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Guest Editorial

TEACHING THE BASIC MEDICAL SCIENCES

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THE PROPORTION OF medical graduates on the staff of preclinical and paraclinical departments like Anatomy, Physiology, Biochemistry, Pharmacology, Medical Microbiology, and Parasitology, in most medical schools, has shown a dramatic decline in recent years. It is very difficult to attract medical graduates to positions in these departments. In the United States, and other Western countries like the United Kingdom and Australia, the proportion of medically-qualified staff now falls short of "educationally desirable" levels (Glover and McCloskey, 1976). This happens at a time when curricula of most medical schools are being geared towards including more medically relevant courses in the preclinical and paraclinical disciplines. The cause of the problem is that there are serious disincentives, of both salary and career prospects, in these areas.

"Crisis in preclinical medical sciences" was the striking title used by the British Medical Association (1971) in describing the staffing problem in basic medical sciences. Before we can be convinced that a crisis – situation exists, (as in the Department of Biochemistry in the University of Malaya where almost 100% of the staff are non-medical graduates) we have to convince ourselves that medically-qualified staff are vital for the teaching of preclinical and paraclinical subjects to medical students. Amongst the compelling reasons (Rose, 1975) are that doctors as teachers will have the personal experience of the training for and of the practical requirements in medicine, that such staff members can convince the student of the relevance of his pre and paraclinical studies to clinical work based on the teacher's personal and enthusiastic involvement with medicine, and the fact that with the increasing use of man to illustrate scientific principles in all these subjects, supervision should be undertaken by medically-qualified staff. Davidson (1971) emphasised the importance of a medical qualification as a desirable asset in a preclinical teacher in these words, "... that a medically-qualified teacher has at one stage in his life been a medical student himself. Since he knows how medical students live and think, he can appreciate their outlook on life and should be in a better position to understand their peculiar problems and points of view than can his non-medical colleague. These considerations are perhaps of greater importance than is usually appreciated."

There is a striking discrepancy in salaries offered to staff in clinical departments compared to those in preclinical and paraclinical areas (excepting Pathology and Medical Microbiology). "Financial incentives" ranging from about $400–$1200 per month (in the form of a clinical allowance) are now being offered to clinical staff members. This obviously results in the young doctor gravitating towards these financially lucrative fields – resulting in ultimate harm to pre and paraclinical disciplines. Employment as a medical academic must not be allowed to become a second-rate career. The only remedy, short of giving a specialist allowance to all medically-qualified staff, irrespective of the department they serve in, is to place medically-qualified individuals higher on the salary scales or to give them an inducement or deprivation allowance – as is the practice in most enlightened medical schools today. An alternative would be to appoint these staff members on a joint-appointment basis with clinical departments thus making them eligible for

the receipt of the clinical allowance. A less desirable avenue would be to allow staff of these departments to indulge in private practice, after office hours and during week-ends, in order to supplement their meagre income.

No medical practitioner can disagree with the statement made by the Association of University Clinical Professors of Australia in 1972. "Experience has shown the great importance of teachers in these (pre and paraclinical) subjects having a medical degree and the broad education in medicine this implies. Science graduates, however, brilliant, have no training in pathology or medicine. With rare exceptions, they lack comprehension of human disease and the needs and interests of doctors in training."

To quote Glover and McCloskey (1976) "We suggest that each University should be permitted to earmark posts in preclinical departments which they consider must be filled by medical graduates. These posts would be distinguished from those which could be filled by science graduates by means of a title, such as lecturer in clinical (or applied or medical) physiology, and so on, or by making the appointment a dual appointment, say, to the departments of Physiology and Medicine, or Anatomy and Surgery, and people holding these positions should be on the same salary scale as their clinical colleagues."

It is suggested that the highest consideration be given to retain and attract more medically-qualified teachers in the pre and paraclinical departments. Medically-qualified teachers of the Basic Medical Sciences are being overlooked, ignored, and discriminated against compared to their clinical counterparts. Since this problem is going to affect the training of our future doctors, the whole problem must be viewed seriously and tackled immediately. It would be very unfortunate if the teaching of medical students, in the initial stages, is left entirely in the hands of people who have not themselves studied medicine. If steps are not taken to reduce the disparity between the salaries of clinicians and medically-qualified personnel in preclinical and paraclinical departments, a medically-qualified member of the latter departments would become a rarity in the next decade.

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REASONS UNDERLYING THE MATERNAL CHOICE OF MIDWIVES IN RURAL MALAYSIA

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INTRODUCTION

IN MANY PARTS OF the developing world, a proportion of domiciliary deliveries are still attended by traditional birth attendants, known variously as *dukun bayi* (Indonesia), *bidan kampung* (Malaysia), *mohtamyae* (Thailand), *hilot* (Philippines), *dai* (India, Pakistan, Bangladesh) *daya* (Middle East) and *matrone* (Africa). In Malaysia the majority of these traditional birth attendants have never received any training in modern obstetrics or hygiene, while a proportion have had some training usually conducted by local government health staff. With the development of rural health services, an increasing number of trained midwives are being introduced into rural areas, so that, at the present moment many rural areas are served by all three types of midwives, namely, untrained *bidan kampung,* partly-trained *bidan kampung* and trained government midwives. The rural Malay mother is at liberty to choose the type of midwife she prefers. The purpose of this paper is to briefly describe the type of midwife found in rural Malay communities and to examine the reasons given by a sample of mothers for having selected the type of midwife who attended her most-recent-birth.

TYPES OF MIDWIVES

As has been mentioned earlier, there are three basic types of midwives who are available to the rural Malay mother.

The Untrained *bidan kampung*

The untrained *bidan kampung* has been the traditional source of midwifery care in rural Malaysia. She continues to remain prominent and in 1972 was responsible for 55% of all births in the predominantly rural state of Trengganu. During pregnancy she is responsible for providing advice and instructions concerning antenatal behaviour (taboos and behavioural avoidances), but does not provide antenatal care in the modern sense of the word. Once she has been booked she does not leave the village and is available to come as soon as she is called.

Once labour begins, she is not only responsible for the actual delivery but is also expected to take all the traditional precautionary measures to keep evil spirits at bay, provide reassurance to the mother, ritually bathe the mother, supervise the disposal of the afterbirth, wash all soiled linen, bathe the newborn, manage the umbilical stump and swaddle the newborn in an abdominal binder.

During the first 44 days after delivery, she is expected to provide advice and instructions concerning dietary and other taboos, to supervise the "roasting" of the mother's body, a process known as *bersalai* or *berdiang,* and the "roasting" of the abdomen, known as *bertungku* (Fig. 1). She is also expected to provide "heating" medicines and is responsible for the traditional *urut-mengurut* (massage) and the health of the newborn until the stump of the umbilical cord has dropped off (Chen, 1973). To the rural Malay mother, the trained government midwife only performs two of these several duties, namely, the actual delivery and the care of the newborn.

Traditionally, *bidan kampung,* do not have delivery kits. Standards of hygiene are generally

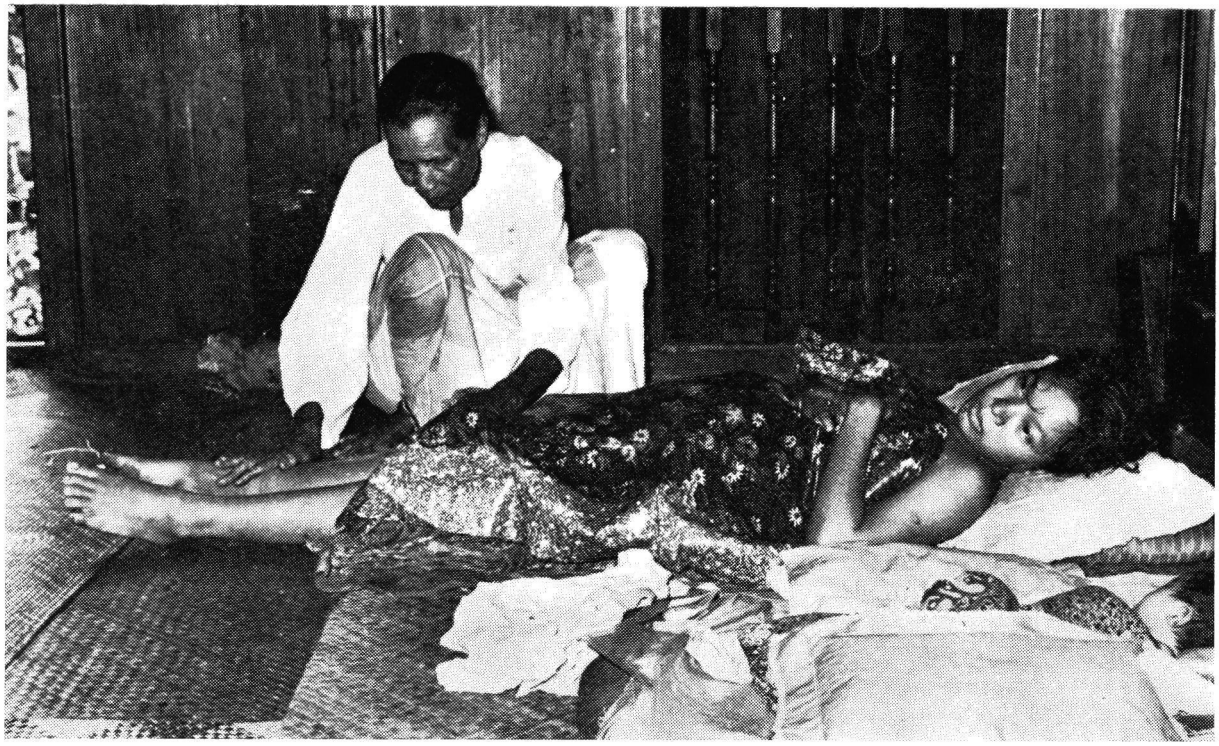

Fig. 1. An untrained *bidan kampung*, the traditional birth attendant, massages a new rural Malay mother with herbs. On her left lies the newborn baby.

low and the umbilical cord is usually cut after it has been rubbed with ashes from the kitchen hearth, knotted seven times and cut over a piece of tumeric "to keep the wind out", the cord being cut witn a freshly prepared *sembilu* (sharp sliver of bamboo). The risk of neonatal tetanus is obviously great.

The Partly-trained *bidan kampung*

Some *bidan kampung* have been partially trained by the local health staff. Training is usually brief and may consist of a dozen classes on elementary hygiene and the need to refer obstetrical complications to the hospital. After training, some are given UNICEF delivery kits while the others are required to buy their own locally assembled delivery kits containing soap, nailbrush, basin, bowls, artery forceps, scissors, antiseptic solution, flavin-in-spirit, cord ligatures, cotton swabs and gauze.

Supervision is generally poor as there is a shortage of health staff. It most usually takes the form of a monthly "supervision class", when the delivery kit is inspected, stocks are replenished and a talk or discussion is held (Fig. 2). These talks are usually on simple hygiene or the need to refer complications. Inspite of the limitations, partly-trained *bidan kampung* are more hygienic in their practices and have the advantage that they are able to call for help should complications arise. In addition, unlike the untrained *bidan kampung*, the partly-trained *bidan kampung* refer the majority of their patients for antenatal care available from the trained midwife.

The Trained government midwife

Trained government midwives are auxiliary midwives who have received from 18 to 24 months of training and who have passed the necessary examinations to enable them to be officially registered. Unlike the majority of the *bidan kampung*, trained midwives are educated and are relatively young. Like the *bidan kampung*, many of the trained midwives live among the villagers she will serve in a specially designed building, half of which is her home while the other half is a clinic from which she operates. Up to 1974, 1236 such midwife stations had been completed.

The trained midwife provides antenatal care to the bulk of pregnant women in her area. In the community studied she provided antenatal care to

Fig. 2. A group of eight partly-trained *bidan kampung*, traditional birth attendants, each holding a delivery kit, listens to a talk at a monthly "supervision class".

96% of the mothers although she eventually only delivered 47% of the mothers, the remaining 53% being delivered by the partly-trained *bidan kampung* (43%) and the untrained *bidan kampung* (10%).

METHODS

In order to study the reasons given by rural Malay mothers for selecting the type of domicilliar midwife who attended her most-recent-birth, a sample of 284 mothers resident in a community in the District of Kubang Pasu, Kedah, was selected and interviewed. Of the 284 mothers, 132 (47%) were most recently delivered by trained midwives, 123 (43%) by partly-trained *bidan kampung* and 29 (10%) by untrained *bidan kampung*. In the paragraphs that follow, the reasons given by the mother for selecting the midwife of her choice are presented. The data presented in this paper was collected in the course of field work towards a doctoral thesis submitted to the University of Malaya (Chen, 1975).

RESULTS

Reasons for selecting the untrained *bidan kampung*

A total of 58 reasons given by 29 mothers for selecting the untrained *bidan kampung* are summarised in Table I, the average number of reasons given by each respondent being two reasons. The principal reason, which was given by 24 (83%) of the mothers, was that the untrained *bidan kampung* provides many services. As was noted earlier, a large number traditional duties are expected of her, including such services as the disposal of the afterbirth, the washing of soiled linen, and the rendering of the traditional *urut-mengurut* (massage), the trained midwife being perceived to perform only two of these duties.

The fact that the untrained *bidan kampung* is a relative is mentioned by 13 (45%) of the mothers, while eight (28%) claim that acquaintanceship and familiarity are important reasons for their selection of the untrained *bidan kampung*, and four (14%) say

that they chose the untrained *bidan kampung* because she is the traditional source used by generations before them.

The fact that the midwife lives nearby is mentioned by seven (24%) of the mothers, indicating that geographical proximity is an important factor determining utilization patterns, since there is a tendency to utilize the nearest midwife. Two (7%) mothers indicated that they selected the untrained *bidan kampung* when the trained midwife was not available. Thus, mothers tend to choose the untrained *bidan kampung* for the reason that she provides many services, is a relative or acquaintance, is traditionally used and lives nearby.

Reasons for selecting the partly-trained *bidan kampung*

A total of 193 reasons given by 123 women for selecting the partly-trained *bidan kampung* as the principal midwife for their most-recent-births is summarised in Table II. As in the case of the untrained *bidan kampung,* the principal reason, offered by 67 (54%) of the mothers, for selecting the partly-trained *bidan kampung* is the fact that the partly-trained *bidan kampung* provides many services. Similarly, geographical proximity is important, although in the case of the partly-trained *bidan kampung,* this is mentioned by an even larger proportion (45%) of the mothers than was the case (24%) with those selecting the untrained *bidan kampung*. The fact that the midwife is a kindred, that the mother is acquainted or familiar with her way of life, and that the partly-trained *bidan kampung* is the traditional source used by past generations, is another important set of reasons, as was the case with those selecting the untrained *bidan kampung*. A total of eight (7%) of the mothers mentioned that they selected the partly-trained *bidan kampung* as the trained midwife was not available when they required her services, while 16 (13%) of the mothers mentioned that the partly-trained *bidan kampung* had government approval since she had received some form of training at the monthly "supervision classes", and nine picked on the partly-trained *bidan kampung* as a result of a fear of hospitalization or rudeness on the part of the trained midwives.

In other words, like the untrained *bidan kampung,* the partly-trained *bidan kampung* was selected by mothers for the reason that she provided many services, lived nearby, was a relative or acquaintance, shared her cultural norms, and was traditionally used by past generations. However, unlike the untrained *bidan kampung,* the partly-trained *bidan kampung* was selected for the additional reason that she had government approval and training, insignificant as the training might seem relative to that of the trained midwife. She thus appeared as an acceptable substitute to nine mothers who feared hospitalization and rudeness (imagined or real) of trained midwives.

Reasons for selecting the trained midwife

A total of 142 reasons given by 132 mothers for selecting the trained midwife as the principal midwife for their most-recent-births are summarised in Table III.

The fact that the service offered by the trained midwife is modern and safe, is given as the reason for her selection by only 37 (28%) of the mothers,

Table I

Reasons given by 29 mothers for selecting the untrained *bidan kampung* as the principal midwife for their most-recent-births

Reasons for selecting the untrained *bidan kampung*	Number of responses	Per cent of respondents expressing the reason
1. Provides many services (e.g. washes soiled linen)	24	83
2. Kindred of midwife	13	45
3. Acquainted or familiar with midwife's way of life	8	28
4. *Bidan kampung* is the traditional source used by past generations	4	14
5. Midwife lives nearby	7	24
6. Trained midwife was not available	2	7
Total number of responses	58*	

* on the average each respondent gave two reasons.

Table II

Reasons given by 123 mothers for selecting the partly-trained *bidan kampung* as the principal midwife for their most-recent-births

Reasons for selecting the partly-trained *bidan kampung*	Number of responses	Per cent of respondents expressing the reason
1. Provides many services (e.g. washes soiled linen)	67	54
2. Midwife lives nearby	55	45
3. Kindred of midwife	17	14
4. Acquainted or familiar with midwife's way of life	14	11
5. *Bidan kampung* is the traditional source used by past generations	7	6
6. Trained midwife was not available	8	7
7. Midwife has government "approval"	16	13
8. Afraid of hospitalization and rudeness of trained midwives	9	7
Total number of responses	193*	

* on the average each respondent gave 1.6 reasons.

clearly demonstrating the lack of successful health education of the mothers with respect to the advantages of modern maternity care. Eight mothers (6%) indicated that they were attracted by the fact that the service is free. A total of 38 mothers indicated that they chose the trained midwife since she was an acquaintance or had been recommended to choose the trained midwife. As in the case of the other types of domiciliary midwives, geographical proximity was another reason although this was mentioned by proportionately fewer mothers than in the case of the partly-trained or untrained *bidan kampung*.

A total of 24 (18%) mothers mentioned that they chose the trained midwife as a result of their desire to *turut undang-undang* (abide by the political directive for them to use government facilities and services), while six (5%) mentioned that they had specifically been instructed by the partly-trained *bidan kampung* to select the trained midwife.

In other words, as in the case of the two types of *bidan kampung*, some mothers selected the trained midwife since they were acquainted with her, and since she lived nearby although geographical proximity was less important than in the case of the *bidan kampung*. However, unlike the services of the two types of *bidan kampung*, the services offered by the trained midwife were thought to be modern and safe by about a fourth of the mothers and appreciated as free by others. On the other hand, a degree of pressure was perceived to have been exerted on mothers by both political sources as well as health agencies acting through the partly-trained *bidan kampung*, to select the trained midwife.

DISCUSSION

When the reasons expressed by mothers for their choice of domiciliary midwives are examined, three main features stand out. The first two revolve around the human interaction between mother and midwife, while the third concerns geographical proximity.

Bloom (1963) in examining the interaction between the medical worker and the patient, notes that their roles can be categorised into two: the "instrumental" role and the "expressive" role. He notes that "Instrumental roles are designed for solving problems, and emotion has little place in them. Expressive roles are patterned for the expression of feeling or emotion and are not concerned with getting anything done".

In terms of the "instrumental" role, it is seen that only 38 of the 284 mothers perceived that trained midwives are modern and safe. On the other hand, it is noted that 67 mothers selecting the partly-trained *bidan kampung* and 24 others selecting the untrained *bidan kampung* mentioned that they did so since the *bidan kampung* offers many more services than the trained midwife. In other words, in the eyes of the consumer, there is a short-coming in the extent of services offered by trained midwives and

Table III

Reasons given by 132 mothers for selecting the trained midwife as the principal midwife for their most-recent-births

Reasons for selecting the trained midwife	Number of responses	Per cent of respondents expressing the reason
1. Modern and safe service	37	28
2. Free	8	6
3. Acquainted with midwife	32	24
4. Recommended by friend	6	5
5. Midwife lives nearby	19	14
6. *Turut undang-undang* (abide by political directive to use government services)	24	18
7. Requested by partly-trained *bidan kampung* to select trained midwife	6	5
8. *Bidan kampung* not available	10	8
Total number of responses	142*	

* on the average each respondent gave 1.1 reasons.

that the best compromise seems to lie in the selection of the partly-trained *bidan kampung* who is a blend of the extreme two.

In examining the "expressive" role, it is noted that this manifests itself positively as *rapport* and that in the case of all three types of midwives it is the product of a combination of kinship feelings, acquaintance, and cultural familiarity. It is also noted that, in relation to this, the untrained *bidan kampung* stands out as the one who achieves the highest level of *rapport*. Fear of hospitalization and rudeness (real or imagined) on the part of trained midwives are the negative manifestations of the "expressive" role. In other words, the consumer holds that *rapport,* in the form kinship feelings, acquaintance and cultural familiarity, is an important component of the interaction between the medical worker and the consumer and that it influences the consumer's acceptance or rejection of the various resources available to her.

The third feature pertains to geographical proximity. It is noted that geographical proximity, with the accompanying advantages of convenience, promptness, and familiarity, is another important factor underlying the selection of the midwives available to the mother, and that the *bidan kampung* rather than the trained midwife is more likely to be selected for this reason.

SUMMARY

Many rural areas in Malaysia are served by a variety of midwives, namely, untrained *bidan kampung* (traditional birth attendants), partly-trained *bidan kampung* as well as trained government midwives. The rural Malay mother is at liberty to choose the one she prefers, choice being largely dependent on how the mother perceives the "instrumental" and the "expressive" roles of the midwife and whether she lives in close geographical proximity or otherwise to the mother.

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ECLAMPSIA – A REVIEW OF 48 CASES

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INTRODUCTION

IN SPITE OF advances made in obstetrics and gynaecological practice and in the dissemination of medical education, foetal and maternal deaths from eclampsia continues to be an important cause of perinatal and maternal mortality in Malaya (Marzuki and Thambu, 1973). In more advanced countries, namely England, eclampsia as a cause of perinatal and maternal mortality has fallen considerably. Maternal deaths in 1952–1954 were 1094 of which 110 were from eclampsia alone, while by 1970–1972 there were 355 maternal deaths with 29 due to eclampsia only (Confidential Reports, Maternal Deaths, 1952–1954; 1970–1972).

This present study reviews the experience in the management of eclampsia in a relatively modern obstetric unit.

MATERIALS AND METHODS

Over a period from March 1968 to April 1976 there were 48 cases of eclampsia seen in the Labour Ward of the University Hospital, Kuala Lumpur, Malaysia. During the same period, there were 22,848 deliveries.

The patients were either admitted through the Accident and Emergency Unit or brought directly to the Labour Ward. All cases were nursed in the eclampsia room in the Labour Ward.

Sedation was by intramuscular injections of 10 mg. diazepam (Valium), 6 to 8 ml. paraldehyde or lytic cocktail (a combination of 50 mg. pethidine, 50 mg. chloropramazine and 50 mg. promethazine). Lytic cocktail has also an antihypertensive effect (Menon, 1956; Sheares, 1957). Convulsions were normally controlled with intravenous doses of 10 mg. diazepam (Lean *et al.*, 1968). Intravenous frusemide (Lasix) 40 mg. was given to reduce the oedema, help in reducing the blood pressure and improve the urinary output in oliguric patients. Mannitol was occasionally given to induce diuresis.

Mild hypertension usually settled with sedation alone. Severe hypertension was treated with intravenous infusions of Neprasol (1, 4 dihydrazino phthalazine) starting with 25 mg. diluted in 500 ml. of 5% dextrose. This was titrated against the blood pressure at an initial rate of 5 drops per minute and increasing by 5 drops per minute until the blood pressure was stabilised at around 120/80 to 130/90 mmHg. It was occasionally necessary to use 50 mg. Neprasol in the infusion drip.

On occasions, moribund patients were curarised with intermittent positive pressure respiration instituted after transfer to the intensive care unit.

General nursing care or expert coma nursing were instituted as required. An indwelling Foley's catheter was inserted. The intake and urinary output was charted. Observations were taken of the patient's general condition, pulse, blood pressure, respiration and temperature. The state of consciousness and the time and duration of any convulsions were noted.

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The pregnancy was assessed abdominally and vaginally after sedation. Depending on the individual case the pregnancy was either conserved or terminated. If labour started spontaneously it was allowed to proceed. Induction of labour was by oxytocin infusion stimulation or amniotomy where the cervix was favourable. Delivery was usually assisted in the second stage. Caesarean section under general anaesthesia was done where the convulsions were uncontrollable and the patient was not in labour or the cervix was not favourable for induction of labour or there was poor progress of labour or foetal distress was present.

RESULTS

Incidence

The incidence of eclampsia in the present study was one in 476 deliveries. This was less common than that of Llewellyn-Jones in 1961 when he obtained an incidence of 1 in 220 deliveries in the General Hospital, Kuala Lumpur, and commoner than that seen by Lean *et al.* (1968) in neighbouring Singapore where the incidence was 1 in 715 deliveries.

Maternal and Social Features

As expected, most were nulliparous (30 patients, 62.5%), of socio-economic classes IV and V (36 patients, 75%) and mostly unbooked (32 patients, 66.7%).

The incidence was significantly higher among the Indians (0.40%) than among the Malays (0.22%) and the Chinese (0.06%) (Table I). It has been generally thought that this was due to better social classes and booking habits seen among the Chinese, but this was not borne out in the present series. There was no difference in booking habit ($X^2 = 0.29$, $P>0.05$) or social class ($X^2 = 7.63$, $p>0.1$). Other undetermined factors were probably responsible.

Clinical Features

Most of the fits occurred for the first time in the University Hospital (54.2%) (Table II). However, out of 3 maternal deaths, 2 of the patients had their first fit outside hospital. There were 27 antepartum eclamptics (56.2%); 14 intrapartum eclamptics (29.2%) and 7 postpartum eclamptics (14.6%). Two maternal deaths occurred in the antepartum eclamptics while the third maternal death was seen among the patient with intrapartum eclampsia. Most patients were in the gestational range of 36 weeks and above (21 patients, 43.7%). Thirteen patients or 27.1% were with unknown maturity. At admission, in 4 patients, no foetal heart sounds were heard. One terminated in a macerated stillbirth and three others as fresh stillbirths.

Table II

Clinical features of the first convulsion

	No. of patient	Per cent
PLACE OF FIRST CONVULSION		
Home	17	35.4
Journey To Hospital	1	2.1
Hospital	26	54.2
Private/Government Clinic	4	8.3
HOURS BEFORE DELIVERY		
<−1	1	2.1
1–6	10	20.8
6–12	11	22.9
12–24	5	10.4
24 and <	9	18.7
unknown	5	10.4
HOURS AFTER DELIVERY		
<−1	2	4.2
1–6	1	2.1
6–12	2	4.2
12–24	2	4.2
	48	100

Obstetric Management

Most eclamptic patients were in labour at admission or went spontaneously into labour later (27 patients or 56.2%). Thirteen patients had induction of labour by either amniotomy or oxytocin

Table I

Racial incidence of eclampsia

	RACIAL GROUPS				TOTAL
	MALAYS	CHINESE	INDIANS	OTHERS	
Number of deliveries	6,337	9,688	6,694	129	22,848
Patients with eclampsia	14	6	27	1	48
Percent	0.22	0.06	0.40	0.78	0.21

$X^2 = 22.435$ $P<0.0001$

stimulation. Spontaneous vaginal deliveries were seen in 19 patients (39.5%). Caesarean section was done in 13 patients (27.1%). The indications for Caesarean section are seen in Table III.

Maternal Morbidity and Mortality

Nineteen patients (39.5%) did not develop any complications. Twenty patients (41.7%) had one complication, while 5 patients (10.4%) and 4 patients (8.3%) had two and three complications respectively. The causes of morbidity are listed in Table IV.

One patient with renal failure and coagulopathy had renal biopsy which showed mild interstitial nephritis. Two patients were moribund with uncontrollable fits and required curarisation with intermittent positive pressure ventilation in the Intensive Care Unit (Chan and Delikan, 1970). There were 3 maternal deaths, giving an incidence of 6.3%. A summary of their clinical features is shown in Table V. At 6 weeks postpartum, 24 patients (50.0%) were found to be normotensive, 7 patients (14.5%) were still hypertensive with 12 patients (25.0%) having defaulted. The blood pressure was not stated in 5 patients.

Foetal Mortality

In the present series, there were 15 foetal deaths giving a total foetal mortality of 30.6%. One foetus died undelivered. The corrected perinatal mortality rate (excluding those infants weighing less than 1000 gms) was 14.6%. There were no neonatal deaths among babies weighing more than 2500 gm. All 3 neonatal deaths were due to prematurity.

Thirty-four infants in this series survived (Table VI). Eighteen of them were premature by weight (2 had associated neonatal jaundice while another 2 had urinary tract infection). One baby with a birth weight of 890 gm. survived. Of the mature infants, 2 had neonatal jaundice and 2 suffered from asphyxia but were well at follow-up.

Table IV

Major causes of maternal morbidity

Cause	Number of cases
Anaemia (including 2 postpartum haemorrhage)	6
Pneumonia	3
Collapsed left lung	1
Disseminated intravascular coagulation	2
Wound infection	1
Puerperal pyrexia	4
Puerperal psychosis	3
Fundi haemorrhages	4
Headaches with blurred vision	2
Infection	9
Anuria (with peritoneal dialysis)	2

Table III

Characteristics of labour and delivery in eclampsia

	NUMBER	PER CENT
a) TYPE OF LABOUR		
Spontaneous	24	50.0
Spontaneous + Oxytocic Stimulation	3	6.2
Amniotomy & Oxytocic Stimulation	13	27.1
Not In Labour	8	16.7
b) MODE OF DELIVERY		
Spontaneous Vaginal Delivery	19	39.5
Forceps Delivery	11	22.9
Vacuum Extraction	2	4.2
Breech Delivery	2	4.2
Caesarean Section	13	27.1
Undelivered	1	2.1
c) INDICATIONS FOR CAESAREAN SECTION		
(1) Eclampsia, not in labour	4	
(2) Uncontrollable eclampsia, 1 in labour	4	
†(3) Induction of labour with slow progress	3	
(4) Induction of labour with impending fetal death	1	
(5) Suspected rupture previous Caesarean scar; placenta increta	1	

† One patient with twin pregnancy

Table V

Clinical summary of maternal deaths

	A. bt A. R/N 051458	Y.K.L. R/N 119841	S.R. R/N 212884
Race	Malay	Chinese	Indian
Age (Years)	26	44	24
Parity	1	10	3
Social Class	II	unknown	IV
Booking	unbooked seen in govt. clinic	unbooked	unbooked
Gestation (age in weeks)	37	32	30
Past History	Nil	hypertension	toxaemia in previous pregnancies
Place Of First Convulsion	hospital	home	private clinic
Convulsion Delivery Interval	20 mins.	52 hrs 20 mins.	died undelivered
Convulsion Death Interval	6 days	4 days	46½ hrs.
Highest Blood Pressure	270/150	290/200	270/200
Clinical Course	hypertensive encephalopathy	hypertensive encephalopathy	oliguria microangicpathy
Cause Of Death	cardiovascular collapse	cerebral haemorrhages	cerebral haemorrhages
Postpartum	Nil	Nil	Nil
Fetal Outcome	fresh stillbirth 2150 gms.	fresh stillbirth 1000 gms.	undelivered

Table VI

Table showing fetal outcome in relation to birth weight

BIRTH WEIGHT (gms.)	FETAL OUTCOME					TOTAL	%
	abortion	macerated stillbirth	fresh stillbirth	neonatal death	normal baby		
0 – 999	3	1†	2	1	1]	8	16.70
1000 – 2500			5†	2	17*	24	50.00
more than 2500					16*	16	33.30
Total	3	1	7	3	34	48x	100.00

† fetal heart not heard at admission
x exclude one fetus in utero, undelivered
* include one set of twins

Subsequent Pregnancies

There were 16 known subsequent pregnancies. Five patients had an uncomplicated pregnancy. Seven patients had toxaemia of pregnancy, one of which delivered a macerated stillbirth. This particular patient had one more pregnancy after that, also complicated by toxaemia but she delivered a normal live-birth. There were 2 abortions, one early and one in mid-trimester. The patient with the early abortion had a normal third pregnancy.

There was no recurrent eclampsia in these known pregnancies. The foetal salvage rate was 81.3%.

DISCUSSION

Eclampsia is still a common and dreaded cause of maternal mortality and foetal loss in Peninsular Malaysia. The aetiology of pre-eclampsia and eclampsia remains unknown, though it is believed the convulsions of eclampsia are due to cerebral anoxia from intracranial vascular spasms, haemorrhage, hypertensive encephalopathy and cerebral oedema. The main pathological alterations are seen in the liver, kidneys, brain, lungs and heart. Dennis *et al.* (1963) described changes in the renal glomeruli and arterioles. One case of renal biopsy done in this series showed mild interstitial nephritis.

The incidence of eclampsia varies in different series, and probably reflects on the geographical locality, its socio-economic development and the availability of health and antenatal services. The reduction in incidence in this series as compared to that seen by Llewellyn-Jones in 1961 is possibly influenced by the better socio-economic status and increased availability of antenatal care. Most patients with eclampsia have no antenatal care and are seen the first time with fits (Bryans, 1963). 66.7% of patients in this series were unbooked.

Chan in 1974, in a series of 504 toxaemia patients, found the incidence of toxaemia to be significantly highest among the Malays. Socio-economic differences were suggested as a possible cause. However, in this series, the incidence of eclampsia was significantly highest among the Indians, and social class was excluded as a causative factor. Other factors may be responsible for this difference.

Sixty to 80% of patients in other series have their first convulsion outside hospital (Crichton and Notelovitz, 1968), while this occurrence was seen in 54.2% in this series. This is of importance because of the availability of immediate treatment. It is significant but that two patients out of the 3 maternal deaths in this series had their first convulsion outside hospital where prompt medical aid is not available; 96.6% of 30 maternal deaths reported by Crichton and Notelovitz (1968) occurred outside hospital.

A higher maternal mortality was demonstrated by Menon (1961) in antepartum and intrapartum eclamptics as compared to postpartum eclamptics, while the rapid improvement in the maternal condition that follows delivery has been universally noted. Due to these factors, many authors have recommended a quick termination of the pregnancy (Menon, 1961; Lean *et al.*, 1968; Leading Article, 1976). Active termination of pregnancy seen in a small number of cases in this series resulted in total foetal survival. Maternal complications however appear similar.

Very often labour occurs spontaneously, as seen in 56.2% here. Delivery was usually rapid and was spontaneous in 39.5%. In recent years a freer use of Caesarean section has been advocated to reduce the maternal and perinatal mortality (Lean *et al.*, 1968; Crichton and Notelovitz, 1968), though we agree with most authors on its more judicious use (Menon, 1961; Dewhurst, 1972; Leading Article, 1976). The Caesarean section rate was 27.1% in this series with a maternal mortality of 6.25%. The three patients that died were very ill at admission.

The principal cause of maternal death is cerebral haemorrhage (Confidential Reports, Maternal Deaths, 1970–1972). Two maternal deaths in this series were possibly due to cerebral haemorrhage. The third patient died of cardiovascular collapse. Autopsies were unfortunately not done. The morbidity is also high, the complication rate in this series being 60.4%.

A high foetal loss is accepted in eclampsia due to prematurity, the toxaemic process itself and the sedatives used. The perinatal mortality rate has varied from 11.1% (Lean *et al.*, 1968) to 32.1% (Mitra *et al.*, 1958). The beneficial results of early Caesarean section in reducing perinatal mortality was shown by Lean *et al.* (1968) and Crichton and Notelovitz (1968). In this series, of the 14 foetal deaths with known birth-weights, 7 were below 100 gms. The corrected perinatal mortality rate was therefore 14.6%.

There were 16 known subsequent pregnancies of which 7 patients (43.8%) were complicated by toxaemia. The recurrence rate of hypertensive complications in recent reports average 35% (Chesley, 1971). The incidence of repeat eclampsia was

2.1% and the foetal salvage rate was 77% (Chesley, 1962). No repeat eclampsia was seen here. The majority opinion, however is that the prognosis for pregnancy following eclampsia is not too unfavourable.

SUMMARY

A review of 48 cases of eclampsia seen in the University Hospital from March 1968 to April 1976 showed that the maternal mortality was 6.3% and the foetal mortality was 30.6%. The corrected perinatal mortality was 14.6%. The prognosis in known subsequent pregnancies was also discussed.

ACKNOWLEDGEMENT

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ANENCEPHALIC PREGNANCIES IN A MALAYSIAN HOSPITAL

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INTRODUCTION

ANENCEPHALY is a common and interesting fetal abnormality. Recent attention has been concentrated on the early antenatal diagnosis of this malformation and such reports are many. However, more basic studies on the relationship of anencephaly to demographic factors like maternal, fetal and geographical factors are few. These have been mainly from the west. Hence, a study of anencephalic pregnancies from the tropical region seems appropriate.

MATERIALS AND METHODS

A retrospective analysis of all anencephalic fetuses delivered at the Maternity Hospital, Kuala Lumpur, Malaysia, from January 1973 to April 1977 was carried out. Data recorded included maternal data, fetal data, labour data and complications during the antepartum period and during labour. Other associated abnormalities of the fetus at birth were also recorded.

RESULTS

Incidence

During the study period, there were 73,307 hospital deliveries out of which 40 were anencephalic pregnancies. The incidence of anencephaly in this study was thus 0.55 per 1000. The incidence was higher in the Chinese (0.77 per 1000) compared to the Indians (0.53 per 1000) and the Malays (0.35 per 1000). It was interesting to note that all patients were third class hospital admissions, that is, they were in the lower social status group.

Maternal Data

Maternal age and gravidity. Table I shows that there is no obvious pattern between the age and gravidity to incidence of anencephaly. This is true for the primigravidae, multigravidae and grand-multigravidae. The majority of patients were multigravidae (75%).

Table I

Anencephalic pregnancies in relation to maternal age and gravidity

Age group (years)	Gravidity 1		2–4		5+	
	No.	%	No.	%	No.	%
<20	4	10.0	1	2.5	–	–
20–24	4	10.0	8	20.0	2	5.0
25–29	2	5.0	6	15.0	3	7.5
30–34	–	–	2	5.0	2	5.0
35–39	–	–	–	–	4	10.0
40 and above	–	–	–	–	2	5.0

Time of diagnosis. Of the 40 patients, the diagnosis was made only at delivery in 30 (75%) patients. Only 6 (15%) patients were diagnosed antenatally. Four (10%) patients were diagnosed during labour before delivery. Of the 22 booked patients, the incidence of antenatal diagnosis of this fetal malformation was 27%.

Maternal complications. During pregnancy, pre-eclampsia was present in 4 out of 37 patients (10.8%), and polyhydramnios was present in 8 out of 37 patients (21.6%). In 3 patients, there was no record of whether these complications were present or not. *During labour,* shoulder dystocia was present in 2 (5%) patients. Both these fetuses weighed less than 2950 gm at birth. There were no patients with post-partum hemorrhage. Maternal injuries encountered during delivery were minor. These included first degree perineal tears in 4 (10%) patients, second degree perineal tears in one (2.5%) patient and minor labial tears in one (2.5%) patient.

Duration of pregnancy. As shown in Table II, 19 (57.6%) patients delivered at term. Eight (24.2%) pregnancies were pre-term out of which, 5 were complicated by poly-hydramnios. Six (18.2%) patients were post-term; none of these patients had polyhydramnios.

Duration of labour. The mean duration of labour was 10 hours 4 minutes. Of the 35 patients included, 11 (31.4%) laboured for less than 6 hours, 11 (31.4%) between 6–12 hours, 8 (22.9%) between 12–18 hours, 4 (11.4%) between 18–24 hours, and one (2.9%) for more than 24 hours.

Mode of delivery. As shown in Table IV, vaginal delivery was achieved in 35 out of 38 patients (92.0%). Caesarean section was done in 3 (8.0%) patients; one for a big breech, one for a shoulder presentation, and one for an impacted face presentation. Two patients who delivered before arrival in hospital were excluded. The majority (60.5%) of the vaginal deliveries were spontaneous cephalic.

Fetal data

Fetal presentation in labour. The presentation was cephalic in the majority of the anencephalic fetuses – 23 (60.5%). Other presentations included breech (21.1%), face (15.8%) and shoulder (2.6%).

Table II

Duration of pregnancy in anencephalic pregnancies*

	Duration of pregnancy (weeks)							
	<36	36–	37–	38–	39–	40–	41–	42+
No.	7	1	–	5	4	7	3	6
%	21.2	3.0	–	15.2	12.1	21.2	9.1	18.2

* out of 33 patients

Mean duration of pregnancy (Table III). The overall mean duration of pregnancy was 38.8 weeks. For those with polyhydramnios, it was 36.1 weeks and for those without polyhydramnios, it was 39.5 weeks. Those patients with polyhydramnios therefore had a shorter duration of pregnancy.

Table III

Mean duration of pregnancy in anencephalic pregnancies

Overall[1]	—	38.8 weeks
Those with polyhydramnios[2]	—	36.1 weeks
Those without polyhydramnios[3]	—	39.5 weeks

NB [1]out of 33 patients
[2]out of 7 patients
[3]out of 26 patients

Labour data

Onset of labour. The onset was spontaneous in 38 (95%) patients while labour was induced in 2 (5%) patients at 35 – 40 weeks, for the relief of symptoms secondary to polyhydramnios.

Table IV

Mode of delivery in anencephalic pregnancies*

Mode of delivery	No.	%
Spontaneous cephalic	23	60.5
Spontaneous face	4	10.5
Spontaneous breech	1	2.6
Assisted breech	5	13.2
Breech extraction	1	2.6
Forceps	1	2.6
Caesarean section	3	8.0

* out of 38 patients

Sex of fetus. It was interesting to note that in this study, the anencephalic fetuses were more commonly males (22 – 55%) than females (18 – 45%). The ratio of male to female fetuses was thus 1.22: 1.

Fetal birth weights. The mean birth weight was 2028.5 gm. Most (57.5%) of the fetuses weighed

more than 2000 gm at birth; 12.5% were below 1000 gm in weight (Table V).

Table V

Birth weight of fetus in anencephalic pregnancies

Birth weight (gm)	No.	%
<1000	5	12.5
1000–	9	22.5
1500–	3	7.5
2000–	10	25.0
2500–	10	25.0
3000–	2	5.0
3500–	0	0
4000 and above	1	2.5

Viability of fetus. Half of the fetuses were live births and the other half were stillbirths. Of the stillbirths, 5 (12.5%) were macerated and 15 (35.5%) were fresh. All 20 live births ended as perinatal deaths.

Other associated abnormalities. In 3 (7.5%) instances other abnormalities were present. These were exomphalos and absence of one limb in one fetus; encephalocele, polydactyly and hydrops in one fetus; and meningomyelocele in one fetus.

DISCUSSION

The incidence of anencephalic pregnancies in this study (0.55 per 1000) is lower than reported figures from the west which vary from 0.76 to 2.43 per 1000 (Cassady, 1969; Fedrick, 1970; Honnebier and Swaab, 1973; Janerich, 1972).

The relationship of maternal age and gravidity to incidence of anencephalic pregnancies in this study does not conform to the described 'U' shaped relationship, i.e., among primigravidae, the younger the mother, the higher the risk; while among the multigravidae, the older the mother, the greater the risk (Fedrick, 1970; Janerich, 1972). However, this pattern is not invariably found.

Polyhydramnios occurred in only 21.6% of our patients compared to reports of 51.5% (Milic and Admsons, 1969) and 73% (Honnebier and Swaab, 1973). This is an important association as it is seen that the mean duration of pregnancy is markedly shortened in its presence, in this study as well as others (Honnebier and Swaab, 1973; Milic and Adamsons, 1969).

Although the relationship of prolonged pregnancy to anencephaly has been stressed, the incidence of prolonged pregnancy in this malformation has varied from 2.3% to as high as 40% (Cassady, 1969; Honnebier and Swaab, 1973; Milic and Adamsons, 1969). It is therefore not an invariable relationship. Nevertheless, the majority of patients go into spontaneous labour, 95% in this study compared to about 78% in others (Honnebier and Swaab, 1973; Milic and Adamsons, 1969).

The problem of shoulder dystocia during vaginal delivery of an anencephalic fetus has, in our opinion, been overstressed. This complication occurred in only 2 patients in this study. There has been no mention of this complication in other reports (Cassady, 1969; Honnebier and Swaab, 1973; Milic and Adamsons, 1969).

Although most studies have indicated a female predominance over males in the fetuses delivered in the ratio 3: 2 or 3: 1, this study showed a male predominance over female in the ratio 1.22: 1. It indicates therefore that it is not always true that anencephalic fetuses are more commonly female.

The low incidence of antenatal diagnosis of this malformation in this study has made us aware that we should be more acute in our clinical suspicion of this malformation. The present trend of research into its early antenatal diagnosis seems justified. In our hospital, we hope to pursue this aspect of the problem when we acquire our ultrasonic scanner and when the facilities for alpha-fetoprotein estimations are increased.

SUMMARY

A retrospective analysis of 40 anencephalic pregnancies seen in a Malaysian hospital is presented. The incidence was 0.55 per 1000. The relationships of this fetal malformation to racial and social class factors, maternal factors, labour and delivery characteristics and fetal factors are presented. The results are discussed in the light of available reports.

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FIBROADENOMA OF VULVA

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FUNCTIONING BREAST TISSUE is located in the vulva of certain aquatic mammals (whales, dolphins, porpoises) and in woman the presence of breast-like tissue in this region is a rare congenital anomaly. We report one such lesion of the vulva thought clinically to be a cyst which on examination showed a marked resemblance to fibroadenoma of the mammary gland.

REPORT OF CASE

A 36 year old Chinese female L.K.E. was seen at the Luke Clinic, Penang, on 25.5.77 complaining of a lump at the vulva of two year duration. It was uncomfortable but not painful and slowly increased in size.

There was no history of pelvic or genital infection.

Physical examination revealed a non-tender and freely movable oval lump located just under the skin of the left labia majus. It was excised and "shelled out" of the tissue without difficulty, and the patient made an uneventful recovery.

Pathological findings:- Gross examination revealed a well circumscribed, oval and nodular, rubbery firm lump, measuring 1.8 × 1.5 × 1.5 cm. It was apparently encapsulated and its external surface which was smooth and lobulated was covered by an elliptical piece of skin tissue. The cut section was solid and uniformly whitish grey in appearance.

Microscopic sections showed a sharply delimited tumour composed of breast-like tissue in which there was benign proliferation of both the epithelial and the fibrous connective tissue elements in varying amounts. In some places the proliferation of the fibrous tissue was uniformly concentric in distribution in relationship to the epithelial structures which did not appear distorted. In other areas the overgrowth of the fibrous tissue lead to invaginate the epithelial components which appeared as compressed narrow spaces between the fibrous nodules. The covering skin was intact and unchanged.

Section of tumour from perineum showing a fibroadenomatous appearance.

The features resembled a simple fibroadenoma of the breast in which both the pericanalicular and intracanalicular patterns were represented.

COMMENTS

As in all mammals the human breast develops in a primitive epidermal thickening known as the

mammary ridge or "milk line". This line runs from the axillary to the pubic region to end on the upper medial surface of the thigh. Thus from the embryologic point of view supernumerary breast structures may be found at any point along this line. This anomaly frequently occurs below the breasts and sometimes in the axilla. It is only rarely encountered in the vulva, and its presence is explainable in this developmental band.

Vulva breasts are capable of behaving in the same way as normally situated breasts and neoplastic change can supervene. Both fibroadenoma (Fisher, 1947; Siegler and Gordon, 1951) and adenocarcinoma (Hendrix and Behrman, 1956) have been reported.

Although vulval tumours containing breast-like epithelium suggest an origin in rudimentary breast tissue the probability of these having arisen in the epithelium of the vulval apocrine glands has also been reported (Burger and Marcuse, 1954). They describe two cases of intracystic fibroadenoma in the vulva and regard the lesions as a variant of apocrine gland hidradenoma in which the stromal element predominates.

Clinically, these tumours are benign and the symptoms encountered are those of local tumour. They do not recurr unless incompletely excised.

SUMMARY

Supernumerary mammary glands are chiefly found between the axilla and groin. This anomaly is frequently found below the breasts or in the axilla and the vulva is rarely the seat of this malfromation.

We report one lesion of the vulva clinically thought to be a cyst but microscopic examination showed a tumour resembling fibroadenoma of the breast.

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A CASE OF PRIMARY ADENOCARCINOMA OF THE FALLOPIAN TUBE

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PRIMARY ADENOCARCINOMA of the fallopian tube is a rare condition and is the least common malignancy of the female genital tract. Its incidence has been reported to be between 0.1 to 1.6%. In this paper, we report the first case of primary adenocarcinoma of the fallopian tube seen in the University Hospital, Kuala Lumpur.

CASE HISTORY

O.S., a 60 year old Chinese, para 9, was first seen in March 1973 complaining of watery, smelly vaginal discharge for 8 months, and post-menopausal bleeding per vaginam for 3–4 months. General physical examination and vaginal examination revealed no abnormality. Investigations, including full hematological examination, blood urea, serum electrolytes, urine for microscopic and bacteriological examination, chest X-ray and electrocardiogram were all normal. A Pap smear taken on 1-3-73 revealed spindle-shaped epithelial cells resembling transitional cells of the bladder, and parabasal squamous cells. Occasional abnormal cells with hyperchromatic nuclei and irregular margins were present, strongly suggesting malignancy.

Further investigations along the diagnosis of a genito-urinary fistula were done, including a 3-swab methylene blue test, intravenous pyelogram and examination under anaeesthesia with cystoscopy, but all were negative.

A repeat Pap smear on 13-3-73 showed no malignant cells. This was followed by a diagnostic curettage but no curettings were obtained from the endocervical canal or the endometrial cavity.

Repeat Pap smear on 15-3-73 revealed the reappearance of clusters of abnormal cells. A 24-hour urine sample for cytological analysis was negative.

At follow-up, she was still complaining of "leaking" vaginally. This time, she had slight tenderness in the left iliac fossa on abdominal palpation. Vaginal examination revealed a discrete, tender nodule 2 × 2 cm in size, rather fixed to the left border of the uterus. A diagnosis of carcinoma of the fallopian tube was made and a laparotomy decided upon.

Laparotomy was performed on 23-4-73. This showed the uterus to be of normal size, the right fallopian tube and ovary were normal, and the left ovary was normal. The left fallopian tube was enlarged by a nodular, elongated growth (Figure 1) with adhesions to the anterior rectal wall, left ovary and left lateral pelvic wall. The tumour involved the outer half of the tube, leaving the initial proximal half intact and normal. The right lateral pelvic wall was clear, but there were some friable, bleeding nodules on the left lateral pelvic wall. There was no evidence of any secondaries in the peritoneal cavity, pouch of Douglas, liver and the para-aortic nodes.

A total hysterectomy and bilateral salpingo-oophorectomy was done and 800 mg of cyclophosphamide (Endoxan) instilled intraperitoneally.

Histological examination of the operative specimen revealed that sections of the left fallopian tube showed a papillary carcinoma infiltrating its muscle

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coat. The tumour involved the fimbrial end of the tube and was adherent to the ovary. The left ovary was, however, not infiltrated and was free from any primary carcinoma (Figure 2). The right ovary showed normal structural components and was free from any primary neoplasm. The adenocarcinoma showed both a papillary pattern as well as an alveolar pattern in some places (Figure 2), and was composed of cells showing nuclear irregularities, nuclear hyperchromatism and mitotic figures (Figure 3).

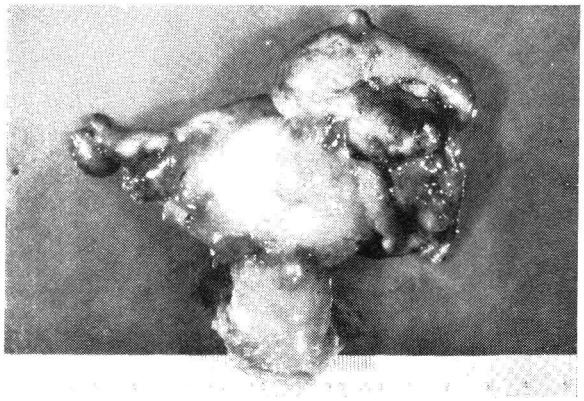

Figure 1

Operative specimen of uterus and appendages, showing the left fallopian tube enlarged by a nodular, elongated mass. The right fallopian tube is normal.

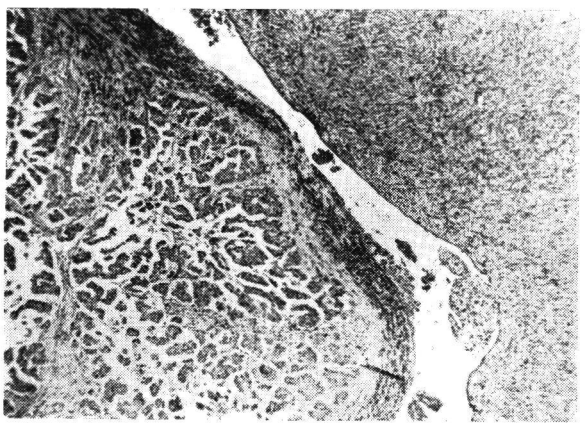

Figure 2

Photomicrograph showing tumour cells in the left fallopian tube arranged in papillary and alveolar patterns. The left ovary is not infiltrated and is free from any primary carcinoma. (× 62.5)

Sections of endometrium and uterine wall in the left cornual end showed no evidence of endometrial cancer. The endometrium was atrophic and the myometrium was fibrotic. The cervix was fibrotic and showed no evidence of cancer.

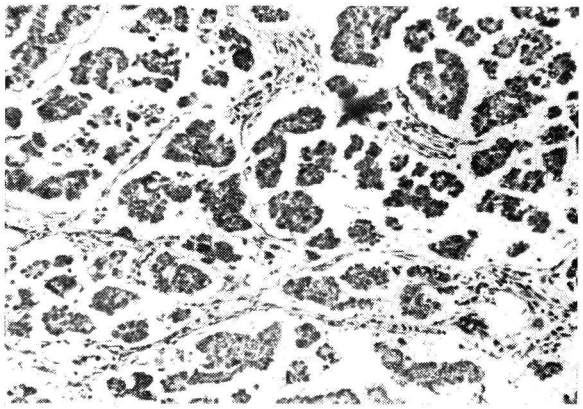

Figure 3

Photomicrograph showing carcinomatous cells with marked hyperchromatism of nuclei and nuclear irregularities. (× 125)

Further treatment was instituted in the form of intermittent massive dose infusions of Endoxan at monthly intervals, viz: 1600 mg on 1-5-73, 1000 mg on 1-6-73, 1000 mg on 1-7-73, and 1000 mg on 28-7-73. Abdominal and vaginal examinations at follow-up visits revealed no recurrence of tumour.

In June, 1975, she complained of neck swelling, lower abdominal pain and low back pain. Examination revealed 4 enlarged lymph nodes in the right supraclavicular region, and a firm fixed mass above the vaginal vault. A biopsy of one of the supraclavicular nodes on the right side revealed metastatic carcinoma. Chest X-ray was clear and X-ray of the lumbo-sacral region showed no evidence of any secondaries. She was given another course of Endoxan 1600 mg.

She requested continuation of therapy in Alor Star General Hospital. She died in November, 1975 of metastatic carcinoma.

DISCUSSION

Tumour staging in this patient is Stage IV, FIGO Classification. Prognosis for this stage is a 5-year survival of less than 15% (Boutselis and Thomson, 1971; Erez, Kaplan and Wall, 1967; Schiller and Silverberg, 1971). In fact, the overall 5-year survival rate for primary tubal cancer is poor, less than 35% in most reports (Boutselis and Thomson, 1971; Erez, Kaplan and Wall, 1967; Green and Scully, 1962; Schiller and Silverberg, 1971; Sedlis, 1961).

Treatmentwise, most authors recommend initial total hysterectomy and bilateral salpingo-oophorectomy supplemented by radiotherapy (Boutselis and Thomson, 1971; Erez, Kaplan and Wall, 1967; Fogh, 1969; Sedlis, 1961), and in some instances, by chemotherapy as well (Boutselis and Thomson, 1971; Erez, Kaplan and Wall, 1967; Green and Scully, 1962; Phelps and Chapman, 1974). The main chemotherapeutic agents used are alkylating agents.

Although most reports indicate that post-operative radiotherapy is not that beneficial, Boutselis and Thomson (1971), and Fogh (1969) have reported improved survival especially with super-voltage therapy. Phelps and Chapman (1974) noted an improved survival in those patients who received supplementary chemotherapy. Our patient received supplementary Endoxan therapy but survived for only $2\frac{1}{2}$ years after initial surgery.

Most patients with primary tubal cancer are between 50–60 years of age when first seen (Boutselis and Thomson, 1971; Erez, Kaplan and Wall, 1967; Fogh, 1969; Persaud and Burkett, 1971; Sedlis, 1961). Our patient was 60 years of age.

The problem in primary tubal cancer is usually one of diagnosis prior to surgery. As Persaud and Burkett (1971) put it "the clinical diagnosis is extremely difficult and is almost never made prior to surgery". The diagnosis was, nevertheless, made pre-operatively in our patient. Clinical suspicion was based on the following features in our patient: postmenopausal bleeding, watery vaginal discharge, positive cytology, negative endometrial curettage and no cervical lesion. The presence of the adnexal mass helped to strengthen the diagnosis.

The laparotomy and histopathological findings in this patient conform to the pathological criteria necessary for diagnosis, i.e., the tumour is a papillary growth in the endosalpinx; there is a transition between normal and abnormal tubal epithelium; the uterus is normal and the ovary is normal.

Primary carcinoma of the fallopian tube is therefore rare, the pre-operative diagnosis difficult and treatment modalities are still unsatisfactory. Nevertheless, one must suspect this diagnosis in any gynaecological patient in whom the suspicion of cancer is high but yet all initial investigations have proved to be negative. Although present day treatment only provides for either supplementary radiotherapy or chemotherapy, a probable logical approach to treatment would be to supplement surgery with radiotherapy as well as chemotherapy.

SUMMARY

A case of primary adenocarcinoma of the fallopian tube is presented. The clinical presentation, treatment and follow up are outlined. Points stressed include difficulty in diagnosis pre-operatively, the lack of a satisfactory regime of treatment, and the overall poor prognosis of this tumour.

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THE MANAGEMENT OF NEONATAL TETANUS

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INTRODUCTION

TETANUS, in particular neonatal tetanus, is a major problem in many developing countries. The global incidence of neonatal tetanus has been estimated to be in the order of one million cases annually and it accounts for more than 30% of total neonatal deaths in certain communities (Gordon, 1961; Marshall, 1968; Schofield *et al.*, 1961; and Tompkins, 1958). In Malaysia, although the incidence of neonatal tetanus has declined progressively through a more efficient antenatal immunization programme and improvement in the delivery of trained obstetric care, the disease is still encountered occasionally. During the period between January 1969 and June 1977, 62 cases of neonatal tetanus were admitted to the University Hospital, Kuala Lumpur. With conservative drug therapy, the mortality rate for this serious illness has been reported to be as high as 90 per cent (Adams *et al.*, 1966; Marshall, 1968; and Low, 1961). The introduction of total paralysis with intermittent positive pressure ventilation regime in the management of neonatal tetanus has reduced the mortality rate to about 20 to 40 per cent (Symthe *et al.*, 1974; Ganendran, 1974). Both these methods of treatment have been employed at the University Hospital. This paper reports our experience in the management of this disease.

PATIENTS

The diagnosis of neonatal tetanus was made on the characteristic clinical findings: trismus, risus sardonicus, muscular rigidity, and spasms of voluntary muscles. All infants below the age of 28 days presenting with at least 3 of the above features were included in the study. Whenever doubt existed as to the diagnosis, lumbar puncture was performed to exclude plrulent meningitis. In addition, blood calcium, magnesium and glucose levels were estimated to ensure that convulsions were not related to these metabolic disturbances. The severity of tetanus was graded according to the criteria of Patel and Joag (1959), one point being awarded to each of the following:

(a) incubation period $\leqslant$ 7 days

(b) inability to suck

(c) presence of muscular spasms

(d) onset of spasms occurring within 48 hours of first symptom

(e) rectal temperature $\geqslant$ 100°F within 24 hours of admission.

Of the total group, 89% of patients belonged to grades IV and V. Table I summarises the relationship between severity of illness and mortality rate.

TREATMENT

General measures: Upon admission, most patients required urgent relief of their muscular rigidity and spasms. This was accomplished by a slow intravenous injection of diazepam *(Valium)* in a dose of 5–10 mg. Once relaxation was achieved, the umbilical stump was excised and all septic wounds were cleansed with hydrogen peroxide and surgical spirit. An intravenous infusion was then set up in a peripheral vein and subsequently all drugs were

Table I
The relationship between severity of neonatal tetanus and mortality rate

Severity of illness	No. of patients	No. of patients requiring IPPV	Mortality rate %
Grade I	0	0	0
Grade II	1	0	0
Grade III	6	3	16.6
Grade IV	29	15	13.9
Grade V	26	22	23.1
Total	62	40	16.1

either administered intravenously or through a nasogastric tube; intramuscular injections were avoided. The infant was nursed in an *Isolette* incubator (Fig. 1). This provided a constant environment and allowed frequent visual observations to be made with minimal disturbance to the patient. In monitoring, particular attention was paid to the pulse rate, respiratory rate, colour and frequency and severity of muscular spasms. A clear airway was ensured by periodic change of posture and by naso and oropharyngeal suction whenever secretions accumulated. Urine collection was made on small urine bags sealed over the perineum and the daily output was measured. Gentle compression over the suprapubic region was at times necessary to aid voiding of urine; in no case was bladder catheterisation required. Eye toilet was performed daily with sterile saline solution and chloramphenicol ointment was instilled several times a day. Saline enema was prescribed when faecal masses were present on abdominal palpation. As a rule, the patients were nursed in the open ward near the nurses' station, and only senior doctors and trained staff nurses were involved in their management.

Fig. 1. Neonate with tetanus nursed in an incubator. The infant is heavily sedated through a continuous intravenous infusion of diazepam.

Antibiotics and tetanus antitoxin: All patients received crystalline penicillin in a daily dose of 100,000 to 400,000 units divided into 2 to 4 intravenous injections for a period of 7 to 10 days. A broad spectrum antibiotic, effective against gram-negative organisms (e.g. kanamycin or gentamicin), was added if pneumonia or other septic complications occurred. There was no consistent regime for serotherapy. Generally, these infants were given 1,000 to 40,000 units of equine anti-tetanus serum without prior test dose. Eight infants, however, did not receive any tetanus anti-serum.

Sedation: In the first group of 43 patients, muscle relaxation and sedation were achieved by systemic diazepam (2–10 mg/kg/day in 4 divided doses) and intragastric phenobarbitone (5–8 mg/kg/day in 4 divided doses). If spasms occurred despite the above basal medication, bolus doses of 2–5 mg of intravenous diazepam were administered. Failure to control spasms after 2 to 4 additional doses of diazepam were regarded as indication for curarization and maintenance of respiration by intermittent positive-pressure ventilation (IPPV). Of the 43 patients in this group, 33 subsequently required the latter form of treatment.

In the second group of 19 patients, the maintenance dose of diazepam used was increased to 20–40 mg/kg/day and that of phenobarbitone to 10–15 mg/kg/day. It was observed that convulsions were often stimulated during intravenous injection of 'push' doses of diazepam. To circumvent this problem, the total daily dose of diazepam was suspended in dextrose-saline solution and administered as a continuous intravenous infusion. During the period of parenteral therapy, care was taken to ensure that the percutaneous intravenous needle was not dislodged as skin necrosis can result from subcutaneous perfusion of the drugs. Tetanic convulsions tended to increase during the initial 2 to 5 days after hospitalisation and the dose of diazepam was gradually increased to a maximum of 40 mg/kg/day according to patients' requirement. Additionally, 2–5 mg of diazepam was given intravenously in between therapy if spasms were severe and frequent. A few patients had distressing hiccups that often provoked continuous spasms; this was effectively controlled by 2–5 mg of intravenous chlorpromazine. Once spontaneous spasms had ceased, the dose of diazepam was reduced every third day by approximately 10% of the previous dose. Should spasms recur, the last effective dose was restored. As soon as the patient could tolerate nasogastric feeding, all drugs were administered via this route. In the majority of patients this was achieved after 5 to 10 days of parenteral therapy. Of the 19 patients who received the second treat-

ment regimen, 7 ultimately required assisted ventilation. The indication for IPPV was similar to that of the first group.

Total paralysis with IPPV: This was reserved for those infants in whom conservative therapy failed to control spasms and apnoeic episodes became life-threatening. Forty infants received IPPV during the eight and a half year period. Eighty-five per cent of them required this form of treatment within 24 hours of admission. These infants were transferred to the intensive care unit of the same hospital where nursing care was provided by trained staff nurses on the basis of one nurse per patient per shift. All previous sedatives were discontinued and tubocurarine was employed to provide muscle relaxation. The patients were intubated with a Jackson-Rees nasotracheal tube (Rees and Owen-Thomas 1966) and IPPV was maintained using a volume-cycled respirator. Tracheostomy was performed in 3 patients. The duration of artificial ventilation ranged from 2 to 52 days (mean 18.8 days). Details of the anaesthetic care provided and the hazards of treatment encountered have been reported elsewhere (Ganendran, 1974).

Feeding: Fluid and electrolyte balance was maintained by intravenous fluids during the first 48 hours when there was an increased risk of aspiration. consequent on uncontrolled convulsions and intestinal ileus. Thereafter, nasogastric feeding was introduced with 5% glucose solution. The stomach was aspirated before each feed; milk feeds were not started until there was no residue. If gavage feeding was not established by the third day, additional nutrition was provided intravenously by 7.5–10% dextrose solution, amino acid infusion (*Sohamin G* 20 ml/kg/day), vitamins and lipids (*Intralipid* 2–4 gm/kg/day). The acid-base status, urea, glucose and electrolyte levels were determined twice weekly during the period of intravenous therapy.

Tetanus toxoid: Patients who recovered from tetanus received a full course of tetanus toxoid as the disease does not confer long-term immunity.

RESULTS

Fifty-two patients survived the illness. The mortality rate was 16.1 per cent. One infant died from asphyxia soon after arrival at the University Hospital and another succumbed at the age of 3 months from complications of tracheostomy. Respiratory failure from tension pneumothorax or extensive bronchopneumonia was the cause of death in the remaining 8 patients; all had previously received IPPV. Among the survivors, the average time taken to re-establish complete oral feeding was 33.4 days; the mean period of hospitalisation was 43 days. Thirty-one patients had at least one follow-up evaluation after discharge. Of these, 5 showed clinical evidence of neurological or developmental impairment. Neurological damage was probably the result of brain anoxia from asphyxiating laryngeal spasms and apnoeic spells rather than from the effects of tetanus toxin.

DISCUSSION

Neonatal tetanus is an entirely preventable disease. Improving the level and acceptance of obstetric and post-natal care will reduce but not preclude the occurrence of neonatal tetanus. A far more effective and economical method of prevention is through active immunisation of pregnant mothers. Standfield and Gall (1970) has documented that 2 doses of absorbed toxoid in the antenatal period afford complete protection against neonatal tetanus. Until universal antenatal immunisation becomes a reality, however, the clinician will continue to be confronted with the problems in the management of this disease.

The treatment of tetanus should be directed to several goals: elimination of organisms producing the toxin; neutralisation of any circulating toxin; provision of skillful care to prevent death from tonic seizures while the fixed toxin is being metabolised in the body. The first two aims can be accomplished by antibiotics, surgical excision of the wound, and by administration of antitoxin. Penicillin effectively kills the vegetative forms of *Cl. tetani*. In order to be effective, the antibiotic must reach the multiplying bacilli, so that if there is a large area of necrotic tissue into which penicillin cannot reach, treatment may fail unless surgical debridement is adequate. The therapeutic effect of antitoxin depends on the neutralization of toxin that is passing from the wound to be taken up by the neural tissue. Antitoxin cannot reverse the effects of the toxin once it has penetrated into the central nervous system (Webster and Lawrence, 1963). The value of antitoxin is thus limited and clinical trials have suggested that administration of 10,000 units of equine tetanus antitoxin is sufficient for treatment (Vakil *et al.*, 1968). Human antitetanus immunoglobulin is preferable to the equine preparation (Editorial, *Lancet,* 1974) because of its relative freedom from allergic side-effects and from risk of immune elimination. The value of human antiserum injected intrathecally into the cerebrospinal fluid is currently being investigated (Ildirim, 1972).

Until an agent becomes available which can displace tetanus toxin from the neural tissue or can effectively antagonise its actions, treatment must remain symptomatic. In a disease which needs

almost continuous observations and therapeutic modification until recovery, it is hardly surprising that the most important contributory factor towards success in treatment is the quality of the nursing care (Smythe *et al.*, 1974). This can only be provided for on a 24-hour basis in major hospitals, so that treatment of tetanus is best confined to these medical centres. In addition, all current therapeutic regimes of proven value carry with them serious hazards in the hands of the inexperienced.

Curarization with IPPV was the mainstay of treatment for tetanus, at the University Hospital until 1973 (Ganendran, 1974). The mortality rate was 23% among 34 patients treated. Although the mortality rate was low, one or more serious therapeutic complications, viz., pneumothorax, pulmonary atelectasis, bronchopneumonia, blocked endo-tracheal tube, apnoea and cardiac arrest from mechanical failure of the respirator occurred in almost every patient. In addition, strained facilities and the prohibitive cost of treatment from prolonged mechanical ventilation, prompted us to seek an alternative form of therapy.

Diazepam was first used successfully in tetanus by Weinberg (1964). Hendrickse and Sherman (1966) subsequently reported the use of this muscle relaxant in 53 patients with neonatal tetanus. In their experience, although diazepam (up to 4.4 mg/kg/day), was useful as an adjunct for relieving muscle spasms, the mortality rate of 53% when employing other drugs for sedation, was not improved upon. Our experience with low dosage of diazepam (<10 mg/kg/day) in neonatal tetanus has been similarly disappointing; 76.7% required curarization with IPPV after initial trial of diazepam. The introduction of large doses of diazepam (20–40 mg/kg/day) in treatment, reduced the rate of therapeutic failure to 36.8 per cent. However, in our experience, increasing the dose beyond 30 mg/kg/day did not significantly reduce the failure rate. Diazepam is not soluble in water and forms a fine precipitate when diluted in infusion fluid. This does not however cause a reduction in its therapeutic potential nor does it result in any adverse reaction (Smith and Masotti, 1971). The major side effects of this form of treatment was the induction of severe drowsiness and coma. In these patients there was a constant risk of inhalation and asphyxia from pooling of secretions, so that the most meticulous nursing care must be provided. Respiratory arrest is another potential hazard (McMorris and McWilliam, 1969). However, in our patients, the continuous infusion of diazepam did not seriously depress respiration nor did it adversely affect the hepatic, haematological or renal function. Upon withdrawal of the drug, consciousness was gradually regained and in patients who did not suffer prolonged episodes of cerebral anoxia, the subsequent neurological and developmental growth had progressed normally. The judicious use of high dosage continuous intravenous infusion of diazepam will thus reduce but will not eliminate the need for total paralysis with IPPV in the treatment of neonatal tetanus. Clearly, the search for more effective muscle relaxants and sedatives must continue.

SUMMARY

This paper reports our experience in the management of 62 cases of neonatal tetanus at the University Hospital, Kuala Lumpur. In the first group of 43 patients, relaxation of rigidity and muscle spasms was achieved by the intermittent administration of phenobarbitone (5–8 mg/kg/day) and diazepam (2–10 mg/kg/day). In a latter group of 19 patients, diazepam was administered as a continuous infusion in a daily dose of 20–40 mg/kg body weight. When conservative drug therapy failed to control the spasms, total paralysis and intermittent positive-pressure ventilation was instituted (IPPV). It was observed that the use of continuous diazepam infusion reduced significantly the proportion of patients that subsequently required IPPV. Problems related to these forms of therapy are discussed. The overall mortality rate was 16.1%. Among the survivors, 16.3% had significant neurological sequalae at follow-up evaluation.

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A REVIEW OF CASES OF OSTEOSARCOMA ADMITTED TO THE UNIVERSITY HOSPITAL KUALA LUMPUR

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IT WAS Samuel Gross (1879) who first described the differentiation between bone sarcoma and metastatic carcinomas. Even at that time he stressed the futility of local excision and recommended ablation inspite of its high mortality of thirty percent.

During the recent years three facts have evolved about the relentless course of this tumour from clinical, radiological and pathological material.

These are firstly, the situation of the tumour in the metaphysis of long bones, secondly the metastatic spread to the lungs which manifest only too late, and thirdly the metastatic spread to other parts of the body, (Enneking, 1975; Dahlin, 1975).

The possible etiology has been an enigma over the many years of its study. Chemical, viral and radiation carcinogenesis have been studied as possibilities (Pritchard *et al.*, 1975).

Clinically possibilities have evidenced themselves in its association with Pagets disease, induction by radiotherapy, possible epidemiologic grouping and hormonal relationships.

The traditional treatment of osteosarcoma has been amputation. In doing so, one hopes for the absence of micrometastasis. The five year survival rate after such treatment has been very unsatisfactory. It may well be that open biopsy followed by amputation or disarticulation would possibly provoke metastasis, but even with frozen section and immediate ablation the results are not significantly different.

Many studies and trials in management of this unfortunate illness which often affects the younger age groups are being carried out in many countries. These will be discussed later in this paper.

The present series of patients treated at the University Hospital consists of twenty-one patients and is the basis for the present retrospective study.

CLINICAL MATERIAL

During the period under review there have been twenty-one patients with osteosarcoma admitted for treatment. Seven of these patients have been from the state of Selangor, three from Negri Sembilan, four from Johore, three from Perak, two from Malacca, one each from Trengganu and Sarawak. This distribution is not statistically significant to ascertain whether there is a rural or urban distribution. In a previous study, Bovill, Silva and Subramanian (1972) showed an indication that in both the Malay and Chinese ethnic groups there was a higher incidence in the urban dwellers. Table I shows the analysis of the present series.

The ethnic distribution

The ethnic groups most commonly affected were the Chinese, there being sixteen patients, while only three patients were Malays and one an Indian. In the earlier study of both East and West Malaysia there were thirty-four Chinese as opposed to twenty-two Malays.

This tumour thus appears to afflict the Chinese community more than the Malays while the Indian race seems to be the least involved.

Table I showing analysis of patients with osteosarcoma

Case No.	Age (yrs)	Sex	Ethnic Group	Duration of Symptom at 1st Visit (mths.)	Site of Lesion	Histology	Previous Treatment	Present Treatment	Follow/ Up (mths)	Duration at Time of Study
1.	42	F	Indian	2½ – ulcer	(L) Ulna	Osteosarcoma	Nil	Above-elbow amputation	3	Lost to follow-up
2.	19	M	Indian	4 – pain	(R) Fibula head	Osteosarcoma	Nil	Above-knee amputation with deep x-ray therapy	21	Died – pulmonary metastasis
3.	4	F	Chinese	6 – pain	(L) Lower 2/3 Tibia	Osteosarcoma	Biopsy G.H. Ipoh	Above knee amputation with deep x-ray therapy	3	Died – Localised metastasis
4.	16	M	Chinese	2½ – pain	(L) Upper 1/3 Femur	Osteosarcoma (x-ray)	Nil	Referred for deep x-ray therapy	Died	Died in hospital – pulmonary metastasis
5.	13	M	Chinese	4 – Pain	(L) Lower 1/3 Femur	Osteosarcoma (x-ray)	Sinseh	–	Died	Died – Pulmonary metastasis
6.	13	F	Chinese	1½ – Pain	(L) Fibula head	Osteosarcoma	Nil	Excision biopsy with deep x-ray therapy	4	Defaulted – mass recurred.
7.	16	M	Malay	2 – Pain	(R) Upper 1/3 tibia	Osteosarcoma (x-ray)	Nil	–	Nil	Lost to follow-up – Pulmonary metastasis
8.	21	M	Chinese	2½ – Pain	(R) Upper Humerus	Osteosarcoma	Nil	Advised deep x-ray therapy	Nil	Defaulted
9.	15	M	Chinese	3 – Mass	(R) Shaft Femur	Osteosarcoma	Nil	Subtrochanteric amputation with deep x-ray therapy	20	Alive and well – no metastasis
10.	19	M	Malay	8 – Pain	(R) Upper end tibia	Osteosarcoma	Deep x-ray therapy – G.H., K.L.	Deep x-ray therapy	Nil	Lost to follow-up
11.	12	M	Chinese	5 – Pain & Swelling	(R) Upper Humerus	Osteosarcoma	Nil	Deep x-ray therapy	Died	Died – pulmonary metastasis
12.	22	F	Chinese	4 – Pain & Swelling	(L) Lower Femur	Osteosarcoma	Nil	Deep x-ray therapy, above knee amputation chemotherapy	9	Lost to follow-up – pulmonary metastasis
13.	9	M	Chinese	3 – Pain & Swelling	(R) Upper Fibula	Osteosarcoma	Nil	Advised deep x-ray therapy	Died	Died – pulmonary metastasis
14.	21	M	Malay	3 – Pain	(L) Lower Femur	Osteosarcoma	Nil	Disarticulation (L) hip with deep x-ray therapy	13	Died – pulmonary metastasis
15.	22	M	Chinese	5 – Swelling	(R) Lower Femur	Osteosarcoma	Nil	–	Nil	Died – Refined surgery
16.	7	M	Chinese	2 – Pain & Swelling	(R) Lower Femur	Osteosarcoma	Sinseh	Advised deep x-ray therapy	Defaulted	Died
17.	16	M	Chinese	4 – Swelling	(L) Pubic bone	Osteosarcoma	Nil	Deep x-ray therapy	Nil	Died – multiple metastasis
18.	18	M	Chinese	6 – Swelling	(R) Upper tibia	Osteosarcoma	Sinseh	Subtrochanteric amputation with chemotherapy	5	Died – multiple metastasis
19.	16	M	Chinese	3 – Pain & Swelling	(L) Lower Femur	Osteosarcoma (x-ray)	Deep x-ray therapy	–	Nil	Transferred to G.H., K.L.
20.	15	F	Chinese	3 – Pain & Swelling	(R) Shaft Femur	Osteosarcoma	Nil	Deep x-ray therapy	Nil	Referred to G.H., K.L.
21.	21	M	Chinese	7 – Pain & Swelling	(L) Upper Tibia	Osteosarcoma	Nil	Above knee amputation and chemotherapy	12	Died – pulmonary metastasis

Sex

In this study there were sixteen males as compared to five females showing a male preponderance. In the earlier study concluded for Malaysia, a similar trend was seen there being forty males and twenty-eight females. Figure 1 shows the ethnic and sex distribution in the present study.

The age group most affected in the present series was the second decade there being twelve patients. This is the unfortunate significance of osteosarcoma, in that it affects the flower of youth. In the 1969 – 1972 study the same age group was again the most commonly involved. Figure 2 shows the age distribution in the present series.

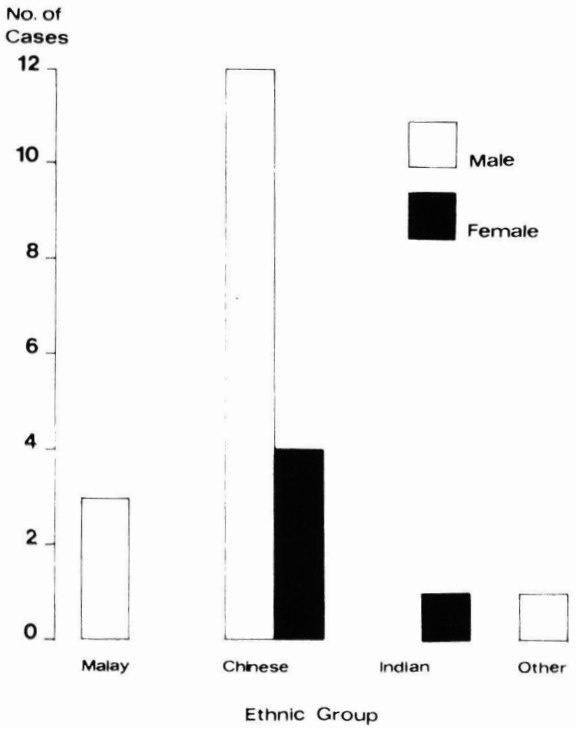

Figure 1. shows the ethnic and sex distribution of 21 cases of osteosarcoma.

The sites of the lesion

Figure 3 shows the sites of the lesion in this study. Fourteen of the patients had the neoplasm around the knee joint, thus conforming to the general pattern of this tumour. The lower femur was involved in six cases, the upper tibia in five and the fibula in three. Of the remaining seven, three were in the upper femur.

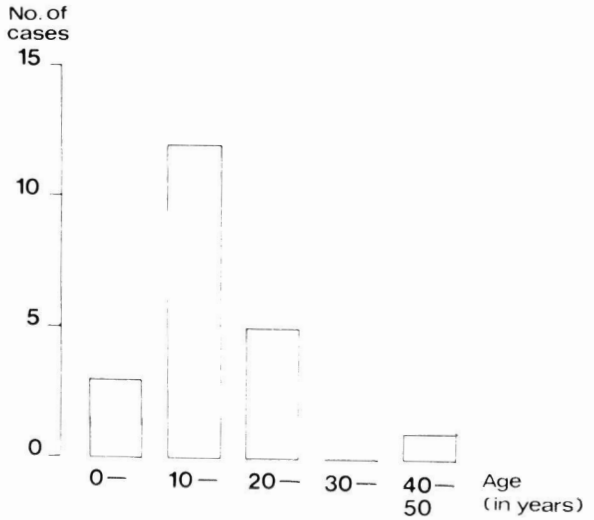

Figure 2. shows the age distribution of 21 cases of osteosarcoma.

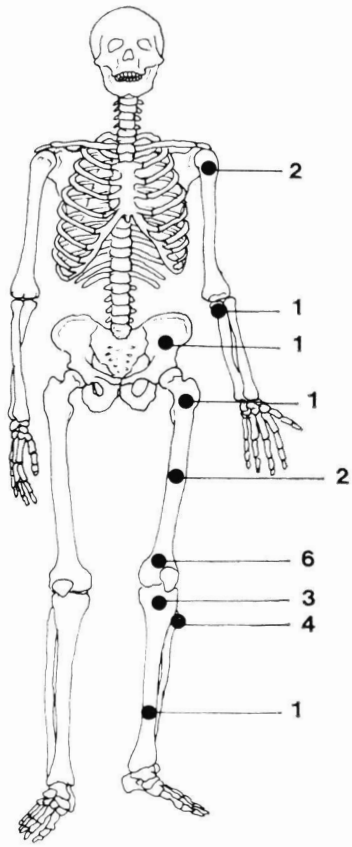

Figure 3 shows the sites of the lesion.

Metastasis

Seven patients had pulmonary metastasis. Three patients have had metastasis in under three months while three have developed this complication in seven, eight and nine months respectively.

Three cases had metastasis in the lungs when they were first seen at the University Hospital.

One patient was alive and well with no pulmonary metastasis at twenty months.

In eight patients there was no follow up possible on a written questionnaire.

Three patients had generalised metastasis and in one there was a local recurrence. (Table II).

Table II

Condition of patient at time of study

Condition	Number of patients
Death with pulmonary metastasis	7
Death with localised or multiple metastasis	3
Death – condition unknown	2
Alive and well	1
Lost to follow-up	8
Total:	21

Duration of symptoms

The duration of symptoms in patients with this neoplasm is significant from the point of view of survival. In a tumour with such a poor prognosis early admission is vital, to have a high percentage of five year survivals even with the most modern forms of combined therapy.

In the present series seven cases have had symptoms for two months, thirteen for three months and five for four months.

Management

The management of these patients has been a problem, in that neither the patients nor their relative favour radical surgery.

Under these circumstances seven patients discharged themselves against medical advice and six patients had only a course of deep x-ray therapy. These thirteen patients however were lost to follow up.

Four patients had deep x-ray therapy followed by radical surgery. Of these one patient was lost to follow up. Two were dead with metastasis while one is alive at twenty months. Three patients had adjuvant chemotherapy in addition to surgery, one of whom was lost to follow up. One patient had only an amputation as a palliative procedure to make life tolerable in the terminal stages.

Table III shows the analysis of the treatment given in the present series. Figure 4 shows the level of the lesions and site of ablation in the patients who consented to surgery.

Tibial lesions have had above knee amputation thus leaving a joint intervening between the lesion and the amputation. In the femoral lesions however one has had a high amputation, another a disarticulation while the others have had amputations above the level of the lesion.

Here again the problem to some extent has been the reluctance of patients to have a radical procedure while in others the surgery has been for the sole purpose of excision a fungating mass.

Table III

Types of treatment given to patients with osteosarcoma

Type of treatment	Number of cases
Deep x-ray therapy	7
Deep x-ray therapy with amputation	4
Deep x-ray therapy with amputation and chemotherapy	1
Amputation and chemotherapy	2
Amputation	1
Defaulted	6
Total:	21

DISCUSSION

The surgical management of osteosarcoma involves either a biopsy which may be open or needle followed by amputation. In the alternative, the amputation is done if the patient is free of metastasis six months after a course of radiotherapy (Cade, 1947, Cade, 1955).

The advantage of such a regime is that fewer patients are subjected to radical surgery. Further the survival rate of those operated on is improved (Sweetnam, 1975). As for biopsy which could be open or a drill biopsy there is no advantage in

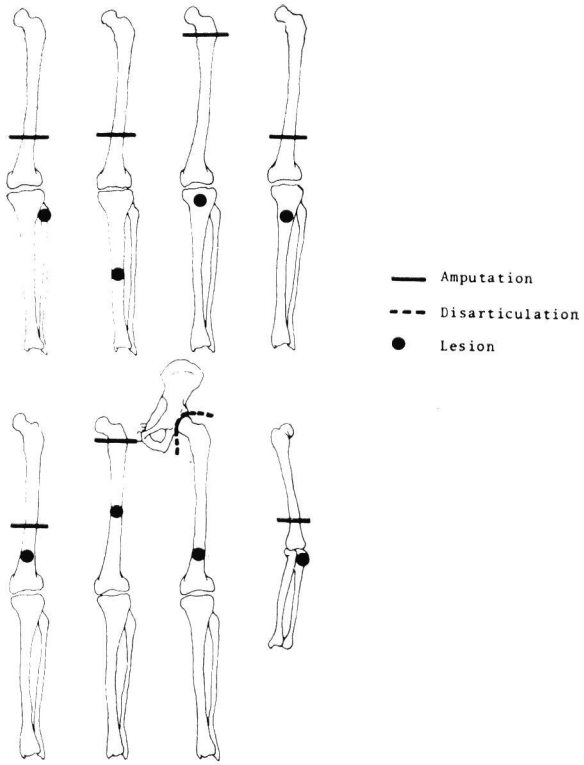

Figure 4 shows the sites of lesion and level of amputation or disarticulation.

avoiding it. In a series of nineteen patients operated without biopsy only two survived (Sweetnam, 1969). For biopsy an open technique is preferable as drill biopsy does not give adequate tissue for study.

There does not appear to be a real difference between primary ablation and that after radiotherapy. In either case the metastasis appear after an interval of ten months. The disadvantages of following the routine of radiotherapy and delayed amputation as advised by Cade (1955) are the problems that arise in the terminal stages of the disease such as pain, fungation and even a pathological fracture. In the present series the patients did not report as early for treatment as one would like. Hence the chances of these complications are much more likely.

In the present series only one case was subjected to amputation after radiotherapy while deep x-ray therapy alone was offered to six patients and one patient had only an amputation while another had chemotherapy as an adjuvant.

There is no proof that disarticulation is better than high amputation, there being no adequate study to prove that the one is better than the other.

However should recurrence appear in a stump it would lead to intolerable suffering. Hence disarticulation may be considered the better procedure. Dahlin and Coventry (1967) recommend through femur amputation. They had ten stump recurrences.

Pulmonary metastasis

The current trend is to treat the pulmonary metastasis aggressively (Martini *et al.*, 1971). In patients treated by multiple wedge resections the five year survival rate went up to forty-five per cent at a three year follow up, while it was only five percent without (Marcove *et al.*, 1975). At five years, fifteen were alive with disease and twelve with disease elsewhere. This latter factor is what causes failure after multiple thoracotomies.

However in an untreated series with pulmonary metastasis, fifty percent were dead at the end of the first year (Marcove *et al.*, 1973). The important criterion is the early detection of the pulmonary tumour and if possible to know when it started.

Bilateral staged thoracotomies followed by immunotherapy and chemotherapy would be the answer provided there was no involvement of the myocardium, the bronchial tree or a blood stained pleural effusion. In this series one patient had a pneumonectomy for secondaries. None were subjected to multiple thoracotomies.

Radiotherapy

Irradiating the tumour and delaying ablative surgery for six months meant that fewer patients came to surgery and hence a longer survival rate in those subjected to it (Poppe *et al.*, 1968; Sweetnam *et al.*, 1971). Irradiation of the lung with 1700 rads in ten fractions is claimed to improve the survival rate at twenty-four months to sixty per cent in the treated group, whereas it was thirty percent when the lungs were not radiated (Suit & Phil, 1975). None of the patients in this series were offered this routine largely owing to their late presentation.

The host immune response

Statistical projections based on the known rate of mitosis and gene replication show 10,000 mitotic errors to occur daily in man (McMaster *et al.*, 1975). Although most cells are non viable, the low incidence of neoplasia in humans suggest the possibility of the existence of a system to eliminate these aberrant cells after their identification.

Thus a cellular immunity may be responsible for cancer surveillance (Weinert *et al.*, 1974).

Foreign cell membranes are distinct from host cells antigenitically and could so produce a lymphocyte medicated hypersensitivity leading to their ultimate rejection.

A failure on the part of lymphocytis to recognise these cells could well be the factor responsible for neoplasm production.

Hence adjuvant immunotherapy is useful to increase the five year survival of osteosarcoma.

BCG and allogenic sarcoma tumour cell vaccine are two possibilities. One ampoule of B.C.G. should be given intradermally at weekly intervals into the groin or axilla.

Allogenic sarcoma cell vaccine 1×10^7 tissue culture cells was given once a week for three months and there after every two weeks for three months.

The sarcoma cells are now prepared from several tumours (Eilber *et al.*, 1975; Jaffe *et al.*, 1969). Immunotherapy however does not increase the response to chemotherapy. It is an additional mode of independent attack on the tumour. The time of death was the same in patients who received chemotherapy alone and those that were given both immunotherapy and chemotherapy. Hence it seems advisable to give chemotherapy immediately after surgery to reduce the tumour cell population in the patient. Immunotherapy could possibly then reinforce the action by stimulating an immense response in the host. The latter action is still not conclusive.

Chemotherapy

In the past, the cure rate for osteosarcoma was 10 – 20 per cent. The interval between diagnosis and metastasis was ten months, and death occurred about six months after the appearance of the first metastatic deposit (Sinks *et al.*, 1975). Chemotherapy has improved this situation. A choice of several combinations of chemotherapy are available either Adriamycin alone, 30 mg/M^2 daily for four to six weeks after amputation or a combination of more than one drug. Jaffe *et al.* (1974) suggested methotrexate with citrovorum rescue and incristine. A multi drug regime commonly used and efficacious is Cyclophosphamide, Vincristine, L-Phenylalanine Mustard and Adriamycin, known as Conpadri I (Sutow *et al.*, 1974). With this treatment they had a 55 per cent two year survival. Adding a high dose of methotrexate (Conpadri II) to the above has also been tried out, (Sinks & Mendell, 1975). The toxic effects of these drugs should however be appreciated such as haemopoetic depression, gastro-intestinal ulceration and alopaecia but with their use, surgical removal of pulmonary metastasis have been made possible thereby prolonging life.

Thus what one has to decide in which is the most useful combination of drug therapy and in this light which is the most useful surgical approach. Reinforcement of these modalities of treatment with immunotherapy and deep x-ray therapy to the lung fields will probably help in the long term survival rate.

Perfusion of the osteosarcoma has also been tried and is claimed to help in prolonging life (Tateishi & Sekine, 1976).

This multifaceted approach which also must be multi displinary will help our patients, who generally come late for treatment.

SUMMARY

The management of osteosarcoma is indeed a sad and difficult task. This is more so when patients present themselves late for treatment. This has been evident in the present series.

This paper is a retrospective study of patients with osteosarcoma admitted to the University Hospital. In evaluating their management, the current trends in treating this unfortunate disease have been discussed and the newer approaches highlighted. In so doing the improved techniques available to prolong the life of patients with osteosarcoma have been stressed. To achieve this end the need for a combined therapeutic approach using all the modalities of treatment available at present, has been suggested as the most plausible way to achieve the longest possible survival rates.

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ORAL MANIFESTATIONS OF MICROBIAL DISEASES

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INTRODUCTION

THE ORAL MUCOSA and alveolar bone respond to a wide variety of generalised diseases, including viral, bacterial and mycotic infections. In the past decade, a considerable body of new ideas about oral manifestations of microbial diseases has emerged. This paper summarises the major conditions which might produce local signs and symptoms in the oral cavity and should be of interest to general practitioners and specialists alike.

VIRAL INFECTIONS

These may produce a characteristic clinical picture providing an easy or spot-diagnosis or may require histopathological and laboratory aids to arrive at the correct diagnosis. The virus may be confined to the oral mucosa exclusively, as in Herpes simplex infections, or may involve the oral mucosa as part of a widespread involvement of skin and other mucous membranes, as in chicken-pox or measles. The typical lesion produced, in the oral cavity, by viruses as an erythema and a vesicular eruption, and it is on a knowledge of the extent and distribution of these lesions that the clinician arrives at a correct diagnosis. Cases that still defy diagnosis may even require elaborate investigations like viral and immunological studies. The important viral infections are summarised below.

Localised viral infections

Herpes simplex infections – These are caused by Herpes simplex I virus and usually occur in older children and young adults exposed to the virus after the protection conferred by maternal antibodies has waned off. There is a prodormal phase lasting 24 to 48 hours. In primary herpetic infections, there is initially an acute gingivitis, and the gums are red and swollen but do not undergo necrosis. The tongue shows non-specific coating probably resulting from the associated pyrexia. Scattered vesicles may appear in any area of the oral cavity and rarely do they fuse to produce bullae. They rupture after 24 hours leaving shallow ulcers which have no zone of erythema surrounding them, and heal after 12 to 18 days without any scarring. The diagnosis is essentially clinical and rarely is cytological study required. Characteristic cytological features seen are the presence of giant-cells with large, hyperchromatic nuclei displaying nuclear inclusion or elementary bodies. Herpes simplex virus is notoriously known to produce recurrent infections which manifest clinically as Herpes labialis or "cold sores". The virus resides latent in the oral epithelium and may be activated by such precipitating factors as fever, trauma, psychological tension, exposure to sunlight or even prolonged kissing. Groups of vesicles surrounded by a zone of erythema and oedema appear beyond the vermillion border of the lips, producing intense pain, irritation and pruritis. The lesions usually rupture after 24 to 48 hours leaving behind shallow ulcers which generally heal after 2 to 10 days.

Herpangina – This condition is caused by Coxsackie Group A, Type IV virus. Typically, there is an intense inflammation of the oropharynx and posterior areas of the oral cavity like the soft palate, tonsillar area, and rarely the posterior third of the tongue. Small vesicles may appear but may not become apparent due to the intense erythema. Recurrent

herpangina is unusual and is seen in patients undergoing treatment with immuno-suppressive drugs like corticosteroids.

Generalised viral infections

Hand-foot-and mouth disease – This is a rare condition produced by Coxsackie Group A (A-5, A-10, A-16) virus. There is patchy erythema of all areas of the oral mucosa, but the palate, oropharynx and gingivae are spared. A vesicular eruption appears later and again small ulcers result from rupture of these lesions. The diagnosis becomes apparent when the characteristic vesiculo-papular lesions with purpuric borders appears on the palms, soles, heels, knees and legs.

Chicken-pox (varicella) – This common condition is produced by primary exposure to varicella-zoster virus. Oral lesions accompany or may rarely preceed the more pronounced skin eruptions. There may be a generalised erythema in addition to vesicles which usually rupture producing ulcers which heal in 10–14 days. In severe cases, bullous lesions and large areas of ulceration can occur.

Herpes zoster (Shingles) – This condition is produced by recurrent infection with varicella-zoster virus. If the trigeminal ganglion is involved, a unilateral, linear, vesicular eruption appears on the buccal mucosa, gingiva, palate or tongue. The ulcers secondarily produced heal without scarring. In some patients, post-herpetic neuralgic pain may be an unpleasant sequealae. Herpes zoster affecting the geniculate ganglion of the facial nerve (Ramsay-Hunt Syndrome) produces vesicular eruptions in the anterior two-thirds of the tongue or in the ear accompanied by a facial palsy.

Measles (Rubeola) – Twenty-four hours prior to the appearance of the skin rash, there is an intense erythema of the oral mucosa, and this is the significant oral manifestation of measles (Shklar and McCarthy, 1976). The so-called Koplik's spots are rarely seen and are supposed to be white spots on a background of inflammed buccal mucosa.

Infectious Mononucleosis – This is characterised by the presence of a low-grade fever, fatigue, lymphadenopathy and a sore-throat. The oropharynx is inflammed and an exudate with scattered superficial erosions may be present. In severe cases, extensive necrosis and sloughing occurs. This condition can produce a false-positive serological test for syphilis.

Mumps (Epidemic Parotitis) – This viral infection generally involves the parotid gland unilaterally or bilaterally, and only rarely are the sublingual and submandibular glands affected. The patient may complain of an unusually dry mouth (xerostomia) due to diminished production of saliva, and on examination, the papilla at the orifice of the parotid duct, in the vestibule opposite the crown of the upper second molar tooth, may be intensely inflammed.

Vaccination (Vaccinia) – After successful vaccination against smallpox the child may rub the lips or cheeks against the vaccination site, thus secondarily innoculating the virus in these areas. A large raised area with a necrotic centre, surrounded by erythema and oedema appears. Though alarming in appearance, the lesion heals within a few days. Smallpox (Variola) itself produces insignificant oral involvement, in the form of vesicles and ulcers, compared to the extensive cutaneous involvement.

BACTERIAL INFECTIONS

The oral mucosa is relatively resistant to entry by bacteria. There is a protective mechanism provided by lymphocytes and plasma cells present in the lamina propria of the oral cavity. The oral mucosa also harbours some nonpathogenic bacteria, like *Borrelia vincenti,* which only become invasive in times of lowered tissue resistance produced by other systemic diseases or physical and emotional stress. Oral lesions of nonbacterial origin, like ulcers produced by trauma or following rupture of vesicles caused by viral infections, may become secondarily involved by bacterial infections.

Localised bacterial infections

Vincent's Stomatitis (Acute necrotising gingivitis) – This infection is caused by *Borrelia vincenti* and *Bacillus fusiformis* which form part of the normal flora of the oral cavity. The organisms become invasive in times of lowered resistance produced by trauma, malnutrition, leukemia, severe systemic infections and the use of immuno-suppressive and antimetabolic drugs. The gingivae, on their unattached margins only, are inflammed and the gingival papillae between teeth undergo necrosis, producing a "punched-out" appearance. Later, ulceration occurs on the unattached gingival margins, producing a grayish-white slough or pseudo-membrane which, if removed, leaves a raw bleeding surface. The necrosis and suppuration produce a foul taste in the mouth and the patient transmits a fetid odour. In severely debilitated patients, the buccal and labial mucosa may undergo necrosis, destroying the lips or cheeks and producing the clinical condition known as Noma (cancrum oris or gangrenous stomatitis).

Generalised bacterial infections

Syphilis – The organism causing this disease is the *Treponema pallidum* and may infect the foetus transplacentally producing congenital syphilis, or be innoculated during sexual intercourse producing acquired syphilis. In acquired syphilis, the incubation period is approximately 3 weeks but may vary from 12–90 days. The typical lesion is a chancre at a site where the organisms enter via a breach of the mucous membrane. In extra-genital areas, this may be on the lips or the tongue. A papule which progressively enlarges and eventually ulcerates and is characteristically painless, is found. The regional lymph nodes would be palpably enlarged. Untreated, the lesion heals in 3–6 weeks.

Secondary syphilis is produced by dissemination of the organism through the blood and lymphatic stream producing systemic manifestation like fever, lymphadenopathy and skin rashes. The oral lesions consist of a diffuse, erythematous pharyngitis; mucous patches which are elevated, erythematous areas with a grayish-white exudate; or erythematous macules and papules on the palate. Tertiary syphilis manifests itself in the oral cavity in the form of a gumma of the tongue or palate or as an interstitial glossitis. Gummatous lesions are necrotic or proliferative and in the palate may produce a perforation, and in the tongue, if multiple, may produce a lobulated tongue. Interstitial glossitis is characterised by an obliterative vasculitis producing atrophy of papillae ("bald-tongue") or muscular wasting ("wrinkled tongue"). Leucoplakia may eventually appear and precede a carcinoma of the tongue. Congenital syphilis used to be aptly summarised by the triad of Hutchinson consisting of blindness (caused by interstitial keratitis), deafness and tooth defects, but other lesions may also be present (Bradlaw, 1953). Gummas may occur on the palate, jaws or facial bones and the tongue may display interstitial glossitis. Linear scars extending from the corners of the mouth, known as rhagades, are also frequently seen. If the decidous teeth are involved, enamel hypoplasia usually results. Permanent central incisors usually display hypoplasia with an increase of antero-posterior dimension and mesio-distal narrowing of incisal surface with or without notching. The first molars usually display a narrow crown with several underdeveloped cusps (mulberry molars).

Tuberculosis – In primary infections, a nodule appears at the site of innoculation in the oral cavity and undergoes ulceration after 2–3 weeks. Regional lymphadonepathy is pronounced. If the resistance of the patient is high, the lesion usually heals.

Secondary tuberculous infection produces a wide range of clinical manifestations. Tuberculous ulcers of the tongue are irregular, or sharp and linear, with undermined borders and with a purulent exudate in the bases. Surrounding induration is minimal. Granulomas may be periapical or on the buccal mucosa. If the mandible is involved, suppuration may extend to the skin producing tracts and fistulae (Cawson, 1960). In secondary infections, the cervical lymph nodes are also involved producing hard masses.

Scarlet fever – The organism causing this condition is the Group A, hemolytic streptococcus. The oral signs include an acute pharyngitis, and the inflammation may extend to the tonsilar areas. Acute stomatitis is present at some stage of the condition and the tongue may have a non-specific white coating. The fungiform papillae usually stand out prominently producing the so-called "strawberry tongue".

Gonorrhoea – Like extragenital chancres, gonorrhoea in the oral cavity is produced by oro-genital contact. The oro-pharynx is red, ulcerated and necrotic and a pseudomembrane is generally seen (Schmidt *et al.*, 1961).

Leprosy – Oral manifestations of leprosy will be dealt with in a paper in the Malaysian Dental Journal (1978).

FUNGAL INFECTIONS

These are relatively rare, and the only one of any significance is thrush (oral moniliasis or candidiasis). The organism, *Candida albicans,* is a yeast normally resident in oral cavity, and becomes pathogenic when the normal bacterial flora of the oral cavity is destroyed by broad-spectrum antibiotic therapy, or in states of lowered resistance, like prematurity, debilitating diseases, diabetes, and the use of immunosuppressive drugs. Fungal infections may be classified as superficial or deep.

Superficial mycoses

Candidiasis (thrush) – The typical lesions are creamy, milk-curd exudates, scattered in the oral cavity, with a bright red base. They strip with difficulty and leave a raw bleeding surface. Diagnosis is essentially clinical and rarely are smears or cultures necessary.

Deep mycoses

Actinomycosis – This is caused by *Actinomyces israelli,* an obligatory anaerobe which thrives in devitalised tissue like apical dental lesions, deep periodontal pockets and area of trauma. A granulomatous lesion appears in the oral cavity and spreads

via subcutaneous planes to involve the skin where a reddish-purple nodule appears and breaks down to form sinuses. Yellowish sulfur granules emerge from the orifices of the sinuses, and microscopically these are seen to be teeming with the causative organism.

Other very rare deep mycoses like blastomycosis, histoplasmosis, muromycoses, sporotrichosis and coccidiomycosis produce ulcerative, granulomatous, or proliferative lesions.

CONCLUSION

In many cases, a thorough examination of the oral cavity is an essential step in arriving at a correct diagnosis of a systemic disease. This paper has only high-lighted the oral manifestations of microbial disease, but it must never be forgotten that systemic, immunological, neurological, metabolic, nutritional, and congenital diseases can have their own specific signs and symptoms displayed in the oral cavity.

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CHARACTERISTICS OF 17β-ESTRADIOL BINDING PROTEINS

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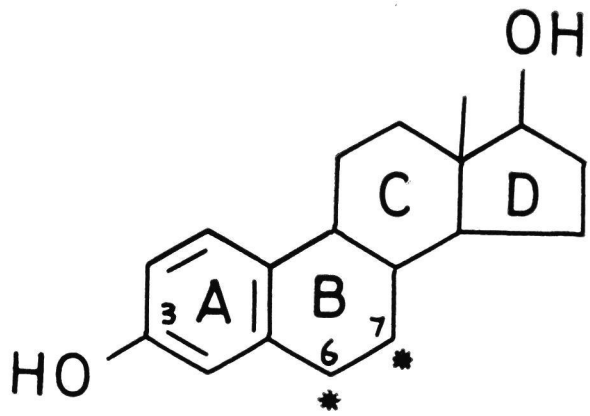
INTRODUCTION

THE PRESENCE OF a protein with high affinity and which binds specifically with 17β-estradiol has been demonstrated in the uterus (Toft and Gorski, 1966). This receptor protein molecule was thought to exist in a free form or is only very loosely bound to structural elements in the cytoplasm.

To date, one of the proposed mechanisms of steroid hormone action is that the hormone initially acts by binding to a specific cytosol receptor protein. The complex that is formed is then transported to the nucleus of the cell wherein it reacts with the nuclear chromatin. This combination in turn influences the synthesis of mRNA that will act as a template directing the synthesis in the endoplasmic reticulum of a specific enzyme protein.

The clinical importance of 17β-estradiol receptor assays has made inroads in the prediction of response to endocrine therapies in patients with metastatic breast cancer (McGuire *et al.*, 1975). Hence, several assay methods were developed for measuring estrogen receptors, e.g. sucrose density gradient, gel filtration, electrophoresis, tissue-slice and dextran-coated charcoal (DCC) techniques. The DCC assay was the most popular technique and was the method adopted in this study. The labelled hormone employed was 17β-estradiol tritiated at positions 6 and 7 of the steroid structure as shown below.

It is our aim in this study to isolate, purify and characterize these binding proteins from the rabbit tissue cytosol and thereby to study their characteristics in different tissue such as liver, uterus and kidney. These binding proteins have sometimes



been referred to as the hormone receptors. It is therefore realised that a study on 17β-estradiol binding proteins will throw more light in the understanding of the mechanism of estradiol action.

MATERIALS AND -ETHODS

Materials

17β-estradiol, Norit A and Dextran were purchased from the Sigma Chemical Co. (U.S.A.).

6,7-^{3}H estradiol (500 mCi/mmol) was purchased from the Radiochemical Centre (Amersham, England).

Experimental Animals

Adult female rabbits (New Zealand White) were obtained from the Central Animal House, Faculty of Medicine, University of Malaya.

Animals (7 days pregnant) were killed by cervical dislocation and the liver, uterus and kidney were quickly removed and placed on ice. All subsequent procedures were carried out at cold room temperature (4°C) unless indicated.

Preparation of 17β-Estradiol Binding Proteins

The fresh tissues of liver, kidney and uterus were homogenized (Sorvall-omnimixer) in six volumes of iced-cold 0.01 M Tris/HCl buffer (pH 7.4). The homogenate obtained was centrifuged (Sorvall, SS-3 automatic) at 755 xg for 20 min at 4°C and the resulting supernatant further centrifuged at 4°C for 20 min at 10,000 xg. The pellet was discarded and the supernatant recentrifuged at 10,000 xg for 20 min. Centrifugation at 100,000 xg (Beckman ultracentrifuge L2-65B in a 60 Ti rotor) was then carried out on the supernatant for 1 hr at 4°C. The resultant supernatant contained the 17β-estradiol binding proteins, also referred to as cytosol extract.

Precipitation of Binding Proteins with Ammonium Sulphate

The digest mixture containing 100 μl of labelled estradiol (37,000 cpm), 200 μl of cytosol extract of varying protein concentration and 0.01 M Tris/HCl buffer (pH 7.4) in a final volume of 500 μl was incubated at 37°C for 90 min. 500 μl of saturated ammonium sulphate solution was added at 0°C and the mixture allowed to stand in ice for 10 min. The mixture was then centrifuged at 6,000 xg for 15 min. The precipitate obtained was washed with 500 μl of saturated ammonium sulphate solution and re-centrifuged at 6,000 xg for 15 min. The resultant precipitate was transferred into a vial containing 5 ml of toluene-Triton X-100 scintillation cocktail. The vials were counted for 5 min each in a Beckman LS-100 Liquid Scintillation Counter.

For competitive binding studies, estradiol was added to the reaction mixture together with the labelled hormone.

Separation of Bound and Free Estradiol by Charcoal Adsorption

Labelled estradiol of varying volumes (10 to 200 μl, i.e. 2,000 to 40,000 cpm), 200 μl of cytosol extract, and buffer in a total volune of 500 μl were incubated at 37°C for 30 min and then cooled in ice. 1 ml of the suspension of dextran-coated charcoal in Tris/HCl/EDTA buffer (pH 7.4) was added. The contents were mixed and kept in ice for 10 min. The charcoal was spun down at 1,000 xg for 20 min and 500 μl of the supernatant collected into the counting vial containing 10 ml of Bray's scintillation mixture.

For competitive binding experiments, different amounts of the unlabelled estradiol were added to the reaction mixture together with the labelled hormone. In some cases, the cytosol extract was preincubated at 37°C for 30 min with the unlabelled 17β-estradiol prior to the addition of the labelled hormone.

The above standard procedure was modified with regard to incubation time, temperature, pH, ion and detergent concentrations.

RESULTS

Comparison of Separation Methods of 17β-Estradiol Binding Proteins

Ammonium sulphate precipitation appeared to yield slightly higher values of percentage binding than those obtained by dextran-coated charcoal (Fig. 1). The lower values in binding with the latter method could be due to the removal of some of the labelled estradiol from the bound hormone protein complex by the charcoal.

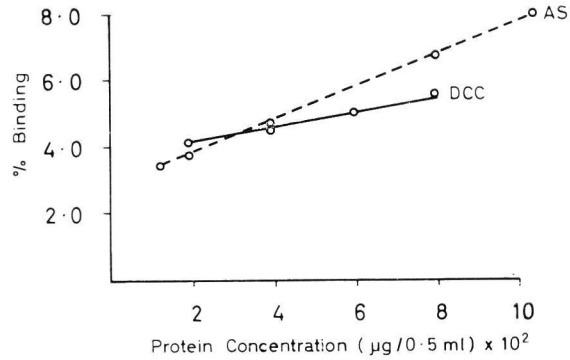


Fig. 1. Comparison of Dextran-coated Charcoal and Ammonium Sulphate Precipitation.
Increasing amounts of protein (200 μg – 800 μg/200 μl) were incubated with 100 μl of tritiated estradiol (37,000 cpm) at 37°C for 90 min. Separation of the bound from the free estradiol was effected by using (a) ammonium sulphate precipitation (AS) and (b) dextran-coated charcoal technique (DCC).

Influence of Incubation Time on the Binding

The rabbit uterine cytosol (700 μg/100 μl) was incubated with 100 μl of labelled 17β-estradiol (37,000 cpm) and 300 μl of Tris/HCl/EDTA buffer (pH 7.4) at 37°C for various time intervals ranging from 5 min to $2\frac{1}{2}$ hr.

The results showed a gradual decline in the binding of labelled hormone (Fig. 2). This decline in binding was seen in the first 30 min after which the percentage binding remained fairly constant. Anyway, there was no appreciable loss in binding

activity with time. The decrease in percentage binding within the first 30 min of incubation could be indicative of a denaturing process (Brecher *et al.*, 1967).

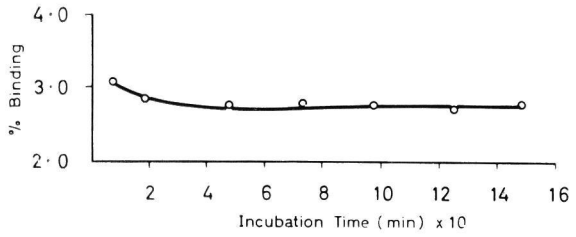


Fig. 2. Influence of Incubation Time on Tritiated Estradiol Binding.
The digest mixture consisted of rabbit uterine cytosol (100 μl), 100 μl of tritiated estradiol (37,000 cpm) and 300 μl of Tris/HCl/EDTA buffer. The digest was incubated at 37°C for various time intervals.

Binding as a Function of Cytosol Protein Concentration

Varying amounts of the tissue extracts were used for incubation with 100 μl of the labelled estradiol. In the liver and uterine cytosol, the binding of the labelled hormone increased with increasing protein concentration (Fig. 3). But the percentage binding in liver cytosol was higher than that in the uterine cytosol. The kidney cytosol did not change significantly in binding ability with varying protein concentration.

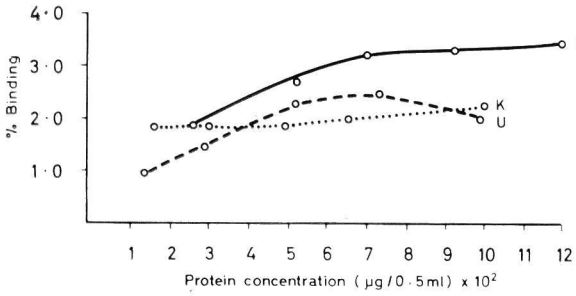


Fig. 3. Relationship between Protein Concentration and Percentage Radioactivity Bound
L = Liver cytosol, K = Kidney cytosol,
U = Uterine cytosol
Varying amounts (975–9,600 μg/200 μl) of tissue extracts, 100 μl tritiated estradiol (37,000 cpm) and buffer in total volume of 0.5 ml were incubated at 37°C for 30 min.

The binding of labelled estradiol to the cytosol proteins was a saturable process with respect to the labelled hormone concentration. The failure of kidney cytosol to show significant increase in binding despite increasing protein concentration indicated that the protein receptors had been saturated with the labelled hormone.

Displacement of Labelled 17β-Estradiol by the Unlabelled Hormone

Increasing amounts of cold estradiol (10 pg to 1,000 pg) were added to the incubation medium containing 500 μg of cytosol proteins and pre-incubated for 30 min at 37°C. 100 μl of labelled hormone (10,300 cpm) was then added and the mixture incubated for a further 30 min.

From the results obtained, the displacement effect by the unlabelled hormone appeared to be most significant in the 10–200 pg region for liver and uterine cytosol (Fig. 4).

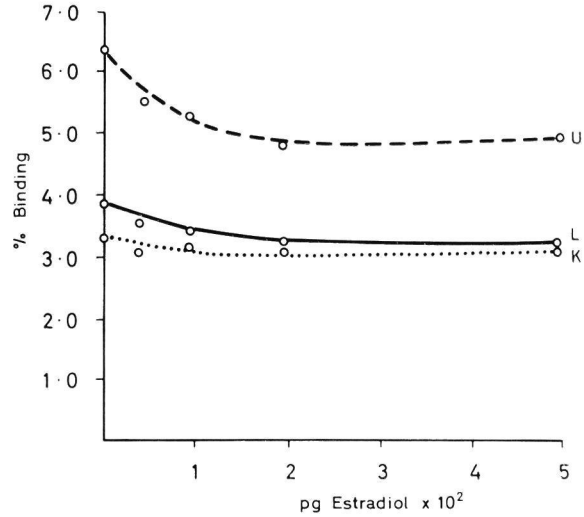


Fig. 4. Influence of Unlabelled Estradiol on Binding.
Protein concentration of the uterine, liver and kidney cytosol extract was 975 μg/200 μl, 9600 μg/200 μl and 3,300 μg/200 μl respectively.

Influence of Temperature on Binding

The digest containing a mixture of 50 μl of labelled estradiol (10,300 cpm), 100 μl (500 μg) of cytosol proteins and buffer in a final volume of 500 μl, was carried out at temperatures ranging from 4°C to 60°C for 30 min.

Temperature appeared to have a marked influence on the binding of labelled hormone (Fig. 5). For uterine cytosol, binding was maximum at 35°C – 40°C. Liver cytosol also showed a maximum binding at this range of temperature. However, kidney cytosol showed a maximum binding at a lower temperature of 25°C. In general, the uterine binding proteins were more sensitive to temperature changes.

Influence of pH on Binding

100 μl (500 μg) of cytosol proteins and 50 μl of labelled hormone (10,300 cpm) were incubated

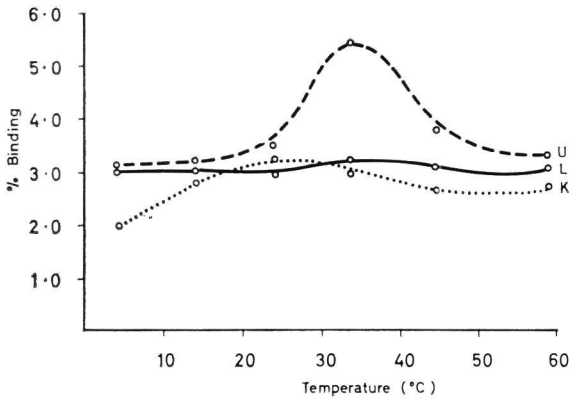


Fig. 5. Influence of Incubation Temperature on Binding.
U = Uterine cytosol, L = Liver cytosol,
K = Kidney cytosol

under hydrogen ions concentrations ranging from pH 3.0 to 9.0 for 30 min at 37°C. Bound estradiol was separated from excess free estradiol by charcoal adsorption.

A maximum binding was observed at pH 7.4 in the uterine cytosol (Fig. 6). Binding in the acidic medium was lower than that in a neutral or alkaline medium. In liver cytosol, maximum binding occurred in the range of pH 6.0 to 7.0. Kidney cytosol also showed a pH optimum of 7.0 for maximum binding.

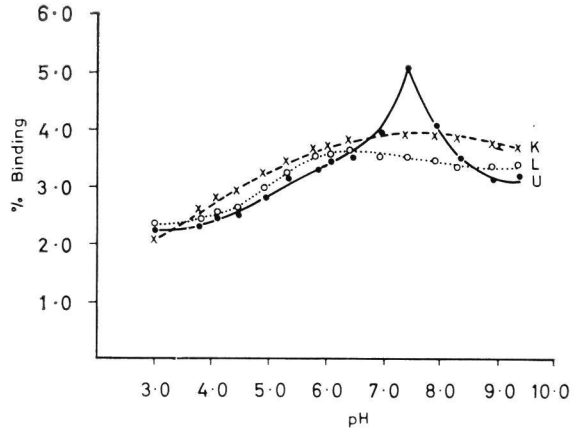


Fig. 6. Influence of pH on Binding.
K = Kidney cytosol, L = Liver cytosol,
U = Uterine cytosol

Effect of Magnesium Ions on Binding

100 μl (500 μg) of cytosol proteins, 50 μl of labelled hormone (10,300 cpm) were incubated at pH 7.4 in a medium containing magnesium ions ranging from 1 mM to 1,000 mM. The bound estradiol was separated from the free hormone by using a dextran-coated charcoal suspension in Tris/HCl buffer (pH 7.4) which did not contain EDTA.

In kidney cytosol, the binding appeared to decrease slightly in the presence of magnesium ions when present in a concentration of 5 mM to 10 mM (Fig. 7). Above this ions concentration, there was a slight increase in binding. The liver cytosol was not significantly affected by the magnesium ions. Uterine cytosol showed a marked sensitivity to magnesium ions in binding ability. Calcium ions gave similar binding pattern to that of the magnesium ions.

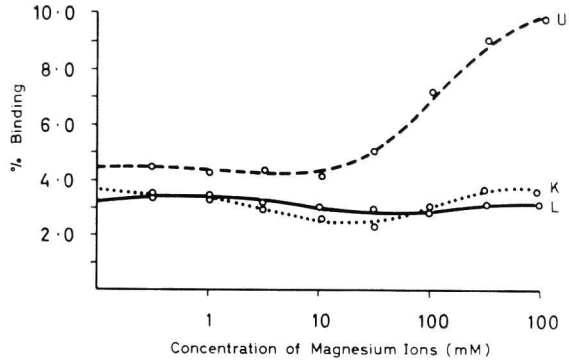


Fig. 7. Effect of Magnesium Ions
U = Uterine cytosol, L = Liver cytosol,
K = Kidney cytosol
100 μl (500 μg) of cytosol protein, 50 μl of labelled estradiol (10,300 cpm), 100 μl of buffer and 250 μl of magnesium ions of molar concentrations ranging from 1 mM to 1,000 mM were incubated at 37°C for 30 min.

Effect of Ionic and Non-Ionic Detergents on Binding

The ionic detergent used was sodium deoxycholate, "Triton X-100" and "Span" were the two non-ionic detergents employed. The incubation medium with a final volume of 500 μl contained 50 μl of labelled estradiol (10,300 cpm), 1 mg of cytosol protein and increasing amounts of the respective detergents ranging from 0.1% to 1.0% (v/v in the case of Triton X-100 and Span, w/v in the case of sodium deoxycholate). Incubation was carried out at 37°C for 30 min.

(i) *Rabbit Liver Cytosol*

Binding of labelled hormone increased with increasing concentration of the three detergents (Fig. 8). With Triton X-100 or sodium deoxycholate, a sigmoidal type relationship was observed.

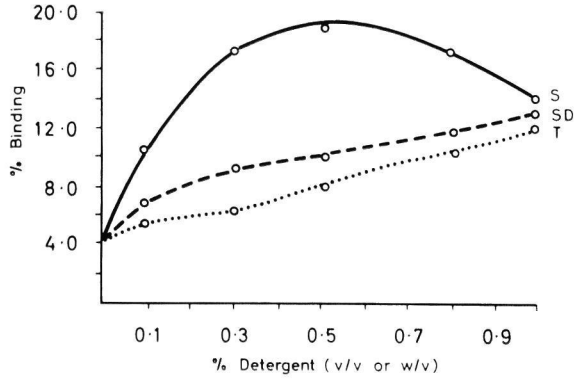


Fig. 8. Effect of Ionic and Non-Ionic Detergents on Binding in Rabbit Liver Cytosol.
T = Triton X-100, S = Span, SD = Sodium deoxycholate

(ii) *Rabbit Kidney Cytosol*

Generally, the detergents used enhanced the binding of labelled hormone (Fig. 9).

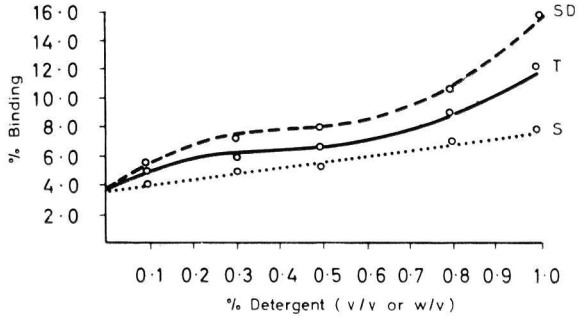


Fig. 9. Effect of Ionic and Non-Ionic Detergents on Binding in Rabbit Kidney Cytosol.
T = Triton X-100, S = Span, SD = Sodium deoxycholate
(Similar curves were obtained for uterine cytosol)

DISCUSSION

Although ammonium sulphate precipitation appeared to give a higher percentage binding than the dextran-coated charcoal method the latter was adopted because it was simpler and less time consuming. This method also gave better duplicate readings.

The binding of labelled estradiol to the cytosol proteins was a saturable process with respect to the labelled hormone concentration. The failure of kidney cytosol to show significant increase in binding despite increasing protein concentration indicated that the protein receptors had been saturated with the labelled hormone.

In the displacement experiment, both labelled and unlabelled estradiol competed for the same binding sites in the tissue cytosol extracts. Hence, a decrease in the binding of labelled hormone in the presence of cold estradiol was observed. In the target organs e.g. uterus, the amount of specific receptors of high affinity binding system present in the cytosol is larger in quantity than that of non-target tissues, such as liver or kidney. Since the binding of estradiol to this system is reversible, the addition of excess of cold estradiol will result in displacement of the labelled hormone. From the curves, it can be seen that the bound tracer could not be reduced to zero even with large excess of the competitor. The effect is clearly caused by the large excess of low affinity binding sites. The relatively high concentration of the low affinity sites rendered them less sensitive to displacement.

The measurement of the amount of estradiol bound by the tissue extract is one indication of the amount of specific receptors present. The charcoal method employed distinguishes the "specifically-bound" from the "non-specifically-bound" estradiol by removing most of the latter together with the excess of free estradiol. The suppressibility of the binding of labelled estradiol by unlabelled hormone which competes for the same specific receptors in the tissue extracts is a second and probably better indicator of the amount of specific receptors present.

The affinity of various steroids to the estrogen receptor has been investigated (Hahnel and Twaddle, 1974). Highest affinity to the estrogen receptor was found if the steroid structure had all three of the following features: (1) an aromatic ring A; (2) a phenolic hydroxyl group on carbon-3; and (3) an alcoholic hydroxyl group on carbon-17 in the β-configuration. The most important of the three structural requirements is the phenolic hydroxyl group, both with regard to position on the ring and its nature (i.e. phenolic or alcoholic).

The position and the nature of the oxygen function on ring D are not as critical. On the basis of these results it was postulated that binding of estradiol to the receptor requires a two-point attachment. Binding is initiated by attachment of the C-3 phenolic hydroxyl group to a highly specific centre. The strength of this attachment is influenced by steric factors (for instance, planar aromatic ring A versus chair or boat configuration in saturated ring A) and functional groups (for instance, weaker hydrogen bonding through C-3 alcoholic hydroxyl group versus C-3 phenolic hydroxyl group). Once the initial attachment between the C-3 phenolic hydroxyl group and the primary binding centre has been established, a specific change in configura-

tion of the receptor may be triggered which brings the second binding centre into closer proximity of the C-17β hydroxyl function of 17β-estradiol and facilitates binding.

Above an optimum temperature for maximal binding of the tissue cytosol, the percentage binding decreased rapidly. This was probably due to irreversible denaturation of the receptor protein. Temperature optima could be indicative of the involvement of hydrophobic interactions in binding (Talwar *et al.*, 1968).

The sensitivity of the binding to pH changes suggested stringent conformational requirement for binding (Ellis and Ringold, 1971). The receptors are irreversibly destroyed at low pH (Toft and Gorski, 1966).

Several reports have indicated that certain divalent ions either increase the extent of binding (Emanuel and Oakey, 1969) or stabilize the receptor in some way. It was found that a large excess of calcium ions causes aggregation of the receptor which is probably caused by charge neutralization. However certain other divalent ions e.g. Mn^{2+} and Zn^{2+} appear to cause a reduction in receptor binding.

The sigmoidal type relationship obtained in the experiment of detergents on binding suggested a a heterogeneity of the estradiol binding molecules in the tissue extract or possibly the involvement of cooperative interactions in the binding of the steroid to the receptor molecules in the presence of detergents. The increase in binding with labelled estradiol in the present of detergents was probably due to changes in conformation of the receptor molecule, exposing more of the binding sites to labelled hormone.

In conclusion, our studies indicate the presence of a protein which binds specifically with 17β-estradiol. This binding protein possesses certain characteristics which are different in various tissue cytosol as evidenced by the experiments on effect of temperature, pH, ion and detergent concentrations.

Further characterization of the binding proteins are being carried out using gel filtration and isoelectric focussing.

SUMMARY

17β-Estradiol binding proteins were isolated from female rabbits using differential centrifugation. Ammonium sulphate precipitation and charcoal adsorption techniques were used in the separation of the bound from the unbound hormone. The binding of estradiol was proportional to the amount of protein receptors present and excess of unlabelled estradiol caused displacement of the bound estradiol from the binding sites. The proportion of bound estradiol decreased with increasing tritiated estradiol in the incubation medium. Binding was dependent on the time of incubation and was also sensitive to temperature and pH changes. Calcium and magnesium ions affected binding only when high concentration of these were used and both ionic and non-ionic detergents increased the binding ability.

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OBSERVATIONS ON A CHROMOGENIC AND A STARCH-IODINE METHOD FOR THE ROUTINE MEASUREMENT OF SERUM AMYLASE

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INTRODUCTION

THE starch-iodine method described by Wootton (1964) has long been in use in our laboratory for the measurement of serum amylase, primarily because of the simplicity of the procedure and its low cost. However, much objections have been raised (Rosalki and Tarlow, 1973) against starch-iodine methods, among which are: reaction not zero order kinetics (substrate concentration being sub-optimal), colour development interfered by serum proteins, different results obtained with starches of different origins, and the methods appeared less able to detect increased amylase activity in a number of sera shown to be definitely elevated by the saccharogenic and the chromogenic methods. Also precision was noted to be generally poor. With these drawbacks, consideration should be given to more satisfactory methods for the routine assay of serum amylase.

Chromogenic methods are more attractive than saccharogenic methods as the former are generally rapid and simple to perform, and hence, ideal for routine use. Several chromogenic methods have been assessed by Rosalki and Tarlow (1973), and found highly satisfactory for the determination of amylase. One of such methods is in the Amylochrome Kit (Roche Diagnostics, U.S.A.) which uses amylose-cibacron blue 3G-A as the substrate. A quick appraisal of this Kit was made in comparison with Wootton's method.

MATERIALS AND METHODS

Amylochrome Method

Amylase hydrolyses the water-insoluble amylose-cibacron blue 3G-A substrate, releasing the soluble dye complex. The unhydrolysed portion of the substrate is removed by centrifugation, and the absorbance of the blue dye complex, which is proportional to the amylase activity, is measured.

Reagents and Procedure: refer literature accompanying the Amylochrome Kit (Roche Diagnostics).

Wootton's Method

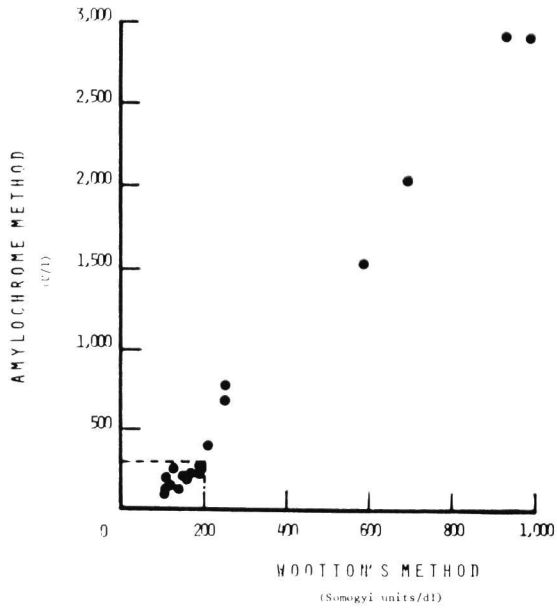
Starch is hydrolysed by amylase, and the remaining starch is reacted with iodine to form a blue colour which is measured. The decrease in colour, which gives a measure of the starch utilised, is proportional to the amylase activity.

Reagents and Procedure: refer Wootton (1964)

RESULTS AND DISCUSSION

Twenty patient samples were assayed by both methods, and the results shown in Fig. 1. Excellent correlation between the Amylochrome method and Wootton's method was noted, $r = 0.99$, $p<0.001$. This finding differs from that of Rosalki and Tarlow (1973) who showed that the starch-iodine method as developed by Caraway (1959) correlated poorly ($r = 0.10$ to 0.52) with both the dye methods studied and a saccharogenic method. We feel that Wootton's modification improved the performance of the starch-iodine method.

Serum samples were analysed in duplicates by the two methods. The precision of the Amylochrome method was found to be much better than that of Wootton's method (Table I). Greater sensitivity was also observed for the Amylochrome method;



Correlation between the Amylochrome and Wootton's method.

example, for the same enzyme value, the absorbance change in the method was twice that of Wootton's method. Further, the error contributed by instrument fluctuation was more pronounced in Wootton's method (Table II). An instrument fluctuation of 0.005 absorbance unit is not unusual, and while such a change means a 8 U/l amylase activity (a $\pm$ 2.7% error if activity is at 300 U/l) for the Amylochrome method, the same fluctuation causes a 15 Somogyi units /dl difference in Wootton's method ($\pm$7.5% error at 200 Somogyi units/dl). A larger error in Wootton's method, which is three times more than that for the Amylochrome method, can, therefore, easily arise from instrument fluctuation.

As documented in the literature accompanying the Amylochrome Kit, linearity is possible to 2,000 U/l. No dilution of a serum sample is therefore required for amylase activities up to about seven times the upper limit of normal. In Wootton's method, the test is performed on a 1 in 10 diluted serum (with normal saline), and the result holds good if activity is less than 400 Somogyi units/dl, which is only two times the upper normal limit. To avoid substrate exhaustion, further dilution is required if the activity exceeds this level.

Of the twenty human sera tested, two cases with 251 and 254 Somogyi units/dl (upper normal limit, 200 Somogyi units/dl) were found to have definite elevation of 769 and 683 U/l (against a normal upper limit of 300 U/l), respectively, by the Amylochrome method. This finding, also noted by Rosalki and Tarlow (1973), is thought to be due to inhibition in Wootton's method, probably by the

Table I
Precision data from the Amylochrome and Wootton's methods

	AMYLOCHROME METHOD U/l	WOOTTON'S METHOD Somogyi units/dl
Normal Range	upper limit 300	upper limit 200
Number of samples = 20 (in duplicates)		
Range of values obtained	122 to 2,920	98 to 980
Mean	852	343
Standard Deviation	22	18
Coefficient of Variation	2.6%	5.2%
Precision (95% limits) for the range of values obtained	$\pm$5.4%	$\pm$11.0%

Table II
Error due to instrument fluctuation, and sensitivity for the two methods

Method	Change in Absorbance	Calculated Amylase Activity	Error from instrument fluctuation
Amylochrome Method	0.185	300 U/l	
	$\pm$0.005*	8 U/l	300 $\pm$ 2.7%
Wootton's Method	0.065	200 Somogyi units/dl	
	$\pm$0.005*	15 Somogyi units/dl	200 $\pm$ 7.5%

* Absorbance fluctuation of instrument

benzoate which is added in the substrate preparation. Two very elevated cases gave 924 and 980 Somogyi units/dl by Wootton's method (about 5 times the upper limit of normal). The values obtained by the Amylochrome method were, 2,920 U/l for both cases (approximately 10 times the normal upper limit). Although both methods returned clearly elevated values, the Amylochrome method demonstrated greater capability for measuring high amylase activities.

In Wootton's method, the colour of the starch-iodine complex decreased rapidly on standing; the absorbances of the control and test fell disproportionately, resulting in false higher amylase activity being derived. It is, therefore, essential that the absorbances are read without delay. The colour obtained on the Amylochrome method was very stable, and remained unchanged up to more than 2 hours.

The many disadvantages and technical failings observed in the starch-iodine method point to the need for a more satisfactory method for the routine assay of serum amylase. The dye method examined here proved to be superior and robust, besides having a simple and rapid procedure, and can, therefore, be considered for replacing the less sensitive Wootton's method.

SUMMARY

A comparative study was made on the amylochrome method, marketed by Roche Diagnostics, U.S.A. against a starch-iodine method described by Wootton (1964), the latter presently used by our laboratory for the routine assay of serum amylase. Although both methods are rapid and simple, the dye method has the advantage of giving a stable colour, while the colour from the starch-iodine complex decreases rapidly on standing. The dye method also gave better precision, and demonstrated greater capability of measuring high amylase activities. Excellent correlation between the two methods was noted.

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PHYTOBEZOAR: A CASE REPORT

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BEZOARS may be trichobezoars, phytobezoars or one of the atypical types such as xylobezoar, silicobezoar, lignibezoar etc. Phytobezoars are masses formed from vegetable material and are rare in occurrence.

CASE REPORT

A 38 year old Indian man presented with epigastric pain off and on for about 4 years. Antacids gave him little relief. A laparatomy was done and a gastro-jejunostomy with vagotomy was performed for an ulcer in the first part of the duodenum. The patient was discharged after recovery. However 3 months later the patient returned with severe abdominal pain from intestinal obstruction. Laparatomy revealed a mass about 10 cm from the duodenojejunal junction which was the cause of obstruction. An enerotomy was done and the mass, a phytobezoar, (Fig. 1 and Fig. 2) was removed. The patient made an uneventful post-operative recovery.

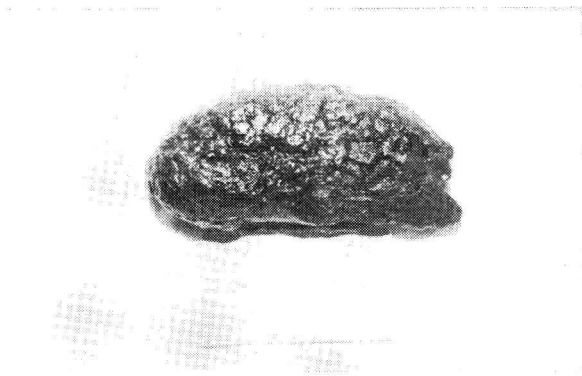

Fig. 1: Photograph of the phytobezoar removed from the patient.

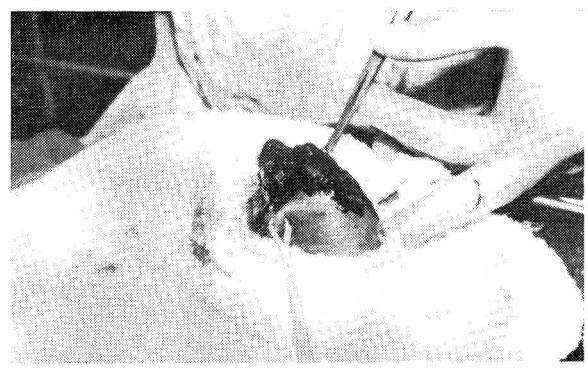

Fig. 2: The phytobezoar being surgically removed.

DISCUSSION

Phytobezoars may be formed from persimmons, celery, pumpkins, leathers, grape skin, prunes, raisins, mellows, wild beet, and iniobezoar of coconut fibre etc. "The Harpanahalli" bezoar is a unique variety and has a specially dangerous effect. It is formed by the blood of a species of chameleon to which certain drugs are added. It is neither vomited out nor passed through the pylorus, but produces gastritis in about 2 weeks and death from inanition in about 3 months. It is commonly used in homicidal poisoning. A rare form of bezoar, potato skin bezoar, has been reported by Wilde (1965) in gastrectomised patients. Any of the bezoars may lead to

low ileal obstruction or gastro-intestinal perforation of which the fatality rate is over 70%. Phytobezoars also occur following Bilroth I and gastro-jejunostomy. Delayed emptying favours the incidence. Bezoars may slip into the efferent limb and cause small intestinal obstruction (Chin and Dinan, 1965). Most phytobezoars require surgical removal although some attempts have been done to disintegrate the bezoar. For example 1% hydrogen peroxide with mineral oil may be used for a starch bezoar formed from the ingestion of large quantities of laundry starch.

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A RECORD OF LIMNATIS MACULOSA (BLANCHARD) (HIRUDINEA: ARYNCHOBDELLIDA) TAKEN FROM THE NASAL CAVITY OF MAN IN SABAH, MALAYSIA

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INTRODUCTION

A NUMBER OF reports on nasal leech infestation in man, domestic and wild animals in Southeast China, Ceylon, India, Vietnam, Malaya and Borneo have been made by Chin (1949), Audy and Harrison (1952), Walton (1955), Harrison (1953), Smythies (1960), De Silva & Anderson (1964) and Keegan *et al,* (1970). The species commonly responsible for this kind of internal infestation is *Dinobdella ferox.* This is a common leech species in Borneo where they are locally referred to as *"lingungud".* Species of several other genera of aquatic leeches have also been incriminated in internal hirudiniasis, but those which have caused the greatest variety of symptoms and have produced the most suffering are members of the genus *Limnatis* (Faust & Russell, 1964). One such infestation described in this report is probably the first known recorded case caused by a member of this genus of Hirudinea, to occur in man in Sabah.

CASE REPORT

A middle-age, small built Kadazan woman reported for medical treatment at the Queen Elizabeth General Hospital in Kota Kinabalu in early 1977. Her presenting complaints were bleeding from the right nostril which was the focus of all her complaints. There was no foul smelling discharge or hemoptysis, no difficulty in breathing and no past history of similar symptoms. She had these complaints for about a week before she came for treatment and during this time she had been working in the rice fields. The diagnosis was obvious when she was seen as the leech was already moving out of her right nostril. The leech was gently removed with forceps. After removal, bleeding stopped and the patient was not seen again. It was presumed that symptoms ceased after the leech was removed and the patient had recovered.

This single leech, which appeared to be well blood-fed is shown in Fig. 1 and has the typically large posterior sucker and possesses a groove extending from the mouth to the dorsal margin of the anterior sucker, and has salivary papillae on the jaws. The total length of this specimen was 40 mm. The diameter of the posterior sucker was 9 mm and the greatest width of the body was 12 mm. The greatest dorso-ventral thickness of the body was 3 mm. These measurements were taken after a longitudinal section was taken on the ventral aspect. After the

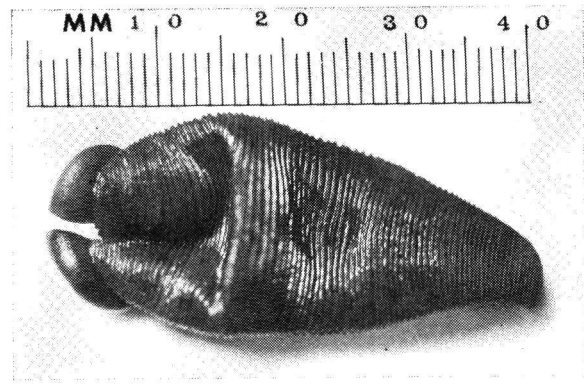

Fig. 1. Specimen of the leech, *Limnatis maculosa,* **taken from the right nasal passage of a woman in Sabah, Malaysia. Note the slit of the ventral aspect of the posterior sucker.**

section was made, the alimentary tract was filled with fresh blood. The reproductive organs were simple with rudimentary ducts. No trace of a color pattern was present in this specimen. The leech shown in Fig. 1 was grayish black when preserved in 4% formalin but was deep reddish when alive. Definite identification is not possible as the specimen was damaged. The tentative identification of this specimen is *Limnatis maculosa*.

DISCUSSION

This infestation was acquired in Kinarut, 24 km south of Kota Kinabalu in the west coast of Sabah. It was not unusual that the patient was aware of the leech in her nose. Our impression of the mode of infestation was that the leech attacked her while she was working in the rice fields and reached her nose from the legs or her head as she was bending down in her work or to drink from the streams. This is probably the first known record of a nasal leech infestation by *Limnatis maculosa* in man in Sabah.

A *Limnatis maculosa* which measured 8–12 cm long has also been reported from Singapore. It was picked up during the act of drinking and was localized in the pharynx or nasopharynx. It can also be found in the trachea (Dr. J.R Palmieri and Dr. Mak Joon-Wah,pers, comm., Faust and Russell, 1964). Another species, *Limnatis nilotica* has been reported to infest man in the Mediterranean region. Typical symptoms are illustrated by three patients seen by Levonian (1950) in Palestine. These individuals, all from Nazareth, gave histories of gradually increasing hoarseness accompanied by occasional expectoration of blood-tinged sputum. One patient seen by Cameron (1950) vomited blood. According to Keegan *et al.* (1969), this is apparently a rare occurrence with such infestations.

It was thought that the infestation had been acquired at least three to four weeks before onset of symptoms judging by the size of the leech. In studies made in Japan, young free-living specimens of *Dinobdella ferox* which averaged 7 mm in length and 1 mm in width, were allowed to enter the nostrils of a rabbit. When they were removed 30 days later, they averaged 45 mm in length and were 8 mm wide. They had also undergone a color change from milky white to grayish black (Keegan *et al.*, 1969).

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A SEVEN YEAR STUDY OF OPIATE DEPENDENCE IN MALAYSIA*

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INTRODUCTION:

DEPENDENCE on opium and its derivatives had been known for centuries. The opium wars in China in the nineteenth century bear witness to the entrance of opium as a lucrative item of international trade. As recently as 1940, the British Colonial government was actively engaged in the opium trade in Malaya through a string of legally authorised retail shops supplying the narcotic to addicts.

Opium is the sun dried exudate obtained by incising the unripe opium poppy *(Papaver somniferum)* pod. This exudate when refined gives rise to such products as morphine and heroin both of which have been used quite legally for medicinal purposes. After its relatively free trade opium and its derivatives ceased to be available openedly at the end of World War II in Malaysia. In this country, opium abusers and addicts were elderly Chinese who brought the habit with them when they migrated from China. A smaller but significant number of Indians principally Sikhs were dependent of opium and its derivatives – especially morphine. However, Wagner and Tan noted in 1970 that there was no attraction for opium among the young in Malaysia. In the late sixties, figures from Britain started to show a steep rise in the number of young drug and especially opiate (United Kingdom, 1968) addicts. The same has been true of drug addicts in the U.S.A. (Freedman, 1975), Hong Kong and Philippines (Cameron, 1968).

The picture of opiate dependence (dependence on opium and its derivatives) in Malaysia has only recently started to come to light. Tan in 1972 and Navaratnam in 1976 have done studies in Penang to show an increasing dependence on opiates among young people. In a matter of years, the problem has spread like a "large scale communicable disease" (Cameron, 1968) across cultures and countries with amazing speed.

AIM OF STUDY

The aim of this retrospective study is to note the changing characteristics of opiate dependence as seen from admission of male opiate addicts to the University Hospital for treatment over the seven year period from 1970 to 1976. These opiate addicts were admitted to the Psychiatric Unit for withdrawal from addiction to opiates.

METHOD OF STUDY:

All case records of male opiate addicts admitted to the Psychological Medicine Unit of the University Hospital from 1970 to 1976 were reviewed. Data relating to ethnic groups, age, and type of opiates abused were obtained for study and analysed.

RESULTS

Ethnic Group of Addicts

Chinese:

The Chinese formed by far the largest single ethnic group of the addicts treated during the seven year period. There were a total of 90 Chinese out of the total of 209 constituting 43.1%. They constituted only 20% in 1970 but by 1976, they had formed 37.9% of the yearly total. In the years 1973 to 1975, they were the largest single ethnic group treated for opiate addiction.

* Based on a paper presented at the 11th Malaysia-Singapore Congress of Medicine, Kuala Lumpur, August 1976.

Table I

Opiate dependence study – 1970–1976 ethnic groups of addicts

Ethnic Group	1970		1971		1972		1973		1974		1975		1976		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Malays	0	0	2	14.3	3	4.3	6	17.7	5	25.0	17	36.2	23	39.7	56	26.8
Chinese	3	20	5	35.7	5	23.8	20	58.8	11	55.0	24	51.1	22	37.9	90	43.1
Indians excl. Sikhs	7	46.7	1	7.1	6	28.6	5	14.7	3	15.0	1	2.1	3	5.2	26	12.4
Sikhs	5	33.3	6	42.9	7	33.3	3	8.8	0	0	3	6.4	9	15.5	33	15.8
Europeans	0	0	0	0	0	0	0	0	1	5.0	1	2.1	0	0	2	0.95
Eurasians	0	0	0	0	0	0	0	0	0	0	1	2.1	1	1.7	2	0.95
Total	15	100	14	100	21	100	34	100	20	100	47	100	58	100	209	100

Indians :

The Indians (Indians, Pakistanis and Ceylonese) as a group accounted for a total of 59 out of the 209 addicts treated (or 28.2%). However, an interesting sub-group in this ethnic group stood out by their over-representation. This were the Sikhs who constituted a total of 33 or 15.8% of the total number of addicts. In the years, 1970, 1971 and 1972, Indians were the largest single group of addicts treated making up 80%, 50% and 61.9% respectively in those years' totals. The Sikhs as a sub-group totalled 33 out of the total of 59 Indian addicts treated during the period.

Malays :

As a group, the Malay addicts were grossly under-represented in the earlier years of the study. Thus in 1970, there were no Malay opiate addicts treated and in subsequent years, their numbers remained far lower than their population representation in the country would suggest. However, in 1974, there were 5 (25%) Malay opiate addicts out of 20 treated. In 1975, this number rose to 17 (36.2%) and by 1976, they formed no less than 23 (39.7%) of the total number treated for opiate addiction. Because of their gross under-representation in the earlier years, the total number of Malay opiate addicts treated over the seven years only totalled 56 (26.8%).

Others :

There were only four others (2 Europeans and 2 Eurasians) treated for opiate addiction during the period of the study.

Age Groups

Another change that occurred during the period of the study was the change in the age groups of opiate addicts admitted for treatment. In the period 1970 to 1972, more than half the addicts were aged 26 years or more but after this period, their number dropped to less than third of the total number treated (Table II). On the other hand, the number of addicts below the age of 26 increased rapidly from less than 50% in the years 1970 to 1972 to more than 50% after that to reach almost 70% in 1976. The number of addicts in the age group 16–20 years, rose from 6.7% to 24.1% over the 7 years while the first addicts in the 10–15 years age group came for treatment in 1975 and 1976 (Table III). The age group 21–25 years had the largest number of addicts among all age groups and in total numbered 81 or 38.8%. They rose from 26.7% in 1970 to 43.1% in 1976.

Opiates of Dependence

The types of opiates that addicts were dependent on seemed to undergone a revolution in the seven years of the study. In 1970, morphine was the opiate of dependence in 12 (80%) of those who were treated. There were no heroin addicts and only 3 (20%) were opium addicts. This picture changed dramatically over the next three years to one of heroin dependence by 16 (47.1%) in 1973 followed by morphine dependence – 13 (38.2%). By 1976, the place of heroin as the principal opiate of abuse had been fully established. That year 50 (86.2%) of the addicts were heroin dependent and only 7 (12.1%) morphine dependent. The first heroin addict was treated in 1972 but by 1976, heroin addicts formed 115 out of the 209 addicts studied over the seven years – amounting to over 55%. This was followed by 65 morphine addicts (31.1%) and opium – 25 addicts or 11.9% out of the 20 dependents. Another four addicts took more than one opiate regularly.

DISCUSSION

The opiate dependence disease has undergone a revolution and is perhaps still undergoing one today. Over these seven years, the characteristics of those dependent and their dependence have changed dramatically. The Indian and especially the Sikh addicts of 1970 to 1972 were essentially morphine dependent and dominated by their numbers the opiate dependents treated at the University Hospital. However, the Chinese took over as the largest single ethnic group in 1973 – the same year that heroin made a big entrance into the drug addiction problem among those treated. The Chinese addicts were the largest single group for three years up to 1975. In 1976, the Malay opiate addicts (of whom there were none in 1970) took over as the largest single group among addicts treated at the University Hospital. Sikh addicts have been over-represented in this study and also seem to be increasing in number.

The age groups of the opiate addicts as was shown in Figures 2 and 3, has also reversed in the seven year period. Most of the addicts (68.9%) in 1976 are below the age of 25 and opiate addicts have also been noted in the 10–15 age group. The older age group addicts such as those in the 36–40 years and 41–45 years have remained small throughout.

Considering these changes, one is confronted by the important question – why? There does not seem to be simple answers to that question. There appear to be complex and wide ranging factors at work – some social, some political, some economic and yet others unknown. Certainly, the worldwide

Table II

Opiate dependence study – 1970–1976 age groups of opiate addicts

Age Group in Years	1970		1971		1972		1973		1974		1975		1976		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<26	5	33.3	2	14.3	10	47.6	19	55.9	14	70	32	68.1	40	68.9	122	58.4
>26	10	66.7	12	85.7	11	52.4	15	44.1	6	30	15	31.9	18	31.1	87	41.6
Total	15	100	14	100	21	100	34	100	20	100	47	100	58	100	209	100

Table III

Opiate dependence study – 1970–1976 age groups of addicts

Age Groups	1970		1971		1972		1973		1974		1975		1976		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
10 – 15	0	0	0	0	0	0	0	0	0	0	1	2.1	1	1.7	2	0.9
16 – 20	1	6.7	1	7.1	1	4.8	9	26.6	6	30	7	14.9	14	24.1	39	18.7
21 – 25	4	26.7	1	7.1	9	42.9	10	29.2	8	40	24	51.1	25	43.1	81	38.8
26 – 30	6	40	2	14.3	4	19.1	5	14.8	3	15	9	19.2	12	20.7	41	19.6
31 – 35	1	6.7	1	7.1	3	14.3	2	5.9	1	5	3	6.4	2	3.5	13	6.2
36 – 40	2	13.3	3	21.4	1	4.8	3	8.8	1	5	1	2.1	0	0	11	5.3
41 – 45	0	0	5	35.9	2	9.5	2	5.9	0	0	2	4.3	3	5.2	14	6.7
46 <	1	6.7	1	7.1	1	4.8	3	8.8	1	5	0	0	1	1.7	8	3.8
Total	15	100	14	100	21	100	34	100	20	100	47	100	58	100	209	100.0

Table IV

Opiate dependence study – 1970–1976 opiates of addiction

Year	1970		1971		1972		1973		1974		1975		1976		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Opium	3	20	6	42.9	3	14.3	5	14.7	4	20	3	6.4	1	1.7	25	12.0
Morphine	12	80	8	57.1	16	76.1	13	38.2	4	20	5	10.6	7	12.1	65	31.1
Heroin	0	0	0	0	1	4.8	16	47.1	11	55	37	78.7	50	86.2	115	55.0
Mixed Opiates	0	0	0	0	1	4.8	0	0	1	5	2	4.3	0	0	4	1.9
Total	15	100	14	100	21	100	34	100	20	100	47	100	58	100	209	100.0

spread of narcotic traffic and sales is having an impact on our drug addicts. The steep rise in heroin dependent persons is not a coincidence – heroin is the most easily available narcotic to the opiate addict today. The younger addict we see today may be the result of the greater economic power of younger people today coupled with a paradoxical sense of purposelessness and loss of direction. The boom years of 1973 and 1974 may also have something to do with the prominence that heroin has come into but its continued spread may not be so easily explained. The rapid economic and urban growth in Malaysia has thrust thousands of young people into a highly competitive urban society, perhaps ill-prepared for the tribulations and emotional uncertainties that follow, and heroin may be offering them a false sense of soothing security.

The reasons for the dramatic changes in opiate dependence as seen by the hospital admissions of opiate addicts are indeed complex. But what is obvious is that the menace is growing rapidly. What is needed therefore, are a recognition of the gravity of situation, further studies to identify vulnerable groups and urgent preventive, treatment and rehabilitation measures to combat the disease.

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NEEDS-ORIENTED POSTGRADUATE TRAINING IN ORTHOPAEDICS

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INTRODUCTION

FOR a developing country, Malaysia has a good health care delivery system. This health care delivery system provides for the control of communicable diseases and also provides curative and health services. Specialists in medicine, general surgery and obstetrics and gynaecology are available in all the general hospitals throughout the country as well as in some of the district hospitals and in the private sector, so that specialist care is now available to the people in most urban parts of the country. However, orthopaedic units are found only in the general hospitals and the time is now ripe for attention to be directed towards the provision of further specialist services and a program of training for orthopaedic surgeons. However, we must develop a program relevant to the national needs and the local situation, which means that the training is best done locally.

LOCAL TRAINING

Local training has several advantages. The trainee grows in the local environment and becomes familiar with the local population and the local disease patterns. He also becomes familiar with the local health care delivery system and fits in easily to the system at the end of his training.

There are skills, knowledge and attitudes relating to the delivery of orthopaedic care in the community that are not stressed in the training programme that are now available in developed countries. Many do not have any understanding of the economic, social and cultural problems involved in the organisation of health care and are not prepared for the local situation at the end of their training. The result is that often there is a discrepancy between the society's health needs and disease problems and the response of the orthopaedic surgeon. Further, the needs of one developing country differ from those of another. Does Malaysia need two levels of training for the orthopaedic surgeon as has been suggested for developing countries like India and Africa which have very large populations and poor doctor-population ratios? Rather than two levels of training for the orthopaedic surgeon in Malaysia, the need is for a broad based training of the orthopaedic surgeon who should also receive a sound training in general surgery, together with an adequate training in orthopaedics for those who are being trained as general surgeons. Primary orthopaedic care in all the district hospitals is now provided by general surgeons many of whom have had inadequate training in orthopaedics as many were trained for the system of medical care found in developed countries.

NEED FOR A SOUND GENERAL SURGICAL TRAINING

Many of our general hospitals have at least one general surgeon and one orthopaedic surgeon. However, in a single man station each covers the others area of work. Consequently, the trainee in orthopaedics will benefit from exposure to general surgery, plastic surgery and neurosurgery. "It is singularly useless for a highly specialised orthopaedic surgeon to deal expertly with a shattered tibia while the patient is dying because the surgeon cannot diagnose and if necessary remove a ruptured spleen or diagnose and drain a haemopneumothorax" (Holdsworth, 1970).

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In designing the curriculum stress should be laid on local disease patterns. Table I shows an analysis of the elective orthopaedic operations done in the University Hospital, Kuala Lumpur during the five year period 1968 – 1972. Most of the operations were for deformities due to poliomyelitis, leprosy, cerebral palsy, rheumatoid arthritis, bone and joint tuberculosis, pyogenic infections of bones and joints and congenital deformities. In addition, spinal surgery and amputations were of importance. Table II shows an analysis of the operations done for neglected trauma which is rarely seen in developed countries. Trainees must therefore spend time in the developing countries if they are to gain experience in relation to such problems.

Table I

Elective orthopaedic operations done at the University Hospital, Kuala Lumpur from 1968 – 1972

Operations for	Number
Amputations	207
Post-polio deformities	200
Cerebral palsy	63
Leprosy	56
Rheumatoid arthritis	48
Spina bifida	8
Pyogenic infections of bones and joints	180
Tuberculosis of bones and joints	113
Congenital deformities	82
Bone tumours	29
Soft tissue tumours	84
Spinal surgery	133
Prosthetic replacement	41
Total	1244

TRAINING IN ACCIDENT AND EMERGENCY SERVICES

Malaysia is developing rapidly and injuries due to road traffic accidents and industrial accidents are becoming more common. In 1974 there were 51213 road accidents with 20915 people injured and 2303 killed. In 1975 there were 55148 road accidents resulting in 21973 people injured and 2317 people killed. Consequently, the hospital emergency room is an important area for the training of the orthopaedic surgeon and several educational objectives can be achieved in an emergency room setting (Morton and Milton, 1968).

Table II

Elective operations done for neglected trauma at the University Hospital, Kuala Lumpur from 1968–1972

Operations for	Number
Non-union or malunion of femur	133
Non-union of tibia	80
Fractures of forearm bones	84
Fractures around elbow	58
Fractures of ankle	38
Fracture shaft of humerus	26
Fractures around knee	47
Unreduced dislocations of elbow	28
Unreduced dislocations of hip	13
Unreduced dislocations of shoulder	19
Total	526

1. Certain diseases or injuries can only be observed in an emergency setting.

2. Skills in rapid but accurate assessment of injured patients, their resuscitation and definitive treatment can be acquired.

3. Skills in effective communication, with patients and relatives at the time of crisis, can also be acquired.

SUB-SPECIALITY TRAINING

Among many sub-specialities one could consider hand surgery and spinal surgery. During the five year period from 1968 to 1972, 548 operations on the hand were done at the University Hospital. These were for bony injuries of the hand (202), tendon repair (102), nerve repair (45), and skin cover (199), and for leprosy and rheumatoid arthritis. It would therefore appear that there is a special need for some exposure of the trainee to the principles and practice of hand surgery. During the five year period under review 133 operations on the spine were carried out. They were for tuberculosis of the spine (55), spinal cord tumours (29), prolapsed intervertebral discs (11), spinal fusion (16), spinal plating (5) and correction of scoliosis (17). I do not think that the trainee at the end of his four year period of training will be able to do spinal surgery competently. Further training at special centres in the country or abroad will be necessary for this.

TRAINING IN MEDICAL ASPECTS OF ORTHOPAEDICS

It would be better to call the speciality orthopaedics rather than orthopaedic surgery since a substantial portion of the work is medical. Some aspects of internal medicine, endocrinology, neurology, rheumatology related to orthopaedics and rehabilitation medicine must be included in the curriculum.

SKILLS IN ORGANISATION AND MANAGEMENT

Learning of skills in organisation and management is neglected in undergraduate medical education and at the postgraduate level as well. The doctor learns these skills by trial and error. As a consequence the delivery of orthopaedic care sometimes suffers because of poor organisation by the surgeon. An orthopaedic surgeon's effectiveness depends not only on his clinical skills but also on his ability to manage clinics, rehabilitation units, orthopaedic workshops and on his ability to work as a team with social and welfare staff. It is thus crucial that the trainee develops skills in management in addition to clinical skills.

SUMMARY

Specialist care is now available in all the general hospitals and some of the district hospitals in Malaysia. The time is now ripe to embark on a program for the training of orthopaedic surgeons for Malaysia. The training must be relevant to the national needs. To achieve this the training must be done locally for the trainee grows in the local environment, becomes familiar with the local disease patterns and fits in easily to the local health care delivery system, particularly since certain skills, knowledge and attitudes relating to the delivery of orthopaedic care in the local community are not stressed in the training programmes available in the developed countries and neglected trauma, leprosy, bone and joint tuberculosis and poliomyelitis are also rarely seen in the developed countries. There is also a need at present in Malaysia to provide adequate training in orthopaedics for those who are being trained as general surgeons.

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A HISTORY OF PSYCHIATRY IN PENINSULAR MALAYSIA, 1830 – 1975

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INTRODUCTION:

The British settled on the island of Penang in 1786; incooperated Province Wellesley to Penang in 1800, founded Singapore in 1819 and took over Malacca from the Dutch in 1824. By 1929, Penang had a lunatic asylum with 25 inmates, consisting of 13 Indian convicts, 11 Chinese and a Portuguese lunatic (Ward and Grants, 1830). In 1830, Penang was reduced to the status of a Residency. Together with Malacca and Singapore, it became directly dependent upon British India. The Straits Settlements Act, 1866, constituted the four settlements of Singapore, Malacca, Penang and Labuan (in Sabah now) as a Crown Colony (Bastin and Winks, 1966).

Malay folk medicine with Malay magic (Skeat, 1967), Malay poisons and charm cures (Gimletter, 1929) incorporated the Malay world view, including the concept of natural and supernatural causation of mental illness (Muhammad Taib, 1972). The bomohs (Malay medicine man), mainly part-time practitioners, may be consulted for common misfortunes or ailments. The healing rituals showed some early Hindu and Islamic cultural influences. Herbs may be used. Later, Chinese and Indian folk medicine and folk rituals or spirit-mediumship (Shaw, 1973) contributed to the evolving social-medical tradition.

THE FIRST PHASE, 1874-1910

From 1874, following the role of the British as advisers to the four states which later formed the Federated Malay States (on 1 July 1896) efforts were initially directed at making the environment safer through public health measures (Strahan, 1948). By 1895, except for Pahang, in each of the other three states, there was a lunatic asylum situated in a major tin mining town. In Kuala Lumpur, of the 130 patients, (112 males and 18 females), nearly all were Chinese. Melancholia was the most prevalent diagnosis. 68 of them were discharged as cured while 21 died. "The accommodation for lunatics in Selangor is both insufficient and unsuitable and many have been sent for treatment to the Colonial Asylum in Singapore" (Selangor, 1896). In Taiping, of the 145 patients (including 104 new cases), 29 died from a sudden attack of diarrhoea (Perak, 1896). In Seremban, all lunatics were removed to the General Hospital, where a portion of one of the main wards was divided off for them. 13 cases were treated, of which 3 were discharged as cured, one absconded (but was recaptured); 3 died and 6 remained under treatment at the end of the year (Negri Sembilan, 1896).

In 1898, the old goal near the pauper hospital, Kuala Lumpur (the current General Hospital) was converted into a lunatic asylum (Milne, 1948). "The building which is used as a lunatic asylum leaves much to be desired in form and in situation. It was constructed 17 years ago when the town was still in comparative infancy and was intended to be used as a prison. Having been vacated by the convicts on the completion of the Pudu Prison, it has since been used as purpose to which it is now applied. But its form renders it unsuitable for the intelligent treatment of lunatics, its capacity is inadequate in view of the number of patients now sent in from other states, and having in consequence of the growth of the settlement being surrounded on all sides by the houses of the European officers, it is

far more in evidence than is pleasing or desirable. A new building in a more remote situation will soon be a necessity. (Selangor, 1903).

In 1905, an epidemic of beri-beri broke out in the Kuala Lumpur Lunatic Asylum. Out of 219 patients, 194 persons were affected, of whom 27 died. A district surgeon showed that the eating of uncured (Siamese) rice was related to the occurrence of beri-beri while there was no occurrence of beri-beri among another group of patients who were eating cured (Indian) rice. The only difference between cured rice and the uncured variety was that the former was boiled and dried before being milled. (Fletcher, 1907). The death rate at the Lunatic Asylum, Kuala Lumpur in 1907 was 22.22% – of the total of 270 patients treated, 60 died. (Selangor, 1908).

THE SECOND PHASE, 1911-1945

The remote situation finally chosen was Tanjong Rambutan (T.R.), Perak. The Federal Lunatic Asylum was scheduled to receive lunatics not only from the Federated and Unfederated States, but also the Straits Settlements of Penang, Malacca and for a period, Singapore. On 7 November 1911, the officials at the Lunatic Asylum, Kuala Lumpur sent all their certified lunatics to T.R. (Selangor, 1912).

With a new dumping place, little effort was made to treat lunatics in the asylum nearer their community, e.g. 128 lunatics were passed through the Lunatic Asylum, Kuala Lumpur and transferred to T.R. during 1917 when certified. Only 26 lunatics were directly discharged from Kuala Lumpur in that year. (Selangor, 1918). This attitude and practice plus further immigration probably accounted for the rapid increase of not only beds but actual patients in Tanjong Rambutan.

Within the first three years of its function, the number of patients at the end of the year exceeded the total number of beds. In 1912, there were 280 beds but 359 patients (Perak, 1913), and in 1913 there were only 493 beds for 520 patients (Perak, 1914). By 1928, there were 2,211 patients at the Federal Lunatic Asylum, Tanjong Rambutan, renamed the Central Mental Hospital. That year was the first time that the patient population showed a decrease compared with the previous year – due to the transfer of 189 Singapore patients to the new Singapore Mental Hospital. (Perak, 1929).

Confusional insanity primary dementia (dementia praecox) and melancholia headed the diagnosis list. The following were then common "causes" of mental illness: syphillis, gastro-intestinal system infestation (namely, ankylostomiasis), cardio-vascular degeneration, alcohol and haemopoietic system. The rise in syphillis is due to a certain extent, to a much careful examination and a greater use being made of the Government laboratory, but the rise of alcohol is just the more or less steady rise it has maintained for some years ... Against this, I would point to the three cases of drugs, none of them opium, but all hashish." (Samuels, 1929). An earlier Report of the Commission appointed to enquire into certain matters affecting the health of estates in the Federated Malay States (1925) had recommended that while toddy might be sold openly, restriction should be placed on alcohol. The open sale of opium then contributed to the revenues of the Government.

Among the staff at Central Mental Hospital in 1928 were: 1 medical superintendent, 1 assistant medical superintendent, 4 European male and 4 European female attendants, 1 senior assistant physician, 1 assistant physician, and a second assistant physician. There were two nurses, one matron, one work mistress, one steward, one storekeeper, one inspector and one assistant inspector for numerous attendants (Perak, 1929).

An important part of the milieu then was the farm attached to the Asylum. Vegetables and padi were planted. In 1916, there was a piggery and the dairy yielded 7,739 pints of fresh milk. Games, such as cards, dominoes, draughs were encouraged and supplied (Perak, 1917). By 1938: The farms as usual provided all the pork, fruit and vegetables required for the patients and occupational therapy was extended, a large number of useful articles being made from waste material and condemned clothing." (Perak, 1939).

The recovery rate in 1919 was 37.41% and the death rate 19.29% (Perak, 1920). In 1938, 1,264 patients were admitted. A total of 781 were discharged – of which 312 were classified as "recovered", 365 as "relieved" and 104 as "unimproved". The number of deaths was 275, giving a death rate of 6.68% (Perak, 1939).

In 1937, Madras Presidency, with a population of 47 million, the number of lunatics in institutions was under 2,000. Malaya, with a population of $5\frac{1}{4}$ million people, maintained nearly 4,500 lunatics. There were 1,054 lunatics in Singapore, 2,883 in Tanjong Rambutan who came from the Federated Malay States and the 557 lunatics in Johore. In all these three mental institutions in Malaya, the incidence among the Malays (0.81, 0.85 and 0.59 per 1,000 population respectively) was about half that in the other races. Indians showed almost the

same incidence throughout (1.47, 1.58 and 1.57 per 1,000 population respectively). MacGregor (1938) attributed the higher rate for Chinese in the Federated States (1.53 per 1,000 population) than Singapore (1.25 per 1,000 population) to a lower death rate in T.R. and possibly because of easy repatriation of Chinese from Singapore. The rate for Chinese in Johore was 1.15 per 1,000 population.

The significantly larger proportions of southern Indians being hospitalized in Malaya when compared to Indians in Madras and the differences in the race of the Malaysian patients probably reflected the stress on the migrants and how the absence of kinship contributed to their hospitalization.

At the Central Mental Hospital, Tanjong Rambutan, the population had increased steadily to 3,154 patients at the end of 1941. Officially, between 1 January 1942 to 30 September 1945, 5386 patients were treated in the Central Mental Hospital. 3850 deaths were officially recorded, presumably from dysentery or beri-beri. All the British staff, and a few local staff in the hospital had left before the arrival of the Japanese Military Administration. Among the patients were 996 psychiatric patients transferred by the Japanese Military Administration from Sabang Island, near Sumatra in January 1943 and 600 patients transferred from the Woodbridge Mental Hospital, Singapore in November 1944 (Woon, 1971).

THE THIRD PHASE, 1946-1975

With the return of the British Administration, rapid social and political changes continued. After the formation of the Federation of Malaya (Persekutuan Tanah Melayu) in 1 February 1948, the Emergency was declared on 12 July 1948. Between 1946-1950, the annual population of Central Mental Hospital, Tanjong Rambutan increased by about 600 annually – from 448 in 1946 to 2,750 in 1950 (Hospital Bahagia, 1974). The Tampoi Mental Hospital was opened in 1952. The Mental Disorders Ordinance, 1952 defined the certification of patients for observation or treatment. Some patients were temporarily confined to mental cells in district or general hospitals before transfer to one of the two mental hospitals.

Tampoi Mental Hospital, served the states of Kelantan, Trengganu, Pahang, Malacca, Negri Sembilan and Johore. By 1957, there were 1,200 patients at Tampoi. Central Mental Hospital served for the catchment area of Perlis, Kedah, Penang and Province Wellesley, Perak, Selangor and Raub District in Pahang. The overcrowding condition in Tanjong Rambutan had existed since 1951, when the total number of inpatients had exceeded the bed capacity of 3,000 in the hospital (Hospital Bahagia, 1974). Two mental health consultants who were sponsored by the World Health Organization, Dr. S. Mackeith (1954) and Miss I. Marwick (1956) reported on the grossly inadequate treatment of mental patients and the unsatisfactory psychiatric nursing training and practices respectively.

A commission was authorised to enquire into the conduct and administration of the Central Mental Hospital since 1st June 1955 and to make recommendations to the High Commissioner concerning such conduct and administration. At the end of their enquiry in 1957, the number of inpatients was 3,900. The number of doctors (including the Medical Superintendent) in the Hospital was still the same as in 1928, namely 5! The Medical Superintendent, being the only qualified psychiatrist then, was the only expert witness who was frequently called to give evidence in the Courts in all parts of the Country. This necessitated too frequent absences from the hospital where he was responsible for both the clinical and administrative functions. The Commissioners compared the over-crowded A-wards for third class patients to the cattle-sheds in veterinary station – except for the low wooden sleeping platforms on which the patients live. "In the A-wards, 900 patients sit about with absolutely nothing to do, with no hope of any improvement in their condition because no one has time to treat or even to examine them, and with no recreation or amusement of any sort to occupy them." (Central Mental Hospital, Tanjong Rambutan, 1957). The Commission felt that if the monthly visits of the Board of Visitors were to have any value at all, they should be genuine inspections and that the Visitors should be requested to make arrangements to spend the whole day at the hospital if necessary. Numerous recommendations had been implemented since the Report. A recommendation that had been unable to implement till today related to the building of two more 2,000 bed mental hospitals in the Peninsular Malaysia.

On 31st August 1957, Malaya attained her independence. Health became the responsibility of the Federal Government. Recognizing that rural health services were neglected earlier, intensive efforts were directed towards rural health services (Abdul Majid, 1974). The first outpatient clinic in a general hospital at Ipoh was for discharged psychiatric patients from Tanjong Rambutan in 1958. A psychiatric unit with inpatient and outpatient services was started in the General Hospital, Penang in 1959.

On 31st July 1960, the Emergency ended. The Faculty of Medicine, University of Malaya and the University Hospital were established during the

Second Malaya Plan (1961-1965). For the first time in a Malaysian medical school, a Department of Psychological Medicine was established. Psychiatry became an important part of the undergraduate medical education (Tan and Wagner, 1971). A psychiatric unit in the University Hospital setting, with facilities for child and adult psychiatric services encouraged not only early diagnosis but also management near the community. In the Central Mental Hospital, between 1958 and 1974, 201 psychiatric Assistant Nurses have been trained. Between 1971 and 1974, 90 Junior Hospital Assistants were trained at Tanjong Rambutan and Tampoi (Haq, 1975).

The highest population of 4,922 patients was recorded in 1969 for T.R. In 1971, significant changes took place. The hospital was renamed *Hospital Bahagia,* Ulu Kinta while the Tampoi Mental Hospital was renamed *Hospital Permai,* Tampoi. With effect from 16 December 1971, the post of Medical Superintendent was replaced by that of Director of the Hospital. A new post of Senior Administrative Officer was created while the old post of Hospital Secretary was abolished. With no psychiatric social worker, a lone Social Welfare Officer seconded from the Social Welfare Ministry tried desperately to cope with requests for his service (Hospital Bahagia, 1972). Further progress occurred on 1st November 1972 with the establishment of a third unit, under Dr. E.B. McGregor. This unit was responsible for (a) the reorganization of rehabilitation services and (b) the organization and running of teaching programmes in Hospital Bahagia (1974).

The Director, Dr. Edward Tan, commented on the 1,347 patients in 1972 and the 1,494 patients in 1973 with first admission to the *Hospital Bahagia.* "There is an approximately 2:1, male: female ratio. The largest number of admissions are in the 21-30 age group. Malay and Chinese admissions are about equal, an interesting feature when the resident hospital population has a 1:2 Malay: Chinese ratio. Indian patients have a disproportionately high rate of first admissions compared to the resident population ratio of 1:2 for Indian: Malay." In 1973, the rate of admission per 1,000 population was 0.26, 0.29 and 0.46 for Malay, Chinese and Indian respectively (Hospital Bahagia, 1974). Compared with the incidence of psychiatric inpatients in Malaya for the three ethnic groups, about forty years ago (MacGregor, 1938), the relatively lower rate of admissions for the Chinese and Indian population is probably due to the fact that the migrant nature of those populations had given way to a permanent resident type of population. With industrialization and urbanisation, a new public health and social problem, drug addiction had appeared among all the ethnic groups (Tan, 1973; Im and Mahadevan, 1976).

Decentralization of psychiatric services has been suggested by a W.H.O. Consultant, Dr. Cunningham Dax (1962, 1969) and had been incorporated in the programmes of the Ministry of Health under the Second Malaysia Plan (Abdul Majid, 1974, Haq, 1975). There was a shortage of staff to provide adequate services. Attempts towards the local training of staff resulted in the initiation of the Master of Psychological Medicine course at the University of Malaya in 1973 and the post-basic psychiatric nursing programmes at the School of Nursing, General Hospital, Kuala Lumpur in 1975.

The Ministry of Social Welfare (through their children and family services) and the Ministry of Education (through their Guidance and Counselling Service) had begun to play important roles in preventive psychiatry. Public voluntary organizations had begun to cater for the needs of communities which were not adequately served by the existing Government services – e.g. the Selangor Association for Mental Retarded Children, the Perak Mental Health Society (a pioneer in a Psychiatric Day Care Centre) and the Befrienders, Kuala Lumpur with their telephone facilities for people in crisis.

In 1975, the Family Practitioner, a journal of the College of General Practitioners, Malaysia, published five articles on the theme of Psychiatry. It's editorial reiterated that psychiatric illness was among the commoner causes of consultation in general practice. It advocated close cooperation between the general practitioners and psychiatrists for the further improvement of psychiatric care in the country (Lee, 1975).

A DEVELOPMENT AND SOCIOLOGICAL VIEW OF PSYCHIATRY, 1830-1975

The events during the three chronological phases may be viewed developmentally as phases which merged imperceptibly into the next phase. In the background was the indigenous folk medicine and healing rituals. The First Phase was a record of the small lunatic asylums in the three mining towns of Kuala Lumpur, Taiping and Seremban. The Second Phase which merged into the Third Phase, was a history of the evolution of institutional, custodial psychiatry. The new asylum was soon overcrowded. It became the death-house during the Japanese occupation and in the 1950's, its third class, chronic wards were like cattle-sheds. Active reorganization and rehabilitation took place in early 1970's. The Third Phase also witnessed the beginning of general hospital and community psy-

chiatry, the development of training for all categories of staff in the government hospitals and University of Malaya. Voluntary organization began to participate in different aspects of mental health.

Lunatic asylum was initially the responsibility of the Medical Department. Psychiatry and mental health had begun to be accepted as the joint service, responsibility and effort of the various Government Ministries, University of Malaya and general public, by the experts and laymen, for the individuals and families with mental illness or in crises.

SUMMARY

Folk medicine, including Malay, Chinese and Indian healing rituals, formed the background of psychiatry in Peninsular Malaysia. Small lunatic asylums in Penang and the three main mining towns preceded the opening of the Federal Lunatic Asylum at Tanjong Rambutan, 1911. The population of the Asylum soon increased faster than the number of beds provided. This trend recurred after 1951 inspite of the opening of Tampoi Mental Hospital in 1952. Active reorganization and rehabilitation took place at the Central Mental Hospital, Tanjong Rambutan, renamed Hospital Bahagia. Ulu Kinta, in the early 1970's. There was a beginning of increased activities in the various aspects of training, general hospital and community psychiatry and participation by other government ministries, University of Malaya and public, voluntary organizations.

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BOOK REVIEWS

World Health Organization (1977) **Environmental Health Criteria 3 Lead,** Geneva, World Health Organization, 160 pp. Sw. fr. 16.

This is the third volume of a series on Environmental Health Criteria. It reviews and evaluates the biological effects and other environmental influences of lead on health. The book begins with a summary and recommendations for further research and contains chapters on the physical and chemical properties of lead and its compounds, sources of lead in the environment, its environmental transport, distribution, levels and exposures, its metabolism and studies of its effects on animals and humans, epidemiological and clinical studies of its effects on man and an evaluation of health risks to man from exposure to lead and its compounds. There is a bibliography of some 600 references.

This book will be of particular interest to Ministries of the Environment, of Health and of Labour, as well as to occupational health physicians, plant engineers, toxicologists, public health workers and those involved in the lead industry.

World Health Organization (1977) **World Directory of Schools for Dental Auxiliaries 1973,** Geneva, World Health Organization, 380 pp. Sw. fr. 42.

The acute shortage of dental manpower in many countries of the world has compelled health planners not only to increase the number and size of dental schools but also to increase the capacity of the individual dental surgeon through the utilization of chairside assistants and other dental auxiliaries. Basically all dental auxiliaries can be classified into operating auxiliaries, who perform a limited range of diagnostic, preventive and curative services in dentistry under the supervision of a dental surgeon, and non-operating auxiliaries, such as dental laboratory technicians and chairside assistants, who do not independently carry out any intraoral procedures.

The World Directory of Schools for Dental Auxiliaries, which is bilingual (English/French), contains data up to 1973 on the schools for these two types of auxiliaries and summaries information regarding conditions of admission, duration of training, language of instruction and curriculum content, and will prove useful to those concerning with dental manpower planning and training.

PAUL C.Y. CHEN

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> The survey (Meyer *et al.*, 1971) showed .....

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