collection of epidemiologic data. We would expect every patient seen at UHKL with signs and symptoms of gonorrhoea to have a cultural examination. General practitioners who do not have such easy access to laboratory facilities may have sent us specimens only from problem cases or cases resistant to treatment with the usual penicillin regime. Patients seen at STD clinics are believed to be highly promiscuous and thus constitute a high risk group.

The MICs of most of our gonococcal isolates conform to the general pattern of antibiotic sensitivity of gonococci isolated from Southeast Asia (Reyn, 1969). The proportion of non-PPNG strains less sensitive to penicillin is considerably lower than that reported from neighbouring countries like Thailand where in 1975 92% of gonococci isolated in Bangkok were less sensitive to penicillin (Suvanamalik, 1977) and Singapore where 96% of isolates in 1977 were less sensitive to penicillin (WHO, 1978a). However, the isolates from these 2 countries were obtained mainly from STD clinics whereas most of the non-PPNG strains we tested were from outpatients of UHKL who probably represent a less promiscuous population. It is well known that antibiotic resistance tends to build up most rapidly in areas where large groups of promiscuous males consort with relatively closed groups of promiscuous females, where antibiotics are freely available or where following treatment no follow up tests are done (Willcox, 1977).

Current therapeutic regimes for uncomplicated gonorrhoea recommend the use of penicillin or ampicillin as first-line drugs. However, in areas where a large proportion of gonococcal infections are due to PPNG, which would not respond to any of the penicillin regimes, the continuous use of penicillin would help to select out the resistant strains. Hence, it may be necessary to use other antimicrobials effective against these resistant strains as first line drugs. The choice of an alternative drug would be influenced by its efficacy on local strains, activity on other STD agents like treponema and chlamydia, side effects, cost, ease of administration and the readiness with which antibiotic resistance develops. Spectinomycin given 2 grams intramuscularly is the best alternative single-dose regime currently available (Siegel *et al.*, 1978). Unfortunately resistant strains have been encountered (Reyn, 1973) and increased usage of this drug as initial treatment could result in the widespread emergence of spectinomycin-

## TABLE II

### Distribution of 43 PPNG infections by Sex, Age, Ethnic group and Clinical Presentation

| Clinical Presentation | No.cases | Sex | | *Age (years) | | | | | | | Ethnic group | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | M | F | <1 | 1-9 | 10-19 | 20-29 | 30-39 | 40-49 | 50-59 | Chinese | Malay | Indian |
| Urethritis | 31 | 31 | | | | | 15 | 13 | 2 | | 25 | 4 | 2 |
| Cervicitis | 6 | | 6 | | | 1 | 3 | | | 1 | 5 | 1 | |
| Conjunctivitis | 2 | 2 | | 2 | | | | | | | 1 | 1 | |
| Pelvic Inflammatory Disease | 2 | | 2 | | | | 1 | 1 | | | 2 | | |
| Spouse of case | 2 | 1 | 1 | | | | 1 | 1 | | | 1 | 1 | |
| Total | 43 | 34 | 9 | 2 | | 1 | 20 | 15 | 2 | 1 | 34 | 7 | 2 |

* The ages of 2 cases, 1 male and 1 female, were not available.

## TABLE III

### Antibiotic susceptibility of Neisseria Gonorrhoeae

| | | MIC mg/l | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Antibiotic | | ≤0.125 | 0.25 | 0.5 | 1.0 | 2.0 | 4.0 | 8.0 | 16.0 | 32.0 | 64.0 |
| | | cumulative % | | | | | | | | | |
| Penicillin | – | 42 | 48 | 72 | 88 | 100 | | | | | |
| | + | | | | | | 5 | 10 | 73 | 84 | 100 |
| Ampicillin | – | 12 | 32 | 47 | 70 | 92 | 100 | | | | |
| | + | | | | | | | 5 | 37 | 90 | 100 |
| Erythromycin | – | 28 | 45 | 63 | 100 | | | | | | |
| | + | 5 | 10 | 26 | 95 | 100 | | | | | |
| Tetracycline | – | | 3 | 42 | 60 | 87 | 92 | 100 | | | |
| | + | | | 10 | 10 | 26 | 84 | 100 | | | |
| Kanamycin | – | | | | 3 | 12 | 43 | 90 | 100 | | |
| | + | | | | | | | 53 | 100 | | |
| Gentamicin | – | | | 2 | 8 | 27 | 93 | 100 | | | |
| | + | | | | 5 | 21 | 84 | 100 | | | |
| Chloramphenicol | – | 13 | 15 | 23 | 50 | 63 | 92 | 98 | 100 | | |
| | + | | | 6 | 28 | 45 | 78 | 100 | | | |
| Spectinomycin | – | | | | | 5 | 13 | 40 | 97 | 100 | |
| | + | | | | | | 16 | 26 | 100 | | |

| | | 0.125/0.025 | 0.25/0.05 | 0.5/0.1 | 1/0.2 | 2/0.4 | 4/0.8 | 8/1.6 | 16/3.2 |
|---|---|---|---|---|---|---|---|---|---|
| Cotrimoxazole* | – | | | 3 | 15 | 28 | 47 | 73 | 100 |
| | + | | | | | | | 16 | 100 |

– 60 non-PPNG

\+ 19 PPNG

* 5 parts sulfamethoxazole + 1 part trimethoprim

resistant strains. Therapeutic trials conducted in Singapore showed that tetracycline, thiamphenicol and cotrimoxazole gave treatment failure rates above 11% and were not recommended for routine use in gonococcal infections but that kanamycin 2 grams intramuscularly is useful as a second-line drug (Rajan *et al.*, 1977). Gentamicin has also been found effective by some investigators (Bowie *et al.*, 1974) but is generally not used for treating uncomplicated gonococcal infections. Erythromycin may be considered for the treatment of pregnant females with penicillin allergy but is ineffective for gonococcal urethritis in the male (WHO, 1978b). At present PPNGs are expected to respond to the same alternative antibiotic regimes as the non-PPNGs as their in vitro sensitivities are similar. Nevertheless, well-controlled therapeutic trials need to be conducted on PPNG infections to correlate in vitro sensitivities with clinical response.

The control of PPNG infections rests on intensive surveillance of high risk populations, effective treatment of cases, re-examination after therapy to detect treatment failures and rapid contact tracing with epidemiologic treatment of exposed partners (WHO, 1978b). This requires the collaborative efforts of responsible health authorities, private and hospital practitioners, social workers and the population at risk. Medical practitioners can contribute vastly just by taking relevant social histories, encouraging patients to return for post-therapy follow up and taking specimens from various sites as urethra, cervix, rectum and pharynx for re-examination to ensure the eradication of *N. gonorrhoeae*.

## SUMMARY

Surveillance for cases of penicillin resistant gonorrhoea was initiated at the University Hospital, Kuala Lumpur in February 1977. Clinical specimens examined were from patients seen at the University Hospital, various general practitioners' clinics and two sexually-transmitted diseases clinics. Out of 211 cases of gonococcal infections diagnosed by the end of November 1978, 43 cases were due to penicillinase-producing *Neisseria gonorrhoeae*. For the University Hospital, an overall 11% of gonococcal infections were by penicillinase positive strains, while the corresponding figures for general practitioners' clinics and the sexually-transmitted diseases clinics were 14% and 33% respectively. Laboratory methods for the isolation, identification and antibiotic susceptibility testing of penicillinase-producing gonococci are described and some clinical features associated with infections by these strains are presented.

## ACKNOWLEDGEMENTS

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# TEMPORARY CARDIAC PACING IN THE CORONARY CARE UNIT

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## INTRODUCTION

TEMPORARY cardiac pacing is an established method of therapy in the emergency control of life threatening arrythmias or their precursors. Although indications vary, the primary aim is to restore regular rhythm and to improve the cardiac output. In situations where arrythmias are due to drugs or electrolyte imbalance, temporary pacing may be life saving until the underlying pathology is corrected.

Heart blocks complicating acute myocardial infarction comprise up to 90% of all patients on short term pacing. Second degree atrio-ventricular (AV) block occurs in 2% — 10% and complete heart block in 1.8% — 8% of all patients with acute myocardial infarction (Hurwitz and Eliot, 1964; Meltzer and Kitchell, 1966; Julian *et al.*, 1964). While the incidence of advanced AV block is higher in inferior (27% — 33%) than anterior infarction (5% — 7%), the mortality is higher in anterior (75%) than inferior (20%) infarctions (Norris, 1969; Schlinger *et al.*, 1970).

More coronary care units providing continous electrocardiographic monitoring have been established in this country. This would increase the recognition of various arrythmias that arise from myocardial infarction and other cardiac conditions. Temporary, and later, permanent cardiac pacing offered in the management of such patients can be expected to increase.

This report of 6 cases describes patients who had successful temporary cardiac pacing. They illustrate the types of cases seen in the Coronary Care Unit, General Hospital, Kuala Lumpur. Indications for their pacing are discussed.

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## CASE 1

C.W., a 51 years old Chinese labourer, was admitted one day after he developed chest pain. Physical examination was normal and electrocardiogram (ECG) showed a recent inferior infarction. Three days after admission he developed first degree heart block. The next day he became hypotensive (Blood pressure 80/60 mm. of mercury) and was in early cardiac failure. Electrocardiogram now showed second degree heart block (mobitz type II) with a ventricular rate of 42 — 50 per minute (Fig. 1). A temporary transvenous endocardial pacemaker was inserted and paced on demand at 80 per minute. The blood pressure improved and cardiac failure subsided. Patient was pacemaker dependent for the next four days. Rehabilitation was well tolerated and the pacemaker was removed one week later. The electrocardiogram on discharge showed no conduction defects.

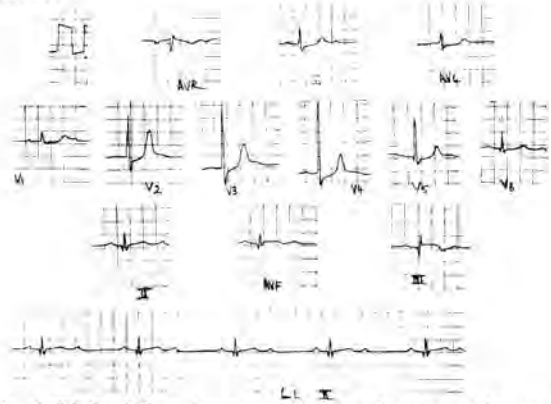


**Fig. 1. ECG of Case 1: Acute inferior infarction with second degree (mobitz type II) AV Block**

### Comments

Second degree heart block with bradycardia caused hypotension and early cardiac failure in this patient with an inferior infarction. Artificial pacing contributed in correcting these complications.

## CASE 2

Y.K.T., a 35 years old Chinese teacher, was admitted four hours after he developed chest pain. Physical examination was unremarkable and electrocardiogram showed an acute inferior infarction. With no complications and recurrence of symptoms he was mobilised on the third day. On the fourth day first degree heart block was recorded which rapidly progressed to complete heart block with a ventricular rate of 40 — 50 per minute. Atropine given intravenously did not produce an appreciable increase in heart rate. A temporary transvenous endocardial pacemaker was inserted and paced on demand at 70 per minute. He remained pacemaker dependent for three days after which he reverted to sinus rhythm. The pacemaker was removed several days later with no recurrence of AV block.

### Comments

This patient with inferior infarction rapidly developed complete heart block on the fourth day. Bradycardia, not responsive to atropine, and his age were the indications for pacing. This provided a satisfactory heart rate while awaiting spontaneous recovery.

## CASE 3

B.M., a 53 years old Malay clerk, was admitted two hours after he developed severe chest pain. On admission he was in cardiogenic shock with a blood pressure of 80/50 mm. of mercury and in cardiac failure. Electrocardiogram showed acute inferior infarction and complete heart block with ventricular rate of 42 beats per minute (Fig. 2). A temporary transvenous endocardial pacemaker was inserted and paced on demand at 80 per minute. Immediate blood pressure response was noticed and stabilised at 130/80 mm. of mercury. Cardiac failure subsided over the following days. He remained pacemaker dependent for the next four days and mobilization was commenced on the fifth day. The pacemaker was left in situ for five days after that before removal with no further recurrence of heart block.

### Comments

Complete heart block arising from acute inferior infarction produced cardiogenic shock and cardiac failure in this patient. Correction of the bradycardia by artificial pacing directly contributed to his subsequent clinical improvement.

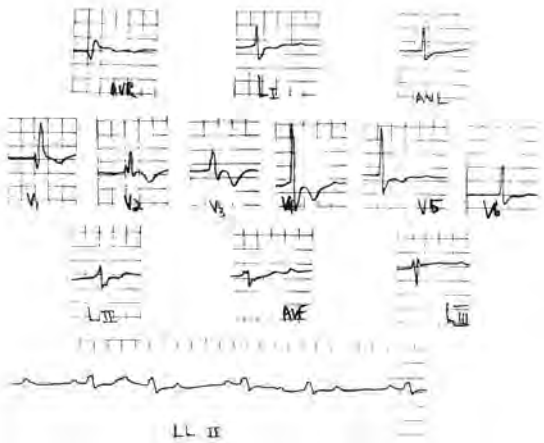

**Fig. 2. ECG of Case 3: Acute inferior infarction with complete Heart Block.**

## CASE 4

L.W.C., a 56 years old Chinese tailor, was admitted two days after he developed chest pain and breathlessness. On admission he was hypotensive (Blood pressure 80/50 mm. mercury) and in gross cardiac failure. Electrocardiogram on admission revealed a fresh antero-septal infarction, right bundle branch block and left anterior hemiblock (Fig. 3). An emergency temporary transvenous endocardial pacemaker was inserted and therapy for congestive cardiac failure instituted with digoxin and diuretics. The cardiac failure resolved over the next three days and the blood pressure stabilised at 140/80 mm. of mercury. Mobilization was then commenced with no untoward consequences. Continous rhythm monitoring did not show a progression to more advanced AV block. The pacemaker was removed seven days later and the patient discharged on his eighteenth hospital day. On last review eight months later, he remained well and electrocardiogram showed an old anteroseptal infarction with left anterior hemiblock.

### Comments

With this patient a prophylactic pacemaker was inserted in anticipation of a progression to complete heart block. Digoxin could also be used with greater confidence with a pacemaker in situ.

## CASE 5

G.R., a 45 years old Indian barber, was admitted with an extensive anterior infarction complicated by cardiac failure. Several hours after

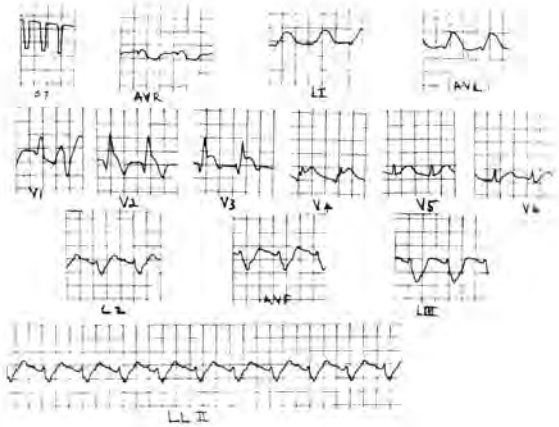

**Fig. 3. ECG of Case 4: Acute antero-septal infarction, right bundle branch block and left anterior hemiblock.**

admission he developed complete heart block with a ventricular rate of 60 per minute. A transvenous endocardial pacemaker was inserted and paced on demand at 80 per minute. He remained pacemaker dependent for one week during which time mobilization commenced with no complications. On removal of the pacemaker ten days after admission the cardiac failure had subsided and he remained in sinus rhythm on discharge.

### Comments

Complete heart block and cardiac failure arising from an extensive anterior infarction were the indications for pacing. Despite the poor prognosis in such patients artificial pacing contributed in his eventual recovery.

## CASE 6

C.Y., a 78 years old Chinese man had been on treatment for hypertension and cardiac failure for several years. He was admitted one day after he developed severe dyspnoea. Several hours prior to admission he was seen and treated by a doctor with intravenous drugs. On admission he was in pulmonary oedema and the electrocardiogram showed complete atrio-ventricular dissociation, complete right bundle branch block, ST and T wave changes but no evidence of an acute infarction (Fig. 4). An emergency transvenous endocardial pacemaker was inserted and paced at 70 per minute and cardiac failure was treated with diuretics alone. From the history digoxin toxicity was suspected and this was later confirmed by plasma digoxin assay of blood sample obtained 6 hours after the intravenous injections were given. It was 3.7 ng/ml. (Normal 1 — 2 ng/ml). He was pacemaker dependent for four days during which time the cardiac failure improved. On reversion to sinus rhythm a repeat digoxin level was 1.4 ng/ml.

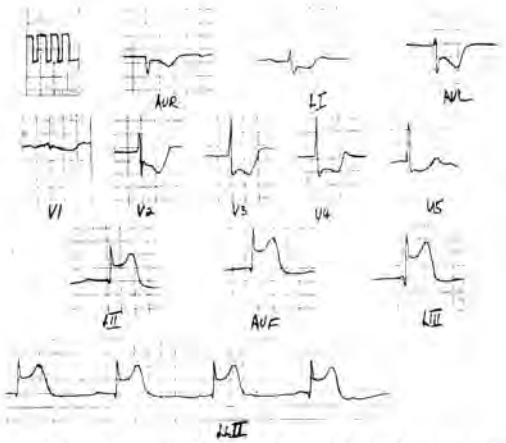

**Fig. 4. ECG of Case 6: Complete heart block, but no evidence of acute infarction.**

### Comments

This patient had complete heart block with no obvious cause on admission. It was later proven to be due to digoxin toxicity. Artificial pacing provided improvement in his condition and also maintained a regular rhythm and rate till this toxic effect of digoxin was corrected.

## DISCUSSION

Patients who develop ventricular conduction defects in acute myocardial infarction face a higher mortality risk. The mortality is higher with anterior than inferior infarctions (Norris, 1969; Schlinger *et al.*, 1970). With anterior infarctions a greater amount of myocardial damage occurs. The block arising is usually sudden in onset, the ventricular complexes are wide and the block occurs below the His bundle. Most of these patients develop severe cardiac failure and circulatory collapse. In contrast, in inferior infarctions, the myocardial damage is smaller in extent with narrow ventricular complexes, and the block lying proximal to the bundle of His. The onset of the block tends to be gradual and lasts a few days.

Irrespective of the site of infarction, temporary cardiac pacing serves to overcome the genesis of bradycardia which results from advanced block. It

has been established that certain conduction defects progress to complete heart block or develop into sudden cardiac asystole. They include Mobitz type II AV block, bifascicular blocks, and alternating right and left bundle branch blocks. The importance of correcting bradycardia in myocardial infarction is to prevent a fall in cardiac output and blood pressure. This was shown by Mather *et al.* (1971), who described a mortality of 49% in patients with a systolic blood pressure of less than 100 mm of Mercury. A higher incidence of ventricular tachycardia, ventricular fibrillation and premature ventricular contractions occur with myocardial infarction complicated by bradycardia (Lown *et al.*, 1967; Adqey *et al.*, 1968). This suggests that bradycardia maybe a precursor to the arrythmias and an important factor in the early high mortality. Furthermore, the ectopics are abolished once the heart rate is increased.

Treatment of tachyarrythmias in myocardial infarction by pacing is more infrequent and less well understood. If arising secondarily to bradycardia, they are usually eliminated by correction of the bradycardia. Tachycardia maybe suppressed by pacing with overriding or in combination with anti-arrythmic drugs.

Although pacemakers are widely used, it is still difficult to assess its effect on mortality rates. Christiansen *et al.* (1973) and Freidberg *et al.* (1968), in their reports stated that the usefulness and benefits of temporary pacing are negligible with no significant reduction in the mortality rates when compared with drug therapy. In contrast, Scott *et al.* (1967), in a comparative study of pacemakers and drug therapy found a mortality rate or 61% among patients treated by medications and 37% among those who had temporary pacemakers. Frequency of anterior and inferior infarctions were however not stated. Some authors would even take the position that to withold pacing is morally wrong (McNally and Benchimol, 1968). When cases are individually considered, it is clear that many patients benefit and are saved by temporary pacing even though some figures may not show it. Mortality should therefore take into account recognised risk factors in addition to advanced AV Block. They include site of infarction, extent of myocardial necrosis, cardiogenic shock, cardiac failure, syncope and QRS prolongation (Friedberg *et al.*, 1969; Norris, 1969).

Permanent pacing may also be of considerable benefit after myocardial infarction. Alone or in combination with anti-arrythmic drugs, permanent pacing is useful in the management of resistant arrythmias. It is also advocated in patients who have a high risk of sudden death after infarction. Such patients are identified based on the electrocardiogram at the time of infarction. They include patients who develop Mobitz type II AV Block, complete heart block and mutliple fascicular blocks. Waugh *et al.* (1973) and Lichstein *et al.* (1973) recommend permanent pacing in such patients, and Atkins *et al.* (1973) demonstrated a significant decrease in the incidence of sudden death of such patients offered permanent pacing.

Temporary pacing has its most frequent application in the management of conduction defects arising from myocardial infarction (Cases 1 — 5). Case 6 illustrates a less frequent situation where digoxin toxicity produced complete heart block and temporary pacing sustained haemodynamic stability until the toxic effect of digoxin was corrected. In addition to these applications, Sowton *et al.* (1967) demonstrated temporary atrial pacing as a stress test for the diagnosis of angina pectoris. Similarly, rapid atrial stimulation is used as a provocative test in the assessment of sinoatrial node automaticity and conduction in patients with the Sick Sinus Syndrome (Narula *et al.*, 1972). Atrial pacing with His bundle electrography has a diagnostic application in the functional assessment of the cardiac conduction system (Damato *et al.*, 1969).

## SUMMARY

Temporary cardiac pacing has a definite role in the management of cardiac arrythmias. 6 patients are described illustrating the types of cases seen in the coronary care who benefitted from pacing. Indications and role of temporary cardiac pacing are discussed.

## ACKNOWLEDGEMENT

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# SEVERE MALARIA WITH DISSEMINATED INTRAVASCULAR COAGULATION

M. ANUAR & P.K. YAP

## INTRODUCTION

DISSEMINATED intravascular coagulation (DIC) occurring in infection with *Plasmodium flaciparum* is well known. We report a case of severe infection with generalised bleeding and acute renal failure due to DIC. This case was also characterised by massive haemolysis occurring over a few hours.

## CASE REPORT

A 44 year old Chinese male was admitted to the University Hospital Kuala Lumpur, Malaysia with a ten day history of fever. He had previously been treated as an outpatient by several General Practitioners with no improvement. One month prior to this he had left Kuala Lumpur to work as a contract labourer in a known malarious region of the country.

On examination then (the patient was admitted at 4 a.m.) he was alert and cooperative. His temperature was 37.6° C and mild jaundice was noted. No bleeding was noted in the skin, mucous membranes or fundi. His liver was palpable 3 finger breadths below the right costal margin. The spleen was not palpable and all other systems were normal. Emergency investigations revealed a haemoglobin of 7.0 mmol/1 (11.2 gm/100 ml), a total white cell count of 39.8 x 10 /1 (neutrophils 72%) and *P. falciparum* trophozites in the peripheral blood film. Oral chloroquine was then started in the usual dosage.

When seen during the morning round (about 8.00 a.m.) the patient's condition was noted to be stable. Further samples of blood were sent for routine investigation. Two hours later the patient became confused and complained of generalised aches. He was then noticed to be pale with a pulse rate of 90/min. and a BP of 110/80 mmHg. Per rectal digital examination revealed malaena.

Fifteen minutes later the patient had a cardio-respiratory arrest. Resuscitation was unsuccessful. During the course of resuscitation profuse bleeding was noted at the site where the central venous pressure line was inserted as well as at venipuncture sites. The patient also regurgitated "coffee ground" material. After the patient had expired, the results of the haematological and biochemical investigations requested earlier were received.

Haematological investigations revealed haemoglobin 3.0 mmol/1 (4.9 g/100 ml), erythrocytes 2.2 x 10 /1, packed cell volume 0.17 (17%), reticulocytes 45 x 10 /1 (0.9%), platelets 11 x 10 /1 (11,000/ul) and white cell count 28.6 x 10 /1 (28,600/ul). *P. falciparum* trophozites were seen in 58.3% of erythrocytes. Fibrinogen was 1.4 g/1, (140 mg/100 ml), fibrinogen degradation products: protamine sulphate was positive and Ethanol gel negative. Prothrombin time: Control 14 seconds (100%), Test 23.2 seconds (30%). Euglobulin lysis time: 150 min.

Biochemical tests showed urea 74.7 mmol/1 (450 mg/100 ml), glucose 3.4 mmol/1 (62 mg/100 ml). Sodium, potassium and chloride were 132, 7.4 and 80 mmol/1 (132. 7.4, 80 mEq/1) respectively. The total proteins were 52 g/1 (5.2 g/100 ml); albumin 22 g/1 (2.2 g/100 ml); globulin 30 g/1 (3.0 g/100 ml), bilirubin 212.0 umol/1 (12.4 g/100 ml), aspartate aminotransferase 106 IU/1; alanine aminotransferase 14 IU/1 and alkaline phosphatase 74 IU/1.

## DISCUSSION

Severe malaria tends to occur in "non-immune" persons. The results of the investigations reveal a marked degree of parasitisation of the

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erythrocytes. The severe thrombocytopenia, low prothrombin activity, low plasma fibrinogen level and the presence of fibrinogen degradation products (FDP) in the blood indicate disseminated intravascular coagulation (DIC). Fibrinolytic activity was normal. The immediate cause of death was probably related to the hyperkalaemia due to acute renal shutdown and massive hemolysis (the haemoglobin fell from 7.0 mmol/1 (11.2 g/100 ml) to 3.0 mmol/1 4.9 g/100 ml) in 6 hours).

DIC occurring in *P. falciparum* infection was first suspected in 1966 based on clearance studies of $I^{125}$ labelled fibrinogen (Devakul *et al.*, 1966). Since then its role in the more serious complications of the infection has been amply confirmed (Reid & Nkrumah, 1972; Jaroonvesama, 1972). In particular, its role in cerebral malaria has been emphasised.

The diagnosis of DIC depends on a high index of suspicion since overt bleeding is very rare. A high parasite count correlated well with the development of DIC (Reid & Nkrumah, 1972). Cerebral symptoms, jaundice and hyperpyrexia should also alert one to the possibility of DIC (Jaroonvesama, 1972).

Complete coagulation studies should ideally be carried out since haemolytic anaemia and thrombocytopenia may occur in *P. falciparum* infections without DIC. Measurement of FDP is probably the most useful single test for DIC in malaria (Reid & Nkrumah, 1972; Jaroonvesama, 1972). Fibrinogen and other clotting factors may be found in normal or even increased concentrations because transient or local increased consumption of such factors may lead to a rebound phenomenon. FDP levels remain elevated for at least 24 hours and occasionally for as long as a week if the initial levels were very high. Lately it has been shown that complement activation triggered immunologically by *P. falciparum* infection also plays an important role in the pathogenesis of DIC (Srichaikul *et al.*, 1975). Hence an increased clearance of complement factor Clq and decreased levels of complement factor C will also contribute to the diagnosis.

## ACKNOWLEDGEMENT

We thank Professor H.O. Wong, Professor of Medicine for allowing us to report this case.

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# THE CRUVEILHIER-BAUMGARTEN SYNDROME

PANIR CHELVAM, ZULKIFLI AHMAD & NG WENG HWA

## INTRODUCTION

THE CRUVEILHIER-BAUMGARTEN Syndrome is a rare clinical entity characterised by the presence of unusual prominent para-umbilical veins, evidence of portal hypertension, splenomegaly and the demonstration of a venous hum, frequently with a thrill, at the site of the para-umbilical circulation. In the syndrome, the umbilical vein is patent as a result of primary liver disease. When the patency of the umbilical or para-umbilical vein is not associated with recognizable significant structural abnormalities of the liver, it is called the Cruveilhier-Baumgarten Disease.

Since the first case report (Pegot, 1933), only 86 cases of Cruveilhier-Baumgarten Syndrome have been described in the literature until 1954 (Cheng *et al.*, 1954). Since then, sporadic case reports have appeared in the English literature (Dikshit *et al.*, 1966; Banerjee, 1969; Fung *et al.*, 1971). The only previously reported case of the Cruveilhier-Baumgarten Syndrome in this region has been that of Fung, Tock and Yu (1971) in a 56 year old Chinese man from Singapore.

We report a further 2 cases of the syndrome, one in a Malay child and the other in an Indian adult, seen in Medical Unit 4, General Hospital, Kuala Lumpur in the past nine months.

## CASE REPORT 1

A 14-year old Malay boy was admitted to Old Ward 13, General Hospital in March 1978 with spastic paraplegia for over 10 years. The consultant neurologist felt that this was probably due to congenital abscence of cortico-spinal tracts within the spinal cord. The neurological investigations including a myelogram was normal. Other relevant physical signs included congenital abscence of digits of left hand; a pigeon chest deformity and a ventricular septal defect with cardiomegaly.

There was no jaundice no spider naeri or palmar erythema. There was grossly dilated veins in the anterior abdominal wall especially around the umbilicus with a large coil of veins 6 cm above the umbilicus. (Fig. 1). The direction of flow of the veins was away from the umbilicus. A palpable thrill was present over the varix above the umbilicus and on auscultation a loud continuous murmur was audible. The liver was not palpable; the spleen was enlarged to the level of the umbilicus. No ascites was detected.

Investigations revealed pancytopenia (haemoglobin, 6.8 gm/100 ml; platelets, 34,000/cu. mm total white cell count, 1,650/cu. mm). Urea and electrolytes were normal. The total bilirubin was 1.3 mg %; alkaline phosphatase, 9 KA units; total proteins, 5.3 gms. % (albumin was 3.1 gm % are globulin was 2.2 gm %); SGPT was 2RF units. The prothrombin time was 2 seconds prolonged. The HBs Ag was negative. Barium swallow did not demonstrate any oesophageal varices. The splenoportogram (Fig. 2) showed dilated splenic and portal veins with a large patient umbilical vein feeding large varices in the anterior abdominal wall. The liver biopsy showed macronodular cirrhosis.

## CASE REPORT 2

A 38 year old Indian gardener was first admitted into Old Ward 13, General Hospital, Kuala Lumpur in December, 1977 with the complaints of abdominal distension, yellow discolouration of eyes, swelling of both feet and loss of appetite for 2 years. No history of hemetemesis or malaena. His consumption of alcohol has been

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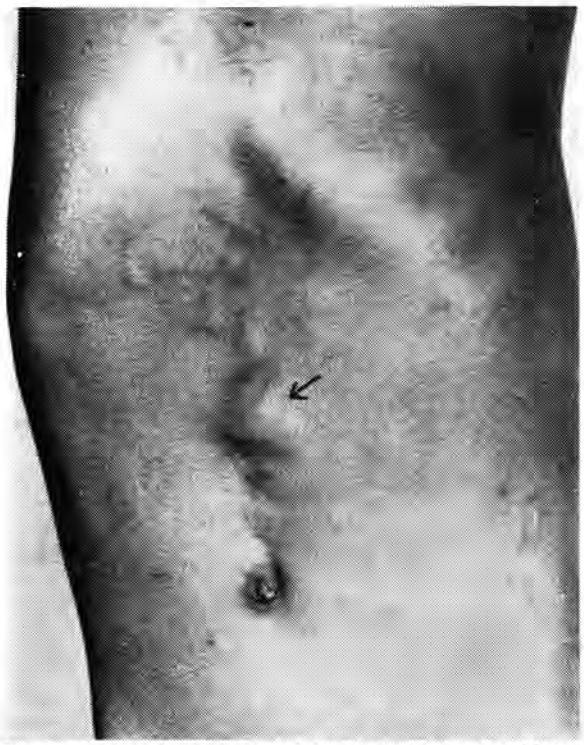

**Fig. 1. Photograph of anterior abdominal wall showing dilated tortuous veins. The arrow indicates the site of the venous thrill.**


**Fig. 2. Splenoportogram of the 14-year old Malay patient, showing dilated portal and splenic veins with a large patent umbilical vein feeding the periumbilical varices.**

heavy for the past 25 years; his average weekly intake includes 4 pints of beer, 10 pints of toddy and 2 small bottles of chinese wine. Physical examination revealed a mildly jaundiced male with pitting ankle oedema with no spider naevi or palmar erythema. His abdomen was distended with ascites but no dilated periumbilical veins were detected then. Liver was palpable 2 cm below right costal margin; spleen was not palpable. He was diagnosed as having alcoholic liver cirrhosis with portal hypertension and was treated with diuretics and Vitamin K. He was advised to refrain from alcohol consumption.

The patient defaulted follow-up and was re-admitted on 17th March 1978 with similar complaints. Examination revealed similar findings as before except that he now had dilated periumbilical veins. Though a bruit was not palpable, a continuous venous hum was audible on auscultation just above the umbilicus.

Laboratory investigations showed a haemoglobin of 11.6 gm %; a platelet count of 74,000/cu. mm with a normal white cell count. Urea and electrolytes were normal. Liver function tests showed a serum bilirubin of 1.7 mg %, serum alkaline phosphatase of 6.0 K.A. units, serum albumin of 2.9 gm %, serum globulin of 5.3 gm %, SGPT of 2 RF units. The prothrombin time was 2 seconds prolonged. The hepatitis B surface antigen (HBsAg) was negative. Barium swallow did not demonstrate any oesophageal varices. Three days after admission the patient developed a spotaneous bleed from his umbilical varices, loosing about 250 ml of venous blood. Only when the bleeder was ligated did the bleeding stop. No blood transfusion was required.

A splenoportogram (Fig. 3) showed a slightly dilated portal vein with a patent umbilical vein feeding the varices around the umbilicus. A liver biopsy showed micronodular cirrhosis.

The patient was discharged with diuretics and vitamin supplement. He is being followed up in the hepathology clinic.

## DISCUSSION

The Cruveilhier-Baumgarten Disease is rare. Until 1972 only eleven cases of the disease have been recorded (Ozsoylu *et al.*, 1972). Unlike the Cruveilhier-Baumgarten Syndrome, the liver is

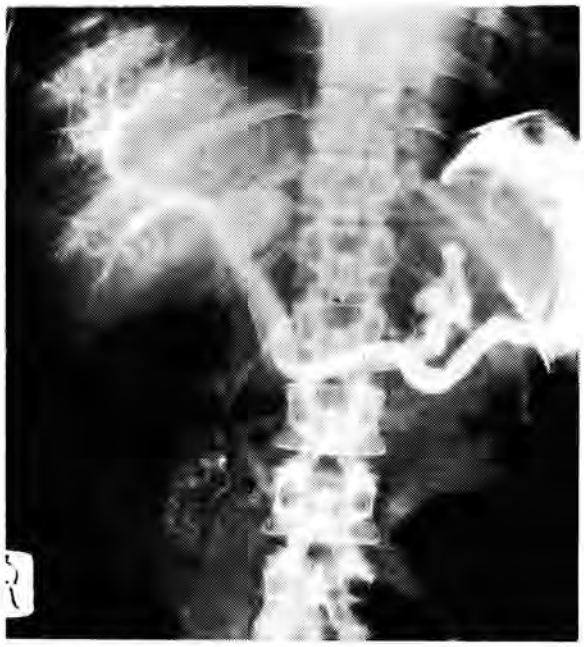

**Fig. 3. Splenoportogram of the 38-year old Indian patient, showing the patent umbilical vein (arrowed) feeding the umbilical varices.**

morphologically normal with no cirrhosis. Our 2 cases are those of the Cruveilhier-Baumgarten Syndrome as they both had underlying liver disease (cirrhosis) to account for the prominent para-umbilical veins with the demonstrable venous hum. In the clinical diagnosis of the disease or the syndrome, the venous hum is of great importance. The mechanism of the production of the murmur is still unsettled, although its dependence upon the venous anastomises is beyond doubt.

In both our patients the venous hum was detected and a patent umbilical vein feeding the umbilical varices was demonstrated in each case with splenoportogram. Splenomegaly has been detected in most of the previously reported cases. The spleen was enlarged in our Malay boy but was not palpable in our second case. Anaemia, leukopenia and thrombocytopenia (hypersplenism) was evident in our patient with the clinically enlarged spleen but not in our Indian patient. Eosinophilia was absent in both our cases. Splenomegaly with or without eosinophilia, hepatomegaly, anaemia and persistent leukopenia have been stated as additional clinical criteria for the diagnosis of Cruveilhier-Baumgarten Syndrome. (Cheng *et al.*, 1954). Our first case is interesting because we believe that this is the first case of a young Malay boy with the Cruveilhier-Baumgarten Syndrome associated with multiple congenital deformities (pigeon-chest, absent digits, ventricular septal defect and perhaps congenital abnormalities in the spinal cord).

We feel that routine clinical auscultation of the periumbilical region in all patients with portal hypertension is necessary to pick up all cases of the Cruveilhier-Baumgarten Syndrome.

## SUMMARY

Two cases of the relatively uncommon Cruveilhier-Baumgarten Syndrome are reported; one in a 14-year old Malay boy; the other in a 38-year old Indian man, both with cirrhosis of the liver. the 14-year old boy had associated multiple congenital abnormalities. Some important clinical features of the Syndrome are discussed. The need for routine auscultation of periumbilical region in patients with portal hypertension is emphasised.

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# MELIOIDOSIS: A REPORT OF TWO CASES

NG TIAN SENG

MELIOIDOSIS was first described in man by Whitmore and Krishnaswami in 1912 in the autopsies of the beggars and derelicts in Rangoon. Staton and Fletcher observed the disease in the guinea-pig colony at the Institute for Medical Research in Kuala Lumpur in 1913. They erroneously attributed the disease to vegetables contaminated by wild rodents. Many years later Chambon demonstrated the natural occurence of Pseudomonas Pseudeomallei (the causative agent of melioidosis) in soil and water. We now know that it is probably a soil saprophyte. Most cases have been reported from Southeast Asia but sporadic human cases have been reported from Korea, the Philippines, Central and South America, the West Indies and Turkey. Endemic areas are now known to exist in Malaysia, Madagascar, Guam and Australia (Howe *et al.*, 1971).

The precise mode of entry into the body is not known but it presumably gains entrance by ingestion or in association with trauma sustained in endemic areas. A report where one-third of helicopter crew were infected in a series of 150 cases suggest that inhalation of organism in dust raised by helicopter rotors may initiate pulmonary melioidosis.

## THE CASES

2 cases of melioidosis with classical high fever, liver involvement without lung involvement are described. The first case seen by the author with lung involvement hepatosplenomegaly and septicaemia died within five days of admission before full investigations and is the reason this author wishes to highlight this disease as early vigorous treatment may save more lives.

### Case I

This Malay boy age 22 was admitted with a history of fever, chills and rigors for two weeks prior to admission. He also had pain in both ankles and was treated for typhoid by private practitioners. When he was admitted he had a temperature of 104° F and hepatomegaly. His chest X-ray was normal, haemoglobin was 13gm%, total white count was 9100 with 70% polymorphs, 29% lymphocytes and 1% monocytes. Blood films for malaria parasites were negative. He continued to have a swinging fever and on the 9th day after admission, an area of cellulitis appeared on the left ankle. An X-ray of the ankle was normal. Meantime he had been given chloramphenical 500 mg six-hourly for five days without much effect. Results from blood culture grew pseudomonas pseudomallei and a pseudomonos pseudomallei-like organism. (This pseudomonos pseudomallei-like organism has been sent to Porton Down in England and Centre for Disease Control, Atlanta for identification and results will be reported elsewhere). Meantime, his melioid titre by indirect haemagglutination was 1:3200. Widal Weil Felix was negative. So were the serologic test for murine, scrub, tick typhus and leptospira. The melioid titre after 14 days rose to 1:12,000 confirming the active disease. The live function test before and after treatment is shown in Table I.

**Table I**

**Case I: Liver function tests before and after treatment**

| | Before treatment | After treatment |
|---|---|---|
| Serum protein | 6.1 gm % | 5.8 gm % |
| Serum albumin | 2.9 gm % | 3.1 gm % |
| Serum globulin | 3.2 gm % | 2.7 gm % |
| A : G | 0.9 | 1.1 |
| Zinc sulphate | 3 units | 5 units |
| Alkaline phosphate | 30.6 K.A. units | 16.6 K.A. units |
| Serum bilirubin | 0.7 mg % | 0.6 mg % |
| B.S.P. (retention) | 13% | 4% |

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He was given intravenous pyrrolidino-methyl tetracycline (Reverine Hoechst) 275 mg eight hourly and the temperature settled promptly after 3 days. After one week of intravenous tetracycline, he was started on oral tetracycline and he was discharged one month after admission with 1 gm of tetracycline four times daily.

One month after discharge, he was readmitted with fever, chills, rigors, pain in the throat and dysphagia. He had high fever of 104° F with a whitish exudate on the tonsillar bed. A swab taken grew *Pseudomonas pseudomallei* sensitive to tetracycline and chloramphenicol. Intravenous pyrrolidinomethyl tetracycline was commenced and he recovered and was discharged with 1 gm of oral tetracycline four times daily. At the last follow-up 3 months later, he was completely well. He was given tetracycline almost continuously for two months.

**Case II**

This 33 year old Indian male rubber tapper was referred with history of abdominal pain, fever and vomiting of about seven days duration. On clinical examination, the patient appeared ill with temperature of 101° F, jaundice and a tender enlarged liver. He was given oral tetracycline (1 gm daily) and meantime his blood culture grew *Pseudomonas pseudomallei.* His temperature and clinical symptoms subsided on the tetracycline and follow-up examination one month later showed that he had recovered completely.

**Clinical Manifestations of Melioidosis**

The clinical manifestations of melioidosis are protean but fatal cases are not common. The clinical cases are usually either chronic draining abscesses or the fulminating septicaemic variety with a high mortality. Those with superficial abscesses and lung absecesses have been commonly found in diabetics but has been reported in normal people. The pulmonary lesions are characterised by nodular infiltrates in the upper lobes, often accompanied by cavitation that mimics radiological features of mycotic or tuberculous infections. The organisms can be recovered from bronchial aspirate or sputum and if confined to the lungs are readily curable with appropriate antibiotics. Spotnitz *et al.* (1967) reported good results in 9 cases of melioidosis penumonitis using tetracycline. In cases where pulmonary resections were undertaken for suspicion of carcinoma or tuberculosis the organism has been recovered from the abscesses in the resected lung.

Melioidosis sometimes occurs as an overwhelming septicaemia which is fatal even with treatment. These were originally described by Whitmore in derelicts. Abscesses were found in the lung, liver, spleen, kidneys but not in the gastrointestinal tract. Even though malnutrition may be a factor, this author found a young soldier with septicaemic melioidoses who had no underlying immunological disturbance.

Chronic melioid with multiple skin abscesses and draining sinuses sometimes occur in diabetics but can occur in any person exposed to it. This presentation can be febrile and can cause systemic spread if the patient is immunologically compromised. However, many cases are not clinically manisfest as studies by Strauss *et al.* (1969) showed with antibody survey in Malaysia. They found that the antibody range from 3% in non-rice growing states to 20% from those in mainly rice growing states. This correlated with another of their study where the micro-organism was found most often in water from fields of wet-rice cultivation and in water accumulating after heavy rains on the surface of cleared land, such as animal pastures and military camps. Thin *et al.* (1971) reported on the recovery of the organism from open spaces like low-lying sports fields confirming earlier findings (Strauss *et al.*, 1969) that tubber, oil palm estates, primary and secondary forests do not harbour the organism as readily as open fields. All these studies still do not answer the questions that whereas the organism is widespread in Malaysia, why is severe disease not common?

**Bacteriology**

Pseudomonas pseudomallei are motile, aerobic, gram-negative, non-acidfast and non-spore bearing rods which have bipolar staining. On solid media, it gives off a musty slightly aromatic odour, are not haemolytic and do not produce soluble pigment but are oxidase-positive. On glycerol-nutrient agar *Pseudomonas pseudomallei* grows initially in characteristic round, smooth colonies which after several days incubation take on a wrinkled, heaped-up appearance that became more pronounced on longer incubation. It grows with smooth pellicle in broth but does not grow in desoxycholate nor in a salmonelia-shigella agar. It can grow at 42 C and will reduce nitrate to nitrite and then to nitrogen gas.

### Chemotherapy

In their report, Eickhoff *et al.* (1970) tested 10 strains of *Pseudomonas pseudomallei* to 20 chemotherapeutic agents. Tetracycline chloramphenicol, novobiocin and sulphadiazine were the most active whereas kanamycin was less active. Certain combinations like kanamycin-chloramphenicol, tetracycline-kanamycin and sulphadiazine-chloramphenicol showed definite antagonistic effects in vitro. Streptomycin, polymycin B and penicillin and its derivatives were ineffective. In actual clinical practice tetracycline is considered the drug of choice. Adequate dosage maintained over a prolonged period is necessary for bacteriological cure and in various reports relapse have occured after one month of medication as occur in our first case. It is stressed, however, that the sensitivity of the bacterium to various antibiotics be carried out so that adequate and effective chemotherapy be given in this potentially fatal infection.

## SUMMARY

Two cases of melioidosis is reported and it is suggested that the bacterium being a saprophyte present in Malaysia should be considered in obscure infections as it is treatable in most cases.

## ACKNOWLEDGEMENT

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# A CASE OF PNEUMOPERITONEUM IN A NEW-BORN CHILD.

RADHAMANALAN S. & THOMAS ISAAC

## INTRODUCTION

TRACHEO-OESOPHAGEAL fistula abnormalities is not a rare anomaly. Oesophageal atresia and tracheo-oesophageal fistula may occur as separate deformitis but, more commonly, they occur together.

In addition to the obvious oesophageal and tracheal abnormalities, concomitant lesions do occur. The most common of these associated lesions are congenital heart diseases, gastrointestinal abnormalities like imperforate anus and duodenal atresia, genitourinary anomalies, skeletal and muscular deformities.

We now present a case report of a newborn child with tracheo-oesophageal fistula who subsequently developed a massive pneumo-peritoneum, probably due to a spontaneous rupture of the stomach.

## CASE REPORT

On the 4th of April 1978, a one-week old female child, the first of a set of twins, was referred to the Surgical Unit of the General Hospital, Tawau, Sabah. The history was that a 28 year-old Bugis female, with a gestational period of about 32 weeks who went into spontaneous premature labour prior to admission. On admission, a diagnosis of polyhydraminios with twin pregnancy was made. She delivered a set of twins, both females, soon after admission. The first twin, with a birth weight of 1.68 kg, was found to have hare-lip and cleft palate. The second twin who was 1.82 kg was normal. The first twin was refered to us due to distension of the abdomen and cyanosis on oral feeding. As we were not able to pass a catheter down the oesophagus, a provisional diagnosis of broncho-oesophageal fistula was made. As the child was referred late and was in a poor general condition, no surgery was attempted. All the same, a gastrograffin study was ordered.

Figure 1 shows the radiograph taken two days after birth. It shows a markedly dilated stomach with the presence of air in the bowel loops. There is also a collapse of the right upper lobe. Figure 2 shows the radiograph taken just prior to the commencement of the gastrograffin study. It shows the

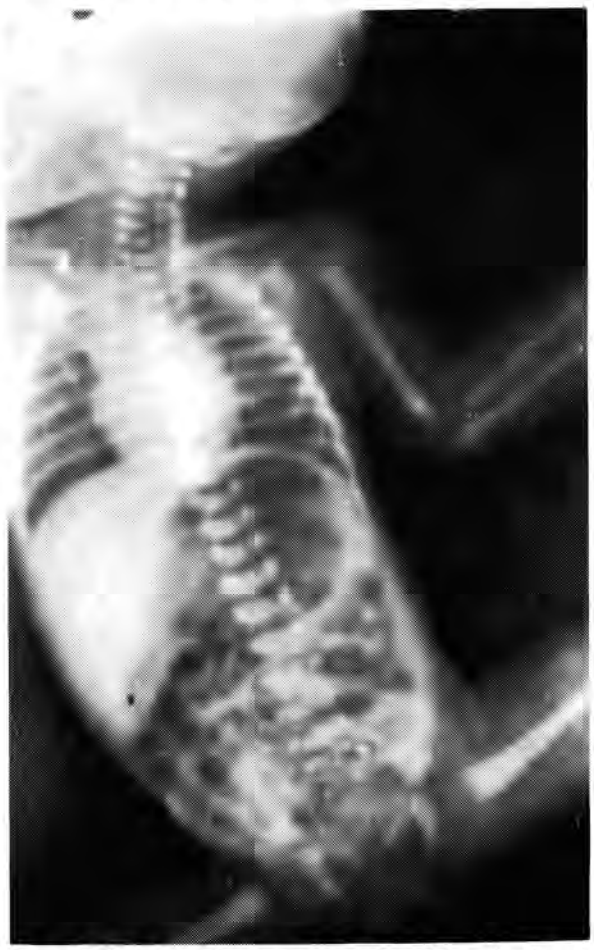

**Fig. 1. Radiograph taken two days after birth, showing a markedly dilated stomach and the presence of air in the bowel loops.**

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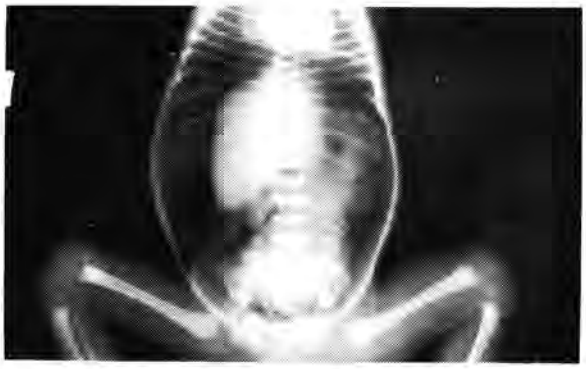

**Fig. 2. Radiograph taken prior to the commencement of the gastrografin study, showing the absence of air in the stomach and bowel loops, but the presence of air in the peritoneal cavity.**

absence of air in the stomach and bowel loops but the presence of air in the peritoneal cavity. The diagnosis of oesophageal atresia with distal tracheo-oesophageal fistula with pneumoperitoneum was then made. The child died a few hours after the gastrograffin study. A request for post-mortem was refused by the parents.

## DISCUSSION

At about the 21st day of embryonic development, the foregut begins to form into the dorsal oesophagus and the ventral trachea. The two organs are separated by a process of septation. An interruption in the septation process results in a fistula between the oesophagus and trachea. A low fistula would by the result of an early 'interruption' and a high fistula the result of a late 'interruption'.

The two conditions which may herald the birth of a child with oesophageal fistula are hydramnios and prematurity. 35 per cent of patients with oesophageal atresia with tracheo-oesophageal fistula are born premature by weight or age while a recognizable abnormality is present in some 50 per cent of these patients.

Though no known pattern of heredity has been established, sporadic cases of sibling being born with oesophageal atresia with tracheo-oesophageal fistula does occur.

Distension of the abdomen, in these children, is a result of swallowing air. Normally, a child will close his glottis while crying and this forces the air through the tracheo-oesophageal fistula into the stomach. The gastric and intestinal dilatation may elevate the diaphragm and respiration may become impaired. It is extremely unusual for patients with distal tracheo-oesophageal fistula to have a gas free abdomen, though reports contrary to this have been cited.

Though spontaneous rupture of the bowel is rare, in cases of congenital deformities such as this, a thinning of the stomach wall or gastrointestinal tract may be present making spontaneous rupture possible.

## ACKNOWLEDGEMENTS

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# CIMETIDINE FOR CHRONIC DUODENAL ULCERATION SHORT TERM CLINICAL TRIAL

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## INTRODUCTION

CIMETIDINE is an effective drug for the short term treatment of duodenal ulcer. In the eight prospective randomised double blind placebo-controlled studies available in the published world literature (Winship, 1978) healing occured in 57 to 87 % of duodenal ulcer patients compared to a healing rate of 19 to 60 % in placebo-treated patients. The duration of treatment was for 4 to 6 weeks and the dose ranged from 0.8 to 2.0 g per day.

We present here a preliminary report of a short term clinical trial of cimetidine treatment of 26 Malaysian patients with chronic duodenal ulceration, using a dosage of 1 gm per day for six weeks.

## METHOD

The trial was carried out at the General Hospital, Kuala Lumpur by the Department of Medicine, National University of Malaysia. Patients entering the trial had symptomatic and endoscopically proven duodenal ulcer (26 patients). Endoscopy using the Olympus GIF type K, JF type B2 and GIF type P2 instruments was carried out in the week before the commencement of treatment. The endoscopy was repeated by the same endoscopist in the first week after the 6 weeks of treatment. Ulcers were recorded as healed or unhealed. All patients were treated as outpatients with regular follow-up at 2 weeks intervals for the period of treatment. The dose of cimetidine used was 200 mg three times a day immediately before meals and 400 mg at night. Antacid tablets were allowed for symptom relief. During a pretreatment interview a detailed history and physical examination was performed. Baseline studies performed pre-treatment included haematological and biochemical blood studies (haemoglobin, haematocrit, red blood cell count, total white blood cell count, differential and platelet count, blood urea, serum creatinine, bilirubin, alkaline phosphatase, SGPT) and urinalysis. These studies were repeated during follow-ups in most of the patients.

At each follow-up a history and physical examination was performed with particular reference to ulcer symptoms, amount of antacids consumed and to side effects of cimetidine.

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## RESULTS

### Patient profile:

Twenty-six patients entered the trial. Of these, 18 were males and 8, females. The racial distribution consisted of 6 Malays, 8 Indians and 12 Chinese. The ages of the patient ranged from 16 years to 64 years, the mean age being 46 years.

### Symptom relief with Cimetidine

The duration of symptoms ranged from 6 months to 12 years with a mean duration of 6.0 years. The most consistent symptom was burning epigastric pain (in 22 patients out of 26), relieved by antacids and/or meals, aggravated by fasting. Sixteen patients out of the 26 had night pains disturbing their sleep in the early hours of the morning.

There was improvement of symptoms in 25 patients out of the 26. The pain relief was complete in 15 patients after the first week of treatment; in another 6, after the second week of treatment; in another 1, after the fourth week of treatment. There was partial relief of pain (i.e. decreased frequency and intensity of pain) in 3 patients, almost no improvement in 1 patient. The use of antacids during the course of treatment could be reduced in all patients except one. All patients with night pain (16 out of 26) had relief of their nocturnal symptoms whilst on cimetidine.

**Ulcer healing with Cimetidine**

Nineteen out of the 26 patients (73%) had complete healing of the ulcer (proven endoscopically) after 6 week of Cimetidine treatment. In the remaining 7 patients, 3 had partial healing and 4 had no healing at all.

Although 22 patients had complete relief of pain after the fourth week of treatment, only 19 patients had complete ulcer healing. Two of the 15 patients, where pain had disappeared after the first week of treatment, had no evidence of ulcer healing at the end of the six weeks treatment. There was no definite correlation between ulcer healing and symptom relief.

Of the 7 patients whose ulcers did not heal with Cimetidine the ages ranged from 16 to 52 years of age. Also the duration of the duodenal ulcer disease did not seem to affect the healing.

**Side-effects of Cimetidine**

There were no serious side-effects in all our patients. All patients tolerated the drug well.

Change of bowel habit was the most frequent untoward side-effect noted in our series. 8 out of the 26 patients complained of constipation; 4 complained of loose to soft stools. No patient developed nausea or vomiting. None had dizziness or headache while on the drug. There was no gynaecomastia or galactorrhoea in our patients. Laboratory investigations did not reveal any evidence of agranulocytosis in all the patients. Of the 20 patients who had serial liver function tests done, none had any elevation of liver enzymes. Of the 18 patient none showed any elevation of the serum creatinine above 2.0 mg % (i.e. clinically significant).

## DISCUSSION

Cimetidine, the most recent and most promising of the histamine H -receptor antagonists is a potent inhibitor of gastric acid secretion in normal subjects, and in patients with duodenal ulcer, (Henn, 1975; Longstreth *et al.*, 1976) hence the main indications for the drug are duodenal ulceration and the Zollinger-Ellison Syndrome (Malagelada, 1978). (Useful indications include treatment of gastric ulcer and pancreatic insufficiency; possible indications are prevention of gastrointestinal bleeding and treatment of peptic oesophagitis).

In 300 placebo-treated patients with duodenal ulcers a healing incidence of 37% has been reported in the world literature (Winship, 1978). The healing incidence of 73% in our series using 1gm of Cimetidine per day confirms the significantly higher healing rate. This healing rate is in agreement with experience elsewhere in the world (Banks *et al.*, 1976; Hetzel *et al.*, 1978).

Cimetidine relieved pain completely in 21 out of our 26 patients. However 3 of these patients showed no healing of ulcer endoscopically at the end of treatment, indicating that symptom relief does not indicate ulcer healing. Ippoliti *et al.* (1978), in his series, states that ulcer healing was not necessary for symptom relief as 18 of 36 patients with endoscopic evidence of ulcer or erosion were asymptomatic.

We did not experience any serious side-effect of the drug. Bowel habit alterations especially constipation was observed in 12 of our patients. Although gynaecomastia, raised serum trausaminares and creatinine have been observed we detected none in our series. Serum prolactin levels have been reported to be raised in patient with Cimetidine. Prolaction levels were not measured in our patients.

We conclude that Cimetidine is an effective drug for ulcer healing and symptom relief for the short term treatment of duodenal ulceration.


## SUMMARY

26 patients with endoscopically proven chronic duodenal ulceration were treated with Cimetidine 200mg three times a day and 400mg at night for 6 weeks. In 19 out of the 26 patients (73%) the ulcer was endoscopically healed at the end of the treatment. All patients received antacids only for symptom relief. Symptomatic relieve did not correlate to ulcer healing. No significant side effects were noted in the 26 patients. This study demonstrates the efficacy of short term Cimetidine in healing of chronic duodenal ulcer and in relieving ulcer symptoms.



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# PHYSIOTHERAPY IN THE MANAGEMENT OF SPORTS INJURIES

GENNY TEOW

## INTRODUCTION

SPORT INJURIES can be divided into 3 main categories:-

1) Extrinsic injuries those involving external violence eg. body contact with an opponent or goal post, being struck by a ball, a bat or a stick. These commonly result in haematoma, ligament sprains and tears and fractures of bone.
2) Intrinsic injuries basically caused by clumsiness or inco-ordination and at times under some external influence. These give rise to muscle component strains and tears and avulsion fractures.
3. Injuries caused by unaccustomed use and overuse. These are similar in pathology but in the former, are seen in the untrained person and the latter, in the trained athlete. These injuries include such conditions as tendonitis, bursitis, joint synovitis and stress fractures.

Physiotherapeutic management of sports injuries should ideally start on the playing field and continued throughout the recovery period. The shortage of therapists has not made this possible and at times lack of proper equipment and insufficient supervised exercises have contributed to unsatisfactory results. The lack of incentive and motivation on the part of the sportsmen can also be a contributing factor to a longer recovery period and lowering of general fitness.

In general, therefore, the physiotherapeutic management of sports injuries can be considered in three stages:-

1. The initial treatment which is essentially First-aid and is usually administered on the playing field, court or gym. In Malaysia, the physiotherapist, does not usually have a role here as most of the first aid is handled by coaches and first aiders with the less severe injuries, the more serious ones being treated by doctors and other qualified personnel.
   Management of less severe injuries will include cold application such as ice, cold water or spirit, application of compression through the use of elastic bandages or elastoplast and support when necessary by slings and strapping.
2. the next stage is the stage of definitive treatment where therapeutic measures are taken in the physiotherapy department to accelerate resolution of the injury.
3. The final stage involves adoption of measures taken to maintain fitness, particularly of the cardio-vascular system.

The injured athlete or player can receive definitive treatment within a few hours, a few days or even after a few months after the injury, depending on the severity and extent of injury and its subsequent swelling and pain or the urgency with which the player is needed to be active again. In this country, sport is considered more a recreational and social event rather than a profession. Hence, physiotherapeutic treatment has often been delayed and this had led to unnecessary complications and discomfort.

Basically, the aims of treatment are:-

i) To resolve the inflammatory process and promote removal of inflammatory products thereby reducing pain and swelling.
ii) To restore joint mobility and proprioception.
iii) To restore muscle strength, power, endurance and extensibility and
iv) To maintain general fitness.

Reduction of pain and swelling of recent injury is promoted by the use of ice, compression, elevation and occasionally, when prescribed by the doctor, anti-inflammatory and analgesic drugs. Once stasis is established, further reduction of

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pain and swelling is accelerated using ice, contrast packs or baths (alternate hot and cold), and/or pulsed ultra-sound.

The choice of heat to accelerate resolution is usually ultra sound for interfascial, intra-muscular and deep joint lesions and microwave (M/W) or short wave diathermy (SWD) for muscular and superficial joint lesions. Frequently a combination of continous ultra sound followed by pulsed sound, or M/W (SWD), followed by pulsed sound is used.

The next stage then involves a gradually progressive exercise program which in majority of the injuries is the most important treatment modality to restore muscle strength, endurance, mobility and proprioception. Exercise is also used as a self-manipulation with the aim of reducing pain. Pain-free movement patterns are established and the patient instructed to "press" into the full range, repeating the exercise a little but often throughout the day, but stressing that exercise should always be performed within the limit of pain and swelling. Exercises are usually incorporated with the application of ice or heat as the relief obtained during the application help facilitate movements.

The fourth aim of treatment is to maintain general fitness and frequently apply to those who are partially incapacitated through a fracture particularly of the bones of the lower limb, rupture of tendon or muscle or a back injury. While the injured area is immobilized or rested, general strengthening exercise are instituted to the unaffected areas. For example a patient with an injured back may still be able to lift light weights in a prone or supine position or propel himself along the gym floor and blanket in a similar position. Specific muscle strengthening can be achieved by the use of weights and pulleys.

There are, however, certain commonly injured joints that merit individual and detailed consideration. The knee and ankle are by far the most commonly injured areas.

**THE KNEE**

The initial treatment for the knee when there is gross swelling and pain, would be the application of an ice pack with elevation, of the leg. Further reduction of swelling is then promoted with compression bandaging. For this the leg, from mid-calf to mid-thigh, is bound with 2 layers of cotton wool and then by cotton or crepe bandages (Robert Jones type). Rest and elevation is continued until the swelling has considerably decreased. Static quadriceps exercises can be started as soon as the pain has subsided. Bandaging is then reduced to facilitate exercises. Exercises are then progressively graded by increasing the resistance using weights and in the number of times the movement is performed. Static and active quadriceps exercises are emphasised to prevent any extension lag. Knee flexion exercises can be instituted when the swelling has decreased. Persistent swelling can be helped with ultra sound (U.S.) and S.W.D. Support strapping can be used to ensure safety in early movement of the knee as with the ligamentous tear that affect the stability of the knee joint. Further strengthening exercises can include cycling, rowing and knee squats.

**THE ANKLE**

An ankle sprain is initially treated by immersing the whole foot in ice, followed by U.S. and compression bandage or support strapping. Active movements of the ankles should be started as soon as pain allows. If swelling is not gross, patient can hobble around with a supportive strapping. Exercises are then increased, emphasising on full range of movement. Ultra-sound (U.S.) & SWD can be applied if the swelling persists. Contrast baths (alternate hot & cold) can be used to help reduce the swelling. Further strengthening exercises would include balancing exercises on balancing board or trampoline, heel-toe movements and cycling.

The treatment programme above do not apply initially if there are fractures involved.

Malaysia has still a long way to go in the management of sport injuries both in terms of equipment and trained personnel. Hopefully, this will improve with the realization that sports injuries do require adequate professional care.

# PRELIMINARY REPORT OF INTER DIALECT GROUP MARRIAGE OF CHINESE IN WEST MALAYSIA

A.O. FRANK,

## INTRODUCTION

IT HAS BEEN reported from Singapore that there is a significant degree of marriage between Chinese people of different dialect groups (Yeh, 1964). The author knows of no report from Malaysia on this subject. However, it is important to be aware of the degree of inter-marriage between different dialect groups as investigators into the aetiology of different disease processes require to look carefully into the racial background. It has already been shown in Singapore that there is a different incidence of nasopharyngeal carcinoma in Chinese patients of different dialect groups (Shanmugaratnam and Tye 1970). This finding is of considerable importance to physicians and rheumatologists as our understanding of the familial predisposition to the rheumatic diseases has been enhanced by the work of Moll *et al* (1974), and the nearly simultaneous finding of the association of certain rheumatic disorders with the genotype HLA B 27 (Brewerton *et al.*, 1973, and Schlosstein *et al.*, 1973).

During 1974 — 1976 a study was conducted into the racial background of patients suffering from Systemic Lupus Erythematosus (S.L.E.). It was found that patients asked about their dialect group (Yeh, 1964) invariably gave the dialect group of their father. Only one patient gave the dialect group of her mother, and one admitted to having parents from different dialect groups. This preliminary study was designed to ascertain the degree of inter-dialect group marriage among patients attending the University Hospital.

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## PATIENTS AND METHODS

Group I consisted of 163 patients suffering from Systemic Lupus Erythematosus who were being treated as inpatients or as outpatients. Data was available from 76 patients in this group.

Group II consisted of 85 patients who were being treated in the Department of Medicine at the university Hospital, mostly as inpatients. They were a selected group matched by age and sex with patients from group I. Data was available from 80 patients in this group.

Group III consisted of all Chinese patients admitted into a female medical ward over a four month period, excluding any patients who were included in Groups I and II.

All patients were asked, through an interpreter when necessary, their age, and the dialect-group to which their parents belonged.

## RESULTS

Table I shows the number of patients in each of the three groups, together with the total number of patients for which information was available, the total number of patients whose parents came from the same dialect group, and the total number of patients whose parents came from different dialect groups.

Information was available from a total of 192 patients, and of these 152 had parents who were from the same dialect groups. Thus nearly 20 per cent of the total sample came from families whose parents spoke different dialects.

Table II depicts the mean age of the different groups.

In each group the mean age of patients with parents of different dialect-groups was less than the mean age of patients with parents of the same dialect group.

**Table I**

**Number of patients in same and different dialect groups**

| Group | Total number of patients in each group | Number of patients of known age and dialect group | Number of patients with parents from the same dialect group | Number of patients with parents from 'different' dialect groups |
|---|---|---|---|---|
| I Patients with S.L.E. | 163 | 76 | 63 | 13 |
| II Control patients for S.L.E. series | 85 | 80 | 59 | 21 |
| III Random Ward patients | 36 | 36 | 30 | 6 |
| TOTAL | | 192 | 152 | 40 |

**Table II**

**Age of patients in same and different dialect groups**

| Group | Mean Age of Total Group (years) | Mean Age of Group with known data (years) | Mean Age of 'Same' Group (years) | Mean Age of 'Different' Group (years) |
|---|---|---|---|---|
| I | 25.6 | 26.5 | 27.7 | 20.6 |
| II | 26.6 | 26.9 | 28.8 | 21.6 |
| III | * | 44.5 | 45.7 | 38.7 |

* Age was unknown for three patients

**Table III**

**Distribution of patients from Groups I, II and III by age and parentage (percentage figures in brackets)**

| Age in Decades | Number of patients who had parents from the same dialect group | Number of patients who had parents from different dialect groups | Total Number of Patients |
|---|---|---|---|
| 10 — 19 | 32 (68.1) | 15 (31.9) | 47 |
| 20 — 29 | 58 (79.5) | 19 (26.0) | 77 |
| 30 — 39 | 22 (84.6) | 4 (15.4) | 26 |
| 40 — 49 | 14 (100 | 0 (0) | 14 |
| 50 — 59 | 13 (100) | 0 (0) | 13 |
| 60 — 69 | 6 (75) | 2 (25) | 8 |
| Over 69 | 4 (100) | 0 (0) | 4 |
| Patients of unknown age | 3 | 0 | 3 |
| TOTAL | 152 | 40 | 192 |

It can be seen that the mean age of patients from Sample III (routine ward admissions) is higher than the mean age of the other two groups. This would be expected as admissions to a general medical ward would include patients of all ages, whilst patients suffering from SLE would predominantly be in the second and third decades. In view of the fact that the third group was smaller and with a wider age distribution than the others a combined t-test was performed on the mean age of the combined total of patients in sample groups I and II only. This showed that the younger age demonstrated in patients whose parents were of different dialect groups was significantly less than the mean age of patients whose parents were of the same dialect group ($0.01 > p > 0.001$).

Further analysis of the age of patients in the two groups (parents of the same dialect group, and parents of different dialect groups) showed that at least two patients with mixed dialect group parents were in the sixth decade. This suggests that marriage between the different dialect groups is not a new phenomenon. The difference in mean ages, however, suggests that marriage between dialect groups is becoming more frequent. This can be confirmed by reference to Table III which shows the numbers of patients with parents of the same or different dialect groups according to their age.

It can be seen that of the 39 patients over the age of 39, only 2 had parents from different dialect groups. This decreased frequency of patients with parents from mixed dialect-group marriages with increasing age was statistically significant ($x2 — 0.05 > p > 0.02$).

Analysis of groups I and II by sex showed that all the men came from same dialect-group marriages (this was not a statistically significant finding). Table IV shows that the numbers of men were small, and that there was no difference in age between the sexes.

**Table IV**

**Distribution of patients in groups I and Ii by age and sex**

| Group | Number of Men | Number of Women | Mean Age of Men (years) | Mean Age of Women (years) |
|---|---|---|---|---|
| I | 8 | 68 | 28.4 | 26.29 |
| II | 10 | 70 | 25.2 | 27.14 |
| Total I + II | 18 | 138 | 26.6 | 26.72 |

## DISCUSSION

The practical importance of these findings is that investigators into social trends, or disease patterns related to ethnic factors will have to take note of the dialect groups spoken by the parents of any subject of study. It is interesting to note that the recent census (Malaysia, 1972) information was only obtained as to the dialect spoken by the subject interviewed. Since this data suggests that nearly 20 per cent of subjects may come from an inter-dialect group marriage, data of this kind will become increasingly hard to interpret.

It is interesting to note that Yeh found in 1964 that 61 per cent of persons interviewed in 1964 in Singapore married persons from the same dialect group (Yeh 1964). Perhaps the urban environment of Singapore predisposed to marriage outside the dialect group compared to the sample of patients in this study some of whom came from rural areas (Frank, A.O. to be published).

It is also important to note that since inter-dialect group marriages are not confined to the younger generation, it is not possible to predict from old data the accuracy of studies involving different dialect groups.

It is recommended that a larger study be set up to confirm these findings in view of the importance of the observations to researchers into medical or social fields.

## SUMMARY

192 patients seen on the wards or in the outpatient clinics of the Department of Medicine at University Hospital were asked to which dialect group their parents belonged. Nearly 20 per cent came from families in which the parents came from different dialect groups. The age of subjects in this group was significantly less than the age of patients whose parents were from the same dialect groups. Nevertheless, they included patients in the sixth decade. The implications of these results are discussed.

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# BOOK REVIEWS

## PAEDIATRIC PROBLEMS IN TROPICAL COUNTRIES

ROBINSON, M.J. & LEE, E.E.

THIS IS THE first paediatric textbook written in Malaysia for the undergraduate medical student, the paediatric medical officer and those doctors concerned with primary child health care in developing countries. In most medical schools the total paediatric curriculum for medical students covers only about 12-16 weeks in a medical school. Hence it is essentially important that students should be able to depend on a textbook in paediatrics which has material expressed in a problem orientated manner. Here at last is a textbook of 52 chapters which I believe fills the gap for any undergraduate and postgraduate student. The emphasis has been on making a correct diagnosis after taking a careful history and performing a thorough physical examination.

The opening chapter on community paediatrics emphasizes the vital role that paediatricians and priamry child health care workers have to play in identifying with the rural health programme and the preventive paediatric measures that can reduce the infant mortality rate. I am happy to see that besides the well documented chapters on low birth weight, jaundice, infections, infant feeding, vomiting and malabsorption, there is a chapter on the child and the family. This again is important as behaviour problems in children present as paediatric problems for the general practitioner and the paediatric doctor. The theoretical and practical aspects of disturbances of fluid and electrolyte metabolism have been explained with clarity. This chapter will be very useful to the young doctor and a good refresher for the continuing paediatric postgraduate doctor.

The chapters on clinical genetics, aspects of growth, and ambiguous genitalia, will strengthen the students endocrine knowledge and provide a new dimension on special problems in paediatrics. The emphasis on an early detection of handicapping conditions such as hypotonia, mental retardation, spastic, visual and hearing defects, speech and learning disorders is stressed in this book and the question of early rehabilitation of these handicapping conditions is important to the medical student. The chapter on practical procedures of infancy and childhood is carefully written with sensible logical sequence and a chapter that most paediatricians would want to refer to in their daily routine work.

Finally a Bahasa Malaysia translation of this paediatric textbook should be an urgent early consideration for future medical, science, and agricultural students and even the nursing professions in undergraduate and postgraduate studies.

S.C.E. Abraham

Churchill Livingstone, Edinburgh, London and New York, 1978, pp. 349.

ROBINSON, M.J. & LEE, E.E.

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