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Editorial

Is there a place for a Pain Clinic in Malaysia?

by A. E. Delikan

EVERY HUMAN BEING experiences pain at some time of life and fundamentally pain can have a functional (emotional) basis or an organic (pathological) basis. The reaction to pain varies. A religious or superstitious person might accept pain as of divine origin, possibly inflicted for the sins of the past, and suffer patiently. Most people, however, are driven to consult a doctor, especially if the symptom persists or becomes worse, despite the usual common remedies available to the lay public. In fact, pain is the commonest cause for a patient to seek medical advice and treatment.

Medical research workers have constantly been developing drugs to contain pain and this accounts for the myriad of analgesic drugs available today for this purpose. Despite the numerous new drugs, morphine and its derivatives still hold sway as a potent painkiller. But these analgesics bring with them the major problem of addiction, especially when dealing with chronic pain.

To some extent, every doctor can deal with pain but today, the value of the anaesthetist is becoming increasingly evident, especially in the management of chronic intractable pain. To remove the sensation of pain is one of the paramount aims when an anaesthetic, (general or local), is administered. Regional nerve conduction blocks, using local analgesic or neurolytic agents, are of special value in dealing with intractable pain, especially in advanced malignancies.

The best way of dealing with the major problem of chronic, intractable pain (intractable pain implies pain which is severe, incapacitating and resistant to all simple forms of treatment by drugs or other physical means) is to tackle it in an organised unit like the Pain Clinic, usually within a hospital run by a panel of consultants; a radiotherapist, a neurosurgeon a neurologist, a psychiatrist, and an anaesthetist, the latter being usually the head of this panel. Patients with chronic intractable pain can be referred to the pain clinic by private practitioners and by doctors in hospitals throughout the country.

Those common conditions requiring referral to a pain clinic are cancer, giving rise to intractable pain, post-herpetic neuralgia, intermittent claudication (for diagnostic or therapeutic sympathetic blocks), trigeminal neuralgia, post-traumatic neuralgia (painful operation scars, phanthom limb pain and painful stumps), causalgia, Paget's disease (for lumbar sympathetic block), osteoarthritis when a nerve root is trapped by arthritic process, angina (for stellate ganglion block), coccydinia and other undiagnosed intractable pain.

The usual pain relief procedures carried out are chemical neurolysis, drug therapy alone, neuro-surgery and deep X-ray or Cobalt therapy. Nerve block provides an alternative method when the cause of the pain cannot be eliminated or when the patient is unfit or unwilling to undergo neurosurgery or radiothe-

rapy. Neurolytic agents, by destroying pain-conducting nerves, might allow patients with advanced malignancy pains to spend the last days of their lives relatively pain-free.

Once a pain clinic is established with a panel of consultants, an education programme on intractable pain must be commenced, aimed at (1), the general medical community to encourage early referral, so that good results could be achieved and addiction problems lessened; and (2), the lay public to make them realise that intensive suffering in cancer can now be controlled by relatively simpler, newer techniques without addiction as an inevitable end-result. The pain clinic is not to be regarded as a diagnostic clinic but one that would deal with patients in whom the cause of the pain has been determined.

In Malaysia today, there is no organised pain clinic and some doctors may feel that the attitude of our peoples to the problem of pain does not warrant the setting up of such an organised unit as yet. This would be a negative attitude; what is required is an energetic approach in the treatment of pain in terminal malignancy.

A Teaching or General Hospital will be a suitable place to set up such an organised pain clinic. Besides the service that will be available to a group of pathetically suffering patients, such a clinic will provide ideal facilities for research where controlled clinical trials of new and old analgesic drugs can be carried out. Teaching of medical students, medical officers, general practitioners and trainee-anaesthetists in the various regional block techniques can be performed under ideal conditions.

Treatment of Pituitary Adenomas:
A study of 66 cases

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ALL TOO FREQUENTLY, the treatment of patients with pituitary adenomas is still considered in the light of the high surgical mortality and poor postoperative results of bygone years. The present study of 66 such patients demonstrates that with modern techniques, the surgical mortality is low and the results of treatment are excellent if the condition is recognised early and appropriate treatment, usually surgical removal of the tumor, postoperative radiation therapy and endocrine replacement therapy are undertaken promptly.

The successful treatment of a patient with a pituitary adenoma can be most gratifying. Restoration of vision, or maintenance of it at a useful level by the arrest of further growth of the tumor, in itself is a boon to any patient threatened with blindness. The efficacy of postoperative irradiation in controlling recurrences is well accepted, [9,10,13,15,23] and long meaningful survivals of up to 25 years [23] and 48 years [12] are not uncommon. The quality of the survival has been such that the majority of these patients can be expected to lead a relatively normal life.

Improved surgical techniques and advances in anesthesia have reduced operative mortality and morbidity, but these alone have not been enough. Of significant importance have been the recognition of pituitary deficiency states, both pre and postoperatively, and the proper use of endocrine replacement therapy prior to, during and after surgery, to enable the patient to withstand the stress of the operation and that of the postoperative period. Since the introduction of steroid substitution therapy [28], a much lower mortality and morbidity with a smoother postoperative course have been achieved. The better understanding of the responses to stress situations of a chronically hypopituitary patient has been a further step in this direction.

The radiosensitivity of the adenomas of the pituitary gland was demonstrated by the better results in those treated by surgery and X-ray when compared with those treated by surgery alone [2,3,9,10,15]. In 1936, Dyke and Hare [7], following a careful analysis, claimed a 26% success rate with only irradiation although admittedly 47.3% of their patients became worse with such treatment. Since then, with X-rays alone, success rates of 42%, [6] 50%, [26] 60%, [15] 70%, [20] have been reported. More recently, Chamlin [5] reported improvement of vision in 62.2%, maintenance of vision in 28% and that 7.9% of his patients became worse. There has thus been a tendency to over-

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emphasise the beneficial effects of radiation therapy upon pituitary adenomas while minimising the failures (those patients who got worse or did not improve) and ignoring the tragic results which can occur when a histologic diagnosis of the lesion present has not been made. Not uncommonly, one may encounter a craniopharyngioma or an aneurysm simulating a pituitary adenoma. It would be ill advised to irradiate such patients, and they may become blind in the interim of waiting for a response to the X-ray treatments. Again, the empty sella syndrome and arachnoidal cysts in and about the sella turcica can present with hypopituitary states and typical visual field defects. Irradiation again is not the answer in such cases.

In the pituitary adenoma patient, it is not possible to state preoperatively the exact extent of involvement of the visual apparatus. Irreversible visual field changes may occur while waiting for the effects of irradiation, and one may drift past the time for optimal intervention [9,10] being misled by what may appear as an apparent check in symptoms. The risk of hemorrhage into the adenoma though small is real during irradiation. Pituitary apoplexy, should it occur, can be rapidly fatal [1]. Immediate surgical intervention then becomes imperative. An emergency operation upon these patients with endocrine hypofunction is attended with much greater risk than one which can be planned and prepared for more deliberately. We, therefore, believe that those patients with impairment, either of visual fields or visual acuity, should be operated upon first and then treated with irradiation. Only patients judged to be suffering from a pituitary adenoma with no visual impairment should be treated with irradiation, without the tumors having been removed and their nature confirmed by microscopic examination. Even then, it is essential that the patient's condition be carefully followed at frequent intervals with a special concern for the development of visual impairment or evidence of hemorrhage into the tumor. The following case is a tragic example of treating what was supposed to be a pituitary adenoma by irradiation without an operation and of not following the patient closely during and after such treatment.

Case Report I.

A 17-year-old white boy was admitted to a hospital on July 16, 1961. He then had complained of severe bifrontal headaches of some 12 years' duration. His parents had also noted a failure on his part to mature both physically and sexually. For some nine years prior to his first admission, he had complained of intermittent episodes of "fuzzy vision". However, repeated ophthalmologic examination during those episodes failed to reveal any visual abnormality. There was no history of generalised weakness, unusual weight gain or weight loss. On examination, he was found to be 62 inches tall and weighed 120 pounds. He was described as being underdeveloped for his age. He showed no evidence of secondary sexual characteristics. Also, he was described as having a preponderance of fat in his gluteal and thigh areas. His skin was thickened, dry and hyperkeratotic.

A review of his systems and, in particular, a neurological examination at that time did not reveal any other abnormalities. His visual fields were recorded as being normal. There was no mention of his visual acuity. Laboratory investigations on his first admission revealed no significant abnormalities other than a low protein bound iodine (2.8 mg%), a basal metabolic rate of −17%, and low 17 − ketosteroids (2.6 mg). These, together with the Robin Kepler power water loading test, supported the diagnosis of significant adrenal insufficiency. In the latter test, none of the 4-hourly specimens or urine exceeded the overnight volume of 700 ml.

Roentgenograms showed open epiphyses appearances compatible with a bone age of 12 years, indicating a 5-year disparity from his chronologic age. X-ray examination of his skull revealed an enlarged sella turcica with deossification of the posterior clinoids. No calcification in or above the sella were to be identified.

An unjustifiable diagnosis of pituitary adenoma was thus made on the basis of his endocrine status and X-ray appearances of the sella turcica. Based on the recommendations in the literature that pituitary adenomas be treated with irradiation without surgical treatment and confirmation of the tumor, he was then given X-ray treatment. He received 6,000 rads in divided doses over a 31-day period. This was completed on 8-23-61. At no time during his X-ray treatment or after, till the time of his admission to our service on October 4, 1961 did he receive a detailed examination of his visual status.

His admission on 10-4-61 resulted following his complaint of progressive visual loss in both eyes, especially his left. Examination revealed that his visual acuity was 20/200 on the right and a paltry 1/200 on the left. Examination of his visual fields revealed large temporal field defects. Funduscopy showed optic atrophy on the left side. The fundus was normal in appearance on the right. Cerebral angiography confirmed a suprasellar mass. At operation, a cystic cra-

niopharyngioma was found and completely removed. Postoperatively, he developed transient diabetes insipidus. He otherwise made an uneventful recovery. He continues to require endocrine replacement therapy. The tragic part of it is that he is blind in his left eye. Fortunately, vision in the right eye has recovered to 20%25.

This case emphasises the need for careful selection of patients prior to advising radiotherapy on the presumptive diagnosis of a chromophobe adenoma. If a craniopharyngioma is suspected, as it should have been in this case in view of the patient's age and the long standing history of headaches and retarded growth and development, one should not temporise with X-ray treatments.

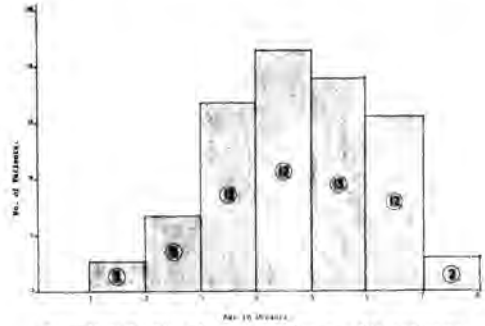
It is the purpose of this communication to report a review of our patients with pituitary adenomas during the past 27 years (1942-June 1969). In addition, we feel that insufficient emphasis has been placed by most writers on the value of steroid and endocrine therapy pre and postoperatively. Further, too many physicians are still influenced by the high operative mortality of bygone years. The long term management of the endocrine deficient patient and the problems associated with it, the management of transient diabetes insipidus and hypopituitary states require expert, careful and constant attention. This is done primarily by one of us (F.L.). Electrolyte balance and the proper understanding of the concepts of inappropriate antidiuretic hormone have also helped calm what formerly was all too often a stormy postoperative course.

The high operative mortality of earlier reports, 13.1% [10], 13.6% [6], 14.1% [16], 11.3% for chromophobe adenomas [2], 7.7% [23], 12.7% [22], 10% [8], 6.8% [27] and a quite commendable 4.9% overall mortality in the Cushing series as reported by Henderson [13] (4.5% for the transfrontal approach), compare strikingly with that of no mortality in 63 consecutive operations for the period 1951-60 in the New Hospital [24]. Our case mortality (two deaths) for the past 27 years ending June 1969, is 4.0%, with an operative mortality of 3.6%.

The present study comprises 66 patients with pituitary adenomas. Of these, 50 were operated upon. Two of these operations were in acromegalic patients without visual compromise of significance, and the rest were for chromophobe adenomas. There were five re-operations for tumor recurrences. Ten patients received X-ray treatment alone. Two patients died shortly after admission. Both were admitted comatose and in circulatory collapse, following pituitary apoplexy. On autopsy, both of them showed evidence of recent sizeable hemorrhages into their pituitary tumors with extravasation into the subarachnoid space. Both patients harboured chromophobe adenomas. Another patient was too ill with renal failure and hypertensive heart disease to withstand surgery. Two patients refused treatment after a diagnosis had been made, and one was operated upon elsewhere after the diagnosis of a pituitary tumor was documented by us.

Age and Sex

Of the 66 patients, 39 were males and 27 females; 86% of the patients were between the ages of 30 and 69, the greatest number falling between 40 and 49 years (fig. 1). Our youngest patient was 19 years old, and the oldest in this series was 75 years of age.



Age distribution histogram in our 66 patients with pituitary tumors

Fig. 1

Symptoms

Visual impairment or visual difficulties was the single most common symptom occurring in 78.8% of the patients. Visual complaints comprised any or all of the following: failing vision, failure to perceive one or both temporal fields or double vision. Not uncommonly, patients were referred by an ophthalmologist with documented visual field defects or documented progressive decrease in visual acuity. Some of these had been detected on routine eye examination. Forty-two (63.6%) of the patients had complaints of endocrine or metabolic deficiencies, e.g. amenorrhea, impotence, acromegaly, obesity, diabetes mellitus, etc. (tables I and II); 21.2% of our patients had headaches. In Rand's series [23] 19% had headaches. Two patients were admitted because they were discovered to have enlarged "ballooned out" sella turcicas when X-ray examinations of the skull were made for some other unrelated condition. One was seen following a

head injury. X-ray examination of his skull revealed an enlarged sella turcica. There were no changes in his visual acuity or visual fields. During an endocrine evaluation, he left the hospital against advice. The other patient was diagnosed as having Parkinson's disease. As was customary in all such patients, an X-ray examination of his skull was made. This also revealed an enlarged "ballooned out" sella turcica. He had no visual changes and following an endocrine evaluation received X-ray treatments.

Diagnostic Procedures

In this category, we include detailed examination of visual acuity and visual fields, X-ray examinations of the skull, cerebral angiograms, radioactive brain scans and pneumoencephalograms. The examination of visual acuity and visual fields should not be treated lightly. Outside of neuroradiologic studies, it is the most useful single examination. It localises the lesion and gives a fairly good indication of the degree of compromise of the optic pathways. Good preoperative visual fields are essential if one is to follow these patients postoperatively in any meaningful way. The examination of the visual fields and visual acuity should not be relegated to an inexperienced person.

In the present series, 46 patients had documented visual field defects preoperatively and 48 showed significant decrease in visual acuity in one or both eyes. Thirty of the 46 patients had bitemporal hemianoptic defects, but when lesser defects in the visual fields, quadrantanopsias, constriction of the temporal fields, etc., are included, 69.7% of our patients had defects in their visual fields. This compares with Cushing's 65% (Henderson), [13] and Olivecrona's 63% (Bakay) [2].

Forty-seven patients (71.2%) had unequivocal evidence of an enlarged "ballooned out" sella turcica. Erosion of the anterior wall with cavitation of the floor and erosion of one or both anterior clinoids contributed variously to the sellar enlargements. Suprasellar calcifications were present in three patients. It should be emphasised here that a normal appearing sella turcica on plain X-ray films does not exclude the presence of a pituitary adenoma, as we have seen several such.

Cerebral angiograms were performed in 43 patients. Thirty-six of these were considered positive for a suprasellar mass as evidenced by tenting and straightening of the first portion of the anterior cerebral artery, with or without associated stretching and lateral displacement of the cavernous or terminal portions of the internal carotid artery.

TABLE I

Complaints	Visual	Endocrinologic	Headaches
Number	52	42	14
Percentage	78.8%	63.6%	21.2%

Presenting complaints in 66 patients

TABLE II

Type	No.
Panhypopituitarism	31
Hypothyroidism	9
Hypoadrenalism	1
Diabetes Mellitus	1
Total —	42

Table of patients with documented endocrine deficits

Nineteen patients had radioactive brain scans. Only four were positive for suprasellar tumors which subsequently were shown to be chromophobe adenomas. The positive scans were those that showed an increased area of isotope uptake in the suprasellar area in both the anteroposterior and lateral views. The uptake in one instance was so intense as to cause us to strongly consider a suprasellar meningioma in the differential diagnosis (fig. 2.).

Plain skull X-ray examinations, with or without spot films of the sella turcica and tomography, together with radioactive brain scans and cerebral angiographic studies, were sufficient to localise structurally the lesion in all but seven of our patients, thus obviating the need for air studies routinely. However, in the preoperative evaluation of the patient, should the skull films and cerebral angiograms be negative, a pneumoencephalogram is in order. Under these circumstances, we prefer to do a fractional air study with the aid of the image intensifier. Should a tumor be present, it can be readily outlined. The procedure is short and performed with little in the way of discomfort to the patient. It is done as follows: The patient is seated with the head flexed. A lumbar puncture is performed. Five to six ml. of room air are then slowly injected. With the image intensifier and television monitoring, the air in the cisterna magna and the fourth ventricle is usually well outlined with this amount of air unless the cisterna magna is unusually capacious. Although air may have entered the third and lateral ventricles, this is usually not seen until a lateral autotomogram is exposed. This, under normal circumstances, outlines, besides the cisterna

Fig. 2

Brain scan with suprasellar pickup (AP and Lateral). Technetium 99^{m} Brain scan in a case of verified chromophobe adenoma.

magna and the fourth ventricle, the aqueduct of Sylvius, third ventricle and some of one or both lateral ventricles. The head is now hyperextended and a further five ml. of air are injected. The prepontine, interpeduncular, parasellar, chiasmatic cisterna and, rarely, the cistern of the lamina terminalis are outlined. By this method, there is a minimum of subrachnoid air laterally to interfere with the visualisation of midline structures. Should a suprasellar tumor be found, it is well delineated by the above method. The patient is then returned to his room. He is allowed up later that evening.

We performed eight pneumoencephalograms by the above method in patients having pituitary tumors. Four were positive for a suprasellar mass.

Mode of Treatment

A total of 50 patients were operated upon. There were five reoperations for recurrences (excepting the patient noted in Case Report II below, these were anywhere from three to eight years after their initial operation) and a total of five patients received X-ray therapy before an operation was thought to be indicated. Ten received X-ray therapy alone (table IV). All 55 operations in the 50 patients were performed by the transfrontal route. Of the reoperations, all were for tumor recurrence. There were no reoperations for the evacuation of blood clots or because of edema postoperatively.

TABLE III

Total Number with Documented Visual Difficulties = 52 (78.8%)		
Field defects 46 88.4%	Decreased Acuity 48 92.3%	Diplopia 6 13.5%

Types and percentage of visual abnormalities amongst 52 patients with visual complaints.

Before the radiosensitive nature of these tumors became established, not all patients received X-ray treatments postoperatively. Since that time, we have not withheld its use whenever so indicated. When it was used postoperatively, it was begun anywhere from seven to ten days after the operation. Each patient received 3,500 – 4,500 rads in divided doses over a four to six week period. Of the five patients reoperated upon for tumor recurrence, three did not receive X-ray therapy postoperatively after the first operation. One did. The other, a 48-year-old man, was initially treated with X-rays elsewhere prior to operation. He is a tragic example of treatment with X-ray alone, without a careful follow-up of the visual status. He became almost blind before being referred for an operation.

Case Report II

A 48-year-old white man saw his doctors in 1947 after two years of headaches and impotence. An X-ray examination of his skull then had shown, apparently, an enlarged sella turcica. He was then treated with X-rays but the number, duration or dosage of X-ray treatments that he received was not available to us. He certainly did not receive an examination of his visual acuity or visual fields during or following his X-ray treatments.

He was first seen by us in September 1954 with complaints of progressive visual loss in both eyes since irradiation. Examination at this time revealed that he could just perceive light in his left eye. The visual acuity on his right was 20/50. In addition, he

had a large temporal field cut on the right side. X-ray examination of his skull showed an enlarged eroded sella turcica. At operation, a chromophobe adenoma with considerable extrasellar extension was removed. In October of the same year, his visual status was unchanged on the left but the acuity on the right eye was recorded as being 20/20 and the large field defect on the right had completely disappeared. He suffered a recurrence in April 1955. At reoperation, extensive lateral spread was found under the temporal lobes. The tumor had also grown upward into the hypothalamus and third ventricle. He was last heard from in August 1955. He is presumed to have died shortly thereafter.

Operative Procedure

As indicated earlier, a transfrontal approach was employed in all our patients; 20% intravenous Osmitrol and continuous drainage of spinal fluid with a malleable needle in the lumbar subarachnoid space were employed routinely. A bifrontal skin flap was raised and the bone flap was "turned" on the side of maximal involvement of the visual apparatus, or on the right side if there was no indication to operate on the left. Through all intradural approach, the frontal lobe was elevated. Whenever the visual pathways are involved by a pituitary adenoma, the tumor will be found to have either stretched the diaphragma sella upward or to have broken through it. The optic nerves will then be seen to be stretched over the mass. In advanced cases, they may be quite flattened and atrophic. The chiasm of the optic nerves is usually hidden from view until some tumor is removed.

In all cases, an attempt at aspiration of the tumor with a fine needle is in order when it is first exposed. Varying amounts of cystic fluid may be evacuated resulting in better visualisation of the surrounding structures. In the days prior to angiography, this procedure was crucial in avoiding a fatal hemorrhage from an aneurysm in this location. Even now, cerebral angiography does not invariably disclose the presence of an aneurysm rather than a tumor, and a fine needle hole is far safer than a stab wound. If no aneurysm is found, the capsule is incised, at which time some soft grayish gelatinous tumor may extrude. The tumor is then removed with small spoons, rongeurs and suction. Because of the usual consistency of these tumors, suction is particularly useful in their removal.

After the tumor has been completely removed, the superior capsule of the tumor can often be separated from the under surface of the brain with gentle traction and blunt dissection. If it is obviously adherent, the surgeon should not persist in attempting to remove it. It is important that the optic chiasm and nerves be completely decompressed in one way or another. In the past when adequate replacement therapy was not available, it was not thought advisable to remove these tumors completely. This is no longer the case. On the other hand, removal of the capsule is not important and obviously can never be complete. If it can be partially accomplished, a complete removal of the tumor can be more readily and certainly obtained.

On completion of the tumor removal and adequate decompression of the visual apparatus, hemostasis is assured. This is followed by a careful dural closure. The dura mater is now tented to the bone edges to prevent possible epidural bleeding postoperatively. When the frontal sinus is opened, and this is to be avoided whenever possible, a periosteal flap is fashioned and sutured to the dura over the sinus. The bone flap is now anchored in place with stainless steel sutures. It is our practice to trephine a bone button in the frontal area for cosmetic reasons. This is also replaced and held by stainless steel sutures. The scalp is now closed in two layers. When the frontal sinus is opened at surgery, antibiotics are given postoperatively for ten to 14 days to prevent a bacterial meningitis.

More recently, there has been a trend towards a transphenoidal approach for the removal of pituitary adenomas. Cushing [13] employed it widely before abandoning it for the transfrontal route with a significant reduction in his operative mortality. Present day antibiotic therapy has largely offset the fear of bacterial meningitis that could follow operations transphenoidally. Further, microsurgery and the image intensifier have enhanced this procedure. We believe that a transphenoidal approach should be restricted to cases where the growth, if it be present, does not extend beyond the diaphragma sella. We further believe it has a real place in elective hypophysectomies for cancer, diabetic retinopathy and biopsy of masses arising from the clivus or its surrounds e.g. chordomas, giant cell tumors of bone, etc. We shall discuss the transphenoidal approach to pituitary tumors later.

Operative Mortality

Patients dying within 30 days of surgery were considered operative deaths. We had two deaths.

One was a 29-year-old man with a nine-year history of progressive visual loss and was almost blind.

He was operated upon in 1946. At operation, he had considerable extrasellar extension of his tumor, necessitating prolonged retraction of his frontal lobes. This was in the pre-steroid era and before the use of dehydrating agents and spinal drainage to reduce the volume of the brain during operation had become common practices. He died on the third postoperative day. Autopsy revealed cerebral edema and infarction of both his frontal lobes, and uncal herniation.

The second death occurred in a 46-year-old woman. Brisk hemorrhage from, in and around the capsule was difficult to control. Postoperatively, she was hemiparetic. Three days later she was decerebrate. She died on the sixth postoperative day. Autopsy revealed a rather large intracerebral hematoma in the temporal lobe that extended to the cerebral peduncle on the left. The two deaths gave a case mortality of 4.0% and an operative mortality of 3.6%.

Histopathology

All but two tumors microscopically verified on surgical specimens were chromophobe adenomas. The two were acidophilic tumors. Both were removed from patients suffering clinically from acromegaly.

Postoperative Course

The postoperative course is largely that of any frontal craniotomy. Transient bloody cerebrospinal rhinorrhea occurred in those where sinuses were opened at surgery. They were kept flat in bed until the rhinorrhea subsided. It usually did so within a day or two. These patients were placed on antibiotics for ten to 14 days postoperatively. We had no occasion to repair the leak surgically in any of our patients. Those patients who developed diabetes insipidus did so anywhere from 12 to 72 hours postoperatively. The management of these patients will be alluded to shortly.

The general postoperative course was otherwise a smooth one. Since 1951, patients received cortisone before, during and after surgery. When dexamethazone became available, it was used postoperatively. Of all factors responsible for a reduction of operative mortality in brain tumors, the most significant has been dexamethazone [19]. When dexamethazone was employed, it was tapered off by the 7th postoperative day. Cortisone replacement therapy was then begun. Anywhere from the 7th to the 10th postoperative day, X-ray treatments were started. Some patients received these on an outpatient basis. Following discharge from the hospital, the patients were closely followed by both the endocrinologist and the neurological surgeon. Periodic checks of the visual acuity and the visual fields were routinely made. This proved to be the most useful single examination for the detection of early tumor recurrence.

Both pre and postoperative visual fields were available for comparison in 40 patients. Of these, 33 (82.5%) showed significant improvement in their visual fields. A total of 13 (32.5%) had complete restoration of their visual fields to normal. Thirty patients (75%) had a significant improvement in their visual acuity, but only seven (17.5%) had restoration of their acuity to normal.

The postoperative fields in those treated with operation alone were compared with those who had X-ray therapy following surgery. In the former group, 72.7% showed improvement in their visual fields, while 86.2% showed this in the latter group (table V for details). It is obvious, however, that these groups are too small for these differences to be significant. Ten patients were treated by X-ray alone. Of these, four had normal vision prior to treatment. Of those with impaired vision, two were improved and one patient had restoration of his vision to normal. It should be noted, however, that this group is not comparable to those who were operated upon as only those with no visual field defect or only minor ones received X-ray therapy alone.

Patients with pre and postoperative studies of their visual fields, whose fields prior to their being seen by us were available, were divided into two categories. Those seen for the period 1942 to 1959 (group I), and those seen from 1960 to 1969 (group II). Twenty-two of the 24 patients (91.7%) in Group II had complaints of under 40 months' duration. Whereas, only six of the 15 (40%) in Group I fell in this denomination, while nine (60%) had had symptoms for more than 40 months. In Group II, 20 (83.3%) showed significant improvement in their visual fields with treatment compared to nine (60%) in Group I.

Admittedly, there are many factors that account for the differences between Groups I and II. Amongst these may be mentioned earlier referrals, improvements in anesthesia, surgery and in X-ray therapeutics. Nevertheless, it appears clear that better results are obtained from treatment, so far as impairment of vision is concerned, in patients whose symptoms have been present for shorter periods of time.

Preoperative Evaluation, Preparation and Postoperative Endocrine Management of Patients Undergoing Pituitary Surgery

Forty-two of the 66 cases in this series showed

evidence of endocrine deficiencies based on clinical and laboratory evaluation. Thirty-one cases showed evidence of pan-hypopituitarism. Nine cases demonstrated only hypothyroidism. One case demonstrated only hypoadrenalism and one case only diabetes mellitus. (table II) One instance of persistent hypercalcemia was noted in a patient with a suspected chromophobe adenoma. In no instance was diabetes insipidus present preoperatively. But in nine cases postoperatively, this complication lasted more than the usual transient four to six day period of time and in two of these instances, this complication has been prolonged (two years). One patient, with a chromophobe adenoma, postoperatively developed diabetes mellitus with hyperglycemic non-ketotic acidosis. A single instance of inappropriate ADH secretion was seen postoperatively.

The pertinent baseline studies consist of serum electrolytes, glucose, calcium, phosphorus, BUN, P.B.I. or T4 and urinary 17 ketosteroids and 17 ketogenic steroids. Cortisone acetate 50 mgm. I.M. q. eight hours is started 48 hours before surgery. On the

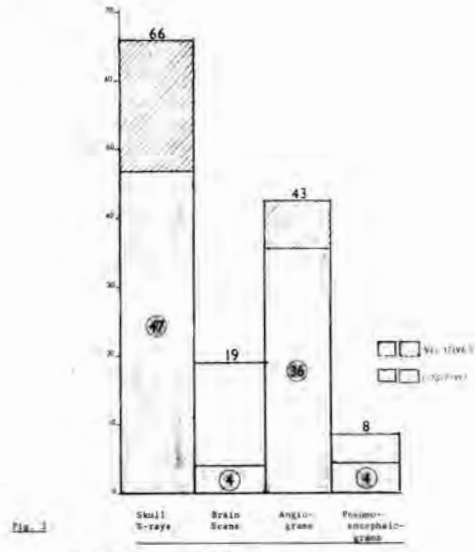


Fig. I

HISTOGRAM OF POSITIVITY OF RADIODIAGNOSTIC STUDIES

(Numbers on top of the histograms indicate the total number of each corresponding study. Those within the histograms, the number that was interpreted as being positive or negative for a tumor.)

Group I (1942-1959) = 15 Patients

Group II (1960-1969) = 24 Patients (See Text for Details)

Fig. V

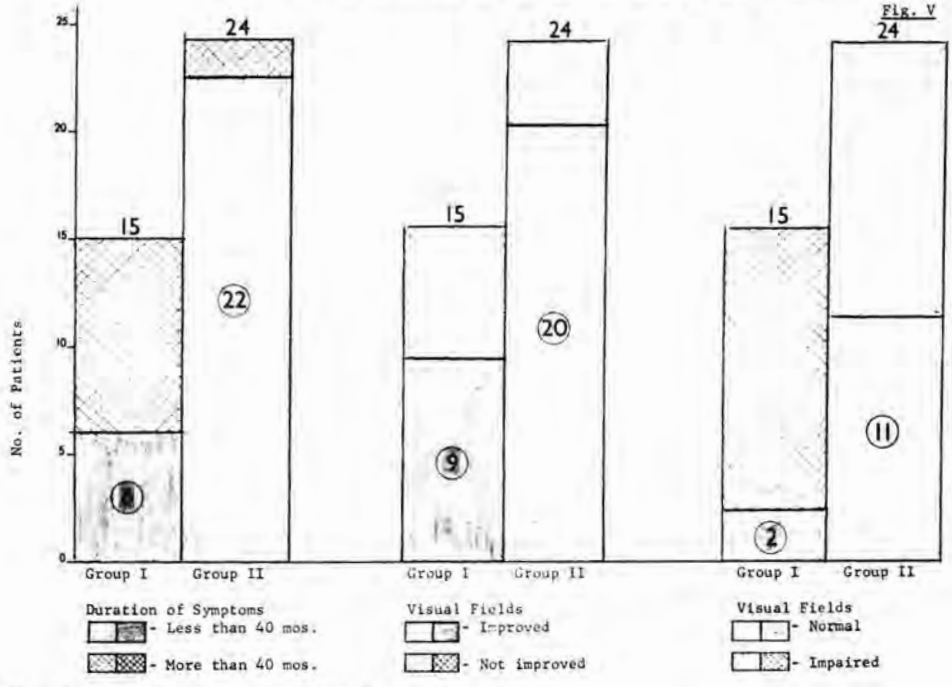


Fig. IV. A COMPARISON BETWEEN GROUPS I AND II

(See text for further details as to postoperative improvement in visual fields.)

morning of surgery, 100 mgm. cortisone acetate is given intramuscularly. Patients weighing 150 pounds or more received 200 mgm. of cortisone intramuscularly instead. At the onset of surgery, an infusion, consisting of 100 mgm. Solu-Cortef dissolved in 500 ml. of 5% glucose, is administered over an 8-hour period. Patients who did not receive dexamethazone postoperatively were given 50 mgm. of cortisone acetate every eight hours for two days. This dose was then reduced in a stepwise fashion so that by the 8th postoperative day, the patient was on this maintenance therapy. This consisted of 25 mgm. of cortisone acetate each a.m. and 12.5 mgm. each p.m. Those receiving dexamethazone postoperatively were not started on the above maintenance therapy till after the dexamethazone was tapered off. This usually took about five days. This course of supportive steroid therapy has eliminated any signs or symptoms of adrenal insufficiency and has allowed the postoperative recovery phase to be smooth and afebrile. This regime of adrenal steroids does not seem to enhance the appearance of diabetes insipidus postoperatively.

TABLE IV

Type	No.
1. No. treated by surgery, X-ray or both	60
2. Pituitary apoplexy	2
3. Refused treatment	2
4. Treated elsewhere Operated by Dr. W. Hamby	1
5. Too ill for treatment	1
Total	66

Methods of treatment of 66 pituitary adenoma patients.

Diabetes insipidus occurs transiently in the majority of the cases postoperatively. It usually occurs 12 to 72 hours postoperatively and is thought to occur when no other cause for diuresis is apparent (urevert, excessive I.V. fluids). It is judged to be present when the urinary output exceeds 200 cc. per hour and/or when the specific gravity of the urine is below 1,005. Transient diabetes insipidus of less than 48 hours' duration is treated with aqueous Pitressin 0.5 to 1.0 units I.M. every six to eight hours. Diabetes insipidus for more than 48 hours is treated with Pitressin Tannate in oil (five units) 1.0 ml. I.M. every 24 to 72 hours. If continued use of Pitressin is indicated, one can switch to the nasal insufflation of powdered posterior lobe extract every four to six hours. Most patients in this series who developed diabetes insipidus postoperatively had this condition for only two to four days, a few for one week and only two patients in the entire series required long term (two years) control of diabetes insipidus. These two patients did not respond to Chlorothiazide therapy.

Although secondary hypothyroidism was a frequent preoperative finding, it was never severe enough to postpone surgery, except in one instance. Thyroid replacement is started one week after surgery with 30 mg. thyroid extract or 0.05 mgm. synthroid daily and gradually increased over a period of several months to full replacement dosages.

Androgen replacement therapy consisting of 15 to 20 mgm. of methyl testosterone sublingually or in the buccal pouch was used in those males complaining of weakness, loss of libido and potency. Estrogen replacement was routinely used in premenopausal females and in post-menopausal females demonstrating osteoporosis.

Discussion

In performing neuroradiologic studies, one should avoid redundant tests. We have found little use for air studies in view of the information derived from the history, clinical examination, visual field examinations, X-ray examination of the skull, radioactive brain scans and cerebral angiograms. However, in the event of these studies being inconclusive, an air study is in order. We performed only eight pneumoencephalograms in this series. Lewtas [21] makes no mention of cerebral angiography in his discussion of radiology in the diagnosis and management of pituitary tumors. He relies on X-ray examination of the skull and air encephalography. We have found cerebral angiography to be particularly useful in excluding aneurysms about the sella turcica and other suprasellar tumors. A tuberculum sella meningioma was thus diagnosed in one of our patients with signs and symptoms not unlike those of a pituitary tumor. Poppen [22] has used cerebral angiography to determine if the optic chiasm is pre or post-fixed relative to the sella turcica. We do not employ cerebral angiography for this purpose, nor feel that it is reliable in this regard.

The need for histologic verification of the lesion with which one is dealing cannot be overemphasised. Our Case I noted earlier would attest to this. However, operation we feel is less warranted in those with evidence of a pituitary adenoma without any visual compromise. The exception to this is the patient with early onset of gigantism or acromegaly.

Recently, opinion has been expressed by Ray [25] that chromophile pituitary adenomas associated with

acromegaly should be extirpated surgically. This position is justified and one which we have come to accept, especially in those patients suffering from acromegaly or gigantism where the somatic effects are not far advanced. In these cases, the primary concern is with the disfigurement of the patient and seldom with vision. It is now established that in early cases of acromegaly, the disfigurement can be arrested or even made to regress in many instances if the offending tumor is promptly and completely removed. These patients are entitled to this possible relief and should not be subjected to less effective radiation therapy merely because their vision is neither involved nor threatened. It is probable that many acromegalics without visual impairment are best operated upon by the transphenoidal approach.

The high operative mortality of early reports were no doubt due in some measure to larger tumors and the unavailability of steroids. Today patients are being seen earlier. This and endocrine therapy, better anesthesia, improved surgical techniques and postoperative care have all been consonant with the reduction in operative mortality and morbidity.

All our operations were performed by the transfrontal approach. We report an operative mortality of 3.6%. Recent reports in the literature [4,11,12] attest to the low mortality and morbidity following a transphenoidal approach to these tumors. Hamlin [11] reported a mortality rate of less than 2% in 104 patients undergoing transphenoidal pituitary tumor excision and Hardy [12] had none to report in a series of 20 consecutive operations for pituitary adenomas. Guiot (personal communication) has extended this procedure to remove craniopharyngiomas, but this he does not do unreservedly. We believe that a transphenoidal approach should be restricted to cases where the growth does not extend beyond the diaphragma sella. We further believe it has a real place in routine hypophysectomies, acromegalic patients without visual field defects, and in small pituitary adenomas. We have employed it in hypophysectomies for diabetic retinopathy, metastatic breast cancer and for the biopsy of sphenoidal masses. Any evaluation of the transphenoidal approach must take into account the known occurrence postoperatively of cerebrospinal fluid rhinorrhea in some cases and the obviously greater risk of intracranial infection with the transphenoidal approach as compared with the transfrontal.

We fail to see, however, how by a transphenoidal route adequate decompression of the optic nerves and chiasm can be assured, especially in those cases where a "meaty" tumor is located above or on these structures. We are agreed that with proper selection of patients, the transphenoidal route may be employed for tumors that are wholly intrasellar. However, except for the patients with acromegaly, there is little indication for recommending surgery for wholly intrasellar pituitary tumors. When suprasellar extension is present a transfrontal approach is best suited for decompression of the visual pathways under direct vision.

Most of the patients undergoing transphenoidal surgery are also being given radiotherapy. As a result, it is difficult to assess the efficacy of this form of treatment. In the cases reported by Hardy [12] 13 of his 16 pituitary adenoma patients had field defects. He does not state what these field defects were. Following operation and X-ray therapy all but three had what he categorises as "complete improvement". But of the cases with "complete improvement", all but one had symptoms of less than ten months' duration. Further, eight in this group had had symptoms for less than six months. It is this category of patient which is often helped by irradiation. Further, it is somewhat early to study these patients from the point of view of recurrence. Most reports in the literature (and our own experience would concur) indicate that should a recurrence occur, it is most likely to appear between the third and the fifth years following treatment.

That X-ray therapy has a definite and important role in the treatment of the pituitary adenoma patient is not disputed. Our best results have been in patients who were treated with X-rays following surgery. Further X-ray therapy reduces the likelihood of a recurrence. Three of our five patients, who had a recurrence, had not received X-ray therapy following surgery.

Svien et al [27] recently reported on a comparison of visual changes in 71 cases of chromphobe tumors before and after surgery, with 74 cases before and after treatment by irradiation alone. They came to the conclusion that radiation therapy is almost as effective as surgical removal in so far as visual changes were concerned. They utilised the American Medical Association recommendation by the Committee on Medical Rating of Physical Impairment, to quantitate visual loss. In their three categories, Stages I, II, III, they had comparable numbers of patients treated by both methods. It is apparent from Table V of their article, that 14 patients (19.7%) had their vision restored to normal after surgery compared to 9 (12.2%) in the irradiated group. This becomes more significant

when it is realised that 34 of the irradiated group had Stage I visual loss, while only 27 had Stage I visual loss in the surgical group. Further, a larger number, 23, in the surgically treated had Stage II visual loss compared to 19 in this stage in the irradiated group. Moreover, 36 patients (50.6%) had visual improvement of 33% or more with surgery, while 30 (40.5%) did so in the irradiated group. If this be extended to those with visual improvement of 67% or more, 23 (31%) did so following surgery, while 18 (24.3%) were able to accomplish this with X-ray.

TABLE V

Type of Treatment	Improved	Unchanged	Worse	Total
Surgery and X-ray X-ray and Surgery	25(10N)	2	2	29
Surgery alone	8(3N)	2	1	11
X-ray alone	3(1N)	4	—	7
Total	36(14N)	8	3	47

N = Normal fields

Post-treatment visual fields (where available) in those treated by the methods indicated.

Surgery would thus seem to have an edge over X-ray therapy alone. There is no doubt from the experience of others [8,10,22] and as in our own series, that those treated by surgery and X-ray had the best results; 86.2% of our patients had significant improvement in their visual fields while 40% had restoration of their vision to normal with this form of treatment. These facts justify the surgical treatment of these tumors as compared with radiation therapy alone. Further, the importance of a histologic diagnosis has already been discussed and this would obtain only in those treated by surgery.

We have indicated that visual fields should be mapped pre and postoperatively and used as a baseline for future management. They are a sensitive index of improvement or deterioration and are most helpful in pointing to a possible recurrence of tumor.

Lewtas [21] is of the opinion that postoperative fields are misleading and not reliable indices of recurrent tumor growth. He recommends approximately annual serial radiographs of the skull to enable him to examine the bony outlines of the sella turcica. However, tumor gorwth, particularly in the suprasellar region where it is most important so far as vision is concerned, is not necessarily associated with bony change and such changes, even if they occur, may lag far behind changes in vision. Further, the judgement of bone density is too subjective and given to technical variables like rotation, projection and quality of the films to make such radiological studies reliable for this purpose. We feel that the examination of the visual acuity and visual fields constitutes a most sensitive, reliable, reproducible index of recurrence. Confirmation and extent of the recurrence can then be studied by other ancillary diagnostic methods.

Summary

1. A total of 66 patients with pituitary adenomas seen and treated from 1942 to June 1969 are reviewed.
2. Progressive visual compromise has been the major criterion for surgery. It was the presenting complaint in 78.8% of our patients.
3. The pre and postoperative roles of steroids and other endocrine therapy have been emphasised.
4. Of those treated by our three methods, surgery alone, X-ray alone and surgery followed by X-ray therapy, 74.5% showed significant improvement in their visual status and of these, 29.8% had complete restoration of their visual fields to normal. The group treated by surgery and irradiation gave the best results (86.2%), had significantly improved vision and 40.0% had restoration of their visual fields to normal.
5. Our operative mortality of 3.6% (a case mortality of 4.0%) compares favourably with those of other series in the literature.

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The early immunisation of infants in Malaysia

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Introduction

CHEN AND DUGDALE (to be published) in a survey of school children (ages six to seven years) in an urban area in Selangor, found that 11% of them had had no previous immunisation with smallpox, 26% had no B.C.G., 69% had no triple antigen (D.P.T.) or dual antigen (D.T.) (of those who had, only 18% had three or more doses) and 94% had no poliomyelitis immunisation (of those who had, only 3% had three or more does). This low rate of active artificial immunisation is one of the reasons why diseases like diphtheria, tetanus and poliomyelitis are still common in Malaysia.

There are many reasons for this low rate of immunisation, one of which is failure of parents to bring their children to clinics for immunisation. But even clinic patients have low rates of immunisation. Dugdale (1969) reported that only 68% of children who attended Municipal Infant Welfare clinics had smallpox vaccination and only 20% had three doses of triple antigen by the age of one year. He also pointed out that about 50% of the clinic patients stopped attending the clinics after the age of six months.

The rate of immunisation could be improved, using the existing services, by giving the maximal number of immunisations in the fewest number of visits, i.e., to combine antigens, and by giving immunisation as early as possible and completing the primary immunisation (other than reinforcing doses) before the child reaches the age of six months. With this in mind, the University Hospital, Malaysia, has adopted the following schedule of immunisation for infants born here since 1968:

At birth	— B.C.G. and smallpox
At 6 weeks	— 1st D.P.T. (triple antigen) and oral poliomyelitis (trivalent)
At 10 weeks	— 2nd D.P.T. and oral poliomyelitis
At 14 weeks	— 3rd D.P.T. and oral poliomyelitis
At 12 – 16 months	— reinforcing doses of D.T. (diphtheria and tetanus toxoid) and poliomyelitis.

This paper reports a study which tests the efficacy of immunising infants early, with regard to smallpox and diphtheria. Three groups of children, a study and two control groups, were used and were tested by means of primary smallpox vaccinations, re-vaccinations and Schick tests.

Methods

(a) Study population

Twenty-one children, who were immunised with

the above schedule, were studied. Schick tests and revaccinations were done at six months of age. Of the 21, 13 of them had a second Schick test between 12 and 19 months of age. These were done before they received reinforcing doses of D.T.

(b) Control populations

During the study, two groups of children were used as comparisons.

(i) The first group, Control I, consisted of 17 healthy children who had not received primary smallpox vaccinations. They were given primary smallpox vaccinations at the time that the study group received revaccinations (age about six months).

(ii) The second group, Control II, consisted of ten children whose ages ranged between four and 19 months. These were convalescent children, from the University Hospital, who had no history of clinical diphtheria or of previous artificial immunisation against diphtheria. They were given Schick tests.

(c) Tests

All Schick tests were done with diphtheria toxin in the left arm (test) and heat inactivated toxin in the right arm (control) and were read on the 4th or 5th day. The smallpox revaccinations were read on the 4th or 5th day and then again on the 7th, 8th or 9th day.

All tests were performed and read by one of the authors (M.M.C.)

Results

All the study children developed either an immune or a vaccinoid reaction to smallpox revaccination. The maximal area of papule or vesicle and surrounding erythema, at 4th or 5th day, was 10 mm., but the majority of them measured 4-5 mm. By the 7th, 8th or 9th day, reaction had diminished. All the Control I children developed primary reactions to smallpox vaccinations.

Everyone of the study children had a Schick negative reaction at six months and again between 12 and 19 months of age, while all the Control II children had Schick positive reactions.

Discussion

An important reason for the low rate of artificial active immunisation in Malaysia is the fact that immunisation is often scheduled to be completed late in infancy, whereas infants often cease to attend clinics by the age of six months. Another reason is the fact that antigens are usually given singly. An example of a schedule practised by some general practitioners, in Kuala Lumpur and Petaling Jaya, is as follows:-

At birth — B.C.G.
At 3 months — Smallpox
At 4 months — 1st D.P.T.
At 5 months — 2nd D.P.T.
At 6 months — 3rd D.P.T.
At 7 months — 1st poliomyelitis
At 8 months — 2nd poliomyelitis
At 9 months — 3rd poliomyelitis

The rate of immunisation can be raised by giving several antigens simultaneously and starting immunisation of children as early as possible and completing the primary immunisation before the age of six months. The aim is to provide maximal protection in the fewest possible visits. However, the following questions have to be answered before the above can be advocated.

Table I

Smallpox vaccination reactions of study children and of control children

Smallpox vaccination Reaction	Number of study children	Number of control children
Primary reaction	0	17
Immune or Vaccinoid reaction	21	0

Table II

Schick reactions of study children and of control children.

Schick Reaction	Number of study children		No. of control children between 4 & 19 months of age
	At 6/12 of age	Between 12 & 19 months of age	
Negative	21	13	0
Positive	0	0	10

(1) Is early immunisation effective?
(2) Do many complications arise as a result of early immunisation?
(3) Does simultaneous administration of several antigens lower immunity or result in adverse reactions?

(1) Is early immunisation effective?

There is a common belief that young infants are incapable of forming antibodies because of immunologic immaturity, and presence of passive immunity. However, studies have shown that even a newborn infant is capable of responding to an antigen by forming antibodies despite the presence of passively acquired antibodies to the same antigen.

Lin (1965) in Taiwan, giving B.C.G. and smallpox vaccination to newborn, found that the successful rate of takes was high and there was no evidence of increased risk of complications. This result is confirmed by Stanfield (1966) in East Africa and by the study, presented in this paper. Our percentage of takes in smallpox vaccinations among the newborn was 95% (545/574) as compared with 97% (65/67) among infants vaccinated for the first time after the age of two months.

Pearlman (1961) and Harris (1966), in their review of literature pointed out that infants, within the first month of life, were capable of producing protective levels of antibodies to diphtheria, pertussis and tetanus. They pointed out that Gaisford had shown that the majority of very young infants immunised with D.P.T. at 1, 5 and 9 weeks of life exhibited a satisfactory antibody level at 15 weeks.

A Schick negative reaction indicates that the individual has more than 1/250 units of diphtheria antitoxins per 1 cu. cm. of blood. A person whose Schick reaction is negative is protected from contracting clinical diphtheria (Hare 1956). The results of our study confirm that diphtheria toxoid, given early in infancy, produces a protective level of antibodies at six months.

Barret (1962) and Da Silva (1958) showed that very young infants were capable of producing antibodies to oral poliomyelitis vaccine, though the response was less compared with older infants (79% of infants fed poliomyelitis vaccine within 18 days of life produced antibodies as compared with 91% of infants fed the same vaccine between 4½ and 26 weeks of life).

(2) Do many complications arise as a result of early immunisation?

The high incidence of complications of primary smallpox vaccination, namely post-vaccinial encephalitis and generalised vaccinia, in infants under one year of age as reported by Wynne-Griffith has resulted in some countries recommending primary smallpox vaccination after the age of one year. However, Edsall (1961), in his review of literature, summarises that "the weight of experience indicates that the risk of post-vaccinal encephalitis can be minimised by universal vaccination beginning in infancy." In Taiwan, Lin (1965) found no evidence of increased risk of complications in infants receiving smallpox vaccination during the neonatal period. In Hongkong, where 80–95% of all newborn were immunised with B.C.G. and smallpox since 1952, Teng (1969 – personal communication) found no evidence of increased risk of complications. In the University Hospital, Malaysia, 75% of all newborn (about 4,500 babies) were given B.C.G. and smallpox vaccination at birth (sick and premature babies were not immunised till the time of discharge). Up to the time of writing, there have been no reports of serious complications in these newborn.

(3) Does simultaneous administration of several antigens lower immunity or result in adverse reactions?

Simultaneous administration of non-viral antigens have been practised for a long time without reduced immunological response or adverse reaction. However, it has been generally recommended (on theoretical grounds) that different live virus vaccines be given at least a month apart whenever possible. Field observations, however, indicate that, with simultaneous administration of certain live virus vaccines, there was no adverse reaction or lower immunity. In West Africa, millions of smallpox and measles vaccinations have been performed concurrently without significant problems. Smallpox vaccination has also proved to be compatible with simultaneous oral poliomyelitis vaccination. Smallpox vaccine has been given simultaneously, but at different sites, with diphtheria, pertussis, tetanus, typhoid, and inactivated poliomyelitis vaccines; the vaccines maintained their full efficacy and there was no intensification of reactions (W.H.O. 1968). Thus simultaneous administration of several antigens does not as a rule reduce immunity or result in adverse reaction.

Summary

Smallpox vaccination and B.C.G. were given to

Table III

Comparison of the suggested schedule of immunisation (for children first seen at birth) with two schedules presently used in West Malaysia

Vaccines	Time of Immunisation			Remarks on Proposed Schedule
	Ministry of Health	Some Private clinics in Selangor	Proposed schedule	
B.C.G.	At birth	At birth	At birth	On the left arm
Smallpox	5 months	3 months		On the right arm
1st D.P.T. (triple antigen)	2 months	4 months	6 weeks (at post-natal visit)	(1) Use alum absorbed type of D.P.T.
1st Oral poliomyelitis (trivalent)	—	7 months		(2) Check B.C.G. & smallpox scars if absent to repeat.
2nd D.P.T.	3 months	5 months	10 weeks	The interval between immunisation should be at least 4 weeks. But there is no upper limit between the interval, that is, there is no need to repeat an injection once it is given, no matter how long the interval has lapsed.
2nd Oral poliomyelitis	—	8 months		
3rd D.P.T.	4 months	6 months	14 weeks	
3rd Oral poliomyelitis	—	9 months		
Reinforcing dose of D.T. (diphtheria and tetanus toxoid)	1½ —,2 yrs. (D.P.T. is used here)	—	12 — 16 months of age (8 — 12 months after the third doses of D.P.T. & polio.)	May give measles vaccine if available.
Reinforcing dose of oral poliomyelitis (trivalent)	—	—		(School age) —
1st smallpox	6 — 7 years	—	booster (School age)	
1st D.T. (alum absorbed) booster	—	6 — 7 years (School age)		
Further smallpox booster	16 — 17 yrs. (Secondary school leaver)	—	Every ten years	
Further D.T. booster	—			
Tetanus toxoid	12 years (Primary school leavers) & again at 16 — 17 yrs. (Secon. Sch. leavers)			

about 4,500 neonates in the Obstetric Unit, University Hospital; 95% of the infants had a primary reaction to smallpox vaccinations and there were no serious complications. To test the efficiency of smallpox vaccinations in neonates, 21 had repeat vaccinations at the age of six months. All showed an immune or a vaccinoid reaction, but a group of controls, who had not had neonatal vaccination, had primary reactions. Vaccination of neonates, therefore, appears to be both safe and effective.

The group of 21 children also had triple antigen given at 6, 10 and 14 weeks of age. Later, Schick tests (21 at six months of age, 13 after one year) showed that all these children were immune to diphtheria. A control group showed no immunity.

In spite of theoretical objections, early vaccination and immunisation with triple antigen appears to be safe and effective. We suggest the following schedules of immunisation for communities, such as Malaysia, in which the majority of infants are delivered by qualified midwives but are rapidly lost to follow-up (tables III and IV).

Acknowledgements

We are grateful to Professor A.E. Dugdale for his advice and help.

Table IV

Suggested schedule of immunisation for a child first seen between 6 weeks and 1 year of age

Time of immunisation	Vaccine	Remarks
X months	B.C.G. Smallpox D.P.T. (alum absorbed)	On the left arm On the right arm
X + 1 month	2nd D.P.T. (alum absorbed) 1st oral polio (trivalent)	Check B.C.G. and smallpox scar, if absent, to repeat.
X + 3 months	3rd D.P.T. (alum absorbed) 2nd oral polio (trivalent)	May give measles vaccine if available when child is 1 year old.
X + 11 to 15 months	Reinforcing doses of D.T. (alum absorbed) and polio (trivalent)	–
Thereafter	Booster doses of smallpox and D.T.	as in Table III (proposed schedule)

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Clinical Trichuriasis in hospitalised Kuala Lumpur children [1]

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IN MALAYSIA, as throughout much of the world, infection with **Trichuris trichiura** (whipworm or **chaching halus**) is common. A 1962 survey revealed **Trichuris** eggs in the faeces of 88.7% of some 1,359 persons studied in seven states (ICNND, 1964), while Lie Kian Joe (1964) found that 62% of 1,031 Kuala Lumpur General Hospital paediatric patients, aged 2-7 years, were infected. Stoll in 1947 estimated that 227 million Asians, and 355 million people worldwide, were infected with **Trichuris.**

The commonness of the worm and the apparent uncommonness of symptoms attributable to it have caused this parasite's pathologic potential to be neglected. Yet, when large numbers of worms are present in children, a distinctive and important clinical syndrome results. Such children suffer from a refractory and often debilitating diarrhoea or dysentery and frequently develop iron deficiency anaemia.

To better characterise this disorder as it occurs in children in Kuala Lumpur, we studied 26 children with chronic or recurrent diarrhoea and high **Trichuris** egg counts who were admitted to the gastrointestinal ward of the Kuala Lumpur General Hospital over a 4-month period. This paper reports our findings.

Materials and Methods

From mid-January through mid-May, 1968, stool specimens were collected from children admitted to hospital with a chief complaint of chronic or recurrent diarrhoea or dysentery. Specimens were placed in a thiomersal-iodine-formalin (TIF) solution in the ward and examined later in the Division of Rural Health Research of the Institute for Medical Research. Worm eggs were counted using the Dunn (1968) modification of the Beaver (1950) direct smear method, and the smears were carefully examined for amoeba trophozoites or cysts. Children with more than 50 eggs per smear of approximately 3 mg. (about 1/300 ml.) of faeces were included in the study. Duplicate counts were made on each of two specimens obtained before treatment. The hospital

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laboratory performed white cell counts, haemoglobin measurements and stool cultures for bacterial pathogens on each patient at the time of admission. The child's mother (or other responsible family member) was questioned concerning the nature and duration of symptoms, including frequency of bowel movements, the presence of blood or mucus in stools, and of rectal prolapse, pica and previous diarrhoeal episodes; the sibling rank of the child; and the family's sanitary facilities and sources of water and milk.

After these preliminaries, the children were randomly allocated to one of four treatment programs consisting of:

(1) a single retention enema of approximately 400 ml. of a 0.2% solution of hexylresorcinol;

(2) this same kind of enema accompanied by orally administered thiabendazole (Mintezol (R) chewable tablets) in a twice daily dosage of 25 mg./kg. of body weight for 3 days;

(3) the same kind of enema with the same dosage of thiabendazole extended to 5 days; or

(4) the same dosage of thiabendazole for 5 days without the enema.

In children with co-existing amoeba infections, the initiation of therapy with emetine followed by Embequine (R), or with one of the assigned trichuriasis regimens was similarly determined by random assignment. All patients were hospitalised for at least six days, with discharge and later therapy ordered as clinically indicated. Most children were seen again as outpatients 1-2 weeks and 3-4 weeks after discharge, with later follow-ups whenever possible.

Results

The 26 children studied (14 males, 12 females) ranged in age from two to seven years (median age, four years). In terms of ethnic classification, there was a strikingly disproportionate number of Sikh and Pakistani children in the study group. Of 346 children aged 2-7 years admitted to the paediatric gastrointestinal unit from January 12 – May 12, 1968, only 6% were Sikhs and 1% were Pakistanis, with 35% Chinese, 34% Indians other than Sikhs, and 24% Malays. In contrast, the 26 children with severe trichuriasis included eight Sikhs (31%), two Pakistanis, four Chinese, eight Indians other than Sikhs, and four Malays. Subjects tended to be young children in large families; fifth was the median family position, with six the median number of children per family. By history, the median number of daily bowel movements was four, with a median duration of one month. A history of blood in the stools was given for 22 of the 26 children, with mucus reported in 16 of 23 and rectal prolapse in nine of 23 (for whom that information was available). Recent diarrhoea in another child in the family was reported for ten of 25 children.

Regarding sanitary facilities, 13 families said they had latrines (usually pit or bucket); nine said they had none. Water supply was from municipal pipes for 15; nine said they used wells. Five families reported the use of unprocessed cow's milk; 14 said they used only commercial milk. We observed no notable geographical grouping of cases, other than the fact that most came from settlements on the fringe of Kuala Lumpur, which were neither clearly urban nor rural.

On admission to the hospital, all but two of the 26 children (92%) were anaemic by World Health Organisation standards (haemoglobin less than 11.5 gm/100ml) (Jelliffe, 1966). The median haemoglobin was 7.3 gm/100 ml and 21 had values less than 10 gm/100 ml. Most children had a mild leukocytosis, with a median white blood cell (WBC) count of 13,000. Eosinophilia (greater than 300 eosinophils/mm. (3)) was found in 18 (78%) of 23 children, with a median value of 1200 eosinophils/mm.(3)

Concomitant **Entamoeba histolytica** infection was detected in eight of the 26 children, with a pathogenic strain of **Escherichia coli** in two of 22 and **Shigella sonnei** in one of 22 children cultured. However, these figures may be below true incidence because of difficulties in obtaining reliably fresh stools for laboratory procedures. **Ascaris** eggs were found in the stools of 11 and hookworm in five of the 26 children. **Trichuris** egg counts on admission (based on the individual mean of duplicate counts on two specimens per patient) gave a median of 134 with a range of 64-660 eggs per smear.

None of the therapeutic regimens used emerged as distinctly superior. Most children improved gradually during hospitalisation without dramatic response to any specific therapy. Egg counts were usually lower at time of discharge than when the children were admitted, but the infection was rarely eradicated. Later counts were sometimes higher, suggesting that therapy might suppress egg production without eliminating the parasite. Children receiving thiabendazole for five days, along with a hexylresorcinol enema, appeared to experience a more pronounced reduction in egg count and more prompt and sustained clinical improvement than those receiving the other regimens. However, some children on each regimen did well and some poorly, and the numbers involved were too

small to permit any rigorous comparison of therapeutic efficacy.

Case Report

J.K. was a 6-year-old Sikh girl with a 4-year history of recurrent episodes of bloody diarrhoea, which had thrice previously led to hospitalisation. She was the sixth of eight children, and a younger sibling had also been admitted to hospital with similar complaints. Her mother reported she often saw the child eating sand and dirt. When admitted, J.K. was pale but otherwise normal. Her haemoglobin was 6 gm/100 ml, WBC 19,500 with 12% eosinophils. Faecal examination revealed many **Trichuris** eggs, a few **E. histolytica** cysts, and a light **Ascaris** infection. **Trichuris** egg counts in duplicate on three different pre-treatment specimens were 63 and 59*, 263 and 240, and 108 and 95 per smear. Results of stool culture for bacterial pathogens were negative.

The child was treated for five days with 375 mg. of thiabendazole twice daily and 1 cc. of Imferon (R) daily; folic acid and vitamin B complex were also given. No anti-amoebic agent was used. Her condition improved and she was discharged a week after beginning therapy, at which time the **Trichuris** egg count was reduced to eight and ten eggs per smear, and the **Ascaris** had disappeared. She was seen in follow-up at ten days and again at three weeks after discharge and was subjectively much better, with normal bowel movements. However, **Trichuris** egg counts had risen to 231 and 168 at three weeks and **E. histolytica** cysts were again found. Ten weeks after treatment, she had again developed bloody diarrhoea and was given a week's course of tetracycline for the amoebae noted previously. **Trichuris** egg counts were 2 and 24, and 22 and 19. She again became asymptomatic and remained so during three more months of follow-up.

Discussion

The clinical syndrome observed in these 26 children corresponds closely to that noted in various parts of the world by Getz (1945), Whittier **et al.** (1945), Jung and Beaver (1952), and Jung and Jelliffe (1952). The diarrhoea is distinctive for frequent passage of small amounts of stool commonly mixed with blood and mucus. The faecal volume is usually small, and straining at defecation often produces rectal prolapse. Although the worms are found throughout the large bowel in post-mortem studies, symptoms in heavy infections seem primarily due to a concentration of worms embedded in the mucosa of the rectum and lower colon, where they can easily be seen on proctoscopic examination.

This location of the parasite makes the use of egg counts to estimate parasite burden relatively unreliable. Dunn (1968) developed his "preserved direct smear" method (used in this study) expressly for field surveys but showed it to be directly comparable in precision to the Beaver (1950) saline direct smear method, which was used in clinical studies of trichuriasis by Jung and Beaver (1952). The utility of both these methods rests on the assumption that mixing of faecal material (including worm eggs) in the bowel is sufficient to make the egg count in a 1-to-5-mg. sample from a single stool an estimate of total egg production and thus of total worm burden. In clinical trichuriasis, not only are most symptom-producing worms so low in the bowel as to minimise mixing, but eggs tend to cluster in bits of mucus adhering to the bowel wall. A child with many worms in his rectum may thus pass several soft stools containing few eggs, then with additional straining (due to rectal irritation) expel large numbers of eggs mixed with mucus. Layrisse **et al.** (1967) compared egg counts from 3-day faecal collections with numbers of worms expelled after administration of stilbazium iodine and found a significant correlation of number of worms passed with total eggs passed in three days, but none with eggs per gram of faeces. However, 3-day stool collections are rarely practicable, and, as Jung and Beaver (1950) demonstrated, even in trichuriasis, direct smear egg counts provide a useful semiquantitative approximation of the intensity of infection.

In contrast to bacterial or viral infections, where the mere detection of a known pathogen is considered sufficient for clinical diagnosis, the presence of small numbers of intestinal nematodes rarely causes disease. The exceptions are the occasional wanderers, such as an **Ascaris** in the common duct, whose chance location does damage (Warren, 1970). The clinician therefore needs to have some idea of the intensity of the infection before he can judge whether the worm is, in fact, causing his patient's symptoms.

A World Health Organisation Expert Committee (1964) has suggested that anaemia only results from infection with **Necator** americanus (the hookworm commonly found in West Malaysia) when the egg count is greater than 6,600 eggs per gram of faeces for men, or 10,200 for women. With trichuriasis, estimates for the egg-count threshold associated with diarrhoea vary from 2,000 to 30,000 eggs per gram of faeces. Our arbitrary cut-off value for inclusion in this study (50 eggs per smear or approximately 15,000 eggs per gram) was based largely on the fact that

*This designates the count of each of two separate smears from a single specimen.

heavier counts are rarely found in asymptomatic children during field surveys. In our series and that of Jung and Beaver (1952), however, 70% of the children with diarrhoea or dysentery had egg counts greater than 100 eggs per smear (approximately 30,000 eggs per gram of faeces). Jung and Beaver estimated that this may represent as many as 1,000 mature worms (male and female), which is interestingly the same figure as the average derived by Layrisse **et al.** (1967) from egg and worm counts on 3-day fecal collections.

Layrisse **et al.** (1967) also studied the relationship of the **Trichuris** burden to anaemia and reported an average blood loss of about 0.005 ml. per worm per day, or approximately 0.25 ml./1,000 eggs per gram of faeces. They estimated that infections of more than 800 parasites (equivalent to approximately 24,000 eggs per gram of faeces or 80 eggs per 3-mg. direct smear) induce anaemia in children by unbalancing iron metabolism. But since egg counts give only a rough (though useful) approximation of worm burden, the counts on any given faecal specimen may be well below this level in an individual whose anaemia (or diarrhoea) is caused by a heavy **Trichuris** infection.

The most striking epidemiologic feature of trichuriasis in our series is its frequency in Sikh children. Probably the outstanding environmental difference between Sikhs and other Malaysians is their keeping of dairy cattle and use of milk products, often home-processed without pasteurisation. However, there is no apparent reason why this should influence the development of **Trichuris** infections, which occur by ingestion of faecally-contaminated soil where the eggs must have incubated for at least several weeks. Perhaps the keeping of cattle is associated with the shaded, moist soil conditions in which **Trichuris** eggs develop best. One of us (H.K.V.) has been particularly impressed with the prevalence of pica amongst Sikh children, and this may well be the major mode of infection.

Concomitant infections with **E. histolytica** occured in about 30-40% of cases in both our series and that of Jung and Beaver (1952). The possible interrelationship of helminth-amoeba-bacteria in producing diarrhoea and dysentery is poorly understood and deserves further study. We should stress, however, as do Jung and Beaver, that heavy **Trichuris** infections alone may produce dysentery and, when both amoebae and **Trichuris** are present, the worm may be at least as important a pathogen as the amoeba.

There is no widespread consensus on the best method of treating trichuriasis. Most drug trials (such as those of Huang and Brown, 1964; Franz **et al.**, 1965), are conducted with older children and adults with light infections, using "cure" (absence of eggs after therapy) as the criterion of efficacy. It is often not clear how to apply such results to treating symptomatic children in an endemic area, where the important goal is to reduce a heavy parasite burden to a level that is innocuous to the host. But its achievement is still more difficult to evaluate, because of the influence of nonspecific host factors and supportive measures (for example, correcting the anaemia or improving nutrition), the limited correspondence between egg counts and worm load, and wide variations in clinical response.

Jung and Beaver (1952) used 0.2% hexylresorcinol enemas (already described) and reported that, while no infections were "cured", all subjects became asymptomatic within 1-10 days. The difficulties with this method are that the buttocks must be protected with petroleum jelly to prevent chemical burn, the solution should be retained for 15-30 minutes (usually requiring attendance of a nurse or competent assistant), and repeat administration may be needed for full effect.

The most promising results reported for treating paediatric trichuriasis are for stilbazium (Monopar (R)) (Layrisse **et al.**, 1967), but reportedly there have been difficulties in achieving a commercially satisfactory formulation of this drug and it is not currently available. Dithiazinine (Telmid (R)) (Frye **et al.**, 1957) is still sometimes cited as the most effective trichuricide, but the high incidence of severe gastrointestinal side effects and the reports of a number of drug-induced deaths (Abadie and Samuels, 1965; Goodman and Gilman, 1965) make its routine use unjustified.

Several textbooks of medicine (Beeson and McDermott, 1967; Wintrobe **et al.**, 1970) now recommend thiabendazole (Mintezol (R)) as the drug of choice in a dosage of 25 mg./kg. twice daily for 2-5 days, but no studies evaluating its use in symptomatic paediatric cases seem to be available. Our efforts in this regard suggest that treatment for 2-5 days with thiabendazole alone is usually not adequate for children with heavy worm burdens that produce clinical illness. Although differences in outcome were not significant and each of several regimens of hexylresorcinol by enema and thiabendazole by mouth gave a spectrum of success and failure, the longer (5-day) course of thiabendazole along with a hexylresorcinol enema distinctly tended to give more impressive re-

sults than the other methods used. Whalen and colleagues (1970) report that prolonged courses of thiabendazole (3-4 weeks instead of the usual 3-5 days), which they found necessary to prevent relapses in infections with **Capillaria philippinensis**, also produced superior results in eradicating **Trichuris** infections. The mode of transmission of capillariasis, including the possibility of auto-infection, is presently uncertain and "eradication of infection" may therefore be therapeutically important. But with trichuriasis in an endemic area (where re-infection is likely soon after leaving the hospital), prolonging therapy to remove "every last worm" is of dubious merit. However, since thiabendazole is nontoxic and at the dosage prescribed (25 mg./kg. of body weight) appears to be well tolerated by children, it would seem reasonable to try longer courses of the drug, with or without hexylresorcinol by enema, in treating refractory cases.

The correction of the frequently concomitant iron-deficiency anaemia and malnutrition and the specific treatment for any co-existing amoebiasis or bacterial enteritis are also important in the management of the trichuriasis syndrome.

Summary

Twenty-six children, aged 2-7 years, admitted to the Kuala Lumpur General Hospital in early 1968 with chronic or recurrent diarrhoea and heavy **Trichuris trichiura** infections were studied. Epidemiologically, the group was notable for the disproportionate number of infections in the Sikh ethnic group. The illness was characterised by frequent bloody, mucoid stools and moderate to severe anaemia. About a third of the cases had co-existing amoebiasis, but amoebae did not appear to be more important than the **Trichuris** in producing symptoms.

Pending further trials and commercial availability of stilbazium, a combination of hexylresorcinol enemas and oral thiabendazole seems to be the most useful therapy available. However, the clinical course of the infection is highly variable, and treatment may need to be prolonged or repeated.

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An outbreak of Typhoid Fever in Malacca: Epidemiology and Aetiology

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Introduction

TYPHOID FEVER is endemic in Malacca. For several years past, an average of one notification per week has been received at the Health Office, Malacca (Health Officer, Malacca, 1965). The true incidence must be considerably higher, as doubtless many cases do not come to the notice of qualified practitioners.

This paper describes and discusses a small but explosive outbreak in a single village, affecting 31 persons – two of them fatally – in a population of 62.

General description of Solok Kampong Baru

Solok Kampong Baru is a small Malay settlement, eight miles from Malacca town (figure 1). At the time of the outbreak, there were 12 houses situated fairly close together on both sides of a cart-track. The population of the village was 32 males and 30 females. Most of the working adults were rubber tappers employed by neighbouring rubber estates. A few were smallholders with 2 – 4 acres of rubber land which they worked themselves. The income of the villagers was generally low. There was no electricity or piped water supply.

Fig 1
Location of Solok Kampong Baru.

Observations (i) Epidemiological aspects

There was a total of 31 cases (see Appendix I for details in support of the diagnosis and Appendix II for a discussion of other cases of typhoid fever occurring near Solok Kampong Baru at the time of the outbreak).

Date of onset of the cases: The date of onset of each case was obtained and checked wherever possible with other members of the household. Inspite of the care taken to ensure that the dates were as accurate as possible, there may well have been errors ranging from a few days to a week in view of the generally insidious onset of this disease.

The earliest date of onset recorded was 6 April with two cases and the last date, 28th April, with one case (figure 2). Bearing in mind the long incubation period of typhoid fever, this grouping of cases within about three weeks suggested a common source of infection.

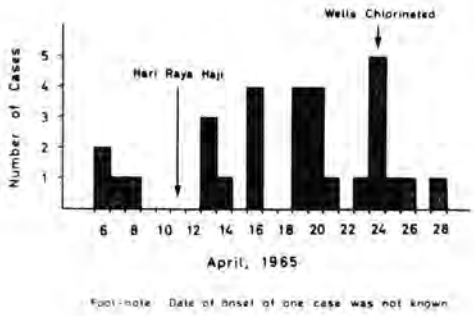

Fig 2
Number of cases of typhoid fever in Solok Kampong Baru by dates of onset.

Persons affected: The attack rate based on the village population was 50%. The proportion of males attacked was 17 out of 32, and females, 14 out of 30 (table I). There were cases in all age groups, except children below one year. In men over the age of 50 years, the proportion attacked – 2 out of 8 – was less than that of the other age groups. A similar decrease in attack rate was not observed among women above the age of 50. Since we are dealing with small numbers, the differences observed could have arisen by chance alone. The occupations of the cases include rubber tappers, students, a teacher, a gardener and a corporal (table II).

AGE (YEARS	MALE		FEMALE		TOTAL	
	PERSONS AT RISK	CASES	PERSONS AT RISK	CASES	PERSONS AT RISK	CASES
0 –	1	0	2	0	3	0
1 –	4	2	1	0	5	2
5 –	2	2	2	1	4	3
10 –	8	5	4	2	12	7
20 –	5	2	6	3	11	5
30 –	3	3	4	2	7	5
40 –	1	1	5	3	6	4
50 and over	8	2	6	3	14	5
TOTAL	32	17	30	14	62	31

TABLE I: Number of persons at risk and the number of typhoid cases by age and sex.

OCCUPATIONS	PERSONS AT RISK	CASES
RUBBER TAPPERS	26	13
STUDENTS	8	7
TEACHERS	1	1
GARDENERS	2	1
CORPORAL (T.A.)	1	1
TAXI-DRIVER	1	0
UNEMPLOYED AND CHILDREN	23	8
TOTAL	62	31

TABLE II: Number of persons at risk and the number of typhoid cases by occupation.

Households affected: Of the 12 households in Solok Kampong Baru, ten had one or more cases (figure 3). The early cases (6 – 8 April) occurred in Households 8 and 10, three in Household 8, and one in Household 10.

(ii) Environmental and Personal Factors

Water supply: 8 out of the 12 households had shallow earth wells close to their homes (figure 3). The villagers used the water from these wells mainly for washing and bathing purposes.

There was one "cement" well in the middle of the village. This well (figure 4) was lined with a prefabricated concrete ring of diameter 3½ feet and height 4 feet, the upper end of which projected 2½ feet above

ground level and served as the parapet for the well. Below the ring, there was no lining of any sort. The depth of the well was eight feet and the water level was usually six feet below ground level. There was no protective cover for the well, but there was a circular, concrete drainage apron 3½ feet wide in which there were large cracks. The exit drain leading from the apron was four feet long and usually water-logged.

Fig 3
Occurrence of cases by households, dates of onset and location of wells and latrines in Solok Kampong Baru in April 1965.

The rainfall for the two months preceding the outbreak was relatively low. However, the villagers stated that there was always water in the "cement" well. Each householder used his own rope and bucket to draw water from it. The women in the village often washed their clothes on the apron.

After an extensive inquiry, it was established that all the households in the village, except Households 11 and 12, drew water from the "cement" well for drinking and cooking purposes, before and during the outbreak. (Households 11 and 12 used water from their earth wells for drinking and cooking). It was reliably learnt that boiling of well water before drinking was not usually practised by the villagers except for making coffee and other hot drinks. It is significant that neither Household 11 nor 12 was affected during the outbreak.

Bacteriological examinations of the water from the "cement" and other wells of the village were not carried out. They were all chlorinated as soon as the outbreak was recognised on 24th April.

Disposal of excreta: The village had no sanitary latrines at the time of the outbreak. The methods of excreta disposal used were:

shallow pit	—	8 households
bush	—	3 households
stream	—	1 household

The sites for defaecation were situated more than 50 yards from the "cement" well (figure 3) and were so situated that it is unlikely that the well was polluted by surface or ground water from any of them. Some householders stated that the same bucket that was used for taking water to the site of defaecation for the performance of the anal toilet was sometimes used for drawing water from the "cement" well.

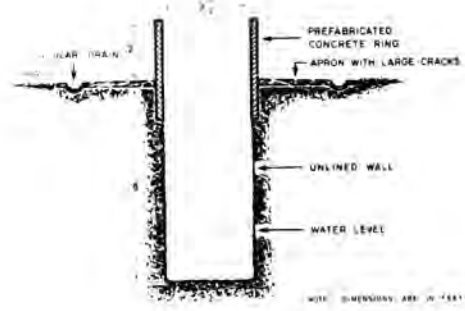

Fig 4
Cross-section of the "cement" wall.

Refuse disposal and flies: Household refuse was usually collected and burnt. Fly-breeding was observed in several of the pits and in the open ground (bush disposal area). However, flies were not numerous either inside or outside the houses. In view of the other evidence, it is unlikely that flies played any part in the transmission of typhoid fever in this outbreak.

Sources of food and sharing of food: Most of the households obtained their provisions from the shops in Bukit Katil Village or occasionally in Malacca town. Rice, sweetened condensed milk and fish were regularly taken. Uncooked food, such as salad and cut fruits, and bread were rarely taken. No fresh milk had been consumed recently.

An ice-cream hawker came irregularly to the village. Most of the villagers interviewed denied having bought ice-cream from him within six weeks prior to the outbreak. The ice-cream hawker was licensed by the Health Department and received T.A.B. vaccination yearly. No laboratory tests were done to exclude him as a typhoid carrier.

Inquiries were also directed towards the practice of sharing of food by a large number of villagers from indifferent households prior to the outbreak. The feast days in the village were Hari Raya Puasa

(2.2.1965) and Hari Raya Haji (11.4.1965). The earliest cases occurred too long after the first of these to be related to it, but those that occurred after 24 April could have been related to the second. The question arises whether the later cases were secondary to those occurring between 6 – 8 April. The latter would begin to excrete typhoid organisms from about the 10th day of their illness, i.e. from the 16 April onwards. Secondary cases would appear after an interval of about two weeks after this, i.e. around 30 April, or a few days earlier if the incubation period was shorter than usual. According to the foregoing reasoning, the only cases which could have been secondary to the primary cases in this outbreak were those with dates of onset 25, 26 and 28 April – one on each date.

Discussion of the aetiology

The outstanding features of this outbreak were:

(a) All the cases occurred within a period of 22 days.

(b) The attack rate was generally high among all groups.

This pattern indicates a common source of infection to which a large number of susceptible persons were exposed at the same time or within a short period of each other. Water and food supplies are the obvious suspects. There was no restaurant in the village, but it has already been noted that there was a communal sharing of food on the occasion of a festival (Hari Raya Haji), five days after the outbreak commenced, which might account for some of the later cases, but could not account for the earlier ones.

Unfortunately, no direct bacteriological evidence was obtained, but there is very strong circumstantial evidence that the water from the "cement" well was the source of infection:

(1) The use of water from the "cement" well for drinking and cooking purposes was a common factor among the affected households. No case occurred among the two households that did not use the water from the "cement" well.

(2) The well was unprotected against pollution.

(3) There were certain practices favourable both to the contamination of the well water and to the spread of infection.

(a) Water was drawn from the well by buckets that were used for other household purposes.

(b) The water was drunk unboiled.

(c) Soiled clothing was washed on the apro of the well.

If the conclusion that the well water was the common source of infection is correct, how was the well water contaminated in the first instance? We have to consider two possible sources:

(a) A case or carrier of typhoid fever among the permanent residents, or

(b) A case or carrier of typhoid fever who visited the village just prior to the outbreak.

Apparently, neither a case of typhoid fever nor a person with symptoms suggestive of typhoid fever occurred in the village within a month before the outbreak. Soon after it occurred, a stool survey was carried out on the unaffected population of the village. Three consecutive cultures at daily intervals of stool specimens from each villager were made. All were negative for salmonella organisms. However, this could not rule out the possibility of an intermittent carrier. Unfortunately, it was not feasible to carry out a survey of Vi agglutinin which has considerable value in detecting carriers of S. Typhi (Cruickshank, 1965). There is the possibility, although this is rather remote, that one of the cases was a carrier prior to the outbreak, but had since suffered a relapse of the disease.

On further inquiry, the villagers could not recall any visitor with symptoms suggestive of typhoid fever present in the village prior to the outbreak. However, the well could have been contaminated by a visitor who was a carrier, through a bucket used by him when cleaning after defaecation, or taken by a second party to a site in the bush where the carrier had recently defaecated, and used soon after for drawing water from the "cement" well. This is the most likely explanation compatible with the evidence available.

Summary

The epidemiological aspects of an outbreak of typhoid fever in Solok Kampong Baru, Malacca, are described. The outbreak was characterised by an attack rate of 50% among a susceptible village population within a period of 22 days. The only common aetiological factor found was the use of water, unboiled, from a "cement" well for drinking and cooking purposes by all the affected households, whereas two households which did not use this water escaped. It is concluded that this was a water-borne outbreak from a single source – a contaminated well. The source of contamination was not ascertained, but is considered most likely to have been an unidentified carrier temporarily resident in the village.

Acknowledgement

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Appendix I

Blood and/or stool cultures for Salmonella organisms as well as the Widal agglutination test were done at the General Hospital, Malacca, on every fever case from the village. Unfortunately, in some cases, the Widal agglutination test was not repeated after treatment with chloramphanicol, and the patients' condition improved. The breakdown of the cases was:

14 had positive cultures for S. Typhi.
4 others showed a rising titre for the Widal agglutination test.
13 were clinical typhoid cases.
TOTAL 31 cases

Appendix II

Cases of Typhoid Fever occurring near Solok Kampong Baru at the time of the outbreak:

(a) Four members of a family of seven in Pengkalan Badak village, about 1½ miles from Solok Kampong Baru, were diagnosed as typhoid cases at the time of the outbreak. The date of onset of one of the cases was 8.4.65 and of the three other cases was 14.4.65. They were all related to the members of Household No. 10 (an affected household) in Solok Kampong Baru and used to take cold drinks and food there two to three times a week before and during the outbreak.

(b) In Kampong Bukit Duyong, about two miles from Solok Kampong Baru, two households were affected, with a total of six typhoid cases (dates of onset from 8.4.65 to 14.4.65). The members of these two households had visited Household No. 6 (an affected household) in Solok Kampong Baru on four occasions before the outbreak.

On further inquiry, it appeared that the affected persons did not take any ice-cream within a month prior to their onset of symptoms. The common factor found was the partaking of drinks and food in the affected households in Solok Kampong Baru. Therefore, the source of infection for these cases was very likely to be the same as those in Solok Kampong Baru.

Experiences of a rural obstetric Flying Squad service

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Introduction

A "FLYING SQUAD" service is a feature of most modern maternity hospitals. This service is essential in any area where domiciliary deliveries take place and its aim is to bring resuscitative measures to the home of the shocked patient prior to transporting her to the hospital.

In Trengganu, an overwhelming majority of deliveries – 90% – occur at home, and of these, 65% are supervised only by an untrained kampong "bidan". Cases of complications and shock are therefore high and produce high maternal mortality rates. In this environment, an effective flying squad service is vital in reducing maternal mortality.

Inspite of many handicaps, a flying squad service has been operating from the maternity unit of this hospital for a number of years. The maternity unit, situated in Kuala Trengganu, serves the immediate needs of the population of a huge area surrounding Kuala Trengganu. It is also the referral hospital for the whole state of Trengganu.

The running and experiences of the squad are reviewed here and an analysis is made of the calls attended during 1969.

Transportation

The squad makes use of the ordinary hospital ambulance and this arrangement has been found to be quite satisfactory.

Staffing

Due to the shortage of medical officers, the service is manned entirely by nursing staff. The maternity staff nurse is the backbone of the service and generally she goes out alone, single-handed. If the pressure of work in the ward and the labour room is light, a staff midwife goes along as well. However, this is the exception rather than the rule. Besides the ambulance driver, an attendant also goes along.

Equipment

Only simple equipment and drugs are taken and no operative or anaesthetic equipment is included. A delivery kit and the following drugs are included:- ergometrine, pethidine, morphine, paraldehyde and methedrine. Intravenous fluids taken are:- 'Haemaccel' two pints, normal saline two pints and 5% dextrose one pint. Due to the scarcity of blood, no blood is taken by the squad.

Area covered

The service covers a wide area indeed, answering calls from a radius of over 30 miles from Kuala Trenggnu itself. This area includes the districts of Kuala Trengganu, Marang and Ulu Trengganu.

Mode of action

The call for the flying squad is taken at the maternity unit by the staff nurse in charge of the ward who

gets all the particulars. On arrival at the home, she undertakes emergency resuscitation and when the patient is fit brings her back to hospital. The sole aim of our squad is resuscitation, and no operative procedure of any sort is performed at home.

All the maternity staff nurses are taught the principles of emergency resuscitation including the giving of intravenous fluids. The details of our management of the various types of cases are given later when discussing the cases themselves.

Analysis of cases seen during 1969

Total number of cases	=	26
Postpartum haemorrhage	=	12
Antepartum haemorrhage	=	4
Eclampsia	=	5
Prolonged labour	=	5
Maternal Deaths	=	nil

Postpartum haemorrhage

This group as expected constituted the largest number of calls on the flying squad. Eleven out of the 12 cases were severely shocked on arrival at home. All the shocked patients were successfully resuscitated in the home prior to the journey to the hospital. The details of the 12 cases are given in Table 1.

The mainstay of resuscitation of shock from blood loss in the home has been the rapid transfusion of two pints of "Haemaccel". This synthetic plasma volume expander has, in our experience proved extremely effective in countering shock. In spite of meeting with severe cases of blood loss and the time delay involved in reaching the patient, every case was successfully resuscitated and made fit for a long and often "bumpy" journey as well to the hospital. As a temporary restorer of blood volume, Haemaccel has been found to be excellent and the squad has not been handicapped by the lack of blood. Of course, once in hospital, suitably crossmatched blood is given as soon as it is available. Manual removal of placenta was undertaken only in hospital.

Antepartum haemorrhage

There were four cases and their details are given in Table 2.

Case	Diagnosis	Condition at home	Resuscitation	Treatment in hospital
1	Ret. P. & PPH	shocked	Haemaccel	MRP & Blood
2	"	"	"	"
3	PPH	"	"	Blood
4	PPH	not shocked	Dextrose	Fluids
5	Ret. P. & PPH	shocked	Haemaccel	MRP & Blood
6	"	"	"	"
7	"	"	"	"
8	"	"	"	"
9	"	"	"	"
10	"	"	"	"
11	"	"	"	"
12	"	"	"	"

Table 1 – Cases of PPH

Case	Gravida	Diagnosis	Resuscitation	Treatment in Hospital
1	8	Accidental haemorrhage	Haemaccel	ARM – N. Del.
2	15	Placenta Praevia	Haemaccel	LSCS
3	10	Accidental haemorrhage	"	ARM – N. Del.
4	2	APH ? cause	Dextrose	ARM – N. Del.

Table 2 – Cases of A.P.H.

Case	Gravida	AN.Care	No. of Fits at home	Fits in hospital	Treatment
1	2	nil	3	nil	ARM – N.Del.
2	5	nil	7	nil	ARM – N.Del.
3	6	yes	4	nil	ARM – N.Del. Stillbirth
4	9	nil	11	nil	ARM – N.Del.
5	1	yes	5	nil	ARM – N.Del.

Table 3 – Cases of Eclampsia.

Case	Gravida	Duration of labour	Diagnosis	Treatment
1	6	3 days	Occipito-Posterior	Forceps Del.
2	1	4 days	Disproportion	LSCS
3	9	3 days	Breech. IUD	Extraction
4	7	3 days	Obstructed labour	LSCS
5	4	2 days	Uterine Inertia	Forceps Del.

Table 4 – Cases of Prolonged Labour.

Three cases were shocked and were resuscitated as described earlier. The fourth case was sedated with pethidine, an intravenous drip set up and the patient brought to hospital.

Eclampsia

The five cases of eclampsia were managed as follows: At home, an injection of 10 ml of paraldehyde was given intramuscularly. This was found to be very effective in preventing further fits during the journey to hospital. Paraldehyde – a specific anti-convulsant – was chosen as it is readily available, rapidly effective and can be administered easily by nursing staff with a wide margin of safety. Further treatment in hospital included the setting up of a lytic cocktail and the induction of labour forthwith by surgical amniotomy. The details of the cases are shown in the table below.

Prolonged labour

A total of five cases were seen. In each case, after sedation with pethidine and the setting up of a dextrose infusion, the patients were brought to hospital. The details of the diagnosis and management are given in the table below.

Discussion

The aim of a flying squad service is to bring resuscitative measures to the home of the patient and to make her fit for the journey to hospital where definitive treatment can be undertaken in safety. It is well recognised that shock is immensely aggravated by movement and to subject a shocked patient to a journey is tantamount to killing her. The sole aim of the squad should be to fulfil this role of resuscitation. Stabler (1947) had, however, visualised a squad capable of performing a Caesarean hysterectomy on the kitchen table if necessary. This view certainly has no place in modern medicine.

Our flying squad is unique in two ways. One, it is manned entirely by nursing staff, and two, we carry no blood. This state of affairs is, of course, not from choice but due to the very limited staff we have and the scarcity of easily available blood. Sophisticated centres, whose flying squad are lavishly staffed and equipped, might consider our squad to be ineffective. However, our figures show otherwise. Every case on which the squad was called out survived and every case of shock encountered in the home (14 in the series) was resuscitated and brought safely to hospital. In all these cases, the squad was responsible for the prevention of a mortality. Further, it also shows that nursing staff with proper guidance from doctors can more than adequately undertake resuscitative measures.

There are many difficulties which this service experiences. One is, of course, the great distances co-

vered over difficult roads. Often at least one to two hours are needed before the patient can be reached. Also, quite often, the house is a mile or two off the main road and the staff have to walk in the last part of the journey. Finding the house can be a problem as many of the kampong houses are without numbers. Trying to resuscitate in crammed conditions without proper lighting adds to the diffficulties.

A major problem after resuscitation is trying to persuade the patient to come to hospital for further treatment. Often, there is a great reluctance to be admitted to hospital and much valuable time is wasted before the patient finally agrees to come in, after consulting with all the relatives. A host of relatives usually follows the patient back so that carrying the patient from the house to the ambulance on the main road poses no problem as there are many willing helpers.

In spite of the difficulties, the nursing staff are most enthusiastic and dedicated to this service, given proper guidance and constant encouragement and support by the doctor. The results speak well for their efficiency and skill and there is no doubt that many maternal lives are being saved by this service in this state. Further, the availability of a flying squad service gives confidence to the midwives working alone in remote areas as they can readily call on the service in case of need. No doubt, in due course with improved facilities, our squad will be manned by doctors as well and blood also will be available. However, the squad in its present form has, I feel, more than justified its existence.

Conclusion

I think our experience shows that it is not necessary to have sophisticated or lavish equipment, vehicles or staff to run an efficient and worthwhile flying squad service. In spite of limited facilities and many difficulties, our squad is playing a vital role in reducing maternal mortality. I would like to pay particular tribute and credit to the nursing staff of the maternity unit of this hospital without whose dedication and skill it would be impossible to run this service.

Acknowledgement

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Depressive illness in private practice

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AN EXTENSIVE LITERATURE exists on depressive illness in various developing countries of the world (Yap, 1965; Pfeiffer, 1962; Asuni, 1962; Lambo, 1956 & 1960; Tooth, 1950). However, as far as can be ascertained, no clinical study has been published on depressive illness in Singapore or its neighbouring country, Malaysia.

Depression, as stated by Fry, is a "non-hospital disease" and only a small proportion of patients find their way to a mental hospital. This is particularly true of the mild forms of depression which are mostly seen and treated in private practice. A study of such an illness seen in private practice will thus give a more accurate impression of depression in the community as the hospital impression may often be distorted.

The use of the term "depression" is often not defined. Most normal people experience fleeting periods in which their mood is below its normal acceptable level (Slater & Roth, 1969). Depression, as a disease entity, may only be said to have set in when these periods become protracted and mood change is intense. Classification of depressive illness is a problem which is still being argued. No attempt is made in this study to place patients into categories such as: Reactive, Endogenous and Involutional. Depression secondary to schizophrenia is excluded.

This paper is done with the hope of bringing to light the pattern and characteristics of depressive illness in a multi-racial and multi-cultural society with a predominant Chinese population.

Method of study

This is a retrospective study of the first 100 patients diagnosed as suffering from "depression" seen and treated by the author in a private psychiatric practice in Singapore. A previous study done by the author of patients suffering from schizophrenia enables a compairson to be made between patients with depression and patients with schizophrenia.

Characteristics of Patients studied

Sex distribution

Table 1

Sex distribution of depressive patients compared with schizophrenic patients and practice population.

Type of patients	No. of male	No. of female	Total
Depressive patients	33	67100	
Schizophrenic patients	55	45	100
Practice population*	272 (54.4%)	228 (45.6%)	500 (100%)

*The practice population consists of the first 500 patients seen and treated at the private psychiatric clinic for two years (1968 & 1969).

Of the patients with depression, there is an excess of women over men. This sex ratio of twice as many female to male is, however, not found among schizophrenic patients.

Age of onset of illness

Table 2

A comparison of age of onset of depressive and schizophrenic illness.

Age of onset of illness	Depressive illness		Total No.	
	No. of male	No. of female	Depressive patients	Schizophrenic patients
13–14	–	–	–	1
15–19	–	6	6	29
20–29	10	24	34	41
30–39	7	25	32	22
40–49	10	8	18	6
over 50	6	4	10	1
Total	33	67	100	100

The incidence of depression and schizophrenia arising from different age groups is shown in table 2. It can be observed that in depressive illness, the number of female patients reaches a sharp peak in the age range of 20–29. For male depressive patients, there is no peak.

Comparing the age of onset of the two major functional mental disorders, it is found that 71 schizophrenic but only 40 depressive patients had their onset of illness in age range of 13–29. This would indicate that schizophrenia begins at an earlier age than depressive illness.

Marital status

Table 3

A breakdown of marital status of depressive and schizophrenic patients compared with practice population.

Marital status	Depressive patients	Schizophrenic patients	Practice population
Married	73	39	263 (52.6%)
Single	22	57	223 (44.6%)
Widowed	3	3	10 (2.0%)
Divorced	2	1	2 (0.4%)
Unknown	–	–	2 (0.4%)
Total	100	100	500 (100%)

There is a higher incidence of depression in married than single patients – 73 are married and 22 are single. In the case of patients with schizophrenia, the position is reversed – 57 are single and 39 are married.

Social class

Table 4

Social class of depressive patients compared with schizophrenic patients.

Social class	Occupation	No. of depressive patients	No. of schizophrenic patients
1	Managerial, professional	47	20
2	Semi-managerial, semi-professional	7	13
3	Skilled worker, clerical	36	30
4	Semi-skilled worker	5	19
5	Unskilled	5	16
6	Unemployed	–	2
Total		100	100

These two groups of patients are assigned into six social classes, according to occupations of the head of the family. As expected, the case materials obtained from a specialist private practice are highly selective, especially with regard to social class. However, this being a comparison, the result obtained should not be affected by such a selective sampling. From table 4, 90 depressive patients but only 63 schizophrenic patients are found in social class 1, 2 and 3. Thus, the social class of depressive patients is found to be higher than that of the schizophrenic patients.

Educational level

Table 5

A comparison of education level of depressive patients and schizophrenic patients.

Category	Educational level	No. of depressive patients	No. of schizophrenic patients
1	University		11
2	Pre-U 1 & 2, college	14	19
3	Secondary 1–4	45	37
4	Primary 1–6	23	27
5	No formal education	7	12
	Total	100	100

The patients are categorised in table 5 according to their educational level. It is observed that there is not much difference in the educational level of the two groups of patients.

Ethnic group

Table 6

A breakdown of the ethnic grouping of depressive patients compared with schizophrenic patients and with the mid-1968 Singapore population.

Ethnic group	Depressive patients	Schizophrenic patients	Singapore population %
Chinese	68	80	74.2
Malay	1	3	14.6
Indian	5	10	8.1
Caucasian	19	5	
Jew	3	–	3.1
Eurasian	3	1	
Others	1	1	
Total	100	100	100%

Ethnic grouping shows an over-presentation of the Caucasian, Jewish and Eurasian groups. Malay in this series is under-represented. It is felt that a further study comparing the patients of the major racial groups in Singapore suffering from depression might provide some insight into inter-cultural differences as well as the dynamics of depressive illness.

Symptoms in depressive illness

When the symptoms of the patients are considered, disturbance in sleep is found to be the most frequent symptom, being present in 78 of the patients and ideas of suicide is next, being present in 72 patients. The other symptoms in order of frequency are:

loss of appetite	55
tension	53
crying	52
excessive worrying	47
irritability	44
feeling of apprehension	44
restlessness	40
loss of interest	30
poor concentration	18
suspiciousness	17
retardation	16
morning depression	12
guilt-feelings	9
sweating	7
dryness of mouth	7
black magic	6
paranoid ideas	4
blaming others	3
jealousy	3

Physical symptoms, such as headache, giddiness, chest pain, difficulty in breathing, epigastric pain, palpitations, constipation and lack of energy are fairly frequent symptoms. In 26 cases, they form an important part of the illness. These symptoms can readily suggest physical disease, especially if the depressive mood is not promiment and if the disorder manifests mainly in hypochondriacal complaints. Such a variety of depressive reaction is termed by some authors as "masked form" of depression (Maslow & Mittelmann, 1951; Hordern, Burt and Holt, 1965). Both Lambo and Field pointed out that depression might be missed because of a veneer of psychosomatic symptoms. As mentioned by Yap, "it is not rare that depressive illness is being masked often by hypochondriacal (psychosomatic) and confusional symptoms".

In the analysis of the symptomatology of depressive patients, the absence of delusion of sin as a symptom is interesting (Yap, 1958 and Lin, 1953). Of the nine patients with guilt feelings, six of them are Caucasians. The severity of the self-reproach in the three Chinese patients is also less severe than that of the Caucasian patients (Murphy, Wittkower and Chance, 1964).

Suicidal attempts

Table 7

A breakdown of age, sex and marital distribution of suicidal patients in depression.

Age of patients	Male	Female		
		Single	Married	Divorced
13–19	–	2	–	–
20–29	2	1	4	1
30–39	2	1	8	–
40–49	3	–	3	–
over 50	–	–	1	–
Total	7	4	16	1

Depressive illness is the mental disorder with the highest suicidal risk. In this survey, 28 patients had made previous attempts at suicide. From the table, a female:male ratio of 3:1 is found. It is noteworthy that over 75% of both male and female patients are under the age of 40. The youngest female is 18. For married women, the peak age-group is 30–39, which appears to be a turbulent period of their life. There are only seven male patients and they are all married.

Table 8

Methods of attempted suicide.

Methods	Male	Female
Barbiturate, hypnotics, tranquillisers and other drugs	4	17
Lysol	–	1
Hanging	1	4
Cutting instruments	2	1
Drowning	1	2
Running at oncoming cars	–	1
Repeated attempts	3	8

Table 8 shows the variety of methods employed as well as their frequency. In both sexes, the use of drugs predominated and accounted for 61% of the methods used. Seven patients had made repeated attempts at suicide. There are three women who made three attempts and one woman who used multiple methods.

Suicide

In this series, to the author's knowledge, there are two suicides. Because of the small number of suicides, the impression obtained about suicide in depressive illness in this study may be inaccurate. Further study is needed to find out about suicide in depression and what proportion of depressive patients commit suicide. According to Etthinger and Flordh, attempted suicides were eight to ten times more frequent than actual suicides. Stengel stated that of surveys in the United Kingdom and in the United States, the number of suicidal attempts was six to eight times that of the suicides, at least in urban communities.

Precipitating factors

In searching for precipitating factors for depressive illness, one faces problems: firstly, whether the stress is a result of the illness rather than a cause of it; and secondly, how much importance the stress plays in patients with personality disorder, especially where the personality and illness emerge imperceptibly the one into the other (Forrest, 1965). However, inspite of such problems, an attempt is being made to list the environmental and medical data which may be considered as significant precipitating stresses in the hundred patients studied.

Social factors

Marital discord	46
Family discord	23
Financial stresses	18
Unhappy with job	17
Domestic problems	9
Rejection by boy/girl friend	6
Business problems	5
Loneliness	4
Separation	4
Unemployment	3
Rejection by family	1

Medical factors

Alcoholism	11
Post-operative	4
Menopause	3
Post-partum	1
Influenza – post	1
Lesbianism	1
Drug – reserpine	1
Post cerebro-vascular accident	2

In the analysis of the precipitating factors, it is often found that it is not a single but several factors which seem to add up and spell mental disorder for the individual.

Discussion

The most striking finding in this study is that in depressive illness, the female predominates. A similar finding has been reported in other studies in different parts of the world for depressive patients seen in private practice (Porter, 1970; Bazzoui, 1970; Watts, 1964). The sex ratio of female:male of 2:1 is in agreement with reports for Affective Reactions obtained from private and general hospitals in the United States (Freeman, Kaplan and Kaplan, 1967). It is again noteworthy that such a ratio is also found by Kellner for neurosis in general practice and Taylor in medical outpatients for both anxiety state and depression.

In this survey, it is found that there is an apparent tendency for the first attack of depressive female patients to occur at the age range of 20–39. Forty of the 49 patients are married and they form an interesting 'housewife group' (Taylor, 1969). In this group, marital and domestic problems are important factors which add up to produce mental disturbance. Yap stated that there is a tendency for the first attack to occur more frequently at an early age in women. The result of this study has shown that six female and no male patients have their onset of illness at the age range of 15–19. In this group of young patients, rejection by family and boy friend, and unhappiness in job are significant precipitating factors for their illness.

In depressive illness, married persons are particularly at risk (Porter, 1970). In schizophrenia, the reverse is the case. This pattern of marital status for affective disorder and other functional psychosis have been repeatedly observed in studies in the United States, Britain and Norway (Faris and Durham, 1959). The social class of depressive patients is also much higher than that of schizophrenic patients. In accordance with reports from other countries, schizophrenics tend to occur mostly in the lower class while depressive illness occupies the upper social class (Myre Sim, 1968; Rawnsley, 1968).

An over-representation of Caucasian patients, especially Americans in such a selected sample, is not unexpected. Of these 19 patients, 15 are women. The Malays are represented by only one patient.

In depressive illness, ideas of suicide is a common symptom and, as shown in this survey, the risk of attempted suicide and suicide is very high. Attempted suicide is more common among the women and the peak level of incidence in women occurs in the age range of 30–39, which is slightly older than that obtained by Tsoi's study of "Attempted suicide in General Hospital".

Summary

The characteristics and clinical features of 100 patients suffering from depressive illness of various degree is presented. In this study, a comparison is also made of these 100 depressive patients with 100 schizophrenic patients studied by the author in a previous paper. The differences between the two groups regarding their sex distribution, age of onset of illness, maritial status, social and educational levels are analysed and discussed.

In the analysis of the symptomatology of the depressive patients, an absence of delusion of sin and rarity of severe guilt feelings among the Chinese population of this sample is interesting.

Depression is a common illness in the community and it may be presented in a "masked form" and be missed because of a veneer of hypochondriacal (psychosomatic) and confusional symptoms. The risk of attempted suicide and suicide, however, is great.

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A radiological appraisal of the paravertebral shadow in diseases of the spine and mediastinum

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Introduction

THE PARAVERTEBRAL SHADOW is that area bounded medially by the lateral border of the thoracic vertebrae and laterally by the paraspinal line. The left paraspinal line is frequently observed in frontal radiographs of the dorsal spine as a thin vertical line running parallel to the vertebral column. It represents the reflection of the posterior mediastinal pleura between the vertebral column and the descending aorta (fig. 1). The fact that this portion of the mediastinal pleura is tangential to the incident rays in frontal views of the chest and dorsal spine makes it visible as a sharply defined line shadow, clearly contrasted against the neighbouring lung (fig. 2). Its radiological anatomy has been discussed by Lachman (1942), Brailsford (1943), Billing (1946) and Knutsson (1955). Because of a slight shift of the right mediastinal pleura across the midline at its reflection in the posterior mediastinum, the right paraspinal line is prevertebral in situation (Cimmine and Snead 1965) and is therefore less well defined.

In a survey of 54 normal subjects, Doyle, Read and Evans (1961) found the width of the left paravertebral shadow to be less than 6 mm. in nearly all their patients below 45 years of age. Above the age of 45, the width of this shadow varied from 0 – 19 mm. They postulated that the increase in width of the shadow with advancing age was most likely due to the presence of marginal oesteophytes which displace the mediastinal pleura laterally (fig. 3). Another likely factor was the dilatation and elongation of the descending thoracic aorta (fig. 4).

Because of the intimate relationship of the paravertebral shadow to the spinal column, sympathetic chains, descending aorta azygos and hemiazygos venous systems and lung parenchyma, any pathological change in these structures invariably causes an alteration in position, shape, density and width of the paravertebral shadow. In this paper, we will discuss some conditions affecting the dorsal spine and mediastinum with particular reference to the paravertebral shadow.

Case 1

R.A., a 60-year-old male Indian, presented with a history of progressive abdominal swelling for two years. He was a known alcoholic for 20 years. Examination disclosed gross ascites with pitting oedema of both legs. The neck veins were engorged and prominent tortuous collateral veins were seen extending from neck to groin on either side. The direction of blood flow was downwards. There was evidence of cardiac enlargement and basal crepitations were heard in the left chest. The clinical diagnosis was liver cirrhosis with superior vena caval obstruction.

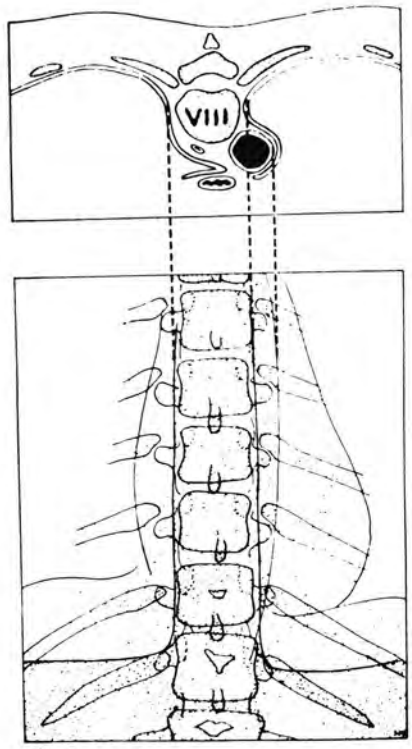


Fig. 1

Upper: Cross section through the posterior mediastinum at the level of the eighth thoracic vertebra. Lower: Diagram taken from a roentgenogram depicting the posterior portions of the visceral and/or parietal pleura as lines along the vertebral column. Dotted lines indicate anatomical substrates of pleural lines and aortic lines in cross section. (From Lachman, E., in Anat. Rec., vol. 83, 1942.)

The chest X-ray showed mild left ventricular enlargement. The lung fields were clear apart from a moderate left basal effusion. The superior mediastinum was widened and a penetrated view revealed widening of the left paravertebral shadow. A superior venocavogram confirmed the clinical diagnosis (fig. 5). There were extensive lateral thoracic and intercostal collaterals draining in the direction of the inferior vena cava and a rather prominent azygous vein. The latter, together with the prominent left paravertebral shadow, accounted for the widening of the mediastinum. The etiology of the superior vena caval obstruction was thought to be due to an idiopathic thrombosis although a fibrosing mediastinitis was also considered.

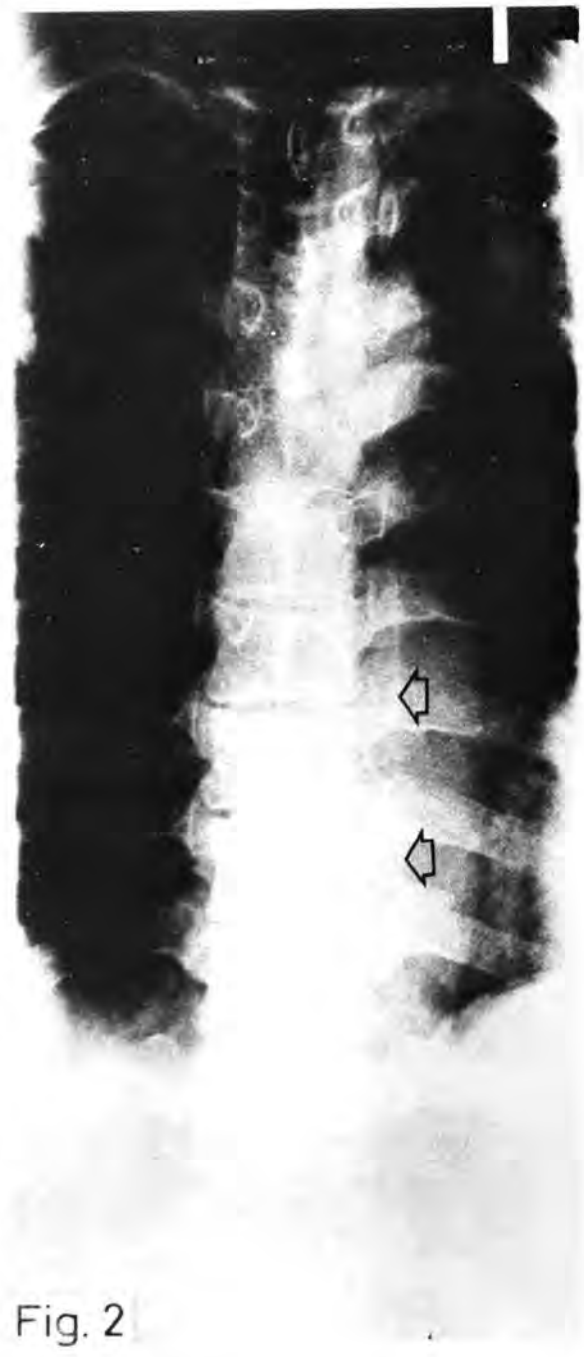


Fig. 2

Normal appearance of the left paraspinal line (arrows).

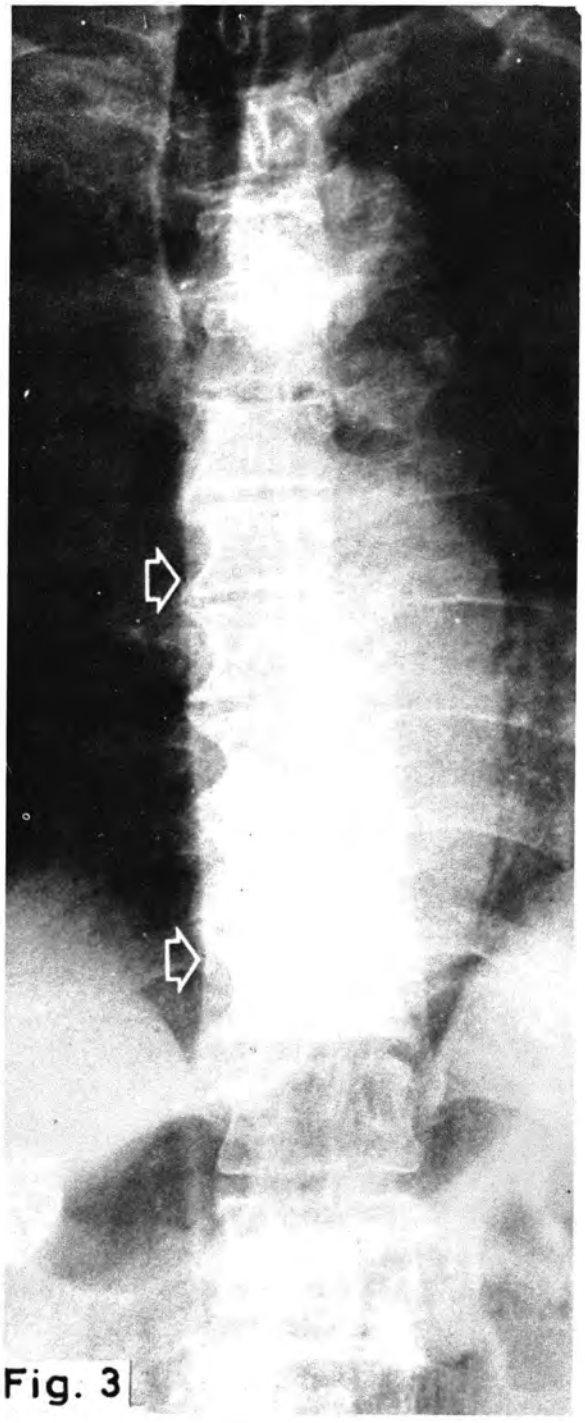


Fig. 3

Marked osteophytic lipping in the lower dorsal spine has resulted in lateral displacement of the right paraspinal line (arrows).

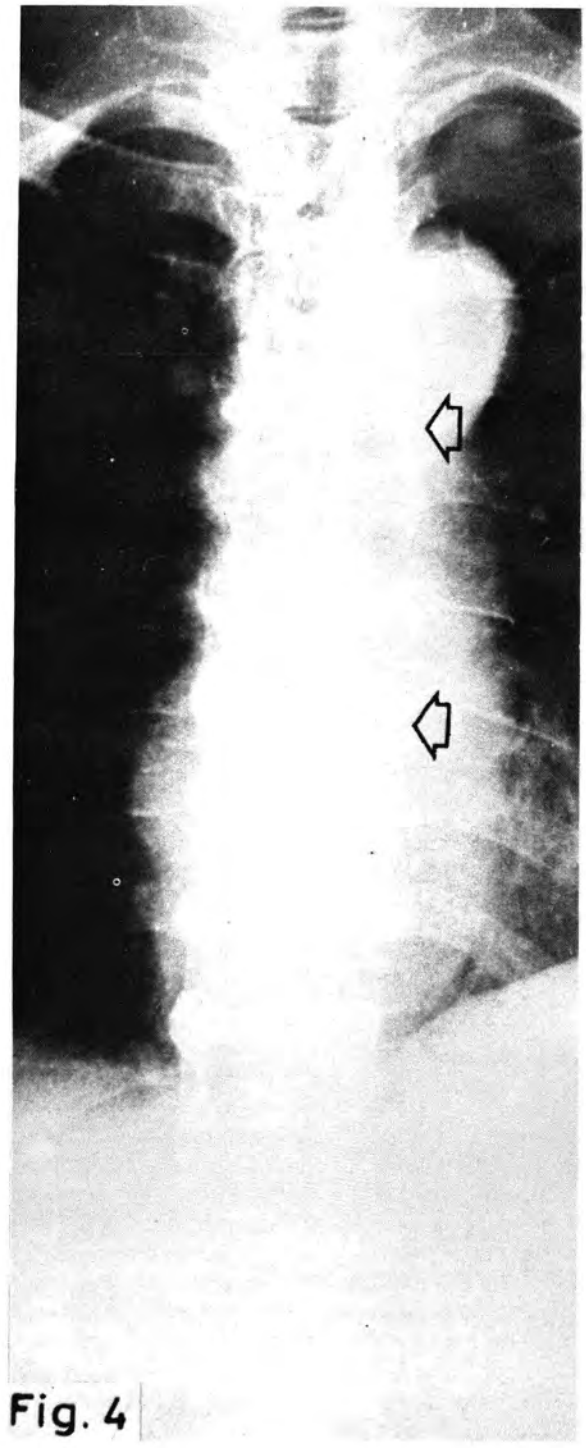
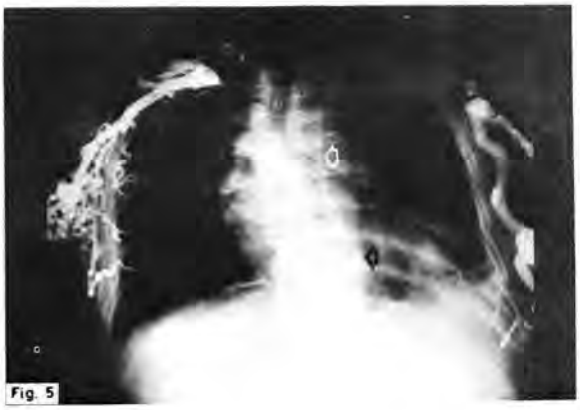


Fig. 4

An unfolded aorta has caused widening of the left paravertebral shadow (arrows).



Superior venocavogram shows obstruction of the superior vena cava and subclavian veins. Notice the huge lateral thoracic veins. Widening of the left paravertebral shadow is shown (arrows), most probably the result of a left mediastinal effusion associated with the left pleural effusion.

Comments

The width of the left paravertebral shadow is, on the whole, increased in patients with portal hypertension. This widening is believed by some to be due to dilatation of the left hemiazygous vein which lies just posterior to the descending aorta. Doyle et al, however, performed post-mortem intraosseous costal venograms on cirrhotic patients with portal hypertension and demonstrated that the opacified left hemiazygous vein did not consistently conform to the lateral margin of the left paravertebral shadow on the radiograph. They concluded that the widened left paravertebral shadow could be a summation of pathological changes inherent in the disease itself, namely excessive fluid retention in the mediastinum and dilatation of the left hemiazygous vein. An increase in width of the left paravertebral shadow, therefore, does not invariably mean a dilated hemiazygous vein. In the case presented, the widening could most likely be explained by the presence of a mediastinal effusion since a moderate collection of pleural fluid was obviously shown at the time of the venogram.

Case 2

C.K.L., a 26-year-old male Chinese, sustained a gun-shot wound in his upper chest posteriorly. The bullet penetrated his back in the region of the left scapula and lodged in the upper dorsal spine. Subsequent to this, he became paraplegic. X-ray examination of the spine confirmed the presence of a bullet in the body of D4. There was obvious paravertebral widening, notably in the superior mediastinum. The swelling had a well defined convex right margin. An area of consolidation was also noted in the left upper zone, due probably to lung contusion. The tracheal shadow appeared normal. An emergency laminectomy was performed to remove the bullet. Extravasated blood and exudates were noted in the paravertebral region and these were thought to be due to the result of tearing of small vessels. Post-operatively, the patient made a gradual recovery. The paravertebral shadow decreased rapidly in size and was no longer apparent two weeks after the operation.

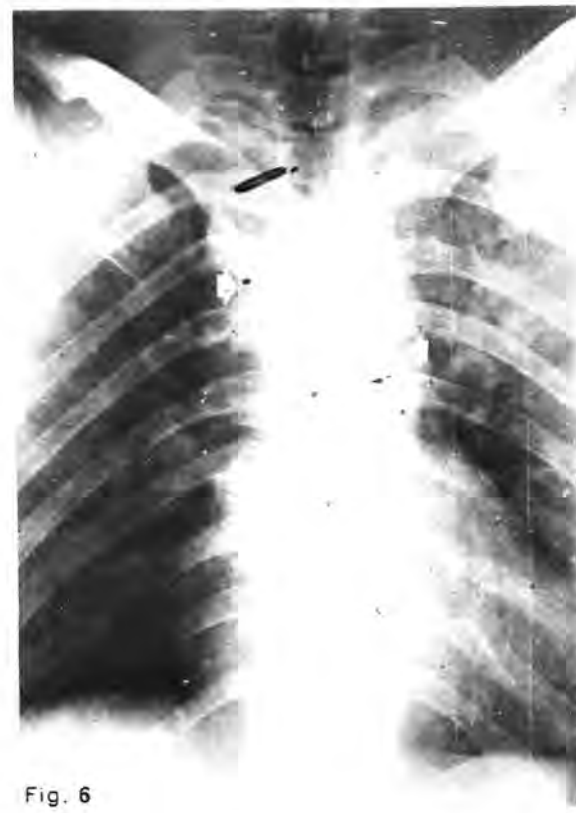


Fig. 6

Haemomediastinum has resulted in widening of the right superior mediastinum and the left paravertebral shadow (arrows). Notice the bullet in the body of D4.

Comments

In this case, the injury was essentially confined to the vertebral body of D4 and the muscular tissues covering the back. Hence, the mediastinal widening

was actually a reflection of the reactive changes in the pre and paravertebral soft tissues. This abnormal radiological appearance was no longer apparent soon after haemostasis had been secured. The fact that the tracheal shadow in this patient was noted to be straight implied that no significant pressure was exerted on the mediastinal structures and thus a good prognosis.

True traumatic haemomediastinum, particularly the result of aortic rupture, carries with it a grave prognosis. Sandor (1967), reviewing a series of 16 cases, noted that four patients succumbed ultimately as a result of shock, severe mediastinal compression and exsanguination, despite a correct diagnosis in every case. Initially, there was marked bilateral widening of the superior mediastinum with well defined convex outer margins. If the patients survived for more than 72 hours, there was a tendency for the mediastinal shadow to be less well defined. A decrease in size was noted as a result of dispersion and absorption of the haematoma. The dimension of the haematoma in some cases was enormous, extending from the clavicular level down to the leaves of the diaphragm. One notable feature in the series was that of deviation of the supracarinal portion of the trachea towards the right. This invariably meant increased pressure within the mediastinum from partial or complete traumatic rupture of the aorta. Daily portable radiography of the chest, therefore, is mandatory in assessing the progress of the mediastinal and paravertebral shadows and the position of the tracheal shadow in relation to the mediastinal mass.

Case 3

T.S.T. was a 15-year-old male Chinese who sustained a fracture of his right femur in April 1970. He was seen a month later and was discovered to have a warm tender swelling at the site of injury. X-ray of the right femur showed a pathological fracture with a "sun-ray" type of periosteal reaction and evidence of soft tissue invasion (fig. 7). A needle biopsy of the mass revealed the histopathology to be consistent with Ewing's sarcoma. Chest X-ray was normal but a repeat examination on 29.6.70 showed opacification in the right upper zone and a nodular density in the right mid-zone, the appearances being in keeping with secondary pulmonary deposits. There was also widening of the right paravertebral shadow but its significance was not fully appreciated until later (fig. 8). Despite deep X-ray therapy, his condition deteriorated and a repeat chest X-ray on 11.8.70 disclosed an obvious paravertebral swelling on either side ex-

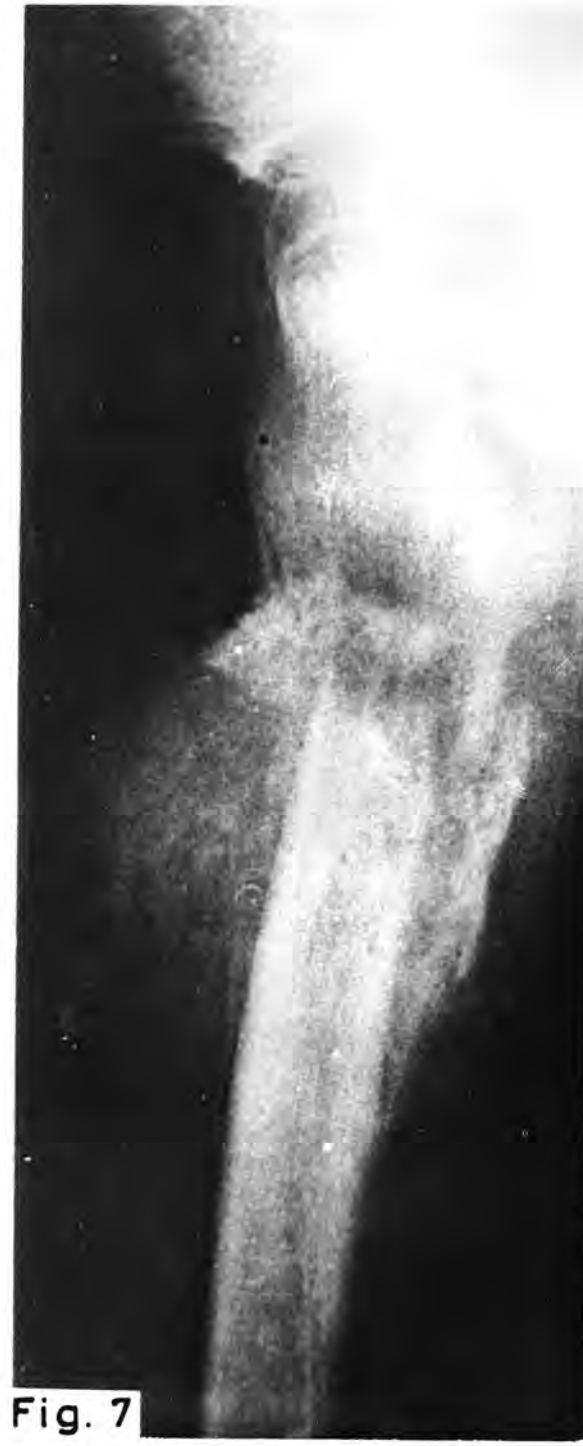


Fig. 7

Pathological fracture of right femur with sun-ray periosteal reaction invading neighbouring soft tissues. Proven case of Ewing's sarcoma.

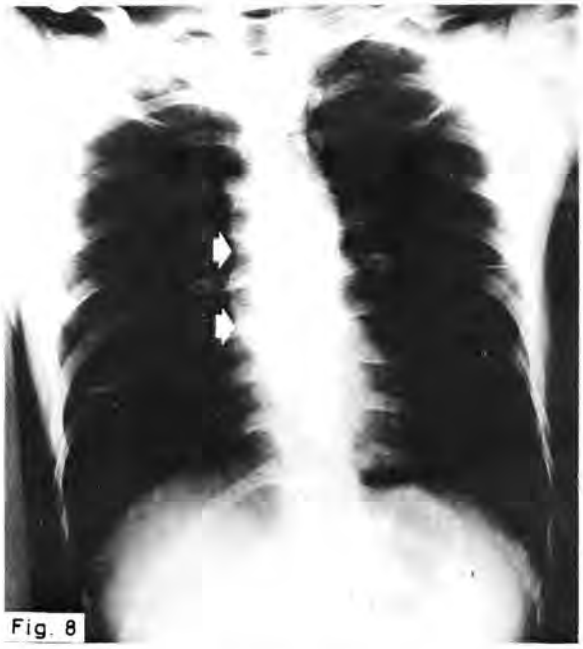


Fig. 8

Chest X-ray of Case 3. Notice the right paravertebral bulge in the mid-dorsal region (arrows).

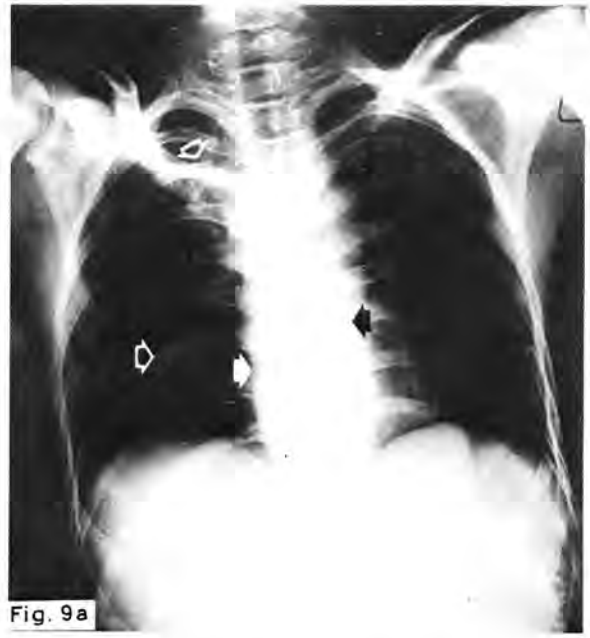


Fig. 9a

Chest X-ray of Case 3 showing further widening of the paravertebral shadow on either side (solid arrows). Open arrows indicate pulmonary deposits.

tending from D5 to D11 (fig. 9a). Antero-posterior view of the dorsal spine disclosed collapse of the bodies of D6, D7, D8, D9 and D10 (fig. 9b). His condition deteriorated further, and he died on 23.9.70.

Comments

With a biopsy proof of Ewing's sarcoma of the presenting lesion in the right thigh, the vertebral lesions with enlarged paravertebral shadows were most certainly due to the same disease process. Whether these vertebral osteolytic lesions represent metastases from the initial lesion in the thigh or independent multicentric foci could not be definitely established on purely radiological grounds. The secondary pulmonary deposits appearing concomitantly with the vertebral destruction seem to favour the former.

Ewing's sarcoma with metastases to the spine was reported by Hamilton (1940), Swenson (1943) and Epstein (1969). The latter reported two verified cases, one of which presented with a large left paravertebral swelling immediately adjacent ot a partially destroyed seventh thoracic vertebra. The cases recorded in the literature showed involvement of one to two vertebrae. Radiologically, Case 3 is unique in that the multiple vertebral involvement from D6 to D10 and the extensive fusiform paravertebral shadowings are salient features reminiscent of spinal tuberculosis. By the same token, an osteolytic type of pyogenic spondylitis must be included in the differential diagnosis.

A few words on the appearance of the paravertebral shadow in two other conditions affecting the spine may be relevant here. Hodgkin's Disease is known to give rise to a paravertebral shadow in about 6% of cases, according to Witten, Fayos and Lampe (1965). A peculiar feature here is the predeliction for the lower left paravertebral space. If the right side is ever affected, the widening is usually noted in the mid-dorsal region.

In middle-aged patients, presenting with osteoporosis, vertebral destruction and a paravertebral swelling, spinal myelomatosis has to be considered (fig. 10). According to Jackson (1968), a paravertebral soft tissue mass is uncommon in vertebral myelomatosis. Garret (1970), on the other hand, reported its presence in all his three cases. The same author noted persistence of these shadows despite clinical improve-

Fig. 9b

Antero-posterior view of dorsal spine shows multiple vertebral collapse with widening of paravertebral shadows (arrows).

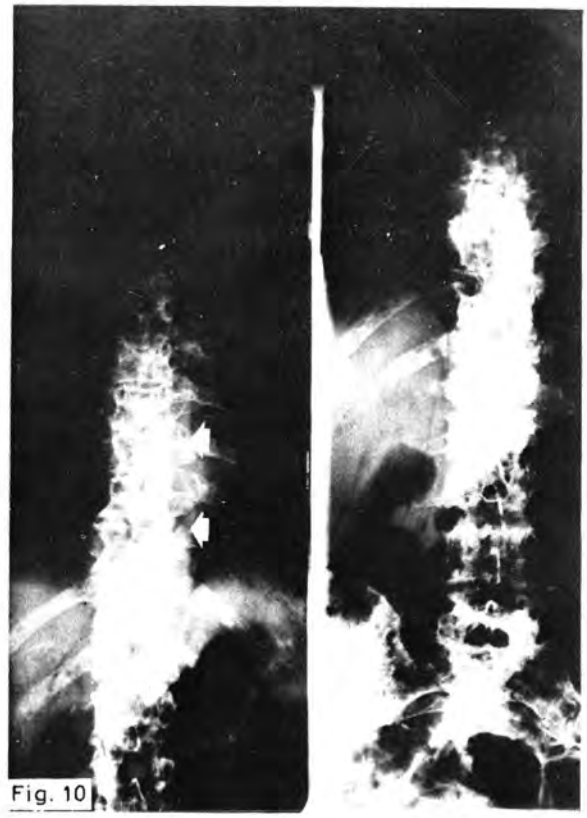


Fig. 10

Diffuse spinal myelomatosis. Arrows indicate slight paravertebral bulging in the left mid-dorsal region.

ment following Endoxan and deep X-ray therapy. According to Epstein (1969), paravertebral shadow widening is usually associated with extensive vertebral destruction with subsequent extension of the deposits into the adjacent soft tissues. An important differential point from other metastatic spinal carcinoma is the relatively infrequent destruction of pedicles in myelomatosis although the vertebral bodies may be collapsed (Jacobson, Poppel, Shapiro and Grossberger 1958; Jackson 1968).

Case 4

P.V.G., a 39-year-old female Indian, presented with increasing pain over the upper dorsal spine for one year. A few weeks prior to admission, she noticed radiation of pain round her chest. Examination showed a toxic looking patient. There was stiffness and tenderness on palpation of the dorsal spine. X-ray of the chest and dorsal spine disclosed a fusiform

paravertebral shadow extending from D2 to D7 (figs. 11a & b). The bodies and transverse processes of D3 and D4 appeared sclerotic. The intervertebral disc spaces, however, were not diminished. The diagnosis was chronic pyogenic osteomyelitis of the upper dorsal spine with paravertebral abscess formation. Exploration at D4 level revealed a thick-walled abscess cavity which was incised and evacuated. Histopathological examination of the evacuated material confirmed the presence of chronic pyogenic osteomyelitis. The post-operative X-rays showed a decrease in the width of the paravertebral shadow.

Case 5

L.L., a 47-year-old Indian man, presented with a history of a discharging sinus in the right flank and swelling in the right iliac fossa for more than one year. The sinus developed following an operation for a lump in the right flank.

On examination, he was emaciated and anaemic, and had a thoracic kyphosis. There was a swelling in the right flank and a tender swelling in the right iliac fossa. The clinical diagnosis was tuberculosis of the spine. A radiograph of the chest was normal. A lateral view of the dorsi-lumbar spine showed a gibbus at D11, resulting from vertebral destruction of the bodies of D12, D11 and D10. The antero-posterior projection showed some calcific densities in the paravertebral region compatible with old abscess formation. A more penetrated view of the spine confirmed the

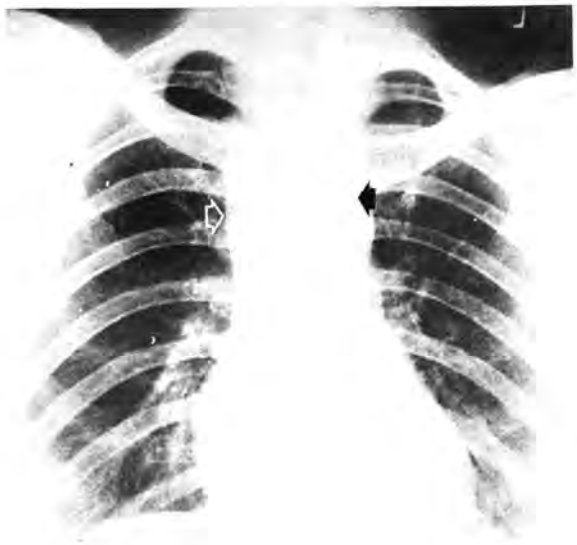


Fig. 11a

Chest X-ray shows obvious bilateral paravertebral bulge (arrows).

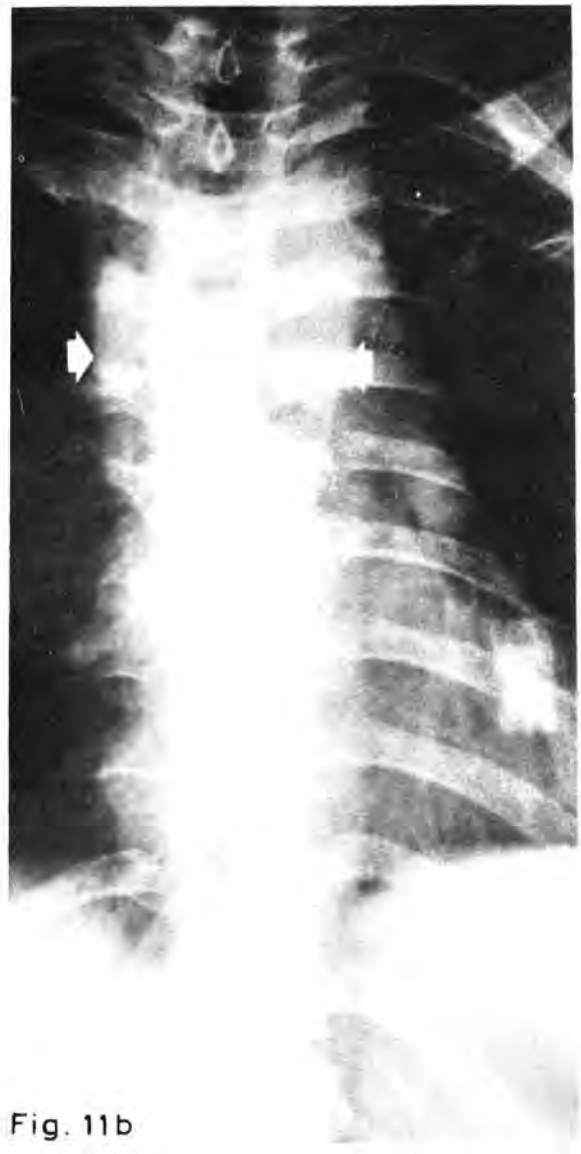


Fig. 11b

Dorsal spine of same patient confirms the size and extent of the paravertebral shadows (arrows). Note the increased density of the affected vertebral bodies and appendages, particularly of D3 and D4.

massive vertebral collapse and widening of the left paravertebral shadow (fig. 12). Calcified debris were noted at the D11/D12 interspace. These findings confirmed the clinical diagnosis of tuberculosis of the spine.

Subsequently, drainage of the paravertebral abscess was carried out followed by sequestrectomy and bone grafting. The histopatholigical findings of the curretted material were consistent with tuberculosis of the spine. Post-operative X-rays disclosed progressive decrease in size of the paravertebral swelling.

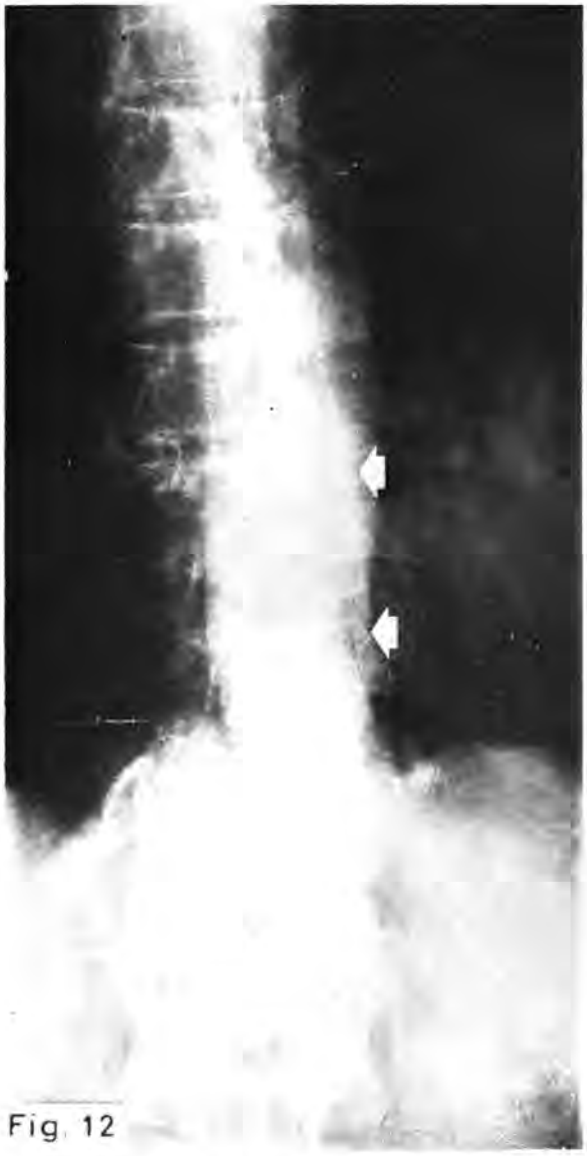


Fig. 12

Antero-posterior view of lower dorsal spine of Case 5 shows obvious vertebral destruction of D10 – D12. Arrows indicate left paravertebral bulge due to abscess formation.

Comments

In pyogenic infection of the thoracic spine, accumulation of inflammatory exudates in the paravertebral region would lead to a lateral displacement of the paraspinal line. This displacement is more obvious on the left and has been regarded as an early sign in dorsal spinal osteomyelitis by Millard (1963). A common observation with widespread infection is loss of definition and widening of the posterior mediastinal shadow. This is caused by localisation of the abscess in the anterior surfaces of the vertebral bodies and appendages. From here, the pus is able to track forward and also laterally into the posterior extrapleural spaces. In the pre-antibiotic era, the outcome of these conditions would most likely be empyema formation and suppurative pericarditis (Solomon and Bachman 1943). The appearance of the spine in chronic pyogenic infection is usually one of increased density due to the adequate time afforded for regeneration of osseous tissues before the patients finally come to the physician or surgeon because of severity of symptoms and a definitive diagnosis made. Equally significant is the complexity of clinical manifestations which may be referred to the abdomen, hips and lower limbs. False assumption of its rarity nowadays is another factor that is attributable to frequent failure of recognition of its exact nature until the disease process has gained a reasonable foothold on the already weakened vertebral column. Careful inspection of the width and outline of the mediastinum, preferably supplemented by a penetrated view, is essential if such conditions are to be recognised early.

In this community, differentiation from spinal tuberculosis still poses a problem to the radiologists. Middlemiss (1961) remarked on the relatively small paravertebral bulge in pyogenic or non-specific spondylitis. Its extent was said to be notably less than that of spinal tuberculosis. Hodgson, Wong and Yau (1969) also pointed out the importance of recognising the discrete appearance of the paravertebral shadow in pyogenic infection. However, the size of the paravertebral abscesses cannot be considered an accurate differential point between the two conditions as their appearances are in many ways dependent on the resistance of the patient and the virulence of the invading organisms. Nevertheless, Hodgson et al attached significance to this point in the assessment of activity of spinal tuberculosis. There seems to be a

direct proportion between the size of the abscess and the activity of the disease. The appearance of the involved vertebral bodies and appendages offer clues in differential diagnosis. Spinal tuberculosis, being a predominantly destructive process, presents more consistently with osteolysis and resultant collapse because of the invasive nature of the lesion, the whole process taking several months before X-ray changes are apparent. On the other hand, vertebral sclerosis is usually the rule with chronic pyogenic spondylitis. However, in fulminating pyogenic infection, vertebral destruction and disc space narrowing can appear in a matter of a few weeks.

Discussion

From the comments made in each of the case reports, it is clear that widening of the paravertebral shadow is only a single feature out of a number of important radiological signs manifested by each disease entity. Its ease of detection on a plain film necessitates its identification in all antero-posterior views of the dorsal spine. In a penetrated frontal view of the chest, it should be sought for particularly behind the cardiac shadow.

Its clinical significance in the early diagnosis of pyogenic osteomyelitis has been discussed. Pyogenic osteomyelitis of the spine is notorious for its protean manifestations which make its diagnosis elusive at times. Hence, in all cases of suspected pyogenic spinal osteomyelitis, the paravertebral shadow should be diligently examined.

The paravertebral shadow assumes prognostic significance in cases of mediastinal haematoma. A mediastinal bulge causing a supracarinal deviation of the tracheal shadow signifies increased mediastinal pressure and although the management is generally one of conservatism, surgical decompression may be indicated. The general outlook, however, remains grave.

The paravertebral shadow is also valuable in assessing response to medical or surgical treatment. In the cases described, the paravertebral shadow is noted to decrease in size with surgical treatment. This is particularly important in spinal tuberculosis where progressive bulging of the shadow, despite intensive medical treatment, invariably means active disease that can only be arrested by surgical decompression. This is also true with pyogenic spondylitis. In the case of Hodgkin's Disease being treated with radiotherapy, a favourable response to treatment would be indicated by a decrease in the size of the swelling. The situation, however, is quite the contrary in myelomatosis where clinical response to radiotherapy or chemotherapy is not reflected in the appearances of the paravertebral mass. A more useful index in such cases appears to be the degree of recalcification of the vertebrae.

Finally, one must be cautious of an apparent spontaneous decrease in size of the paravertebral abscess, particularly in children. In spinal tuberculosis, it often means pointing of the abscess through the pleura into the neighbouring lung tissues and bronchi. Other organs, in which the abscess may penetrate, include the aorta, oesophagus and the peritoneal cavity (Hodgson et al). Rarely, pus from pyogenic vertebral osteomyelitis may spread to involve the lung parenchyma and two cases have been reported by Lorimier, Haskin and Massie (1966) of young infants in which the primary manifestations were respiratory distress and a posterior mediastinal mass on chest X-rays. Fever or systemic toxicity was not apparent until radiological signs had become obvious.

Summary

1. The radiological anatomy of the paravertebral shadow is reviewed.
2. A series of cases illustrating the clinical significance of the paravertebral shadow in diseases of the spine and mediastinum are presented.
3. Its diagnostic and prognostic value is briefly discussed.

Acknowledgements

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The pattern of the pathology of ovarian tumours in pregnancy in the Singapore-Malaysia region

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Introduction

THE OCCURRENCE of ovarian tumours in the pregnant patient is relatively infrequent. But, when they do occur, they present as challenging problems in diagnosis and management, in view of the complications that can be associated with these tumours in pregnancy, namely pelvic impaction, obstructed labour, torsion of the ovarian pedicle, haemorrhage, rupture, infection, and last but not least, malignancy. Malignancy in the ovarian tumour, although the less frequent and least acute of the complications in the pregnant patient, is always at the back of the mind of the clinician, and often the foremost complication in the mind of the medical undergraduates and junior doctors.

Diagnostic criteria

In view of the fact that the ovaries undergo physiological cystic enlargements during pregnancy, especially in the first trimester of pregnancy, and that these physiological enlargements can be of variable sizes, they can pose problems in the diagnosis of ovarian tumours in pregnancy. The diagnostic criteria adopted in this study, for labelling an enlarged ovary in pregnancy as an ovarian tumour is when the enlarged ovary is 6 cm. or more in diameter. The minimum size criteria used in other studies have varied between 5 cm. and 6 cm.

Results

The evaluation of the study of any personal series of such an uncommon condition, as ovarian tumours in pregnancy, may not yield any statistically significant conclusion. It was, therefore, felt worthwhile to analyse the experience of a large obstetrical service, such as that of the Kandang Kerbau Hospital, Singapore, which had consistently been handling just under 40,000 deliveries per annum, during the 1964 to 1966 period under review (Singapore Year Book 1966).

TABLE I

Background data

Place of Study: Kandang Kerbau Hospital
Period of Review: January 1964 to December 1966 (3 years)
Total Deliveries: 118,303
Total Singapore Deliveries: 168,725
% of Singapore Deliveries Studied: 70.1%
No. of Diagnosed and Treated Cases of Ovarian Tumours in Pregnancy: 19
Incidence of Ovarian Tumours in Pregnancy: 1 : 6,226

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Background data

It will be noted from table I that, during the three-year period, 1964 to 1966, there were 118,303 deliveries in the Government units of the Kandang Kerbau Hospital. This represented over 70% of the total mothers delivered in the Republic of Singapore during the same period. In all, there were 19 cases of ovarian tumours in pregnancy, that were diagnosed and treated, and this gave an incidence of ovarian tumours in pregnancy of 1 in 6,226 deliveries, in this study. The incidence of ovarian tumours in pregnancy, as quoted by other authorities, has ranged from just under 1 in 1,000 deliveries to just over 1 in 8,000 deliveries (Gustafson, G.W. et al, 1954); and the incidence of 1 in 6,226 deliveries in this study fits in within the reported frequency range, but of the less frequent occurrence.

TABLE II
Clinical presentation pattern

	No. of Cases	%
Torsion of Ovarian Pedicle	4	21.1%
Pelvic Impaction/Obstructed Labour	8	42.1%
Incidental Finding at Caesarean Section	7	36.8%

Clinical presentation pattern

It is apparent from table II that 63.2% (12 out of the 19) of the cases presented as acute complications of the ovarian tumours in pregnancy, i.e. torsion of the ovarian pedicle 21.1% (4) of the cases and pelvic impaction with obstructed labour 42.1% (8) of the cases. The relatively high proportion (63.2%) of the ovarian tumours in pregnancy presenting as acute complications in this study is due partly to the relatively low "booking" rate of 57.9% in this study (table III) and partly to the lack of routine pelvic examinations at the first "booking" ante-natal visit. In fact, it will be noted that even the remaining 36.8% of 19 ovarian tumours (7 cases) were also diagnosed late, as incidental findings at Caesarean section deliveries. This latter finding also stresses the importance of routine careful inspection of the ovaries at the time of Caesarean section.

TABLE III
Booking pattern

	No. of Cases	%
Booked Cases	11	57.9%
Unbooked Cases	8	42.1%

Booking pattern

Table III shows that only 57.9% (11) out of the 19 cases of ovarian tumours in pregnancy in this study were "booked" cases, i.e. seen for routine ante-natal check-up prior to the onset of labour, the remaining 42.1% (8) of the cases being "unbooked", and hence emergency admissions in labour. As stated earlier, this relatively low "booking" rate of 57.9% is partly responsible for the high incidence (63.2%) of the ovarian tumours presenting as acute complications in pregnancy in this study (Gustafson et al, 1954).

TABLE IV
Ovarian tumour pathology pattern

	No. of Cases	%
Benign cystic teratoma (dermoid cysts)	8	42.1%
Benign serous cystadenoma	4	21.1%
Benign mucinous cystadenoma	4	21.1%
Chocolate endometrial cysts	2	10.5%
Bilateral retention serous cysts	1	5.2%
Malignancy	0	0

Ovarian tumour pathology pattern

In table IV is presented the histo-pathological pattern of the 19 ovarian tumours in pregnancy. It is apparent that the benign cystic teratoma, commonly referred to as the "dermoid cyst", is the commonest type of ovarian tumour (6 cm. or more in diameter) seen in pregnancy. Similar distributional pattern has been reported by other workers (Gustafson G.W. et. al, 1954 and Tawa, K., 1964). In this study, 42.1% (eight out of the 19) of the ovarian tumours in pregnancy were benign cystic teratomas. The benign serous cystadenomas and the benign mucinous cystadenomas each contributed to 21.1% (four cases) of the 19 ovarian tumours in this series. The remaining three cases were chocolate endometrial cysts (two cases) and bilateral retention serous cysts (one case).

TABLE V
Maternal age pattern

	No. of Cases	%
15 to 19 years	4	21.1%
20 to 29 years	11	57.8%
30 to 39 years	4	21.1%

Malignancy pattern

There were no cases of ovarian malignancy amongst these 19 ovarian tumours seen in the 168,725 pregnant women, reviewed in this study. The reported incidence of malignancy amongst ovarian tumours in pregnancy has ranged from 2.2 to 5 per cent (Gustafson, G.W. et al, 1954; Jubb, E.D. 1963; Munnell, E.W., 1963; and Tawa, K., 1964). The absence of malignancy in the 19 ovarian tumours in pregnancy reviewed in this study could be explained by a study of table V, which reveals that all the women were under the age of 40 years, and 78.9% (15 out of 19 women) of them were under 30 years of age. The rarity of ovarian malignancy in women under the age of 40 years, and more so under 30 years, is well established. Although 168,725 pregnant women have been reviewed, there were only 19 ovarian tumours amongst them. Since the reported incidence of malignancy amongst ovarian tumours in pregnancy is 2.2% to 5% (Jubb, E.D., 1963), i.e. 1 in 45 to 1 in 20 cases, it is also possible that another explanation for the absence of malignancy in this series of 19 ovarian tumours, is the fact that the number of cases of ovarian tumours reviewed is inadequate, so that there might be a chance exclusion of the malignant ovarian tumours.

Summary and conclusions

1. The diagnostic criteria adopted for labelling an enlarged ovary in pregnancy as an ovarian tumour is when the enlarged ovary is 6 cm. or more in diameter.

2. Ovarian tumours in pregnancy are relatively infrequent associations, and the incidence of 1 in 6,226 pregnancies found in this study fits in with findings in other parts of the world.

3. A high proportion (63.2%) of the ovarian tumours in pregnancy in this study presented as complications in pregnancy (obstructed labour 42.1%, and torsion of the ovarian pedicle 21.1%), and the reasons for these modes of presentations have been put forth.

4. A histo-pathological study of the 19 ovarian tumours reveals the benign cystic teratoma, commonly referred to as the "dermoid cyst" as the common ovarian tumour seen in pregnancy (42.1%). A finding consistent with other reports.

5. There were no cases of ovarian malignancy amongst these 19 ovarian tumours seen in 168,725 pregnant women. An explanation for this is seen in the maternal age distributional pattern, and the number of cases reviewed.

Acknowledgment

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An evaluation of the Vaginal Hysterectomy-Repair Operation for utero-vaginal prolapse

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THE MODERN TREATMENT of uterovaginal prolapse is operative repair, with or without vaginal hysterectomy. Generally, the choice is between the Manchester Operation and Vaginal Hysterectomy-Repair Operation. In the past ten years, Vaginal Hysterectomy-Repair has been adopted by the University Unit at the Kandang Kerbau Hospital for Women, Singapore, as the method of choice in the treatment of multiparous women with uterovaginal prolapse, in whom there was no further need for childbearing. This has been the policy in the unit, irrespective of whether there was a coincidental medical indication requiring hysterectomy.

The present study was undertaken with a view to evaluating the long-term effects and operative results in a series of 110 cases treated by this method.

Method of Vaginal Hysterectomy-Repair

The operations were performed by three consultants and five senior registrars of the unit. The essential steps of the operation conform to those described in Bonney's Gynaecological Surgery, with these distinctive features:

(1) The suture material used for the pedicles is usually linen.

(2) The stamps of the cardinal ligament and the uterine pedicles are stitched to the vaginal vault in the mid-line.

Preoperative anatomical status

Of the 110 cases, 14 had procidentia, 62 had second degree uterine descent and 34 first degree descent. Ninety percent of the cases were associated with some degree of cystocoele and 60 per cent were associated with rectocoele. Enterocoele was noted in only six patients.

The follow-up investigations

Routine post-operative examination was carried out six weeks after operation. All the 110 cases were seen at this time. In order to assess the long-term results, these patients were recalled for further examination. Forty-eight cases returned and were personally examined by the author.

Immediate post-operative complications

Sixty-five out of 92 cases (i.e. 70%) had a fever of 100 F or more for two or more days during the post-operative period. The causes of the fever are given in table I.

Table I

Causes of fever

Cause of Fever	No. of Cases	Percentage
Urinary infection	37	57
Pelvic peritonitis	1	1.5
Chest infection	1	1.5
No apparent cause	25	39
Total:	65	

Haemorrhage

Intraperitoneal haemorrhage occurred once in this series. The patient went into shock six hours after vaginal hysterectomy. At laparotomy, six pints of blood was found in the peritoneal cavity resulting from the slipped right uterine pedicle. Haemostasis was secured by ligation of both internal iliac vessels. The post-operative recovery was uneventful.

Anatomical and Functional results (Late)

At six weeks post-operative examination, no complications were noted, except for the finding of symptomless vault granulations in 11 cases.

A more detailed analysis of the long-term results of surgery on 48 patients who were examined more than six months after the operation is presented. Seventeen patients were seen between six months to one year after operation and 31 patients were seen between one to three years after the operation.

Vault prolapse

There were two cases of vault prolapse. One developed four months after the operation and a vault slinging operation was carried out with good result after 1½ years. The other patient was symptomless and was sexually inactive.

Enterocoele, Cystocoele and Rectocoele

There were six cases (12 per cent) of symptomless small enterocoele. Recurrent cystocoele occurred in six cases (12 per cent) of which five were mild and one marked. Rectocoele was found in six cases (12 per cent). All of them were mild.

Stress Incontinence

Stress incontinence was found in two patients; one had it before operation and one occurred after the operation. As there were eight cases of stress incontinence in the 48 cases, the cure rate of stress incontinence would be 88 per cent.

Functional result

Of the 48 patients, coitus was satisfactory in 22 and unsatisfactory in five. Twenty-one had stopped coitus even before operation. Of the five cases who had coital difficulty, two had stenosis of vagina and one vault prolapse. One complained of "dryness" during coitus and the remaining refused coitus because of fear of pain even though the anatomical result was satisfactory. From this investigation, it was found that the two cases of vaginal stenosis and the case of vault prolapse with dyspareunia were attributable to surgery.

Discussion

Although many operative procedures have been devised for the surgical treatment of uterine prolapse, only the Vaginal Hysterectomy-Repair operation and Manchester Operation are commonly employed. Over the last quarter century, the Vaginal Hysterectomy-Repair operation has become increasingly popular for the following reasons:-

(1) The potential source of uterine disease, menstrual disorders and malignancy, is removed.

(2) The anatomical restoration is more effective than that of the Manchester Operation. This reduces the recurrence rate.

The late results of the operation may be considered in two aspects, anatomical and functional. Anatomical failure may be said to occur when vault prolapse, stenosis or shortening of vagina occurred as a result of operation (Table II). Functional failure may be said to occur when coital difficulty developed after operation.

Table II

Anatomical results

	No. of Cases	
	Sexually inactive	Sexually active
Shortening of vagina (3 inches or less)	6	0
Stenosis of vagina (1½ finger breadths or less)	0	2
Shortening and stenosis	7	0
Vault prolapse	1	1
Total:	14	3

Although there was a 12% recurrence rate for enterocoele, cystocoele or rectocoele, none of these produced any symptoms in this series. However, in other series recurrent enterocoele appears to contribute significantly to the anatomatical and functional failure rate.

Anatomical failure by definition (including vault prolapse), occurred in 35 percent (17 cases). However, 13 of these were sexually inactive, and in these cases, the operator usually deliberately narrowed the vagina to prevent recurrence of prolapse. Taking this into consideration, the corrected anatomical failure rate would be 8%.

For those who are sexually active, it is the functional result that matters most. From our series, it may be said that there was a functional failure rate of 11% (three cases) and another 7% (two cases) with partial failure as no anatomical reason could be found for the coital difficulty. Watson and Jeffcoate, in two separate series, found that 21% of their cases who were sexually active had dyspareunia; however, only 13% had anatomical reasons.

These failure rates should not be taken lightly and it is felt by the author that the Vaginal-Hysterectomy-Repair Operation should not be carried out for symptomless prolapse, as it has a substantial risk of causing coital difficulty. In order to prevent failure due to vaginal stenosis, it is important to note whether coital function is needed and if so, care should be taken not to excise too much vaginal mucosa. It is better to excise too little than too much in such cases. It may be possible to prevent vault prolapse by stitching the vault to the cardinal ligament pedicles and by buttressing the pre-rectal fascia.

Conclusion and Recommendations

Although the Vaginal Hysterectomy-Repair Operation is now an established gynaecological operative procedure, it has been shown to carry a high morbidity rate and a substantial functional failure rate. As such, this operation should not be carried out for symptomless prolapse. The failure rate may be reduced by taking care not to excise too much vaginal skin, stitching the vault to the cardinal ligament pedicles and buttressing of the pre-rectal fascia.

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Amnioscopy in patients with bad obstetric history and high risk pregnancies

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AMNIOSCOPY WAS INTRODUCED as a technique for assessment of foetal prognosis by detecting meconium in the amniotic fluid (Saling, 1962). Meconium is often taken to be a warning sign of impending foetal death (Wood and Pinkerton, 1961; Barham, 1968). Scanty liquor may be associated with placental insufficiency (Gadd, 1966). Since its introduction, amnioscopy had been used mainly in connection with postmaturity and pre-eclampsia (Huntingford et al, 1968; Henry, 1969), but its use in the management of patients with bad obstetric history and high risk pregnancies has not been stressed.

Patients and Methods
Technique

Amnioscopy is simple and quick to perform with little discomfort to the patient. With the patient in the lithotomy position and under sterile technique, a vaginal examination is performed. The cervical dilatation is assessed and an amnioscope of suitable size selected (figure I). The amnioscope with obturator in place is gently inserted into the cervix with the examining finger as a guide. The obturator is removed, the light source attached to the amnioscope and the characteristics of amniotic fluid studied.

Amnioscopy is usually performed after 37 weeks' gestation and repeated every two or three days until delivery. Serial amnioscopy provides an opportunity to study the natural history of meconium in the amniotic fluid (Barham, 1969).

The value of amnioscopy in patients with bad past obstetric history is well illustrated in the following case summaries:

Fig 1
The 3 amnioscopes of varying sizes with obturators, wool-carrying forceps, and the light source are shown.

Case 1: C.K.T. Gravida 3 with two abortions and no living child. Her expected date of delivery (E.D.D.) was 29.8.70. Pregnancy was complicated by hydramnios in the latter weeks. Serial amnioscopy from 23.7.70 to 18.8.70 revealed clear liquor. In view of the bad obstetric history and hydramnios, low A.R.M. (amniotomy) was done on 19.8.70 but because of poor progress Caesarean section was done on 20.8.70.

Case 2: T.S.E. Gravida 7 but only one child living. In the present pregnancy, she developed mild pre-eclampsia at term; E.D.D. was 13.9.70. Amnioscopy from 29.8.70 to 10.9.70 revealed clear liquor. Low A.R.M. was performed on 11.9.70, followed by vaginal delivery.

Case 3: L.T. All five previous pregnancies ended in disaster. Her E.D.D. was 8.9.70. Serial amnioscopy from 1.9.70 to 11.9.70 revealed clear liquor. Low A.R.M. performed on 12.9.70 was followed by vaginal delivery.

Case 4: L.K.K. Her previous pregnancy ended in intra-uterine death near term. Her present pregnancy was complicated by latent diabetes and mild pre-eclampsia. E.D.D. was 15.10.70. Amnioscopy from 1.10.70 to 5.10.70 showed clear liquor. Low A.R.M. on 6.10.70 was followed by normal delivery three hours later.

Case 5: K.S. All her three previous pregnancies were intra-uterine deaths. This pregnancy was complicated by latent diabetes and hypertension. E.D.D. was 4.11.70. Serial amnioscopy from 17.9.70 to 9.10.70 showed clear liquor. Emergency Caesarean section was performed on 11.10.70 for transverse lie in labour.

Case 6: G.D. She had six previous pregnancies: three were abortions and three were stillborn foetuses. The E.D.D. was estimated to be early November 1970. Amnioscopy from 12.10.70 to 19.10.70 revealed clear liquor but the membranes were accidentally ruptured during amnioscopy on 19.10.70. Caesarean section was performed as disproportion was demonstrated previously at X-ray pelvimetry.

Case 7: S.H.K. She had three previous abortions and only one child alive. E.D.D. was 30.10.70. Foetus was found to be small for dates. Amnioscopy on 16.10.70 and 19.10.70 revealed clear liquor. She had spontaneous vaginal delivery at term.

Case 8: A.M. There were nine previous pregnancies, the last five ending in stillborn foetuses. E.D.D. was estimated to be mid-November 1970. Serial amnioscopy from 28.9.70 to 2.11.70 revealed clear liquor. Labour was induced successfully on 3.11.70.

Case 9: H.B. She had one abortion and one neonatal death, and no live child. Her present pregnancy was complicated by systemic lupus erythematosus and pre-eclampsia. She was uncertain of her dates and E.D.D. was estimated to be around 25.1.71. Amnioscopy from 16.1.71 to 20.1.71 revealed clear liquor of good volume. She had a marked rise in blood pressure and A.R.M. was performed on 22.1.71. However, on account of foetal distress, Caesarean section was carried out.

Case 10: H.A.B. Gravida 4 with one living child and two stillbirths. The E.D.D. was 10.9.70. She was admitted with severe P.E.T. at 37 weeks. At amnioscopy, the cervix was favourable for induction and the liquor clear. Labour was induced and she had a vaginal delivery on 28.8.70.

Case 11: C.C.T. She had one abortion and one stillbirth and no live child. This pregnancy was complicated by diabetes mellitus and mild pre-eclampsia. The E.D.D. was 20.9.70. Amnioscopy on 11.9.70 showed a "ripe cervix" and clear liquor. Low A.R.M. was done followed by vaginal delivery on 13.9.70.

Case 12: P.A. She had two abortions and no live child. Pregnancy was complicated by iron deficiency anaemia. E.D.D. was 19.11.70. Amnioscopy on 16.11.70 revealed clear liquor. Induction of labour was followed by vaginal delivery on 18.11.70.

Case 13: S.G. She had one abortion and one stillborn infant. E.D.D. was 16.10.70. Pregnancy was complicated by latent diabetes. Amnioscopy on 8.9.70 and 10.9.70 revealed scanty liquor. Labour was induced successfully on 11.9.70.

Case 14: Y.M. She had two previous abortions. E.D.D. was 30.12.70. Pregnancy was complicated by mild pre-eclampsia. Amnioscopy on 4.12.70 and 8.12.70 showed clear liquor but on 9.12.70, meconium stained liquor was detected. Low A.R.M. on 9.12.70 was followed by vaginal delivery.

Case 15: A.K. She had two previous intra-uterine deaths; cause was not known. Her present pregnancy was complicated by pre-eclampsia. Serial amnioscopy from 2.12.70 to 7.12.70 showed clear liquor but on 9.12.70, liquor was meconium stained. Low A.R.M. was carried out on 9.12.70. At 7 cm. cervical dilatation, the foetal scalp blood pH was 7.24, and baby was delivered by the ventouse.

Discussion

All 15 patients studied had a bad obstetric history or were high risk cases. They had a total of 52 pregnancies but 44 ended in disaster.

Cases 4, 5, 11 and 13 had diabetes and pre-eclampsia while Case 9 had systemic lupus and pre-eclampsia. These complications are known to carry a very high foetal wastage. In the remaining cases, no cause was found for their poor past obstetric performance in spite of extensive investigations.

Amnioscopy was performed to monitor the foetal condition in these 15 high risk pregnancies. When meconium or scanty liquor was detected, pregnancy was terminated to avoid intra-uterine death as illustrated in Cases 13, 14 and 15. Another important advantage of amnioscopy was that when amnioscopic findings were normal, it avoided unnecessary or premature intervention but allowed pregnancy to go to term as in Cases 1 to 9. However, it was of no value in Cases 10, 11 and 12 because, in spite of normal amnioscopic findings, pregnancy was terminated for other obstetric indications.

All 15 patients monitored by amnioscopy in this series had a successful outcome with live-born infants.

Summary

The use of amnioscopy for monitoring the foetal condition in patients with bad obstetric history and high risk pregnancies is described. The procedure is simple, safe, quick, and easy to perform and provides a convenient method of assessment of the intra-uterine environment in high risk pregnancies.

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Human cases of Filarial Infection in West Malaysia

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A GREAT DEAL has been written about the pathogenesis of filariasis of the adult worm in humans and experimental animals. For the most part, very little attention has been directed towards the fate of microfilariae, and few cases are reported of specific lesions caused by microfilariae in man.

Manson regarded the microfilariae of **Wuchereria bancrofti** and **Wuchereria malayi** as particularly harmless. These were found in the lymphoid tissue close to the parent worm and in the capillaries of the lungs, spleen, kidneys, and other internal organs where in some cases they were surrounded by a fringe of eosinophil leucocytes.

Danaraj et al (1966) have described the pathology of the eosinophilic lung. From the study of 2,000 serial sections of lung tissue from five cases, it was found that dead and degenerating microfilariae were found in both exudative and granulomatous lesions in all but one case. In some of the cases, microfilariae were found to be surrounded by eosinophils separated from a ring of histiocytes by amorphous eosinophilic material.

Nelson (1966), in a detailed review of the pathology of filarial infections, states that the skin microfilariae can be definitely pathogenic, e.g. in onchocerciasis it is the microfilariae which are responsible for the pathological lesions in the skin and eyes. The severity of the lesion is proportional to the density of infection, and this only when the microfilariae are dead. However, it is not unusual to see microfilariae in the conjunctiva or even in the anterior chamber of the eyes of persons with no ocular lesions.

Sapico et al (1967) have described a case of filariasis presenting with gross haematuria. Microfilariae of **Wuchereria bancrofti** were present in the urinary sediment.

A new disease entity, described as endomyocardial fibrosis associated with filariasis, was described in humans by Ive et al (1967) in the provinces of Western Nigeria and also from the Mid-West and the Eastern Region. The lesion consists of scarring of the apex of the heart and inflow tract of the ventricles destroying the normal endocardium, and extending into the myocardium. Either ventricle or both ventricles may be affected simultaneously. The fibrosis interferes with myocardial contractility, and with the expansion of the ventricle during diastole. Microfilariae were present in the blood stream in a high percentage of these cases.

Filariasis in Malaya

Daniels (1908) was the first to notice the presence of filariasis in Malaya when he examined a number of blood films from patients at the General Hospital, Kuala Lumpur and found that three of these were positive. Very few cases of filariasis were seen in hos-

Fig 1
Endemic areas of filariasis in Malaya 1968.

pitals and it was therefore thought that the disease was brought into the country by Indian and Chinese immigrants. Very little attention was paid to the disease in West Malaysia until 25 years later when, in 1934, Strahan and Norris found that the disease was endemic in the rural population living in the coastal rice fields of Province Wellesley. The population in these areas were mainly composed of Malays and the parasite was identified as **Brugia malayi** (fig. 1). From this diagram, it will be noted that the endemic areas of filariasis are along the riverine areas of the country which provide a suitable breeding place for the vectors of the disease.

Two species of parasites are responsible for the causation of filariasis in West Malaysia, i.e. **Brugia malayi** and **Wuchereria bancrofti.**

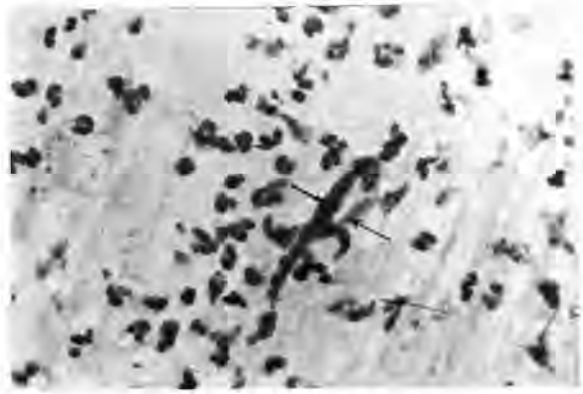

Fig 2
Fragments of microfilaria amidst granulomatous lesion.

1. **Brugia malayi** causes disease among the rural folk of West Malaysia. Two forms of **Brugia malayi** have been recognised in man.

(a) The nocturnally periodic form of **Brugia malayi.** The mosquito vectors of this species are the **Anopheles** and **Mansonia spp.** which are found in the coastal rice fields and some of the inland hilly districts of the country.

(b) The nocturnally sub-periodic form of **B. malayi.** The vectors of this species all belong to the subgenus **Mansonioides,** and are found along the lower reaches of the larger rivers in many square miles of freshwater swamp forests.

2. Wuchereria bancrofti: Surveys carried out by the Institute for Medical Research have revealed that various small endemic foci exist in different parts of Malaya (fig. 1). Wharton (1960) showed that there were two strains of the parasite. The one found in rural areas developed very poorly in **Culex fatigans,** but thrived well in the **Anopheles** species. **Culex fatigans** is the common vector of W. **bancrofti** in other parts of the world. The second which was found in urban areas developed well in **Culex fatigans.** As a result of these findings, two strains of **Wuchereria bancrofti** have been described, viz the "urban" strain and the "rural" strain. The "urban" strain has become very difficult to find recently.

The prevalance rate of the disease varies from 2% – 18% in different parts of West Malaysia.

Case History 1. S.M.D., a female Malay aged 56 years from Bagan Datoh, Telok Anson, West Malaysia, was admitted to the district hospital with a swelling of the abdomen. A provisional diagnosis of a uterine tumour

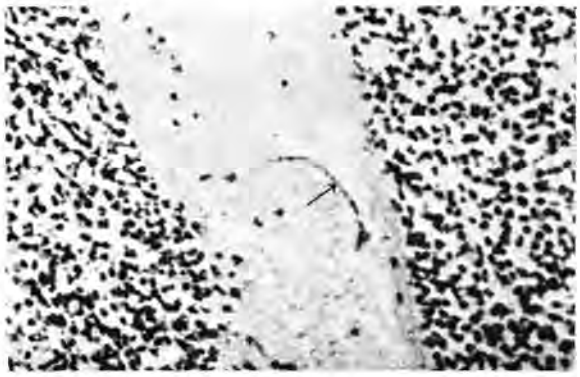

Fig 3
Fragment of microfilaria within blood vessel.

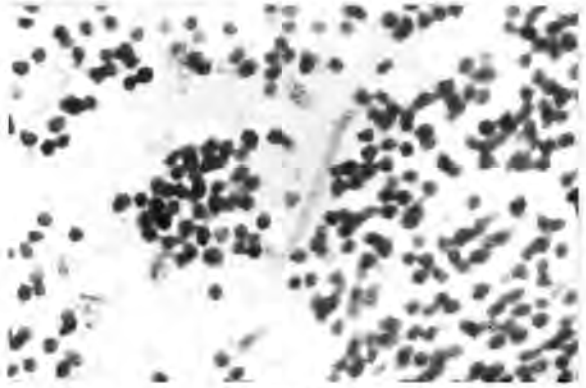

Fig 4
Microfilaria lying in sinus of lymph node.

was made and a total hysterectomy was carried out.

There was a growth in the uterus, the cut surface of which had a whitish appearance. Parts of the tumour mass showed areas of necrosis. Several sections were examined. These showed an extensive granuloma with abscess formation. Most of the inflammatory cells were polymorphonuclears with very few eosinophils. The inflammation had destroyed the muscle in the centre of the lesion while in the periphery it had infiltrated in between the muscle fibres. Fragments of microfilariae were present in the granuloma (fig. 2) and within the blood vessels (fig. 3), and appeared to be responsible for this intensive inflammatory reaction. The nuclei of the microfilariae were well stained and there was no evidence of the presence of microfilarial sheaths being the cause of the inflammatory response. It was clear from the sections studied that living microfilariae were responsible for this lesion and this was not an allergic reaction due to the presence of dead microfilariae or their sheath.

In a survey carried out in this area where the patient lived, it was found that her son had elephantiasis. The mother was admitted to hospital and a 2-hourly blood sample was collected for a period of 24 hours, with the intention of identifying the species of microfilaria but the blood films were found to be negative.

Case History 2. A male Malay, aged 19 years, and a member of the Armed Forces, was seen at the outpatient department of the District Hospital, Taiping with an enlarged cervical lymph node. Histological sections of the lymph node showed the presence of microfilaria lying freely in the sinus without any significant cellular reaction. (fig. 4) The patient showed no other signs of ill-health.

Summary

Human filariasis is endemic in several parts of West Malaysia. Although it does not appear to cause acute debilitating disease, it is a definite cause of chronic illness in areas where it is endemic. Two cases of human filariasis, with different clinical presentations, are described.

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Megaloblastic Anaemia in Malaysia:
A review of 26 cases

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Introduction

ROUTINE HEMATOLOGICAL INVESTIGATIONS of a large number of cases, presented with predominant symptom of severe anemia during the period between 1969 and 1970, revealed megaloblastic anemia in 26 cases. Most of them showed normochromia with a mild degree of macrocytosis and ovalocytosis combined with occasional nucleated erythrocyte in the peripheral blood although bone marrow was frankly megaloblastic. This report draws attention to the fact that occurence of megaloblastic anemia is not uncommon in this part of Malaysia and the anemia is usually manifested with a typical peripheral blood picture.

Materials and Methods

Each case of anemia was admitted, thoroughly examined and treated with a course of combined B12 and folic acid therapy after the confirmation of the diagnosis. Hemoglobin was estimated by the colorimetric cyanomethemoglobin method. Blood film was stained by Leishmann reagent. Sternal marrow smear was fixed in methyl alcohol for 30 minutes prior to staining with Leishmann solution: 3–4 slides were studied in each case.

Results

Clinical

Of 26 cases, 25 were Malay, with ages ranging from five to 60 years. About 75% of them were females. There was one Chinese female in this series. Most of them had severe anemia, moderate hepatosplenomegaly and hemorrhagic retinopathy. Each case responded well with a course of B12 and folic acid therapy.

Peripheral blood picture

In 12, hemoglobin was less than 3 gm%, in 11, 4–6 gm% and in three, more than 6 gm% (table 1). Red cell appeared normochromic with mild degree of macrocytosis, ovalocytosis and occasionally nucleated. Except in few cases megalocytes, pear-shaped or tear-drop erythrocyte, macropolycyte and hypersegmented neutrophil were surprisingly absent (figs. 1 and 2). Mild to moderate degree of thrombocytopenia and leucopenia were usually seen.

Marrow cytology

In all cases, marrow was markedly hypercellular with variable degree of megaloblastic erythropoiesis combined with scattered giant metamyelocytes (fig.

Table – 1

Malay	25	Female	19	**Hemoglobin (gm%)**
Chinese	1	Male	7	Group A (1.5–2.9 gm%) Group B (3–5.9 gm%) Group C (6–8 gm%)
Total	26		26	

Composition of race, sex, and hemoglobin in 26 cases

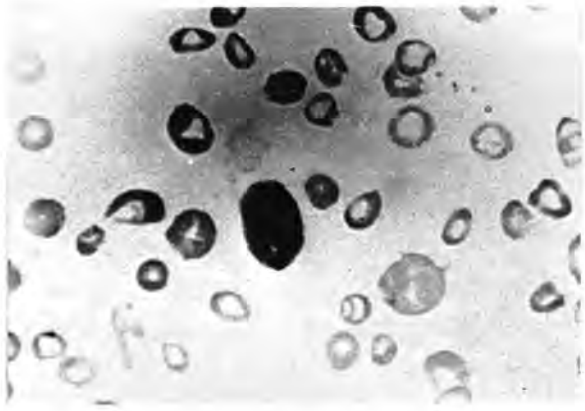

Fig 1
Typical blood picture of megaloblastic anaemia, note marked anisopoikilocytosis, macrocytosis and hypersegmented neutrophil (Leishmann stain x 1800).

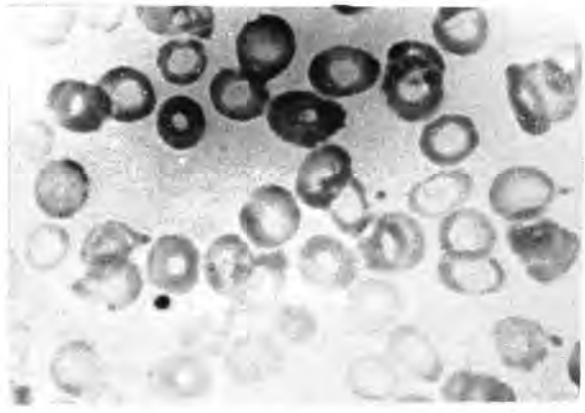

Fig 2
Mrs. R.B.M. a typical peripheral blood picture of megaloblastic anaemia. Note mild anisopoikilocytosis, few ovalocytes and tear-drop erythrocytes (Leishmann stain x 1800).

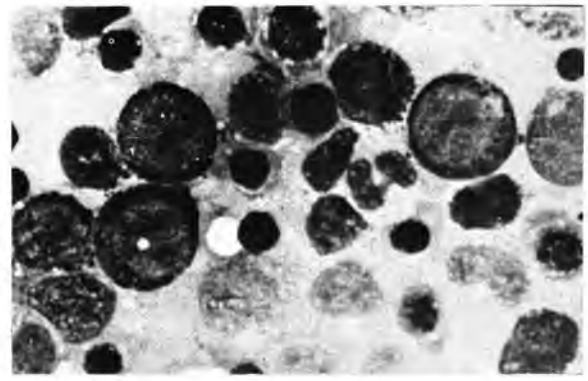

Fig 3
Mrs. R.B.M. bone marrow showing megaloblastic erythropoises (Leishmann stain x 1800).

3). In about 50% cases, megakaryocyte series was moderately hypoplastic and a considerable number of them showed degenerative changes in the cytoplasm and nucleus.

Discussion

Clinically hemorrhagic retinopathy was the constant striking feature present in this series. Cases of hemorrhagic retinopathy associated with megaloblastic anemia are well documented in the literature (Macan Markar et al, 1969).

In severe megaloblastic anemia, peripheral blood picture is usually typical characterised by normochromia with marked macrocytosis, presence of numerous tear-drop or pear-shaped erythrocytes, nucleated red cell and hypersegmented neutrophil but sometimes it may be atypical (Wills, 1948 and Hall, 1953). Macan Markar et al (1969), in their large series of megaloblastic anemia, have reported normal or atypical peripheral blood picture in about 50% of cases, the find-

ing of which is comparable to our series.

Normochromic and mildly macrocytic changes in red cells may be caused by megaloblastic anemia as well as by various diseases without B12 or folic acid deficiency. Therefore, it is more likely that cases of megaloblastic anemia would be missed frequently in this part of the world unless marrow biopsy is performed in such instances.

Summary

Twenty-six cases of severe megaloblastic anemia, of which 25 occured in Malays, are reported here. Most of them were associated with hemorrhagic retinopathy. In most instances, the peripheral blood picture was atypical, characterised by normochromia with mild macrocytosis or ovalocytosis and occasional nucleated red cells. Performance of marrow biopsy in every case of normochromic and mildly macrocytic or ovalocytic anemia in order to exclude or confirm the diagnosis of megaloblastic anemia is emphasised.

Acknowledgement

We wish to thank Dr. K. Ramanathan, Institute for Medical Research, Kuala Lumpur, for taking the photomicrographs.

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Axillary artery thrombosis associated with fracture of the clavicle

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THE LITERATURE on vascular injuries complicating fractures of the clavicle reveal that the lesions are limited to the subclavian vessels and its more proximal components (Dickson, 1952, Ghormley et. al., 1941, Howard and Shaffer, 1965, Penn, 1964, Steinberg, 1961, Stone and Lord, 1955). This report describes a case of axillary artery thrombosis associated with an ununited fracture of the clavicle.

Case report

A 29-year-old male presented with inability to use the right shoulder. Three years previously, as a result of a motorcycle accident, he sustained a closed fracture of the right clavicle with multiple abrasions over the right shoulder region. In his treatment at the local hospital, the arm was kept immobilised in a sling. The abrasions needed eight weeks of surgical toilet and dressings at the hospital due to infection. Since his discharge from the hospital, he noticed progressive weakness and wasting of the muscles of the right shoulder girdle.

Physical examination revealed a healthy young man with obvious deformity of the right shoulder. Irregular scars extended over the supra and infra clavicular regions, overlying the fracture site. Visibly distended veins traversed the front of the upper chest wall and arm. On palpation, grossly distorted fracture fragments were felt. The lateral fragment was tethered to the scar. Finger tip could be easily inserted between the fragments. Radial pulse was absent and so were the brachial and axillary. Other peripheral pulses appeared to be normal. Blood pressure could not be recorded on the affected side. On the opposite side, it was 130 mm Hg systolic and 85 mm Hg diastolic. No appreciable difference in the temperatures of the upper extremities was noted nor did the affected side exhibit any Raynaud's phenomenon.

Neurological examination revealed wasting of muscles of the right shoulder girdle with paralysis of the supraspinatus, infraspinatus and the deltoid muscle. The arm was wasted 1½ inches in girth. Sensation was absent in the cutaneous distribution of the circumflex nerve and diminished along the antero-lateral aspect of the arm.

Laboratory data

Routine blood examination showed values within normal limits and the Kahn test proved to be negative.

X-ray of the region was reported as normal with no evidence of injury to the scapula.

Arteriogram was carried out by percutaneous puncture of the right femoral artery and retrograde advancement of the catheter into the innominate artery. Attempts to negotiate into the subclavian proved unsuccessful. Twenty mils. of urovision was injected and serial films obtained. A segmental occlusion of the axillary artery 1.5 cm. from its origin and about 5 cm. in length was demonstrated. Good distal

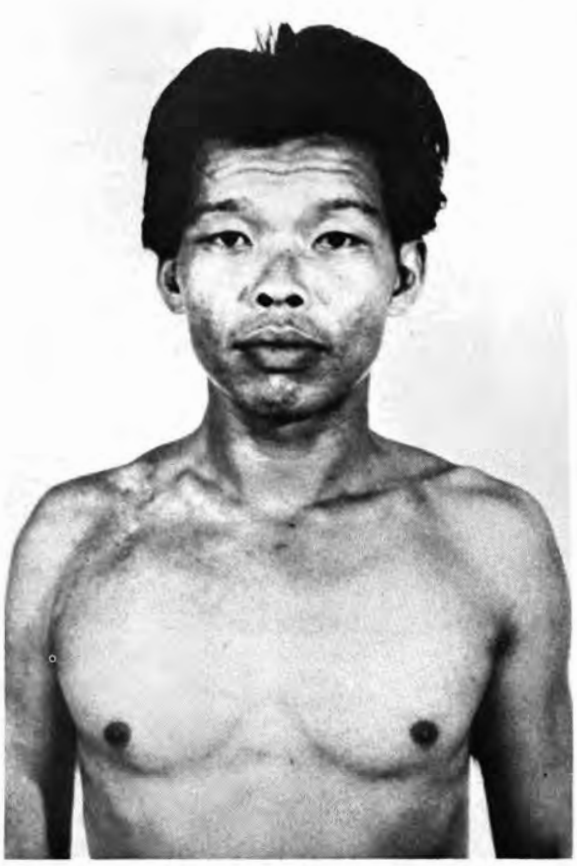

Fig 1

Obvious deformity and wasting of the right shoulder. Inner fragment stands out prominently and scars over the fracture site are visible. The veins cannot be seen in the black and white reprint.

filling from collaterals via internal mammary, segmental intercostal and lateral thoraic artery was noted.

Venogram demonstrated an essentially normal appearance of the vein. ECG was within normal limits.

Operative findings

Trapezius transfer was performed, using extended sabre-cut incision. The operative field was extremely vascular. Mobilisation of the flaps was made difficult by the tethering of the skin to the lateral fragment. The bone was found to be encased in a thick fibrous

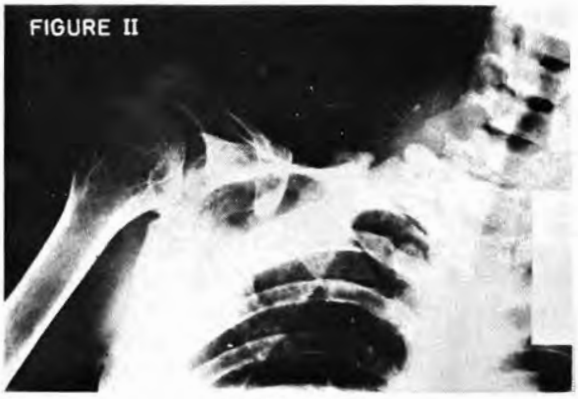

Fig 2

Ununited fracture of the clavicle, showing gross displacement and deformity of the lateral fragment with rounded fracture ends.

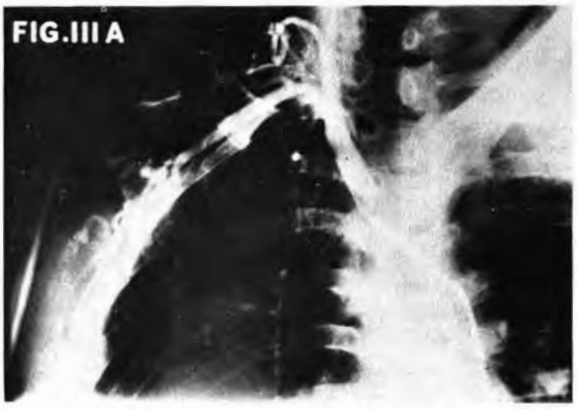

Fig 3a

Retrograde innominate angiogram showing detour taken by the contrast via the internal mammary, segmental intercostal and lateral thoracic artery. Note the block beyond the subclavian.

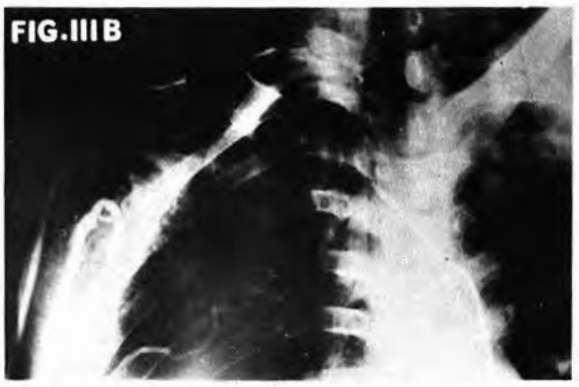

Fig 3b

Passage of the contrast through the lateral thoracic artery entering the distal axillary and into the brachial artery.

sheath and the intervening area between the fracture fragments was filled with intense reactive fibrosis. Beyond this point, the rest of the tissue appeared normal. No attempt was made to display the axillary lesion lest in doing so, more vital collaterals could be interrupted.

Comments and conclusion

Closed fractures and dislocations have been known to be complicated with concomitant vasuclar lesions of the adjacent arteries (Jane and Ghormley, 1950; Johnstone, 1962; and Lowry, Spears and Jane, 1951). The extent of such a lesion may vary from simple spasm to complete severance of the artery. Associated axillary artery lesion have been known to occur with dislocations of the shoulder (Johnstone and Lowry, 1962; Spears and Jane, 1951). In the absence of any history of shoulder dislocation, it seems logical to believe that the thrombosis in this case was the result of possibly a traction type injury to the arterial wall at the time of initial trauma. It would appear that the traumatised intimal wall led to subsequent development of the thrombus.

It is believed that a similar case has not been reported before.

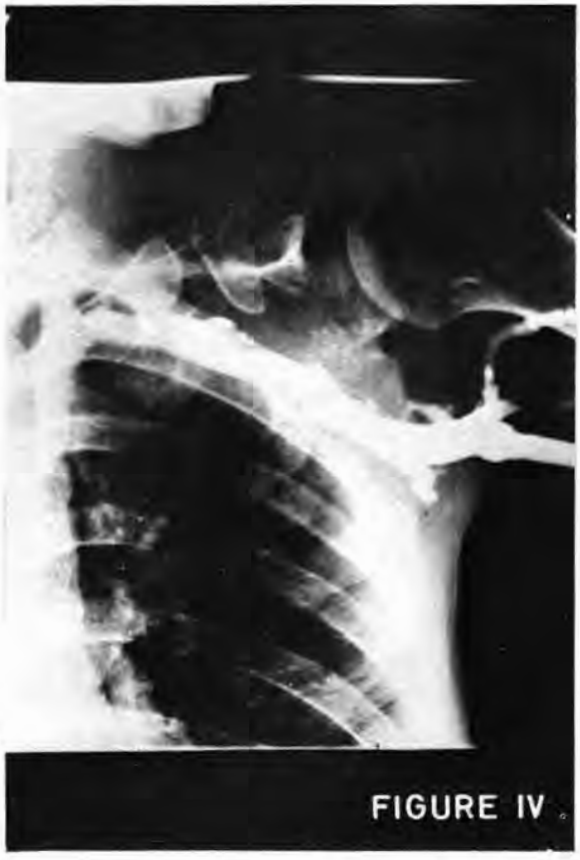

Fig 4
A normal venogram appearance.

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Book Reviews

TEXTBOOK: NEUROLOGICAL EXAMINATION IN CLINICAL PRACTICE by Edwin R. Bickerstaff, M.D. (Birm.). F.R.C.P. (London)

NEUROLOGICAL EXAMINATION in clinical practice can be difficult if only because of the busy schedule of medical practitioners in this region. This book crystallises the examination of the nervous system in more realistic terms, with present day concepts in neurologcial thinking in mind.

Unlike most books dealing with this topic, the author has made a concerted effort to include chapters on ancillary neurological investigative techniques which are neccessary adjuncts to neurological diagnosis.

Chapters on electroenchephalography, X-ray diagnosis including angiography, ECHO-encephalography, and radio isotopic brain scanning are amongst those included to illustrate the usefulness of these investigative measures.

Although the discussions on these topics have not been exhaustive, they are sufficient for purposes of the general practitioner and those concerned with the management of neurological patients. What is more significant perhaps, is the emphasis the author has placed on the interpretive aspects of neurological physical signs and their role in cerebral localisation and diagnosis. I have no hesitation in recommending this book to those involved in neurological diagnosis and investigations.

N. Arumugasamy

MANAGEMENT OF RENAL FAILURE
Ed. by M.D. Milne – British Medical Bulletin Vol. 27, No. 2. May, 1971. Published by the Medical Dept., the British Council, Lond. £2/.

THE SIXTEEN PAPERS contributed by 28 British specialists are addressed to all workers interested in patients suffering from renal failure. It embodies the recent advances in research, analyses and evaluates current work and indicates guide-posts for further investigation.

The subject matter of this symposium includes the management of the acute uraemic emergency, surgical and medical aspects of acute and chronic renal failure, renal failure in the tropics, antibiotics in renal failure, dialysis, the present status of renal transplantation and the use of radiology in diagnosis.

Thus, it would be of interest to the surgeon, physician, pathologist, haematologist, radiologist, and others involved in that branch of clinical medicine which is coming to be known as nephrology.

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