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Editorial

Medical education in Malaysia

by Lim Kee Jin

WITHIN A DECADE, Malaysia has invested in two medical schools. The first at the University of Malaya was established nearly ten years ago. The latest, the Medical School of the University Kebangsaan, will start to take in students this year.

The Medical School of the University of Malaya has conclusively proved that we are able to produce graduates of the highest technical skills with standards comparable to those of the developed countries. Many of these graduates are now serving the country in large and small hospitals and health centres. Yet the main problem of getting doctors to serve in rural areas where the need is greatest, has not really been solved. Investments in medical education are generally extremely expensive and when the graduates are not orientated towards satisfying community needs and put self before service, the problem of brain drain becomes serious. How can societies motivate their medical graduates to work for them, to identify their own needs with those of the community they live in?

The new medical school at the University Kebangsaan will, no doubt, look into the various possibilities in educating our new doctors. They will not sacrifice any standards if possible, but the realities and problems of the situation they face will definitely encourage the Vice-Chancellor and the Dean to consider methods of motivating, stimulating and encouraging students to identify themselves with national aims and aspirations. Studies of new experiments in medical education, particularly in other developing countries and socialist nations may help by suggesting new and novel methods.

A different aspect of medical education concerns the training of specialists. As the nation becomes more and more industrialised, developed and sophisticated, popular demand for specialist attention is growing. This demand, which has been mainly from the urban areas, is luring government specialists into the private sector thereby creating a hiatus among the ranks of government specialists. The need for increasing training facilities for specialists is urgent. The only means of remedying

the situation are by training more specialists ourselves or recruiting them from abroad. The latter course can only be a temporary measure, albeit a necessary one at this stage. Training is done almost entirely by the government now, but in order to encourage more doctors to join the training schemes, more encouragement must be given to those individuals by better prospects for promotion, job satisfaction and better service conditions. Individual specialists, who put in a good deal of effort into training and teaching in addition to their duties, should be encouraged and their help acknowledged.

Professional associations, such as the Academy of Medicine, the Association of Physicians and the College of Surgeons, have a vital role to play in the training and recognition of our local specialists. Local training, however, is only one aspect of the experience which specialists must have. Whenever possible, they should be given opportunities of obtaining wider experience in other centres abroad. It is not for us to discuss this in detail here, but we are sure it can be worked out.

Though one would prefer a leisurely pace of progress in the training of specialists, the meteoric rate of demand for specialist attention from the public makes no concession to a slow approach. Whether the profession likes it or not, pressures will increase to such an extent that unless the professional associations take a hand in the matter, they may be superseded or ignored. We plead for a more positive attitude on the part of our profession, in particular the specialist associations in these crucial times.

MMA House in Jalan Pahang, Kuala Lumpur, which will be declared open by Perdana Mentri Yang Ahmat Berhomat Tun Haji Abdul Razak in April 1973.

RHINITIS-CHRONICA-TROPICA: Clinical, radiological, histopathological, therapeutic and ethnological studies on Chinese, Indians, Malays and 'others'

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Introduction and Scope of Study

IN THE WORLDWIDE EFFORTS to treat tropical diseases, one disease which is very common in many parts of the Tropical Belt and one that is very often neglected is Chronic Tropical Rhinitis.

In comparison with other classical tropical diseases, this condition is considered a minor one and only in the more advanced of the developing countries is some attention paid to it.

Detailed figures from those areas are not available but according to many years of personal experience in West Africa and Southeast Asia, the percentage of chronic tropical rhinitis is very high.

Of the many thousand patients who attended our University E.N.T. Department in the past five years, about 75% of them had pathological conditions of the nose or related to the nasal region.

Owing to the lack of adequate diagnostic facilities (clinical and radiological) in many of these

developing countries, reports on rhinitis of the tropics consist mostly of only clinical observations on response to drug treatment.

Furthermore, the "running and obstructed nose" as mentioned above is considered so common amongst the native population, that many people seeking either temporary relief only by "native medicine" or, if available, with anti-histamines and vaso-constrictor drugs, just accept it as "God-given" and live with it, doing nothing at all about it.

In regions where surgical facilities and professional skill are available, cautery of the turbinates, in most cases "surface cautery" (Jaffè 1957) or submucous cautery (Gnanapragasam 1972) is performed.

In view of the lack of adequate facilities for treatment, its ubiquity and relatively minor tendency to serious complications in spite of neglect or inadequate treatment, it is not surprising that chronic tropical rhinitis has not received the same interest as the more traditional infective tropical diseases.

Surgical procedures in many of the tropical countries are in general still very limited, especially E.N.T. specialist services; therefore treatment either by cautery or by more sophisticated techniques is often a rarity. The fact that in some areas traditional objections against modern surgical procedures still persist further complicates the matter.

Nevertheless, as steady progress in development is made in many of these tropical countries, the results of our five-year experience in the treatment of chronic tropical rhinitis in different ethnic groups (Chinese, Malay, Indian, Ceylonese, Pakistani, Eurasian and European) may be of interest in other regions for the future when their surgical facilities and E.N.T. specialist services improve. Those working in these areas might also find our report encouraging because of the great number of favourable results of our treatment obtained in cases which had proved refractory to treatment by anti-histamines, vaso-constrictors or cautery.

The aim of this present study is to demonstrate that minor surgical approach to chronic tropical rhinitis by means of partial "stripping" of the turbinate performed "lege artis" can be very effective in considerably reducing the symptoms and complaints of the patient. In many instances, it also relieves him of the necessity of further continuous medication and the consequent financial burden and loss of time in visits to the treatment centre. The general and great practical importance for the people living in countries of the Tropical Belt and suffering from chronic tropical rhinitis justifies our effort to present the following data, investigations, statistics, therapeutic procedures, results and conclusions to the interested reader on one of the most common diseases in the Tropics.

Clinical Aspects

A. Patient's Complaints

Nasal blockage, sometimes of the intermittent type, sneezing, lacrimation, loss of smell, nasal discharge of various types, frontal headache, heaviness in the maxillary region, occasional loss of hearing of the conductive type, dry mouth, sore throat, repeated tonsil attacks, irritation of the larynx and tracheo-bronchial tree with hoarseness, cough and expectoration of secretion can occur when the turbinates are chronically inflamed and enlarged as in chronic rhinitis.

B. Inspection of the Nasal Cavity

This may reveal a variety of turbinate shapes, sizes and colours (reddish, bluish, bluish-red, whitish-bluish), oedematous, hyper-plastic, partial atrophic, granulomatous, or combined. In the majority of the cases the *lower* turbinates are enlarged, in cases of previous cauteries with scars left over. There might be fluid in the nasal cavity of watery, mucous, muco-purulent or purulent consistence.

As far as the *clinical diagnosis* is concerned, these features can be found either in chronic allergic or non-allergic rhinitis.

The combination of long-standing *allergic* rhinitis and low-grade inflammation may produce permanent enlargement of the turbinates, particularly of the inferior ones. When this occurs, the turbinate loses most of its ability to expand and to shrink. The result is continuous nasal obstruction.

Nasal drops, anti-histamines and allergic desensitisation do *not* relieve the obstruction.

The *non-allergic* vasomotor rhinitis with intermittent obstruction with or without nasal discharge will not respond to vaso-constrictor nose drops very well, therefore this treatment should be avoided. Over-use might only cause more stiffness of the turbinates increasing with each successive dose. Since the stage of engorgement of the turbinate is controlled by the autonomic nervous system, and since vaso-constrictors stimulate the sympathetic nerves there tends to be a compensatory reaction of the turbinal vessels after the effect of the nose

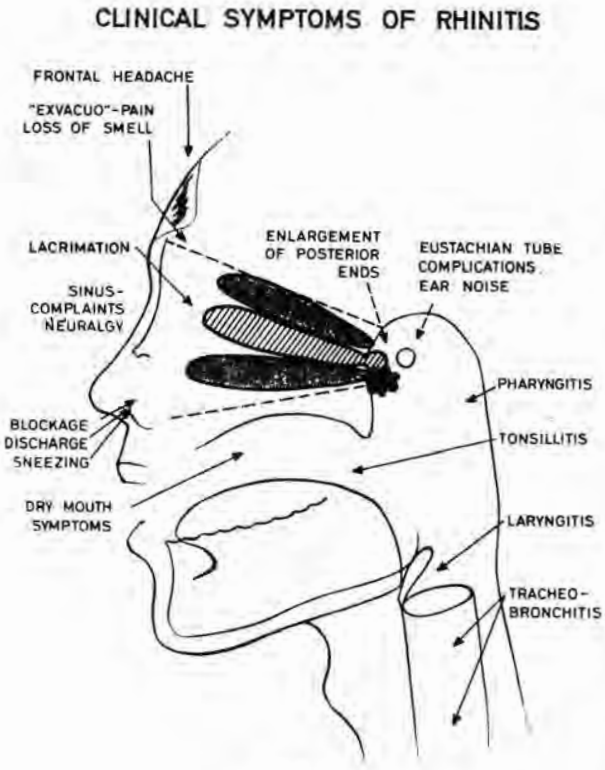


Fig 1

drops is stopped. Thus, after temporary relief the turbinates become more stiff than they were originally.

As a cure, it has been proposed to tolerate a blocked nose for two to three weeks without giving any type of vaso-constrictors. After that period normal function could be expected. In cases where endocrine factors are responsible, specific hormonal treatment is indicated. In nervous-tense persons, psycho-therapy or psychiatric help has been recommended.

C. In our daily practice, the patients seen had mostly a long history of previous treatment with no real permanent relief and consequent frustration, depression and even suicidal attempts as there seemed to be "no way out of the misery".

D. The following are typical treatment histories which clearly show the problems in connection with the blocked and discharging nose:—

1. Nose drops (vaso-constrictors) — Applied over weeks or months with little or no effect.

2. Anti-histamine tablets — In a great number of cases taken over many years without real response, in one case up to a total of 10,000 (!) tablets had been provided previously over the years, leading finally to drowsiness and incapability to work.

3. Cautery (surface or submucous) — With temporary relief only.

4. Repeated cautery — With temporary relief or no relief.

5. Submucous resection of the nasal septum — With temporary relief only.

6. Repeated cautery — No more relief of symptoms.

7. New trial of
   (a) Antihistamine — No response.
   (b) Nasal drops — Only very short relief.

8. (a) Nasal drops — No more response.
   (b) Anti-histamine — No more response.
   (c) Cautery — In some cases up to ten times cautery was performed previously which failed.

Considering the failure rate recorded in the case histories prior to our treatment, the question arises why are there failures?

It has been stated previously that nasal drops and anti-histamines have their special range of indications, but if they are given freely (as the daily practice of unsuccessful treatment histories reveals) they may do more harm than good to the condition as well as produce psychological problems and entail profitless financial burdens.

Another important factor is the proper and complete *clinical diagnosis.*

If, for instance, paranasal sinus X-rays (Werner & Chuah 1972) have not been taken (which was the case in the overwhelming majority of the patients referred to us or who came to seek our clinical treatment because of unsuccessful previous therapy), and pathology of the paranasal sinuses has not been exclused as well as treated, then certainly any local intra-nasal therapy could not be very effective. (See also chapter on X-ray examination prior to our treatment).

The practical consequences arising from the treatment-resistant nose require a method which has proven to us immensely valuable in the last five years, namely partial resection of the turbinates. This method, though already known for a considerable time, is not much advocated in non-tropical countries because of the fear of developing, along with the reduction of the size of the turbinate, another pathological condition instead — atrophic rhinitis (ozaena). As far as the tropics are concerned, with its high temperature and humidity

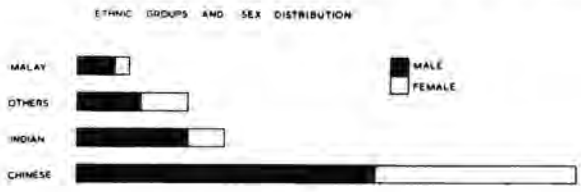


Fig 4

level, the fear of creating ozaena by a partial turbinectomy can be neglected. The following observations, conclusions and suggestions are based on our clinical, radiological and histopathological study of 220 patients who underwent 440 partial lower turbinectomies ("stripping" of turbinates).

Our investigations were not only aimed at clarifying the diagnosis and the reasons for lack of response to previous therapy, but also at seeing the effects of the surgical procedure and to obtain information for analysis concerning the response to them of the ethnic groups in Malaysia (Malays, Chinese, Indians and "Others").

Ethnic Groups and Sex Distribution (Fig. 4)

The different ethnic groups are represented in the following proportions:—

Chinese	61.82%
Indians	18.18%
"Others"	13.64%
Malays	6.36%

The total male and female figures of all ethnic groups are male 62.73% and 37.27% female; nearly twice the number of males as compared with females.

Within the different ethnic groups the percentage distribution between the two sexes is as under:

Chinese	Male	59.56%
	Female	40.44%
Indian	Male	75%
	Female	25%
"Others"	Male	56.67%
	Female	43.33%
Malay	Male	71.43%
	Female	28.57%

Proportions between the sexs are similar in Chinese and "Others", but in Indians and Malays there are nearly three times as many males affected as compared with females.

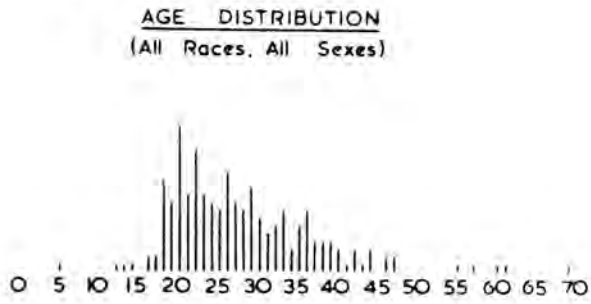


Fig 5

Age Distribution

The majority of cases (all races, both sexes) are within the ages of 20-35 (see Fig. 5).

The distribution *within each of the ethnic groups* according to age (Fig. 6) reveals similar results.

Age and Sex Distribution

Fig 6

In the *older age group* are only occasional cases because the older patients might be either (a) not more concerned about their chronic nasal conditions, (b) disappointed about previous ineffective treatment, (c) not aware of the facilities available for surgical treatment, (d) afraid of surgery, (e) or have already atrophic changes of the nasal mucosa and therefore no more obstruction of the nasal airway.

Children were usually not treated with "stripping". Only in special cases and after other factors such as removal of adenoids or treatment of sinusitis which could produce nasal discharge and obstruction had been eliminated and in whom the symptoms continued despite conservative treatment with vaso-constrictors and anti-histamines a surgical approach was made, first by cautery and if ineffec-

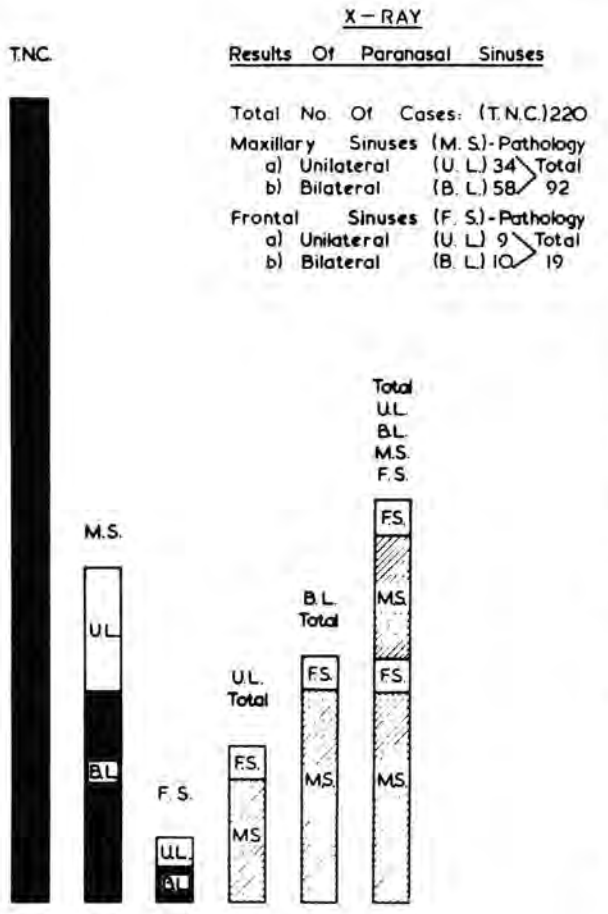


Fig 7

tive followed by "stripping". For this reason, our figures for the children are also low.

The analysis of *X-ray* investigations of the paranasal sinuses reveals the following (Fig. 7):

Out of the total number of 220 cases, the total number with X-ray pathology of the paranasal sinuses was 50.46%.

The detailed figures were as follows:

41.82% of all cases had pathological changes of the maxillary sinuses. 36.96% had unilateral pathology of the maxillary sinuses. 63.04% had bilateral pathology of the maxillary sinuses.

8.64% of all cases had pathological changes of the frontal sinuses. 52.63% had unilateral pathology of the frontal sinuses. 47.36% had bilateral pathology of the frontal sinuses.

86.82% of all cases had deviation of the nasal septum.

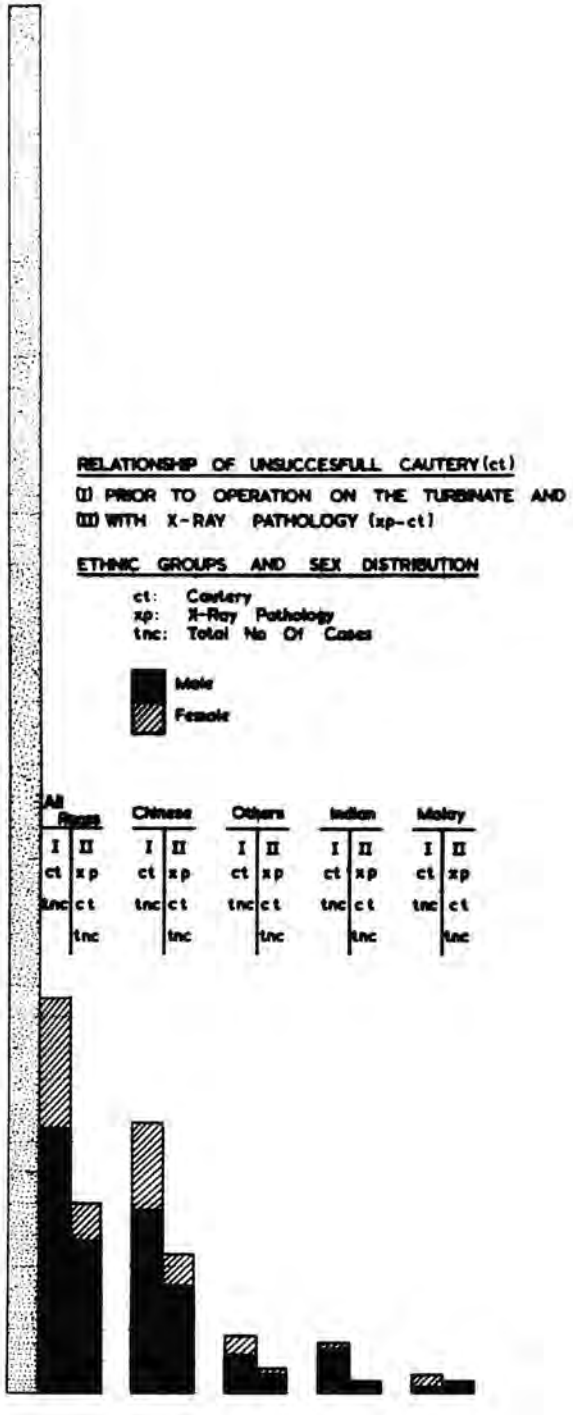


Fig 8

The treatment of the pathological conditions in the paranasal sinuses was therefore of great importance for the treatment of the chronic tropic rhinitis.

Patients with history of Unsuccessful Cauterization and X-ray Pathology Prior to Operation
Ethnic Groups and Sex Distribution (Fig. 8)

A. Relationship of Ethnic Groups and Sex Distribution of unsuccessful Cautery.

Out of the total number of 220 cases we operated on with "stripping" of the turbinate, 28.64% had *previous unsuccessful cautery* (1-10 times), consisting of 66.67% males and 33.33% females. Males, therefore, were twice as much involved as females, which corresponds with the basic relationship of males and females in our study as mentioned previously.

Within the *different ethnic groups* the *previous unsuccessful cautery* proportions are:

Chinese		19.55% out of the total number of cases.
	— Male	67.44%
	— Female	32.56%
"Others"		4.09% out of the total number of cases.
	— Male	66.67%
	— Female	33.33%
Indians		3.64% out of the total number of cases.
	— Male	87.5%
	— Female	12.5%
Malays		1.36% out of the total number of cases.
	— Male	33.33%
	— Female	66.67%

As far as the different ethnic groups are concerned, the figures for males in Chinese, "Others" and Indians appear in similar proportions, twice as many males as females in the Chinese and "Others", whilst the figures for Indian males are seven times higher than the figures for Indian females. Only the Malay group shows reverse proportions where the female figures appear as twice as much as the male figures.

The proportions of 19.55% Chinese, 4.09% "Others", 3.64% Indians and 1.36% Malays reveal also the *previous trend to surgical procedures* which is clearly in favour of the overwhelming majority of the Chinese, whilst Indians and "Others" show a similar tendency. The Malays represent a minority of one-eighth of the Chinese figures.

Relationship of X-ray Pathology to Unsuccessful Cautery (Fig. 8)

B. X-ray Pathology of the paranasal sinuses was present in 13.64% of all 220 cases in which *unsuccessful cautery* attempts have have been made previously. 80% were male. 20% female.

Within the different ethnic groups the following proportions were found:

Chinese	10% out of the total number of cases. 34.92% out of the total number with X-ray pathology. Male 77.27% Female 22.73%
"Others"	1.82% out of the total number of cases. 6.35% out of the total number with X-ray pathology. Male 75% Female 25%
Indians	0.91% out of the total number of cases. 3.17% out of the total number with X-ray pathology. Male 100% Female 0%
Malays	0.91% out of the total number of cases. 3.17% out of the total number with X-ray pathology. Male 100% Female 0%

Comparison between the total number of cases in each ethnic group with the total number of cases with X-ray pathology shows a similar proportion in each group of three times as many with X-ray pathology than those without.

About 50% of cases which had been unsuccessfully treated by cautery and which had X-ray examination done were found to have pathological conditions in the paranasal sinuses. This explains why, even if the cauterization had been successfully done, spreading of inflammation and reinfection from the sinuses would have prevented positive response to the cautery.

The request for paranasal sinuses X-ray examination as well as treatment of paranasal sinuses pathology prior to cautery or intra-nasal surgery is

therefore justified in order to avoid any failures of the intended surgical treatment.

Analysis of the different ethnic groups shows that the majority of the failure cases were males:

In the Chinese group — More than three times the number of females.

In the "Others" group — Three times the number of females.

In the Indian group — Only males were involved.

In the Malay group — Only males were involved.

In comparison of the failure rate with the total number of 220 cases, 10% were Chinese, 1.82% "Others", 0.91% Malays.

Of the total number of paranasal sinus X-ray pathology cases: 34.92% were Chinese, 6.35% "Others", 3.17% Indians and 3.17% Malays. The Chinese group therefore is involved more than five times as often as the "Others" and about ten times as often as Indians and Malays.

Methods of Treatment

A. General: Allergic desensitization, treatment of endocrine disturbance (hypo-thyroidism, hypo-metabolism), psychiatric treatment.

B. Local Medical: Vaso-constrictor drugs, anti-histamines, submucous injection of sclerotising agent.

C. *Surgical* Treatment of Turbinates (Fig. 9).

1. Cautery.
   (a) Surface cautery.
   (b) Submucous cautery.
2. Resection of turbinate bone (Odenal 1930, et. al.).
3. Neurotomy of Vidian-nerve (Malcomson 1959, Golding-Wood 1961, et. al.).
4. "Stripping" of turbinates with or without infraction of turbinate bone.
5. "Stripping" of turbinates with or without submucous resection of nasal septum (S.M.R.).
6. "Stripping" of turbinates with partial resection of turbinate bone (in special cases only).

Comments of Methods of Treatment

As far as *allergic disensitization* in the tropics is concerned, there are very well known tremendous difficulties in connection with such attempts because

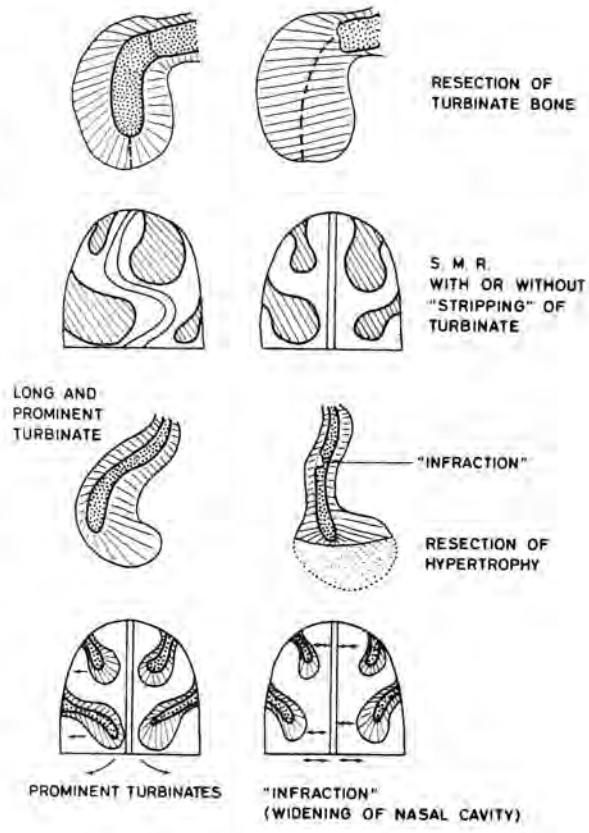


Fig 9

of the multiple factors involved and the psychological problems arising. Even if only one allergen is responsible, it may be difficult to deal with the case owing to the often indifferent approach of the patients as a result of their variable stages of mental development.

The same psychological and therapeutic problems arise with medication by *vaso-constrictor drugs* which might be used and applied by the patient, not in the way as prescribed by the doctor or due to their becoming ineffective after prolonged application or over-use in non-allergic vasomotor rhinitis. This leads to stimulation of the sympathetic nerves with compensatory reaction and reactive enlargement of the turbinates, with or without nasal discharge, and turbinate stiffness, thus reversing the intended effect of increasing the nasal airway with shrinking of the turbinates.

Similar problems of no response to medication can be observed with *anti-histamines* in the case of combination of long-standing allergic rhinitis and low-grade inflammation. A permanent enlargement of the turbinate is the result.

The results of *injection* of a sclerotising agent are also not very encouraging; therefore, surgical methods have been used where facilities as well as professional skill were available. With regard to *submucous resection of the inferior turbinate bone* or *neurotomy of the Vidian nerve,* we did not entertain these techniques.

The effect of *surface* cautery of the turbinate can be seen from Figure 10. In a considerable number of cases observed after this technique had been used elsewhere, an enlargement effect (Fig. 10) was noticed, the temporary reduction of the size of the turbinate having been subsequently reversed.

The problems connected with *submucous* catery might be summarised as follows:

As far as the technique is concerned, (Fig. 10/11) are referred to. Complications are possible depending on the position of the cautery needle. But even in cases where the procedures are performed "lege artis", the *anatomical structure of the*

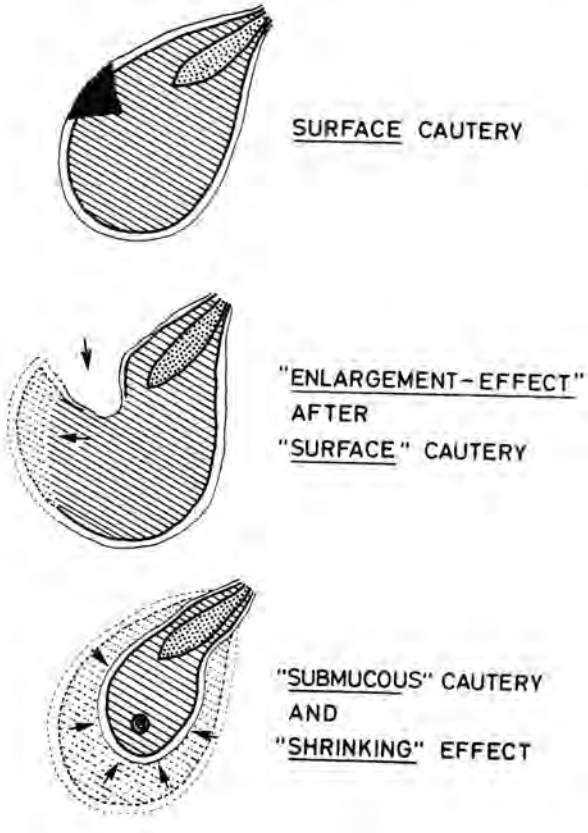


Fig 10

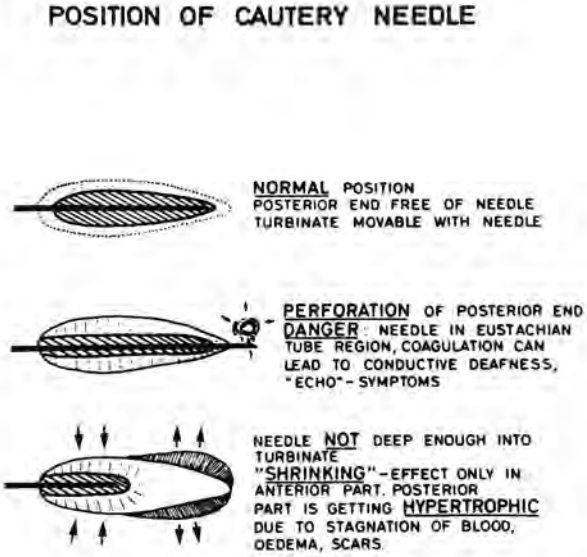


Fig 11

rhino-angiological network A/V type or V/A type (Swindle 1937), as well as circulatory disturbances within the rhino-angiological network as a result of cautery in localised areas of the turbinate may lead to failures with reversion of the intended shrinkage effect.

Our main surgical approach for the past five years has been the partial "stripping" of the turbinate in the overwhelming number of cases of the inferior turbinates where the usual medication showed no signs of positive response or where repeated submucous cauteries failed, or cautery was clinically contra-indicated.

Clinical Evaluation of Size and Shape of Turbinate (as demonstrated in Figure 2/3).

The individual variations depending on the type and reaction to previous conservative and surgical treatment reveal a multitude of possibilities with regards to the "stripping" technique. The soft tissue lining of the turbinate might be easily removable or it might, in other instances, be very difficult to remove due to the adhesion of the scarred soft turbinate tissue to the turbinate bone as the result of one or multiple previous cauteries. In this latter type of case, the danger of fracturing the turbinate or of accidentally removing it with the scarred soft tissue of the underlying bone during "stripping" is considerable.

Not only arterial bleeding, but also change in the basic structure of the physiological nasal airway

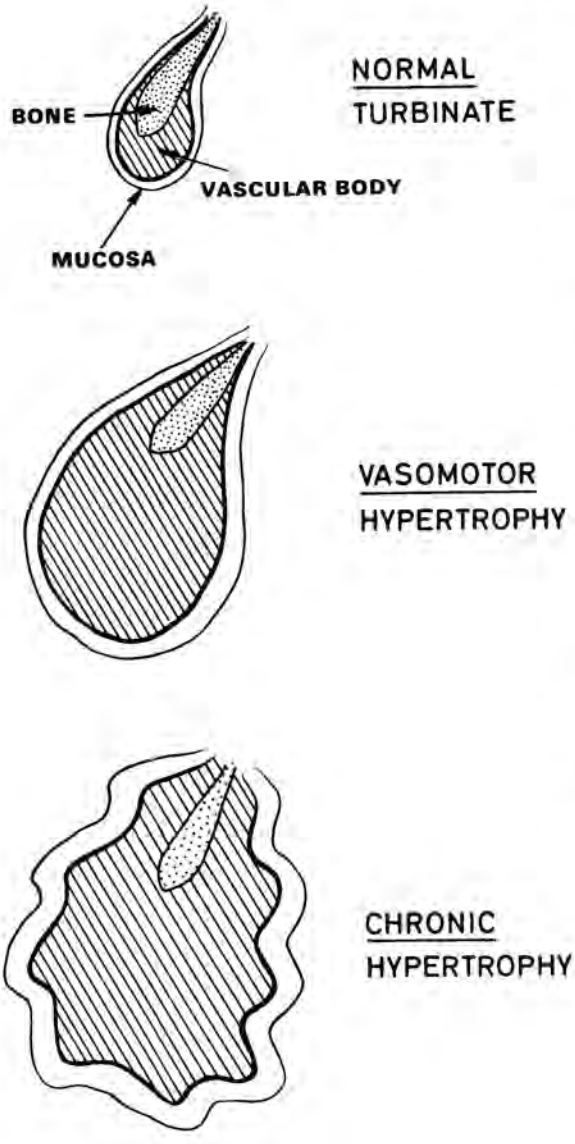


Fig 2

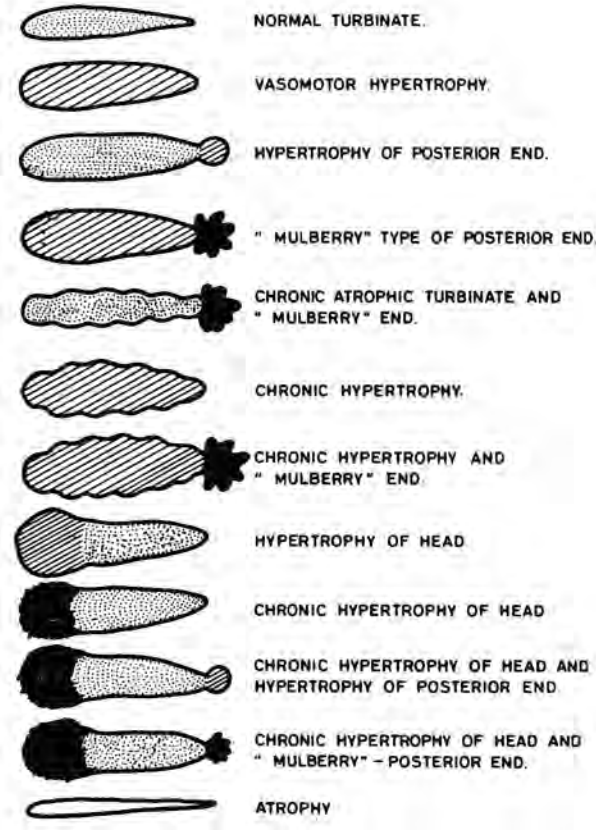


Fig 3

would be the result of partial or total loss of turbinate bone.

In order to prevent such complications a careful partial dissection of the soft tissue turbinate is necessary. (See below).

Our Routine Operating Technique for "Stripping" of Turbinates

'A'

1. Superficial anaesthesia with local anaesthetic (Xylocain spray) of one nasal cavity.
2. Submucous injection of one per cent procaine 1-2 c.c. containing one drop of adrenalin only into the turbinate. (Injection to be done slowly with repeated aspiration to prevent intravasal injection.)
3. Testing of anaesthesia with probe.
4. Incision with scissors starting behind the head of the lower turbinate and resection of enlarged soft turbinate part (Fig. 12); before reaching the end of turbinate, the mobile soft part of the turbinate is pushed backward with a forceps into the nasopharynx without damage to the turbinate bone. If there is enlargement of the posterior end of the turbinate, this will be removed too.

In case of enlargement of soft tissue as well as turbinate bone, additional procedures which may be performed are either infraction with or without partial resection of turbinate bone (Fig. 9/12).

The partially exposed turbinate bone after "stripping" is not to be cauterised to prevent

necrosis, but only covered by nasal packs (technique see below).

5. Nasal packing (Fig. 12)
   (a) Two small gauze packs covering the turbinate wound extending from the nostril to the choanal region.
   (b) One long gauze pack is applied on top of them and fills the remaining part of the nasal cavity.
6. Similar procedures of this technique on the turbinate of the other side.
7. Closure and compression of nostrils by two crossed cellophane or plaster tapes (Fig. 13).
8. External nose pack (Fig. 13).

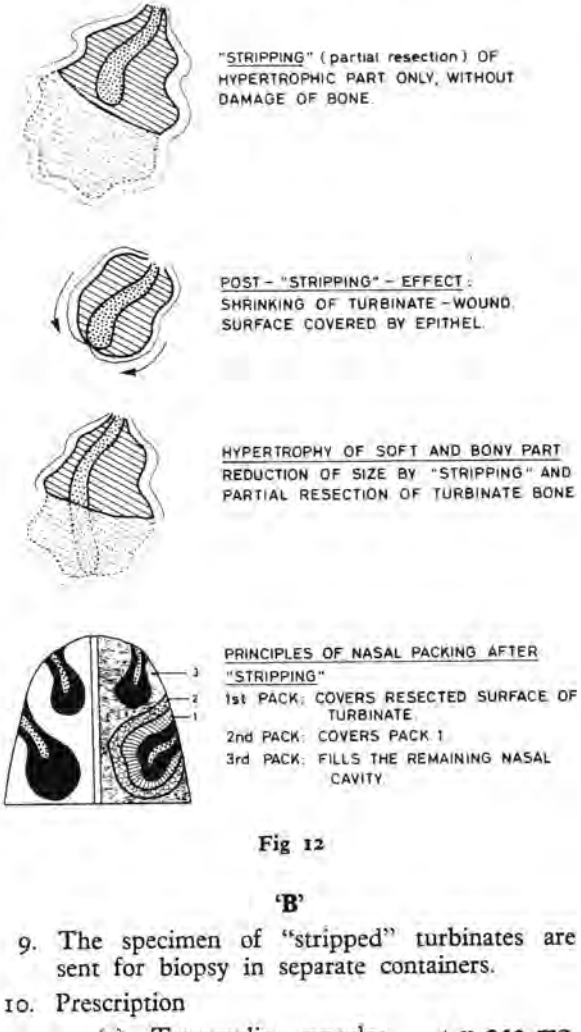


Fig 12

'B'

9. The specimen of "stripped" turbinates are sent for biopsy in separate containers.
10. Prescription
    (a) Tetracycline capsules — 4 x 250 mg. daily for five days.

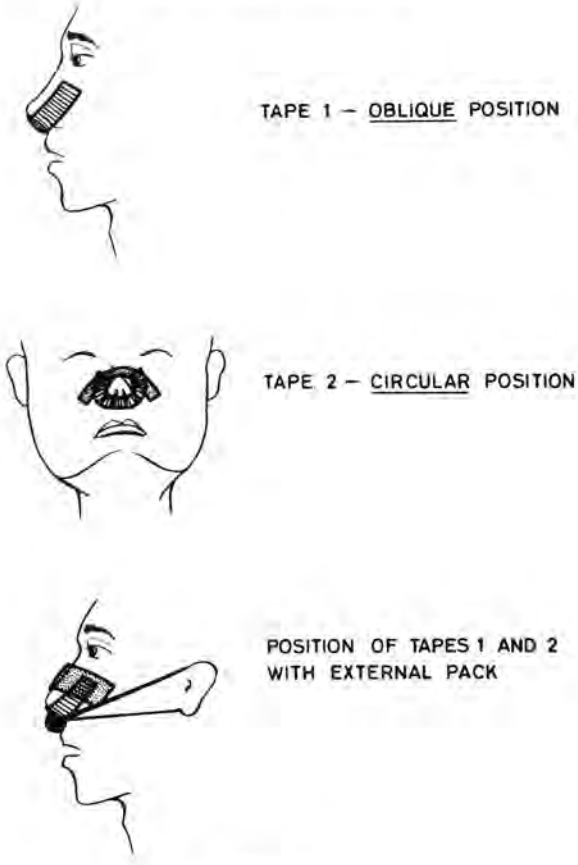
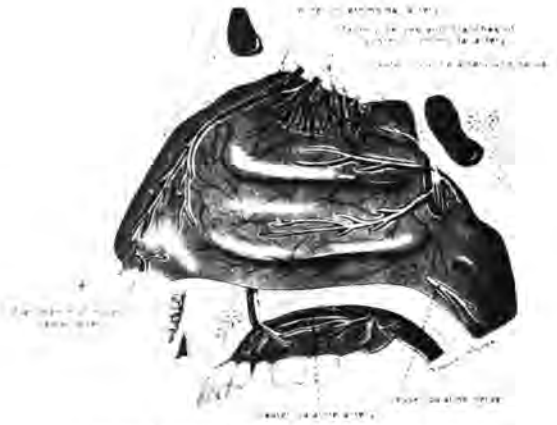


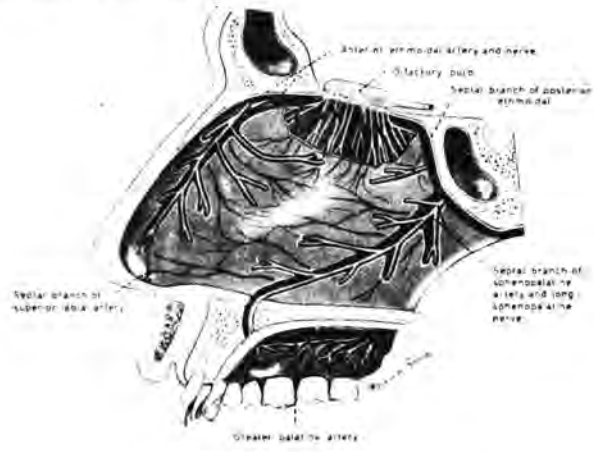
Fig 13

    (b) Analgesic tablets.
    (c) Menthol paraffin nasal drops.
11. Patient is hospitalised at least for one night.
12. Procedures in the ward:
    (a) Half sitting position, head forward.
    (b) Observation of nasal bleeding.
    (c) Icepack around the neck and on nose, (eyes remaining free of pack) for the first 24 hours.
    (d) Change of external nasal pack only if necessary.
    (e) Food. No coffee, no tea, no hot spices, no alcohol, no smoking, no hot diet.
    (f) Mouth cleaning allowed.



(a) The blood vessels and nerves of the lateral wall of the nasal cavity.

Fig 14
From: Sobotta et al (1965)



(a) The blood vessels and nerves of the nasal septum.

Fig 15
From: Sobotta et al (1965)

13. "Medical certificate" (M.C.) for patient for one week's rest.
14. Removal of long nasal pack right and left side one to two days after surgery with or without Xylocain spray anaesthesia or hydrogen peroxide.
15. Removal of the two remaining nasal packs covering the surface of each "stripped" turbinate with or without Xylocain spray, or hydrogen peroxide is done three to four and five to seven days after surgery respectively.
16. After nasal packs have been removed completely, the nose is cleaned and menthol paraffin nose drops applied for one week, either with or without alternating ephedrine nose drops.

Post-Operative Bleeding

This can be coped with satisfactorily if the nasal packing has been done properly and precautions taken as mentioned in the section on post-operative procedures.

Bleeding might occur during the removal of the nasal packs especially if it is done too early and without care. Repacking might therefore be necessary if the bleeding does not stop after the usual time.

It might be a surface bleeding only from the partially denuded turbinate bone (diffuse bleeding) or arterial bleeding from branches of the greater palatine artery and spheno-palatine artery (Fig. 14/15).

In all of our cases, the bleeding could be controlled in the usual way by sitting position with head forward, icepack on nose and forehead, sometimes with icepack around the neck, two small nasal packs in the nostrils, anterior nasal pack and bed rest.

No post-nasal pack had to be applied which might be necessary in the case when, during the "stripping" of the turbinate, accidentally part of the posterior turbinate bone has also been removed. In this instance, cautery of the bleeding spot might be tried or in severe cases the ligature of the internal maxillary artery might help after a Caldwell-Luc approach, with resection of the posterior wall of the maxillary sinus. The final measure would be the ligature of the external carotid artery.

None of these methods mentioned above were necessary in any of our cases post-operatively.

As slight post-operative bleeding might sometimes occur when after all the packs have been removed, the wound membrane is becoming loose, or in female patients prior to menstruation. In order to avoid the latter, we do not operate on female patients in the pre-menstrual period, but only after completion of the menstruation.

Bleeding after operation might also occur from the nasal septum region if the intra-nasal packs have been applied into the cavity too tight after "stripping" of the turbinate and are removed by force and without care. Anatomically involved are the septal branches of the spheno-palatine artery, the superior labial artery and the anterior ethmoidal artery (Fig. 15).

Histopathology

440 biopsies were taken from 440 inferior turbinectomies.

The main histological diagnosis was chronic inflammation.

Out of the total number of 440 biopsies taken, 78 (17.73%) showed positive eosinophilic reaction. (a) 36 (7.55%) showed a moderate number of eosinophilic cells. (b) 42 (9.55%) showed a larger number of eosinophilic cells.

Out of 17.73% of the preparations with allergic signs, rather more than half had heavy eosinophilic infiltration.

As most of our patients received anti-histamines over a short or longer period prior to our treatment, it is now possible to understand why in the overwhelming number these drugs were ineffective because no allergy was present.

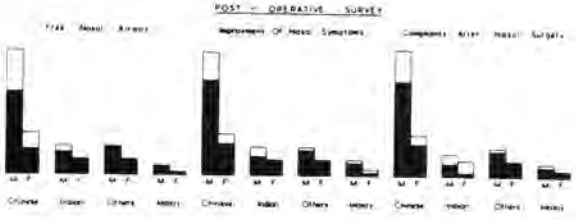


Fig 16

Post-Operative Survey after "Stripping" of Turbinate (Fig. 16)

This took the form of asking the patients the following questions:—

1. Do you have a free nasal airway?
2. Do you have improvement of your previous nasal symptoms?
3. Do you have any complaints after nasal surgery?

The answers were:

1. Free nasal airway: 75% of all the males, 76% of all the females.
2. Improvement of previous nasal symptoms: 76.67% of all the males, 84.84% of all the females.
3. No complaints after the surgery: 73.33% of all the males, 84% of all the females.

The *ethnological evaluation* of these findings within and between the groups of Chinese, Malays, Indians and "Others" revealed the following:

	Free Nasal Airway	Improvement	No Complaints
Chinese			
— Male	66.67%	76.92%	75.00%
— Female	61.54%	76.92%	76.02%
Indians			
— Male	77.78%	66.67%	51.14%
— Female	100.00%	100.00%	20.00%
"Others"			
— Male	100.00%	88.89%	88.89%
— Female	100.00%	100.00%	100.00%
Malays			
— Male	100.00%	80.00%	75.00%
— Female	100.00%	50.00%	100.00%

The restoration of the free nasal airway in both sexes was possible in the majority of cases: 100% in the Malay, "Others" and Indian female group, whilst 60% to 70% of the Chinese males, females and Indian males responded.

Improvement of previous nasal symptoms was 100% in the Indian females and "Others" group whilst the male group of Chinese, "Others" and Indians gave 76% to 88% positive response. The small Malay female group showed a 50% response.

100% of the "Others" and Malay female group had no complaints whilst all the remaining groups had 75% or more. In the Indian female group, a 20% positive response was noted, which might have some relationship to the individual response to nasal conditions.

The Nose after Surgery; Clinical and Functional Evaluation

From the statistics presented in the previous section regarding the patient's comments on the results of the "stripping" of turbinate, it has been noted that an absolute majority of positive answers have been received one to four years after surgery. Post-operative complaints were present only in a minority of cases which indicates the good clinical and functional effect of this type of treatment.

Such results are not surprising as the basic form and shape of the turbinate has not been changed by the operation, but only the hypertrophic part reduced in size, allowing the normal air current function.

Slome (Cit. Scott-Brown et. al. 1965) stated

that it seems clear that except in forced respiration, the respiratory air currents are restricted to the central part of the nasal chambers. Air currents do not pass through the lower part of the nasal cavities nor does any considerable volume pass up into the relatively small olfactory area of the human nose. Narrowing of the nasal cavity in the region of the middle meatus constitutes, therefore, an important obstruction to the free passage of air. Septal deviation, spurs, polypi, mucosal hyperplasia and other causes of obstruction disturb the respiratory air currents. This may result in imperfect conditioning of the air and produce local changes in the mucosa. Valvular function has been attributed to the inferior turbinate. The engorgement and depletion of its mucosa controls the passage of air through the nose. In normal noses the resistance to the flow of air through the nasal passages is low. With partial nasal obstruction, the resistance may be nearly doubled.

No post-operative ozaena has been observed due to the care taken during operation to avoid any damage to the turbinate bone as well as the remaining mucosa lining with regenerated after some time.

Slome (Cit. Scott-Brown et. al. 1965) studied regeneration of the mucous membrane of the paranasal sinuses and stated it has been definitely established that normal, functioning ciliated epithelium can be regenerated following operative removal of the complete lining of the maxillary sinus. This epithelial regeneration occurs mainly by growth from the margin of the operative opening into the sinus and to a less extent from islands of mucosa left behind.

A similar principle applies to the partial denuded turbinate.

In cases of repeated previous cautery, where the turbinate had been deformed by many scars, after "stripping" of the turbinate a new functional epithelial cover of the partially exposed turbinate bone developed.

Under conditions in the tropics with permanent warm weather and high humidity, the phenomenon of a "dry nose" after "stripping" of the turbinate is therefore very unlikely and the fear of creating a post-operative ozaena can be disregarded.

Conclusion and Summary

This study deals with the problems connected with chronic tropical rhinitis, one of the most common diseases in tropical developing countries.

After a review of clinical and therapeutic aspects, the problem of therapy resistance is discussed and our method of "stripping" of turbinate demonstrated.

Results on 220 patients, who underwent 440 operations, who were resistant to the usual methods of treatment by vaso-constrictor drugs, antihistamines and cautery are presented.

Statistics regarding sex, age and racial distribution of patients, X-ray investigations (660 films) and a summary of the histopathology of 440 partial "stripped" turbinates is given. Our operative technique and post-operative care are described. Follow-up records for 1-4 years of the results obtained after surgery as well as the response of the patient to this type of treatment reveal the great practical value of "stripping" of the turbinate (partial turbinectomy) "lege artis" done as a very effective way of therapy in cases of chronic tropical rhinitis resistant to other treatment. Any fear of post-operative ozaena can be disregarded, thanks to our technique and climatic conditions in the tropics, high temperatures and humidity.

Partial turbinectomy, taking into consideration the physiological principles of nasal function as a decisive factor, especially in tropical Malaysia, is very well indicated in the treatment of therapy resistant cases. This refers to various ethnic groups of Malays, Chinese, Indians, Ceylonese, Pakistanis, Eurasians and Europeans.

The excellent results obtained after operations done by seven different surgeons of the department justify the wider use of this minor surgery procedure under the conditions of patient care described.

Taking into consideration the good and lasting effect of this surgical procedure, it becomes in the long run also a help in the socio-economic sectors, because of its time and manpower saving effects for the community. In the developing countries, owing to the fact that a high percentage of the population is affected by chronic tropical rhinitis, effective treatment saves a great amount of money in the health budget by reducing the cost of drugs which would otherwise be used over long periods. The higher initial expenses for the procedures are very well justified, taking into account the savings gained later on. The technique of "stripping" of the turbinate in cases of therapy-resistant chronic tropical rhinitis should, therefore, have a bright future in developing tropical countries.

Acknowledgement

I wish to express my sincere thanks to the authorities of the University of Malaya Teaching Hospital for providing me with the medical records

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Frequency of oral precancerous conditions in 407 Malaysians— with correlation to oral habits

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Summary

ORAL CANCER is the second commonest malignant tumour in West Malaysia. Studies on the frequency of oral precancerous conditions in this country are rare. This paper reports the correlation of the frequency of oral precancerous conditions with oral habits as popularly practised by the various races and sexes in 407 medical workers in West Malaysia and illustrates, incidentally, the many forms of oral stimulants and irritants used by a large section of adult town-dwellers. Seven per cent of the Malays, 8 per of the Chinese and 25 per cent of the Indians had precancerous conditions. In comparison to 8 per cent of the Malay males, 18 per cent of the Indian males had oral precancerous conditions. None of the Malay females had oral precancerous conditions. Whereas 48 per cent of the Indian females had oral precancerous conditions.

Betel-quid chewing appears to be the most important single habit in causing precancerous conditions. In the Malay male, preleukoplakia and leukoplakia of the buccal mucosa and gingivae and smoker's keratosis of the palate were noted most

frequently. They were often associated with multiple habits and single smoking habit. In the Indian male, preleukoplakia and leukoplakia occurred most frequently on the buccal mucosa and less frequently on the labial commissure, tongue and floor of mouth. Multiple habits were most commonly associated with these conditions. In the Indian female, leukoplakia and preleukoplakia occurred most frequently on the buccal mucosa and less commonly on the labial commissure.

Single betel-quid chewing habit was most frequently associated with the lesions. It is indeed interesting to note the town-dwelling Malay male has virtually discarded the habit of chewing betel-quid in favour of smoking. The betel-quid chewing habit seems to have also been discarded by an increasingly large number of the younger group of Malay females and Indian males. Like his Malay counterpart, the town-dwelling young Indian male prefers to indulge in cigarette smoking rather than in betel-quid chewing. The changing trend in oral habits would certainly result in a change in the race and sex incidence and anatomical sites of involvement of oral precancerous conditions and oral carcinoma over the years.

Introduction

Southeast Asia seems to have the highest frequency of oral cancer in the world. Oral cancer is the second commonest malignant tumour in West Malaysia. Among Indian and Malay males, it occupies first place in the data collected so far (Ungku Omar-Ahmad and Ramanathan, 1968). West Malaysia has a population of nearly nine million people consisting of about 50 per cent Malays, 37 per cent Chinese and 11 per cent Indians (Research Paper No. 1).

Between 1967-1971, the Division of Oral Pathology and Oral Medicine, Institute for Medical Research, Kuala Lumpur reported in all 889 histologically confirmed oral squamous cell carcinoma cases. Of these, 64% occurred in the Indians, 20% in the Malays and 16% in the Chinese. The buccal mucosa (43%), tongue (15%), gingivae (14%), palate (13%), lips (7%) and floor of the mouth (4%) were involved in descending order of frequency.

The relation between oral cancer and betel-quid chewing and smoking is well known (Orr, 1933; Khanolkar and Suryabai, 1945; Sanghvi et al, 1955; Marsden, 1960; and Hirayama, 1966). Muir and Kirk (1960) have made a comprehensive account of the sociological significance and composition of the betel-quid. In short, the betel-quid consists of a young betel leaf, sliced betel nut and slaked lime. The Indians, in addition, generally include

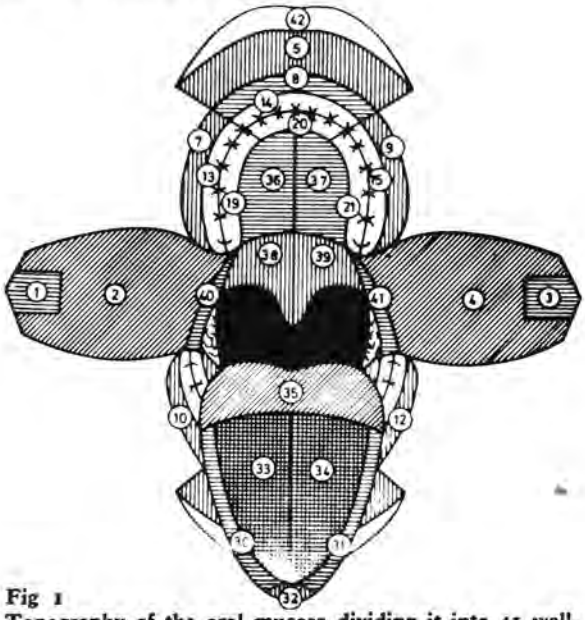

Fig 1
Topography of the oral mucosa dividing it into 41 well-defined regions (after Roed-Petersen and Renstrup, 1969)

tobacco in the quid. The Malays who indulge in betel-quid chewing usually include gambir in their quids. The Chinese as a rule do not indulge in the habit of chewing betel-quids.

Studies on the frequency of oral precancerous conditions in this country are rare. This paper reports the correlation of the frequency of oral precancerous conditions with oral habits as popularly practised by the various races and sexes in this study group and illustrates, incidentally, the many forms of oral stimulants and irritants used by a large proportion of town dwellers.

Material and Methods

The sample consisted of 407 medical attendants and health workers from the following towns: Klang (110), Seremban (76), Raub (61), Kuala Lumpur (59), Tampin (55) and Kajang (46). The group comprised of 248 Malays, 146 Indians and 13 Chinese. None of the workers earned more than $250 a month. The patients were first interviewed for personal data, including details of oral habits, and then submitted to detail oral examination in a well-equipped dental surgery. For purposes of standardisation of examination, the co-authors were standardised to the senior author (K.R.). Colour slides and preliminary clinical trials were conducted. For the anatomical charting of oral precancerous conditions, the topographical classification of Roed-Petersen and Renstrup (1969) dividing the oral mucosa into 41 well-defined regions was used (Fig. 1).

Table — 1

Distribution of 407 persons examined by race, sex and age groups.

AGE GROUP (YEARS)	MALAYS M	MALAYS F	INDIANS M	INDIANS F	CHINESE M	CHINESE F	TOTAL M	TOTAL F
15 — 19	18	—	—	—	—	—	18	—
20 — 29	87	17	38	2	1	—	126	19
30 — 39	68	6	35	10	1	5	104	21
40 — 49	35	5	27	15	4	—	66	20
50 — 59	11	1	15	4	—	2	26	7
TOTAL:	219	29	115	31	6	7	340	67

Definitions of Oral Precancerous Conditions

Leukoplakia is defined as a raised white patch of the oral mucosa measuring 5 mm or more in diameter, which cannot be scraped off and which cannot be attributed to any other diagnosable disease. This definition does not indicate any histological connotation. (This definition was adopted by a WHO meeting of Investigators on Oral Precancerous Conditions in Copenhagen, August 1967 and is now being tested by a group of collaborating centres working with the WHO International Reference Centre For Oral Precancerous Conditions in Copenhagen).

Several attempts have been made to classify leukoplakias into various grades. In this study, leukoplakias are subdivided into (1) homogeneous and (2) speckled types. A homogeneous leukoplakia is a lesion which is characterised by a uniform appearance. In contrast a speckled leukoplakia is characterised by a simultaneous occurrence of red and white patches. The red patches represent areas of atrophy of the oral epithelium, whereas the white patches, often of a nodular appearance, are caused by an epithelial hyperplasia. The speckled leukoplakia may be associated with a candida infection. Epithelial atypia is found in the majority of cases of speckled leukoplakias (Pindborg et al, 1963; Pindborg, 1971).

Preleukoplakia is defined as a low-grade or very mild reaction of the oral mucosa, appearing as a grey or greyish-white, but never completely white, area with a slightly lobular pattern and with indistinct borders blending into the adjacent normal mucosa (Pindborg et al, 1968).

Smoker's Keratosis (leukokeratosis nicotina palati, nicotinic stomatitis) is defined as a thickened, whitish lesion involving the entire palatal mucosa with occasional small nodular excrescences each having a central red dot. In people who indulge in reverse smoking, the palatal changes of smoker's keratosis exhibit greater variations. The entire palate is not always affected and the small red dots on each excrescence are not present in all cases (Pindborg et al, 1971).

Oral submucous fibrosis is defined as a chronic disease affecting any part of the oral mucosa. Occasionally preceded by, and/or associated with vesicle formation, fibrous bands are always present, usually in the buccal mucosa, the soft palate, and the labial mucosa, often associated with pigment changes. In later stages, the oral mucosa becomes stiff, causing difficulty in opening the mouth. Very often the tongue papillae disappear, and the surface of the tongue becomes smooth (Mehta et al, 1971).

In the present study, submucous fibrosis was diagnosed only when the patients exhibited the presence of palpable fibrous bands.

Erythroplakia was diagnosed when the oral mucosa was the seat of a well-defined, red, often fiery red patch, which could not be attributed to other causes (Mehta et al, 1971).

Findings

Age

The age of persons examined ranged from 19 to 54 years. Most of the Malay and Indian males were between 20 to 49 years (Table 1). The majority of Malay females were between 20 to 29

Table — 2

Distribution of 55 Persons with Oral Precancerous Conditions

RACE	SEX	AGE-GROUP (YEARS) 15 — 19	20 — 29	30 — 39	40 — 49	50 — 59	TOTAL	GRAND TOTAL	% of total No. patients
MALAY	M	SK — 1	L — 4 PL — 3 SK — 2	PL — 4 SK — 2	PL — 2	—	L — 4 PL — 9 SK — 5	18	8
	F	—	—	—	—	—	—	—	0
INDIAN	M	—	L — 2 PL — 3	L — 1 PL — 1 SK — 1	L — 2 PL — 2	E — 2 L — 4 PL — 3	E — 2 L — 9 PL — 9 SK — 1	21	18
	F	—	PL — 1	L — 1 SMF — 1	E — 1 L — 6 PL — 3 SMF — 1	L — 1	E — 1 L — 8 PL — 4 SMF — 2	15	48
CHINESE	M	—	—	—	—	—	—	—	0
	F	—	—	PL — 1	—	—	PL — 1	1	14
TOTAL		1	15	12	17	10	55	55	14

E — Erythroplakia; L — Leukoplakia; PL — Preleukoplakia; SK — Smoker's Keratosis; SMF — Submucous Fibrosis

Table — 3

Distribution of 266 Persons who Indulged in Oral Habits

RACE	SEX	AGE GROUP (YEARS) 15 — 19	20 — 29	30 — 39	40 — 49	50 — 59	TOTAL	GRAND TOTAL
MALAY	M	MH — 6 S — 5	A — 4 MH — 22 S — 26	— MH — 15 S — 30	A — 1 MH — 6 S — 16	— MH — 2 S — 3	A — 5 MH — 51 S — 80	136
	F	— — —	A — 1 — —	— BQ — 1 — MH — 1	— BQ — 1 — MH — 1	— — BQ+T — 1 —	A — 1 BQ — 2 BQ+T — 1 MH — 2	6
INDIAN	M	—	A — 2 BQ — 1 — MH — 15 S — 10	A — 2 BQ — 1 BQ+T — 1 MH — 18 S — 3	A — 4 — BQ+T — 3 MH — 18 S — 2	— — BQ+T — 1 MH — 11 S — 2	A — 8 BQ — 2 BQ+T — 5 MH — 62 S — 17	94
	F	—	BQ — 1	BQ — 3 BQ+T — 5	BQ — 3 BQ+T — 9 MH — 3	MH — 2	BQ — 7 BQ+T — 14 MH — 5	26
CHINESE	M	—	S — 1	—	MH — 1 S — 2	—	MH — 1 S — 3	4
	F	—	—	—	—	—	—	0
TOTAL		11	83	80	70	22	266	266

A — Alcohol; Bq — Betel-quid; BQ+T — Betel-quid + Tobacco; MH — Multiple Habits; S — Smoking.

years and in the case of the Indian females, most of them were between 30 to 49 years.

Oral Precancerous Conditions

Fifty-five persons had oral precancerous conditions (Table 2). In comparison to 8 per cent of the Malay males, 18 per cent of the Indian males had oral precancerous conditions. It is also interesting to note that the number of Malay and Indian females examined were approximately the same. None of the Malay females had oral precancerous conditions, whereas 48 per cent of the Indian females had oral precancerous conditions.

The peak incidence of oral precancerous conditions in the Malay male was in the 20 to 29 year age group. This was also the largest group of Malay males to be examined. The peak incidence of oral precancerous conditions in the Indian male was in the 50 to 59 year age group and in the Indian female in the 40 to 49 year age group.

Smoker's keratosis was reported most commonly in the Malay male, preleukoplakia in the Indian male and Malay male, leukoplakia in the Indian male and female. Erythroplakia and submucous fibrosis were reported in the Indians.

Oral Habits

In all 266 (65%) persons indulged in oral habits (Table 3). They consisted of 136 Malay males, 6 Malay females, 94 Indian males, 26 Indian females and 4 Chinese males.

The single habit of smoking was most popular among the Malay male. Multiple habits, consisting of smoking and an occasional drink of beer, brandy or whisky, was the next common habit. Betel-quid chewing was not practised by the Malay male or for that matter by the Chinese in this study. Five Malay females indulged in betel-quid chewing. All of them added gambir to their quid, but only one in addition included tobacco in the quid.

In the Indian male, multiple habits were most popular, followed secondly by the single habit of smoking. Multiple habits usually consisted of chewing betel-quid (often with tobacco), drinking toddy[1] and samsu[2] and smoking cigarettes of locally-made Indian cheroots. In the Indian female, the single habit of chewing betel-quid with tobacco was most popular. Multiple habits in the Indian female often consisted of betel-quid chewing and toddy drinking. All the Chinese females had no oral habits.

Toddy[1] — toddy samples would vary with the degree of fermentation and could fall within the range of 3.8 - 15.1% proof spirit.

Samsu[2] — samsu samples would also vary depending on the brand, whether medicated or illicit and could reach up to 169.1% proof spirit.

Table — 4

Distribution of 407 Persons according to Race, Sex, Oral Habits and Oral Precancerous Conditions

ORAL HABITS		MALAYS			INDIANS			CHINESE			% of total OPC Persons.
		No. of Persons.	Persons with OPC		No. of Persons.	Persons with OPC		No. of Persons.	Persons with OPC		
			No.	%		No.	%		No.	%	
Single Smoking Habit	M	79	7	8.9	17	2	11.8	3	—	—	16.4
	F	—	—	—	—	—	—	—	—	—	
Single Chewing Habit	M	—	—	—	7	3	42.9	—	—	—	27.3
	F	3	—	—	21	12	57.1	—	—	—	
Single Drinking Habit	M	5	—	—	8	1	12.5	—	—	—	1.8
	F	1	—	—	—	—	—	—	—	—	
Multiple Smoking/ Chewing/or Drinking Habits.	M	51	10	19.6	62	15	24.2	1	—	—	50.9
	F	2	—	—	·5	3	60.0	—	—	—	
No Habits	M	84	1	1.2	21	—	—	2	—	—	3.6
	F	23	—	—	5	—	—	7	1	14.3	
TOTAL		248	18	7.3	146	36	24.7	13	1	7.7	100.0

OPC — Oral Precancerous Conditions.

Table — 5

Distribution of 79 Oral Precancerous Conditions by Race, Sex, Anatomical Site and Oral Habits

Anatomical site	Race and Sex	Total Number	No Habits	Single Smoking Habits	Single Chewing Habit	Single Drinking Habit	Multiple Habits
Buccal Mucosa	MM	12	1	3	—	—	5
	IM	22	—	2	2	1	10
	IF	14	—	—	7	—	3
	CF	2	1	—	—	—	—
Labial Commissure	IM	4	—	—	1	—	1
	IF	4	—	—	3	—	—
Lip	IM	1	—	—	—	—	1
Gingivae	MM	5	—	3	—	—	2
	IM	1	—	—	—	—	1
Tongue	IM	4	—	—	1	—	3
Palate	MM	5	—	2	—	—	3
	IM	1	—	—	—	—	1
Floor of Mouth	IM	4	—	—	—	—	4
TOTAL:		79	2	10	14	1	34

MM — Malay Male; IM — Indian Male; IF — Indian Female; CF — Chinese Female

Correlation of Precancerous Conditions with Habits

In the Malay male, of the 51 persons who indulged in multiple habits, about 20 per cent had precancerous conditions (Table 4). Of the 79 persons who indulged in the single habit of smoking, 9 per cent had precancerous conditions. Of the 84 persons who had no oral habits, 1 per cent had precancerous conditions.

In the Indian male, of the 62 persons who indulged in multiple habits, 24 per cent had precancerous conditions. Of the 17 persons who indulged in single smoking habit, 12 per cent had precancerous conditions. Of the 7 males indulging in a single chewing habit, 43 per cent had precancerous conditions. Of the 8 males indulging in a single drinking habit, 13 per cent had precancerous conditions.

In the Indian female, of the 21 persons indulging in a single chewing habit, 57 per cent had precancerous conditions. Of the 5 females indulging in multiple habits, 60 per cent had precancerous conditions.

None of the Indian males and females with no oral habits had precancerous conditions. Of the 7 Chinese females with no oral habits, 14 per cent had precancerous conditions. None of the Chinese males had precancerous conditions.

Correlation of Anatomic Site of Precancerous Conditions with Habits

In the Malay male, preleukoplakia and leukoplakia of the buccal mucosa and gingivae and smoker's keratosis of the palate were noted (Tables 2, 5). They were often associated with multiple habits and single smoking habit.

In the Indian male, preleukoplakia and leukoplakia occurred most frequently on the buccal mucosa and less frequently on the labial commissure, tongue and floor of the mouth. Multiple habits were most commonly associated with these conditions. In the Indian female, leukoplakia and preleukoplakia occurred most frequently on the buccal mucosa and less commonly on the labial commissure. Single betel-quid chewing habit was most frequently associated with these lesions. The

two cases of submucous fibrosis were in a 35-year-old Indian female who indulged in the single chewing habit of betel-quid with tobacco. She also had anaemia. The other was a 45-year-old Indian female who also indulged in the single chewing habit of betel-quid but without tobacco. In addition, she had an erythroplakia of the right buccal mucosa.

Discussion

It is not possible to make an exact comparison of the present study with two previous reports on the frequency of oral precancerous conditions in this country. The two earlier studies had been limited to betel-quid chewers and did not include all the precancerous conditions included in this study. Moreover, Chin and Lee (1970) did not include smoking and alcohol habits in their study. Ahluwalia and Ponnampalam's (1968) observations on the oral habits of the Indian male and female are similar to our findings. In the Indian male, multiple habits of betel-quid chewing, drinking and smoking were most popular whereas in the Indian female the single habit of betel-quid chewing was most significant. This would suggest that the oral habits of the Indians were similar irrespective of whether they lived in towns or in the rural areas.

Seven per cent of the Malays, 8 per cent of the Chinese and 25 per cent of the Indians had precancerous conditions. None of the Malay females had precancerous conditions. This may be due to the small number of Malay females included in the study and furthermore a majority of them belong to a much younger age group. Moreover, a large number of them (79%) did not have oral habits.

The total number of Chinese included in this study is rather small for any valid observations to be made. It is, however, interesting to note that none of the Chinese females had oral habits. Moreover, it is worth pointing out that the records of the Division of Oral Pathology and Oral Medicine show the Chinese female has the lowest incidence of oral carcinoma (4%) in West Malaysia.

In the Indians, in contrast to 18 per cent of the males having precancerous conditions, 48 per cent of the females had precancerous conditions. In this racial group, 35 per cent of betel-quid chewers had precancerous conditions and only 6 per cent of non-betel-quid chewers had precancerous conditions. This would suggest that the most important single habit in causing precancerous conditions is betel-quid chewing.

In this study, the number of betel-quid chewers who did not add tobacco was rather too small to make any significant observation between the two groups. It is worth noting none of the Indians with no oral habits had oral precancerous conditions. Ninety-six per cent of all precancerous conditions occurred in persons with oral habits, whereas about 4 per cent of precancerous conditions (all preleukoplakias) occurred in persons with no oral habits. Probably the preleukoplakias could be caused by irritation from teeth as we observed in one of the two persons in this group. It is also possible in persons with no oral habits for a greater per cent of preleukoplakias and leukoplakias to regress.

In the Malay male, about 2.3 per cent had smoker's keratosis, 4.1 per cent had preleukoplakia and 1.8 per cent had leukoplakia. In the Indian male, 0.9 per cent had smoker's keratosis, 1.7 per cent erythroplakia and 7.8 per cent respectively had preleukoplakia and leukoplakia. In the Indian female, 2.3 per cent had erythroplakia, 6.5 per cent submucous fibrosis, 12.9 per cent had preleukoplakia and 25.8 per cent had leukoplakia.

The high incidence of precancerous conditions in the Indian female could be due to a large number of the sample being from the age group where the peak incidence of precancerous conditions occurs in the Indian female. The peak incidence of precancerous conditions in the Indian female (40-49 years) seems to be at a slightly earlier age than in the Indian male (50-59 years).

Ramanathan et al (in press) in a study of the frequency of precancerous conditions in oral cancer patients have shown like oral cancer, the peak incidence of leukoplakia in the Indian female (40-59 years) occurred at a slightly earlier age than in the Indian male (50-69 years). This was not only because the Indian female, as a rule started the habit of betel-quid chewing at an earlier age but also because the lifetime betel-quid chewing hours (product of the number of quids chewed/day × duration of chewing of each quid × number of years of chewing) was generally greater in the Indian female.

As expected, the incidence of precancerous conditions generally increased with age. The percentage of precancerous conditions for the various age groups were: 15-19 years (5.6%); 20-29 years (13.4%), 30-39 years (9.6%); 40-49 years (19.8%) and 50-59 years (33.3%).

It is indeed interesting to note the town-dwelling Malay male has virtually discarded the habit of chewing betel-quid in favour of smoking. This could explain the highest incidence of smoker's keratosis in this group. The betel-quid chewing habit seems to have also been discarded by an

increasingly large number of the younger group of Malay females and Indian males. Like his Malay counterpart, the town-dwelling young Indian male prefers to indulge in cigarette smoking rather than in betel-quid chewing. The changing trend in oral habits would certainly result in a change in the race and sex incidence and anatomical sites of involvement of oral precancerous conditions and oral carcinoma over the years.

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Cost per anaesthetic

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Introduction

HOW MUCH DOES IT cost to give an anaesthetic?

It will be most interesting and instructive from the point of view of economics to know when one is engaged in the practice of anaesthesia, especially in hospital practice when cost is taken for granted. It is apparent that the components making up the cost per anaesthetic are multiple and variable. Patients in a private hospital have been known to be billed a few hundred dollars for a few days of oxygen therapy by the mask.

The tables on the cost of various anaesthetic drugs given below will be a guideline to encourage and exhort all practising anaesthetists to economise. The figures refer to drugs and gases (pipe-line supply) used in the University Hospital.

The cost of an anaesthetic per se includes cost of premedication; induction agents; maintenance of anaesthesia, best expressed by the hour, either under spontaneous respiration or intermittent positive pressure ventilation (manual or automatic). Special techniques may include regional blocks, ketamine anaesthesia, neuroleptic-analgesia.

The cost of use of disposable syringes, disposable transfusion sets and intravenous cannulae may be included in the total cost of an anaesthetic.

This article will describe mainly the costs of expendable anaesthetic materials which are under the control of the anaesthetist and are dependent on the technique of anaesthesia and the breathing system used.

Table I — Drugs used in Premedication

	Preparation and Dosage	$ cts
Syrup Vallergan	6 mg per ml; 1.5 — 2 mg/kg	2 per mg
Inj. Atropine	0.6 mg	5
Hyoscine	0.6 mg	16
Phenergan	50 mg	20
Pethidine	50 mg, 100 mg	4; 7 cts
Morphine	15 mg, 30 mg	6; 10
Pentazocine	30 mg	70 cts
Water for injection.		5

Comments

Trimeprazine tartrate (Vallergan), commonly used for paediatric premedication, is a strong central sedative, an anti-histamine, anti-emetic, and spasmolytic. The vallergan forte (6 mg/ml) is given 1.5 - 2 mg/kg 1½ to 2 hours before anaesthesia (Cope, 1959).

Atropine and Hyoscine

The belladonna derivatives are about the commonest used, and are relatively cheap. Hyoscine is used more often nowadays for its amnesic and sedative properties in suppressing recall after anaesthesia or reducing the chance of awareness during Caesarean section (Crawford 1971, Liew 1972).

Analgesics

Of the narcotic-analgesics, Pentazocine (Non D-D-A) is most expensive and the advantages over the others are minimal.

Table II — Intravenous Induction Drugs

		$ cts
Thiopentone sodium	0.5 G	43 cts
(2.5% solution)	1 Gm	63 cts
Methohexitone Sodium	500 mg into 50 ml	3.90
(1% solution)	Saline	
Propanidid (Epontol)	500 mg in oily base	70 cts to 1.40
Ketamine Hcl	1% solution (10 mg per ml)	
	20 ml per bottle (200 mg)	6.90
	5% solution (50 mg per ml)	14.90
	10 ml per bottle. (500 mg)	

Comments

Methohexitone (1-1.5 mg/kg) is 2½-3 times more potent than thiopentone. It costs 39 cts per 5 ml of an induction dose whereas thiopentone (3-4 mg/kg) cost 12 cts for an equipotent dose — that is, three times cheaper.

Also a solution of Methohexitone can be safely used up to a period of 10 days, especially kept in a refrigerator. It will be wasteful to open a gram of thiopentone to do a case, unless the balance is left for use by the emergency anaesthetist within 12 hours.

Cost of an Anaesthetic for ECT (University Hospital)

With the non-relaxant intravenous technique (Delilkan, 1969) and use of Ectonus stimulator, using a single intravenous dose of methohexitone (1 mg/kg) premixed with atropine 0.6 mg, the cost is some 45 cents for a 50 kg patient. Similar cost will be for a dental anaesthetic.

Intravenous ketamine Anaesthesia (1.5 — 2 mg/kg)

Intravenous ketamine anaesthesia is usually given when indicated such as for skeleto-muscular operations in the presence of a full stomach; certain abscesses in the head and neck (Delilkan, 1970) or where preservation of airway protective reflexes is desirable. An orthopaedic adult patient may require 500 mg (10 ml of a 5% solution, cost $15.00) for reduction of a fracture lasting 30 minutes. Ketamine is a reserve drug.
Intramuscular ketamine (4-10 mg/kg) anaesthesia is expensive.

Table III — Anaesthetic Gases and Maintenance Anaesthesia

(1 cubic foot = 6¼ imperial gallons;
1 imperial gallon = 4.5 litres)

1. Pipeline oxygen 240 cu. ft per cylinder at $6.50; 24 cylinders in series.
   Cylinders on anaesthetic machine e.g.
   48 cu. ft $2.25.
   24 cu.ft $1.90.
2. Nitrous Oxide
   Pipeline nitrous oxide: 3,600 gallons per cylinder;
   4 cylinders in series.
   Cylinders on anaesthetic machine: 100 gallons (450 L) capacity costs $4.50 - $5.00
   200 gallons (900 L) capacity costs $9.00-$10.00.

Comments

It costs 1 cent per litre or 5 cents per min at a flow of 5L/min or $3.00 for 300 L/hour as calculated below:

Nitrous Oxide: 100 gallons of nitrous oxide cost $4.50. Thus one imperial gallon = 4.5 litres cost 4.5 cents or 1 litre of nitrous oxide costs 1 cent.

Or a 200-gallon cylinder of nitrous oxide containing 900 L which at a flow rate of 5 litres per min lasts 180 mins (3 hours). The cost is thus $3.00 for 300 litres per hour (5 L/min). Nitrous oxide runs at 5 cents per minute at a flow of 5 L/min.

Oxygen

Pipeline oxygen (240 cu ft cylinders).
1 cu ft = 6¼ imperial gallons= 23.32 litres costing 2.5 cents.

Therefore 1 litre of oxygen costs 0.088 cent or 0.09 cent approximately.

The cost of nitrous oxide, litre for litre, is 12 times that for oxygen while it is also used at a flow 2½ times less than that of oxygen (e.g. 5 litres nitrous oxide, 2 litres oxygen). Pipeline oxygen is therefore quite cheap for anaesthetic use. The cost is astronomical only when used at high flows on a patient for days in a ward!

Controlled or automatic ventilation with the Manley Ventilator

This machine is gas driven (expensive), and has a non-rebreathing circuit (expensive). Being a minute volume divider, the patient's minute volume equals the volume of fresh gas from the rotameters.

Table IV — Manley Ventilator

High Flows	Cost per Hour	Total
Oxygen: 3 litres/min	18 (20) cents	$4.40
Nitrous Oxide: 7 litres/min.	$4.20	
Moderate flows:		
Oxygen: 2 litres/min	12 (15) cents	$3.15
Nitrous Oxide: 5 litres/min.	$3.00	

In general, gas-driven ventilators (Manley, Howells) with non-rebreathing circuits are expensive. It is usually extravagant and unnecessary to use more than 7 litres of gases for a 50 - 60 kg patient, whose minute volume is about 5 - 5.3 litres. The fear of insufficient hyperventilation and awareness during light relaxant-nitrous oxide-oxygen anaesthesia is the reason for using high flows of more than 7 litres.

The present trend is moderate hyperventilation (pCO_2 around 30 - 32 mmHg) with a concentration of nitrous oxide between 72 - 74% in oxygen to provide sufficient narcosis (and analgesia) (triad of anaesthesia; Gray, 1960).

The following table showed moderate hyperventilation at moderate flows with a Manley ventilator on two patients undergoing cardio-pulmonary bypass after induction of anaesthesia.

Table V — Manley Ventilator with moderate flow rate of fresh Gases:

		Arterial Blood Gas.
Patient I .50 kg	oxygen 2 (28.5% oxygen)	pCO_2 = 30 mmHg
	nitrous oxide 5	pO_2 = 130 mmHg
Patient II 40 kg	Oxygen 1.8	pCO_2 = 28 mmHg
	Nitrous oxide 4.7	pO_2 = 136 mmHg

The East Radcliffe (basically non-rebreathing) anaesthetic ventilator with incorporation of a soda-lime cannister and reservoir bag (rebreathing) is economical for use during anaesthesia at such flows of oxygen 1.5, and nitrous oxide 3 - 4 litres per minute.

T-piece: For the T-piece for IPPV in paediatric anaesthesia (Rees, 1950), the flow of fresh gas to prevent significant rebreathing is 100 ml/lb (220 ml/kg) body weight with a minimal of 3 - 4 litres in the newborn and young children.

Table VI — Inhalation Anaesthetics and Others

Diethyl ether	500 ml	$ 3.25
Ethyl chloride spray	100 g	$ 1.80
Halothane/Fluothane	250 ml	$69.40
Penthrane	125 ml	$65.00
Soda lime	18 kg	$35.00
Cyclopropane (not used)		$ 1.62

Halothane (1 ml liquid halothane = 211 ml vapour at N.T.P.)

Spontaneous Respiration with Halothane in a Magill circuit

The Magill circuit is now shown to be an efficient system down to fresh gas flow rates probably equivalent to the alveolar ventilation of the patient

(Kain & Nunn, 1967; Norman & Sykes, 1968), e.g. 4 - 4.5 litres alveolar ventilation in a 50 - 60 kg patient.

Vaporisation: 250 ml of Halothane is vapourised to a 1% mixture at
9 litres/minute in about 15 hours (Murray 1966);
at 6 litres/minute in about 22 - 23 hours;
at 4.5 litres/minute in about 30 hours.

Thus at a flow of 4.5 litres per minute of 1% halothane, the cost is some $2.50 per hour.

A Method of Estimation of Cost of Halothane in Various Breathing Circuits

On the Magill circuit, a known volume of halothane is placed in the Fluotec or Goldman vapourizer. Fresh gas, e.g. at a flow of 4.5 litres/minute, is used. The volume left at the end of 1 hour is measured. The difference gives the volume of halothane used in 1 hour.

Use of Halothane in Low Flow Breathing Circuit

Use of halothane in low flow breathing circuit, e.g. VIC (Vapouriser in circuit), (Gurubatham 1971): Halothane from a Goldman Vapourizer in a VIC system with oxygen at 200 - 250 ml per min costs on the average $1 an hour.

Other reports (Synopsis of Anaesthesia 6th ed. p. 203) showed the following costs:

1. 1% halothane in a 6 litres/minute flow will cost 50p ($4) per hour for halothane alone.
2. 3% halothane in a 1 litre flow to a rebreathing system will cost 25p ($2/-) per hour.
3. The cheapest method of administration is the V.I.C.

An azeotropic mixture (Law Gim Teik) consists of halothane 68 (two-thirds) and ether 32 (one-third)) parts by volume usually used in the Goldman vapouriser. It is relatively cheaper.

Comments

The freeze-dried preparation for suxamethonium in solution remains fairly potent up to one week in the air-conditioned theatre. We have not used ampoule preparation of 5% solution (100 mg in 2 ml).

The non-depolaring muscle relaxants cost about the same for equipotent or curarizing doses. Thus 3 ampoules ($1.90) of alloferine containing 30 mg may be used for 2 patients for short operations.

3 ampoules of curare ($1.80) containing 45 mg may be used for one patient for a fairly long surgery.

3 ampoules of pancuronium ($3.15) containing 12 mg may be used for 2 patients.

Alloferine (0.25 - 0.3 mg/kg) is 2½ times more potent, and pancuronium (0.08 to 0.1 mg/kg) is 6 - 7 times more potent than curare (0.6 mg/kg).

Reversal: It will be wasteful to draw up excess neostigmine in a syringe only to squirt the excess on the theatre floor.

Muscle Relaxants and Reversal Agents

1. Suxamethonium (freeze dry)	500 mg; $1.50 per bottle	15 cts per ml of 50 mg
2. d-tubocurare	15 mg in 1.5 ml at 60 cts (45 mg in 3 amp = $1.80) Multiple dose 3 mg/ml x 10 ml = $1.90	12 cents per 3 mg 19 cents for 3 mg in 1 ml.
3. Di-ally-nor-toxiferine	10 mg in 2 ml at 63 cents — $1.05	
4. Gallamine	120 mg in 3 ml at 67 cts	
5. Pancuronium	4 mg in 2 ml at $1.05	
6. Atropine	0.6 mg x 2 = 10 cents	
7. Neostigmine	Paediatric ampoule 0.5 mg/ml	15 cets per amp.
Bulk purchase: Multiple dose 5 ml (2.5 mg/ml) at $1.26		25 cts per ml
Small quantity purchase: $1.80 for 5 ml		35 cts per ml.

Local Anaesthetics and Neuroleptic-analgesics

Lignocaine	0.5% x 50 ml	$6.50 or 13 cts/ml
	1% x 50 ml	$7 or 14 cts/ml
	2% x 50 ml	$7.50 or 15 cts/ml
	5% heavy (spinal)	55 cents
	Xylocard 100 20 mg/5 ml	40 cts.
Bupivicaine	0.5% with 1/200,000 adrenaline x 20 ml	$3.75 or 19 cts per ml
	0.25% with adrenaline x 20 ml	
Haloperidol	5 mg/ampoule	21 cents.
Droperidol	2.5 mg per ml x 10 ml	18 cents per ml.
Fentanyl:	0.05 mg/ml; dosage: 0.1 — 0.2 mg	$1.50 per ampoule.
Phenoperidine	1 mg per ml	35 cents per ml.

Intravenous fluids 500 ml per bottle

Dextrose 5%	$ 1.60
Dextrose/saline	$ 1.60
Haemacel	$ 9.00
Rheomacrodex 10% in N/S or 5% dextrose	$17.50
Normal saline	$ 1.76
Ringer's lactate	$ 2.08
Ringer's lactate with 5% dextrose	$ 2.24

Disposable syringes with needles: 10 cents for 2.5 ml to 10 ml syringes; 15 cents for 20 ml syringes. The convenience and sterility are important in anaesthetic practice. One sees 20 ml syringes open indiscriminately for gastric aspiration, measurement of excreta.

Each endotracheal tube lasts on the average of six autoclavings (Stark and Pask, 1962). Taking the average of 10 autoclavings for each tube in the University Hospital, the cost is 50 cents per intubation.

Discussion

The cost per anaesthetic is described as small and modest — compared with surgical materials and not rising significantly over the years. For example, a disposable drainage tube cost $15 each; and blood for transfusion costs $100 a bottle by the time it is used for the patient. The cost of direct surgical materials and heparinised or ACD blood for a case of open heart surgery may be $1500 — $2000.

There is also a growing concern on the long-term harmful effects on the theatre and anaesthetic staff of breathing small quantities of nitrious oxide, halothane (both expensive agents) and other gases within the environment of the theatre (BJA 1971).

The average cost of anaesthetic may be worked on the following term:

$$\frac{\text{Total Expenditure per year on Expendable Anaesthetic Materials}}{\text{Number of anaethetic per year.}}$$

Resuscitation Drugs and Others

Sodium bicarbonate	50 ml of 7.5%	$ 3.35
THAM - E	36 gm in 150 ml	$22.00
Heparin	5,000 u per ml x 5 ml	$21.00 ($4.20 per ml)
Hydrocortisone succinate	100 mg	75 cts — $3.80
Isoprenaline	0.2 mg per ampoule	$ 1.50
Nalorphine	1 mg per ml amp	53 cents
	10 mg per ml	40 cents
Adrenaline (1/1000)	1 mg/ml	18 cents
Arfonad	250 mg per bottle	$5.30
Endotracheal tube		average $5.00

This is a nonsatisfactory figure, since some drugs and gases (entonox, oxygen, compressed air) are used in other places in the hospital and some anaesthetics are short (e.g. ECT sessions). Ether is often used for cleaning plaster marks; oxygen, compressed air are used in the wards and ICU, carbon dioxide for periotoneoscopy and insufflation. These should therefore not be chargeable entirely to anaesthesia.

The average cost of an anaesthetic for a 550-bed provincial teaching hospital in England may be £1 ($8) (Wilson 1966) based on total anaesthetic drugs and gases bill per year; and £3·55p. ($26/-) for anaesthetists and drugs (Wilson 1961). They commented on the economic modesty of the speciality (Shackleton 1960).

Jones (1957, 1961) showed an overall increase of 30% on the cost of each anaesthetic in 5 years at the Groote Schuur Hospital, between 1955-1960.

The prices quoted in this article refer to bulk purchase and by contract and are less than those when purchased in small quantities.

The ways to economise will be to encourage careful use of anaethetic drugs; use of optimal flow of anaesthetic gases for different anaesthetic circuits; discriminate use of certain expensive drugs and when indicated; more conservative use of disposable syringes, needles, cannulae; and better employment of personnel and better supervision.

Should it include the cost of anaesthetists, a much sought-after world commodity?

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Toxoplasma antibody survey in West Malaysia

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Introduction

IN WEST MALAYSIA, studies of infectious mononucleosis among Asians revealed that a very high proportion of patients whose sera were negative for heterophil-antibody had clinical features typical of toxoplasmosis as well as infectious mononucleosis (I.M.). How many of these I.M.-negative cases were in fact due to toxoplasmosis is not known.

Since the problem of human toxoplasmosis has never been investigated in W. Malaysia, an antibody survey to determine the status of this disease in the population was carried out. The results are presented in this paper.

Material and Methods

Sera were collected from 728 normal persons of different age groups, races and occupations from various parts of W. Malaysia. Among the occupational groups studied were veterinarians, padi planters, oil palm and rubber estate workers, miscellaneous labourers and tin miners.

The antibodies were assessed by the Indirect Haemagglutination reaction (IHA). Formalised and tanned sheep red cells were used for the test. The antigen for sensitisation was prepared according to the method of Jacobs and Lunde (1957). The parasites were obtained from mice previously infected with the Rh strain of Toxoplasma. Initially, the test was done in tubes but later testing was done in plates using the microtiter technique. With the tests done in tubes the significant titre was taken as 1:200 or above and with the microtiter technique the significant titre was taken as 1:160 or above.

Results and Discussion

The overall antibody ratio was found to be 13.9% or 101/728. The highest incidence was in Malays (21.8% or 56/257), followed in turn by Indians (13.5% or 34/251) and Chinese (5.0% or 11/220) — see Table 1.

Table 1
Distribution of Toxoplasma Antibodies among W. Malaysian by Age-Group and Race

Age group (in years)	Malay			Indian			Chinese			Total		
	No. exam.	Pos.	%	No. exam.	Pos.	%	No. exam.	Pos.	%	No. exam.	Pos.	%
0 — 10	50	9	18.0	50	4	8.0	50	7	14.0	150	20	13.3
11 — 20	54	11	20.4	52	9	18.0	51	1	2.0	157	21	13.4
21 — 30	76	11	14.5	69	8	11.6	66	1	1.5	211	20	9.5
30+	77	25	32.5	80	13	16.3	53	2	3.8	210	40	19.0
Total	257	56	21.8	251	34	13.5	220	11	5.0	728	101	13.9

It is now known that toxoplasmosis can be acquired either by the ingestion of infected meat or by the ingestion of Toxoplasma oocysts passed in the faeces of the domestic cat. However, it is not certain as to which of these modes of infection is more important, as far as humans are concerned. In Singapore, porcine toxoplasmosis is quite common where 26% of the animals shows antibodies to the parasite (Zaman *et al.*, 1967). Similarly, antibody surveys done in Malaysia show that 9.5% of goats, 11.2% of buffaloes, 0.1% of cattle and 12.5% of pigs have positive sera (Mulkit Singh *et al.*, 1967).

Inspite of the fact that pigs have the highest infection rates among domestic animals, the Chinese population who consume pork more than any other meat have the lowest infection rate. The explanation for this could be that the Chinese in Malaysia and Singapore usually cook their meat very thoroughly before eating, thus avoiding infection. The Malays as an ethnic group have the highest infection rate. This was also observed in a previous survey done in Singapore (Zaman and Goh, 1969). The greater association of the domestic cat with the rural Malay population could be an explanation for this. In Malay kampongs, dogs are generally not kept for religious reasons, but cats are commonly kept as pet animals.

The incidence in males (14.8% or 86/582) was only slightly higher than that in females (10.3% or 15/146). The age group distribution is presented in Table 1. Antibodies were acquired early in life. A decline in antibody rate may be detected in all 3 races in the 21-30 age group. The reason for this is obscure.

The Malays showed high rates throughout the various ages with the maximum incidence in the oldest age group. The highest incidence in the Chinese, on the other hand, was the youngest group, declining towards the older age groups. This seems to indicate that the Malays are constantly and frequently exposed to toxoplasmosis, whereas the Chinese are exposed mainly during childhood. The Indians also appear to be equally exposed throughout the various age groups.

Of the 5 occupational groups investigated, the padi planters showed the highest incidence (22.2% or 20/90), even exceeding that of the veterinarians (20.0% or 26/130), authough the difference may not be significant (Table 2). Estate workers, working in oil palm and rubber estates, and labourers dealing with anti-malarial work showed moderate rates (13.5% and 10.1%, respectively). The tin miners who work in underground mines had a very low incidence (3.7% or 1/27).

Table 2
Distribution of Toxoplasma Antibodies among five Occupational Groups in West Malaysia

Group	No. examined	No. positive	%
Padi planters	90	20	22.2
Veterinary Staff	130	26	20.0
Estate workers	52	7	13.5
Antimalarial labourers	109	11	10.1
Tin miners (lode mine)	27	1	3.7

Table 3
Racial Distribution of Toxoplasma Antibodies among Veterinary Staff Members

Race	No. examined	No. positive	%
Malay	59	15	25.4
Indian	51	10	19.6
Chinese	20	1	5.0
Totals	130	26	20.0

It is interesting to note that in the veterinary group alone, the racial distribution of antibodies follows the same general pattern, viz. highest in the Malays, lower in the Indians and lowest in the Chinese (Table 3).

As the padi planters exist in a farm environment where domestic animals and cats are often kept, and the veterinary staff come in constant contact with animals, it is understood why their antibody rates are high. Estate workers and labourers also work in a rural environment but do not come in much contact with animals. The tin miners generally have much less animal contact as compared to the padi planters and farmers.

The distribution of toxoplasma antibody titres in the various age groups is given in Table 4. As 2 methods were used, the 2 dilution systems are presented. The majority of the positive sera revealed titres among the lower ranges (1:160 to 1:400). Three had very high titres (1:10,240), two of which belonged to children of 0-10 years of age and one to a teenager. This probably indicated recent infections. Moderately high titres (1:300 to 1:6400) were found mainly among the older age groups due probably to booster reactions. Below these, the titres were more or less equally distributed among the various age groups.

The prevalence of antibodies to Toxoplasma varies widely in different parts of the world (Chandler and Read, 1961). In Southeast Asia, surveys done in Singapore showed a prevalence rate of 17.2% using the IHA reaction (Mulkit Singh *et al.*, 1968). In Indonesia, 8.9% of the population examined in Surabaja were positive (Yamamoto *et al.*, 1970.) In Hongkong, an overall incidence of 6.2% was obtained in the adult population using the dye-test. The same survey showed that 71% of the pigs imported from China were positive (Ludlam *et al.*, 1969). The authors remarked that the lower incidence amongst the predominantly Chinese population of Hongkong could be due to eating pork in "small lumps and only when it is well cooked."

Summary

A serological survey for toxoplasma antibodies employing the IHA test was conducted on 728 normal persons of different age groups, races and occupations from various parts of W. Malaysia. The overall antibody ratio was found to be 13.9%. The Malays were most highly infected (21.8%), followed in turn by the Indians (13.6%) and the Chinese (5.0%). Possible reasons for this are given.

The incidence in males was only slightly higher (14.8%) than that in females (10.3%). Antibodies were acquired early in life and a general upward trend was observed with increase in age.

Of 5 occupational groups studied, the padi planters and veterinary staff showed the highest incidence (22.2% and 20.0% respectively). Estate and anti-malaria workers had moderate rates (13.5% and 10.1%, respectively) and tin miners (of underground mines) had the lowest rate (3.7%).

The distribution of toxoplasma antibody titres in the various age groups was also studied. The majority of the positive sera revealed low titres.

The antibody ratios of some Southeast Asian countries are compared.

Acknowledgement

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Table 4

Distribution of Toxoplasma Antibody Titres in Various Age Groups

	Titres* in macro test	200		400		800		1600		3200		6400			
	Titres* in macro test	160	320		640		1280		2560		5120			10,240	
Age groups (in years)	0 — 10	5	0	7	0	1	0	3	0	2	0	0	0	2	20
	11 — 20	6	0	3	1	5	2	0	0	3	0	0	0	1	21
	21 — 30	2	8	0	3	0	0	2	1	1	3	0	0	0	20
	30+	4	9	3	7	1	3	0	8	0	3	0	2	0	33
	Totals	17	17	13	11	7	5	5	9	6	6	0	2	3	101

*Expressed as reciprocals.

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Treatment of skin diseases: recent trends

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RESEARCH IN THE FIELD of dermatology has made substantial contribution to the understanding of the pathogenesis of many skin disorders. Though cosmetic improvement with reduction in the morbidity of various disorders has been the main aim of advances in the treatment, permanent cure of some disorders does not seem to be far off. Recent trends in the treatment of some common disorders are reviewed in this article.

Psoriasis and Methotrexate

The normal epidermal cells divide approximately every 19 days whereas the psoriatic epidermal cell does it much rapidly, completing the germinative cell cycle every 37 hours (Weinstein and Frost, 1968). Methotrexate prevents DNA synthesis at the S phase of the cell cycle, thus cell replication is stopped. The actively dividing psoriatic epidermis should be selectively more sensitive to methotrexate than other tissues, e.g. normal epidermis. The duration of inhibition of DNA synthesis in psoriatic epidermis following administration of a single dose has been determined to be 12 to 16 hours (Weinstein et al., 1970).

Various regimes of methotrexate has been used for the treatment of psoriasis but Weinstein and Frost (1971) proposed the administration of low-dose methotrexate in three divided doses over the life cycle of the psoriatic cell population. During the 36-hour period, most of the psoriatic cells would, as they enter the S phase, be prevented from completing the germinative cycle, whereas only a relatively small proportion of other actively dividing tissues of the body, such as hair follicle, bone marrow, normal epidermis and the mucous membrane of the gastrointestinal tract, would be

affected with minimal toxic effects. The irreversible damage to the liver on prolonged therapy with this drug is a serious menace which one must bear in mind when we are dealing with a disease which itself is not fatal.

Patients who have had a fair trial of various topical therapy, with no history of past or present liver disease, with intact renal function and women beyond the reproductive age can be considered suitable for methotrexate therapy. They must have pre-therapy liver biopsy, regular blood counts and liver functions tests during the regime. The low dosage regime mentioned above might prove to be more tolerable to patients.

Vitiligo

Development of vitiligo, especially on the exposed part of the body, has both cosmetic and social significance, the latter because of the mistaken belief that it is leprosy. In spite of the specific therapy, available cover-up cosmetics have still a place when the distribution of vitiligo is limited.

To induce repigmentation of the vitiliginous skin both meladinine and 8-methoxypsoralen were used but they were not very effective. A new synthetic compound, furocoumarin derivative, 4, 5', 8-trimethylpsoralen is now used. This is more potent than the previously available preparations in its photosensitising effect and the results of the therapy suggest that it may prove to be a more effective therapeutic agent (Bleehen, 1972).

Two hours after taking the drug, the patient must expose all the affected areas to sunlight, gradually increasing the exposure time depending on the severity of the erythema the vitiliginous skin develops. The effect of the therapy is noticeable after using the drug for a minimum of six months.

The mode of action is not well understood but the observation of perifollicular repigmentation at the initial stages of improvement led to the suggestion that treatment with this substance might induce colonisation of the depigmented skin by the melanocytes originating from the pigmented hair bulbs (Pegum, 1955). However, repigmentation of the mucosa and the genitalia, which is seen with this therapy, is not dependent on the above mechanism. Psoralens with a mitotic effect on the melanocytes (Clark et al., 1968) may activate those found on the border of the vitiliginous spot. Whether the effect produced by this drug is permanent or it has systematic toxic effects is unknown at present.

Acne Vulgaris and Topical Vitamin A

Comedones and seborrhoea are the two chief factors which contribute to the development of acne vulgaris. It is believed that comedone formation is dependent on the production of horny cells which tend to adhere together forming a plug at the follicular opening. In normal person these cells desqumate invisibly at the follicular orifice, as they are loose and non-adherent.

Short of reducing the sebum secretion by anti-androgen, cyproterone, (Cunliffe et al., 1969), which is still in the experimental stage, dislodging the comedones already present or preventing its formation seems an attractive method for treatment of acne vulgaris. The conventional anti-acne agents irritate the surface of the skin to remove the comedones. Vitamin A acid is not only the most potent irritant substance but is also believed to act on the epithelium lining the sebaceous follicle and it inhibits the formation of comedones by increased production of non-adherent horny scales which readily slough and are cast off by desqumation of skin (Kligman et. al. 1969).

On application of Vitamin A topically the skin becomes inflamed, desqumates and crusts. The patient must be warned of this initial effect or he may be frightened and discard the treatment. As with any other anti-acne therapy, continuous treatment for a period of six months is necessary before assessing the results of the therapy.

Urea Cream for the Skin

The degree of hydration keratin decides the softness of the skin and its cosmetic appearance. In ichthyosis and xeroderma, the skin contains much less water than the normal skin and the disorder becomes particularly noticeable on the exposed part of the skin, now that we spend a large part of the day in a low humid air-conditioned atmosphere. Water content of the keratin can be increased first by moistening the skin, then applying grease to the surface to prevent evaporation, or cosmetic improvement can be obtained by keratolytic agents which disperse the scales on the surface. None of these treatments has proved very effective.

Urea binds water and thus it is able to rehydrate the ichthyotic scales (Swanbeck, 1968). It is bactericidal and does not sensitise the skin. However, it is unstable in aqueous mixture. A ten per cent concentration of the substance in a stable emulsified base has proved cosmetically acceptable and has long shelf life (Martin Beare, 1971; Swanbeck, 1968). This is to be applied more than once a day and especially before exposure to the low humidity atmosphere.

Bullous Disorders and Methotrexate

Available evidence indicates that both pamphigus and pemphigoid are autoimmune diseases (Beutner et. al., 1968). The bulla, which is the pathologic marker of both diseases, is intraepidermal in pemphigus and is at the dermo-epidermal junction in pemphigoid. It can be demonstrated that localisation of antibodies corresponds to the site of the pathology and the titre of antibody is proportional to the severity of the disease. Use of immunosuppressive therapy in the form of methotrexate has been found useful in the treatment of both disorders (Lever and Hashimoto, 1969).

Prednisolone was the drug of choice for both disorders but as a lifelong therapy for pemphigus with all its consequent dangers left much to be desired. Methotrexate is a useful alternative for all patients except those with very active disease in whom prednisolone is given initially till the disease is under control and then changed to methotraxate. The mode of action is through both suppression of antibody formation and anti-inflammatory action.

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Simple treatment of jaundice

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Introduction

MANAGEMENT OF JAUNDICE has remained a controversy till today. From the simple treatment of bed rest for the very mild jaundice of hepatitis to the most complex of diets and use of liver metabolites, such as cholin and methionine feeding, steroids, and the exchange transfusion or even total transfusion for the most severely damaged acute necrotic livers. The diagnosis and subsequent management of jaundice and liver disorders have been categorised by textbooks for simple guides to students. An accurate diagnosis of a patient may sometimes leave one in doubt as to whether it may be an intracanincular block, cholestatic jaundice, or extrahepatic obstruction or a combination of such and in a severely jaundiced patient whereby the bleeding tendency is made more acute, liver biopies or laparotomy can be a hazardous operation. Hence, any rapid resolution of jaundice with rapid repair of liver damage is welcome for this nefarious but vital organ, and simultaneously improving liver function for further investigations and management.

Case History

After 3 days of rapidly advancing jaundice, W.C.L., a well-built, 30-year-old urban male, was

admitted diagnosed as hepatitis with marked jaundice; severe nausea, vomited several times daily, right hypochondral pain and tenderness, with a soft liver palpable to two fingerbreadths below right intercostal margin. No past relevant history of note and no previous malaria, hepatitis, blood transfusion, drug treatment or native medicine. At about the same time noticed dark urine and pale stools. He had no chills or rigor but was running a low grade fever of 99°F, Murphy's sign negative and gall bladder not palpable. A provisional diagnosis of infectious hepatitis was made.

Investigations and Management

Serum Bilirubin 48 mg%, Alkaline Phosphatase 12.6 sigma units per ml, S.G.P.T. 560 S-F units/ and Thymol Turbidity 12.2 Maclagen units, urine was positive for bile salts and bile pigments, Urobilinogen (Erhlich's test) positive to dilution of 1/10. Chest X-ray normal, plain X-ray abdomen normal no radiopaquestones, Paul Burnell negative, no malaria parasites seen on blood film.

The patient was admitted on first diagnosis into hospital. He was ordered for bed rest and glucose fluids with a light fat-free diet. On alternate days, glucose 50% I.V.I. 20 ml and parentovite intravenous high potency were given, no other therapy was added. By the 4th day of treatment, his yellow tinge markedly lessened, felt subjectively well, appetite improved, nausea and vomiting subsided. Liver was palpable to 1½f. and still slightly tender.

On the 8th day after having had four injections of glucose and four of parentovite, he felt so well that he asked for home treatment. This was granted as his improvement was so dramatic. Tests repeated showed serum bilirubin 4.8 mg%, S.G.P.T. 114 S.F. unit/ml, thymol turbidity 8.6 Maclagen units and alkaline phosphatase 6.25 sigma units/ml on the 8th day. Urine still showed trace of bile and bile salts, stools were more normal colour.

He was followed up twice weekly for next 14 days at home, and his general condition improved to near normal. Liver by now was impalpable and he had only very slight icteric tinge over sclera and skin. Investigations at 22nd day showed serum bilirubin of 2.4 mg% S.G.P.T. 52 S.F. units/ml, thymol turbidity 2.6 Maclagen units. During the last two weeks, he only had two intravenous injections of glucose 50% and parentovite each alternating twice weekly without much restriction of food except to eating home cooked meals. The patient was able to resume normal duties at this stage, 22 days after a moderately severe attack of infectious hepatitis and jaundice.

Discussion

Glucose-Parentovite therapy dramatically reduced the severity of jaundice in infectious hepatitis, helped rapid repair of liver and quick return to to ambulant stage. In the light of our combined clinical experience with other cases as well, we like to discuss this simple management in general.

Glucose was given slowly intravenously 50% of 20 ml. No undue reaction occured. The parentovite as intravenous high potency paired ampoules were mixed before injection and given slowly. Parentovite was chosen as it has the correct British Pharmacopeia vitamin formulation. A close watch being made for hot flushing, drowsiness, discomfort and paraesthesia, but these were seldom encountered and usually mild, if occured, as a warm sensation and lasted for few seconds only. High doses of Aneurine may induce mild paraesthesia and rarely hypotension. But these were not encountered in this patient or on others of our patients treated by this method.

Parentovite
(Vitamins Limited, Brentford, England)

Formula

Intravenous High Potency

Paired ampoules contain	No. 1	No. 2
Aneurine hydrochloride B.P.	250 mg	—
Riboflavine B.P.	4 mg	—
Pyridoxine hydrochloride B.P.	50 mg	—
Nicotinaminde B.P.	—	160 mg
D-sodium pantothenate	—	5 mg
Dextrose B.P.	—	1000 mg
Ascobic acid B.P. (as Sodium Ascorbate)	—	500 mg
Water for injection B.P. to	5 ml	5 mg
	10 ml	

Doses for Children
(Vitamins Limited, Brentford, England)

14 years and older	—	as for adults
10 — 14 years	—	1/3 to 1/2 the adult dose
6 — 10 years	—	1/3 adult dose

All these have to be modified in individual cases.

We did not treat children under 6 years old by this method as they are unreliable witness of reactions and object to injections. The dose for

the children given from 6 years and above are as above for both the glucose 50% as well as parentovite. Equally good results were obtained from those with infectious hepatitis in children as for adults. Patients were able to be discharged after one week of management, usually after 3 ampoules of each in mild to moderate jaundice in adults. In moderately severe jaundice, patients were retained for longer periods and given two weeks of management, about six to seven injections of glucose 50% and parentovite each. No undue side effects were observed and no anaphylactoid reactions so far encountered. Mild sensation of warmth was seen in one out of 3 patients, not enough to discontinue therapy.

We feel that this is an easy, safe, not expensive and simple way of clearing jaundice of the non-haemolytic type in most patients, especially infectious hepatitis cases. But may equally be applied to improve liver function in those with surgical jaundice, alcoholic cirrhosis, drug induced liver damage, and perhaps hyperemesis gravidarum.

We have tried on similar jaundiced patients firstly glucose 50%, then parentovite alone and then parentovite in Dextrose 5% infusions; but the best and quickest clinical result obtained was still the glucose 50% alternating with the parentovite intravenously neat. The glucose helps phoshorylation in microsomal liver cell metabolism and the vitamins in parentovite, especially of the B group, may provide the catalytic enzymatic boost for the rapid repair of liver disorders. The glucose parentovite therapy seemed to have hit the right combination.

Summary

This case report is to highlight and illustrate the usefulness of glucose-parentovite therapy in jaundice patients, especially those having infectious hepatitis. Its simplicity, relative safety and ease of administration make it most useful in rural areas where no laboratory exists.

Glucose parentovite therapy for jaundice (non-haemolytic type) has the following beneficial effects.

1) It rapidly reduces the severity of jaundice, especially in infectious hepatitis.
2) Quickly improves liver function and aid liver repair, thereby shortening hospital stay by half.
3) Simple, safe and relatively inexpensive.
4) Rapidly improves patients' clinical condition to ambulant stage and rapid cure of symptoms and signs.
5) Prevents further deterioration of liver damage.

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We wish to thank the Sisters and staff of Our Lady's Hospital for their kind and gentle ministration of our patients. Parentovite intravenous high potency used is from Vitamins Limited, Brentford, England.

Study of perinatal mortality 1970, Maternity Hospital Kuala Lumpur*

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THE PERINATAL MORTALITY in any community is influenced by the personal and social characteristics of the mother, as well as by the standard of medical service they receive. It is widely regarded as one of the most important indices of the standard of obstetric care in any community. This study was undertaken to find out the factors influencing the perinatal mortality at the 225-bed Maternity Hospital, Kuala Lumpur, the largest maternity hospital in Malaysia.

Materials

The study was carried out from January 1970 to December 1970. The Maternity Hospital, Kuala Lumpur is a large metropolitan hospital and not only provides the main obstetric service in Kuala Lumpur, but also receives most of the abnormal obstetric cases from the outlying midwifery centers and district hospitals. Some of the abnormal obstetric cases are airlifted from the rural areas, but others have to be transported by road.

Data

The data obtained have been tabulated as follows.

TABLE I
Maternity Hospital Statistics for 1970

Total number of obstetric beds	225
Premature nursery beds	45
Total number of antenatal first visit	8,390
Total number of subsequent visits	14,226
Total number of admissions	11,258
Total number of deliveries	8,054
Total number of booked deliveries	6,262
Total number of unbooked deliveries	1,792

The above table shows that although there were 8,290 hospital bookings at the antenatal clinics, subsequently only 6,262 of them delivered in the hospital. This is due to the practice that some patients have their antenatal care at the hospital, but have their delivery as domiciliary case or in private nursing homes. The number of unbooked deliveries was 1,792; this high figure was due to the practice that the maternity hospital received most of the abnormal obstetric cases of the region.

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TABLE II
Social Class/Ethnic Group/Parity/Deliveries

Factor		Booked	Unbooked
Social class	First	953	9
	Second/ Third	5,309	1,783
Ethnic group	Malays	2,486	548
	Chinese	1,625	628
	Indians	2,118	614
	Others	33	2
Parity	Primigravida	1,805	432
	Gravida 2 — 5	2,789	807
	Gavida 6+	1,668	553

Table II shows the relationship of social class, ethnic group, parity and booked or unbooked deliveries. The designation first, second and third class are based on the socio-economic factor, and the first class patients belong to the higher social class and second and third class to the lower social groups. As shown in Table II, there was a fair distribution of three main ethnic groups, Malays, Chinese and Indians. Because of the great demand upon the beds, it was necessary in 1954 to introduce a system of priorities for women seeking admission. All women showing abnormalities in the present pregnancy or who had previous abnormal pregnancies or confinements; all primigravidae; and all women in their sixth or subsequent pregnancies were accepted for admission, and women pregnant for the second to the fifth time were advised domiciliary deliveries, unless social or obstetric conditions required hospital deliveries.

TABLE III
Social Class/Ethnic Group/Booked/Unbooked/Parity/Neonatal Death.

Social class	Ethnic group	Total		Primigravida		2 — 5		6 +	
		Booked	Unbooked	Booked	Unbooked	Booked	Unbooked	Booked	Unbooked
I	Malays	4	1	—	—	3	1	1	—
	Chinese	2	—	—	—	2	—	—	—
	Indian	6	—	—	—	5	—	1	—
	Others	—	—	—	—	—	—	—	—
	TOTAL	12	1	—	—	10	1	2	—
II & III	Malay	13	25	2	5	7	13	4	7
	Chinese	14	22	5	5	4	13	5	7
	Indian	6	10	3	—	2	2	4	5
	Others	—	—	—	—	—	—	—	—
	Total	33	57	10	10	13	28	13	19

Table III shows that the majority of the neonatal deaths for the three ethnic groups were for the unbooked cases belonging to social class two and three, and in the higher parity group, since the hospital received most of the abnormal obstetric cases from the outlying rural areas, a certain number of patients presented themselves for treatment with severe degrees of foetal distress and inspite of resuscitation, antibiotics, Caesarean section, neonatal resuscitation and care, the neonatal loss was high in the unbooked cases.

TABLE IV
Social Class/Ethnic Group/Booked/Uubooked/Parity/Stillbirth

Social class	Ethnic group	Total		Primigravida		2 to 5		6 +	
		Booked	Unbooked	Booked	Unbooked	Booked	Unbooked	Booked	Unbooked
I	Malay	2	—	2	—	—	—	—	—
	Chinese	1	1	—	—	—	2	—	—
	Indian	2	—	—	—	2	—	—	—
	Others	—	—	—	—	—	—	—	—
	Total	5	1	2	—	2	2	—	—
II	Malay	32	35	6	6	11	17	14	13
&	Chinese	28	53	4	5	15	33	8	14
III	Indian	45	36	8	8	19	14	18	14
	Others	—	—	—	—	—	—	—	—
	Total	105	124	18	19	45	6 4	40	41

Table IV shows that the majority of stillbirths were for the unbooked cases, of social class two and three and belonging to the high parity group. The abnormal cases from the rural areas like cephalo-pelvic disproportion cord prolapses, placenta praevia, accidental haemorrhage and transverse lies were referred for treatment. These cases contributing to perinatal mortality are amenable to treatment by Caesarean section, but a number of such patients, by the time they reach the hospital, present themselves with a dead baby making Caesarean section obviously useless for foetal salvage.

TABLE V
Social Class/Ethnic Group/Stillbirth/Neonatal deaths.

Social Class	Ethnic Group	Stillbirth		Neonatal death up to 1 week	
		M.S.B.	F.S.B.	Less than 5 lbs.	More than 5 lbs.
I	Malay	1	1	4	1
	Chinese	1	1	2	—
	Indian	—	2	1	5
	Others	—	—	—	—
	Total	2	4	7	6
II	Malay	29	39	28	10
&	Chinese	46	34	26	10
III	Indian	40	41	10	6
	Others	—	—	—	—
	Total	115	114	64	26

Table V shows that for stillbirths there was an equal distribution of 115 macerated stillbirths to 114 fresh stillbirths. For the neonatal deaths, the majority were premature babies, 64 deaths out of a total of 107 neonatal deaths. Although the W.H.O. classification gives $5\frac{1}{2}$ lbs. and below as premature baby, at the maternity hospital we classify prematurity as 5 lbs. and below.

TABLE VI
Maternal conditions/Neonatal deaths/Stillbirths

Maternal condition	Stillbirth		Neonatal Deaths		Total (percentage)	
	FSB	MSB	5 lbs.	5 lbs.		
Toxaemics of pregnancy						
Preclampsia/Eclampsia	37	37	10	3	87	(23.0%)
Hypertension	1	0	0	0	1	
Nephrities	0	0	0	0	0	
Antepartum Haemorrhage						
Placentae Praevia	16	6	9	2	33	(26.9%)
Abruptio Placentae	35	6	11	6	58	
Anaemia	1	28	4	1	34	(10.1%)
Multiple pregnancies	5	7	7	0	19	(5.6%)
Abnormal presentation	35	21	20	4	80	(23.4%)
Pyrexia	0	4	1	0	5	(1.5%)
Cephalo-pelvic disproportion	1	6	0	2	9	(2.5%)
Hydramnios	0	5	0	1	6	(1.7%)
Unknown	25	40	26	14	105	(31.3%)

Table VI shows that the main maternal condition associated with perinatal deaths were antepartum haemorrhage (26.9%), abnormal presentations (23.4%), toxaemia of pregnancy (23.0%) and anaemia (10.1%). It is interesting to note that in 31.3% there were no associated maternal conditions.

TABLE VII
Causes of Neonatal Deaths

Disease	Neonatal deaths	Percentage
Congential abnormalities	6	5.8%
Neonatal infections		
(a) Broncho-pneumonia	7)	21.3%
(b) Gastro-enteritis	15)	
		0.9%
Birth injuries	1	7.9%
Asphyxia neonatorum	8	
Haemorrhagic disease of newborn	7	6.7%
Respiratory distress synd.	18	17.4%
Neonatal jaundice	5	4.8%
Prematurity	36	34.9%

Table VII shows that the three main causes of neonatal deaths were prematurity (34.9 per cent), neonatal infections (21.3 per cent) and respiratory distress syndrome (17.4 per cent). Prematurity has always remained as the most important cause of neonatal deaths at the Maternity Hospital. It is well established that the risk with prematurity has been associated with lower socio-economic groups, and these groups are known for their tendency to premature delivery and the birth of small babies.

TABLE VIII

		Perinatal Mortality		
		Total	Booked	Unbooked
	Deliveries	41.9	23.9	102.1
Class	1st	19.8	17.8	22.2
	2nd & 3rd	43.5	25.1	101.5
	Malays	37.2	20.6	113.1
Ethnic group	Chinese	53.2	27.6	110.8
	Indians	38.4	27.8	74.9
	Primi	26.8	17.1	67.1
Parity	2 — 5	46.1	25.4	117.7
	6 +	51.7	23.9	112.1

Table VIII shows that the perinatal mortality rate for 1970 at the Maternity Hospital was 41.9, but the rate for booked cases was only 23.9 and for unbooked cases it had increased to 102.1. From this study it was observed that the perinatal mortality was influenced as follows:

(a) **Social Class:**— the rate was lowest in the higher socio-economic group.

(b) **Parity and Age:**— the rate was lowest in the primigravidae and increased with increasing parity and age. The lower rates in the primigravidae was due to early booking, greater care and supervision during the prenatal period and labour.

(c) **Ethnic Factors:**— the rate was not influenced by ethnic factors and the apparent difference was due to socio-economic, nutritional and booking or unbooking, rather than to pure ethnic factors.

Comments:

The perinatal mortality in any community is influenced by biological and social factors like age, parity and socio-economic status. It is known that the perinatal mortality in the under 20 age group is lower than at any other age period, and that gradual deterioration occurs with increasing age. It is also known that socio-economic status influences age at marriage; age at the birth of the first child; the spacing and number of subsequent children; type of antenatal care sought; the place and conditions under which delivery takes place; the domestic life and attitude to pregnancy; and physique and general health of the mother. It is well known that the rates were lower in the upper socio-economic groups.

The perinatal mortality is also influenced by the standard of obstetric care available and this depends on a booked or unbooked case, and the place where the delivery takes place, home, private nursing home, district hospital, or a maternity hospital. The overall perinatal mortality could be reduced by careful selection of cases, that is by allowing normal cases to deliver at home or a nursing home, while the high risk patients should deliver in hospitals. As such the perinatal mortality will be always higher in a hospital series than a domiciliary series.

Efforts to reduce perinatal mortality should be directed to: the long-term improvement of the general health and living conditions of a population; to encourage family planning: to improve the obstetric and neonatal care services of the rural areas.

Acknowledgement

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Maternal mortality in the goverment hospitals, West Malaysia 1967—1969*

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MATERNAL MORTALITY is widely accepted as one of the most important indices of the standard of medical care in any community. This study was undertaken to find out the factors responsible for the maternal deaths in the Government hospitals of West Malaysia over the period 1967 to 1969. West Malaysia has eleven states and in each state, there is one large metropolitan type general hospital, a number of district hospitals, main health centres, sub-health centres and mid-wife centres. The purpose of this excellent infrastructure of maternal and child health clinics is to enable each clinic to cover a population of two thousand, so that abnormal obstetric cases from the rural areas can be referred to a district hospital or general hospital for treatment.

Materials

The study covers all maternal deaths in the Government hospitals of West Malaysia over the period 1967 to 1969.

Data

The data obtained have been tabulated as follows:

Table I
Maternal Deaths 1964 to 1969

Year	Total deliveries	Number of deaths	Maternal mortality
1964	83,654	224	27/10,000
1965	84,292	215	26/10,000
1966	87,101	209	23/10,000
1967	87,761	253	29/10,000
1968	89,230	219	23/10,000
1969	92,583	211	22/10,000

Table I shows that inspite of an increase in the number of deliveries in Government hospitals from 83,654 in 1964 to 92,583 in 1969, the maternal mortality had fallen from 27/10,000 to 22/10,000. The maternal mortality rate in Government hospitals was higher than the national maternal mortality rate because of the practice of referring all abnormal obstetric cases to hospitals for management.

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Table II
Cause of Maternal Deaths

Cause	Number of deaths			Death in percentage		
	1967	1968	1969	1967	1968	1969
Haemorrhage	134	104	91	52.9%	42.9%	43.1%
Toxaemia	31	29	29	12.2%	13.2%	13.2%
Infection	12	22	12	4.7%	10.0%	5.7%
Other complications of pregnancy, child birth and puerperium.	58	48	65	22.5%	21.9%	30.8%
Associated non obstetric disease.	20	16	14	7.9%	7.2%	6.6%

Table II shows that haemorrhage still ranks in the forefront of the causes of maternal deaths representing 52.9% in 1967, 42.9% in 1968 and 43.1% of maternal deaths in the Government hospitals of West Malaysia in 1969. The second important cause was toxaemia, 12.2% in 1967, 13.2% in 1968 and 13.2% in 1969, and the third cause was infection which accounted for 4.7% in 1967, 10.0% in 1968 and 5.7% in 1969.

Table III
Deaths due to Haemorrhage

Type of Haemorrhage	Number of deaths			Death in percentage		
	1967	1968	1969	1967	1968	1969
Ante-partum Haemorrhage	27	26	16	10.7%	10.8%	7.6%
Post-partum Haemorrhage	107	78	75	42.3%	35.6%	35.6%

Table III shows that post-partum haemorrhage was the most important cause of maternal deaths, and it is encouraging to note that over the years, there has been a gradual reduction in maternal deaths from 49.5% in 1964 to 35.6% in 1969. In the rural areas, midwives find post-partum haemorrhage a major problem because of the co-existence of anaemia in pregnancy and such a combination carries a high mortality risk. Because of the very high avoidable factor in deaths due to post-partum haemorrhage, the authors have suggested an active method of management of the third stage of labour for the rural midwives. The authors feel that intra-muscular syntometrine with controlled cord traction be introduced as standard methods of the management of the third stage of labour by midwives in the rural areas.

Table IV
Toxaemia of Pregnancy

Type	Number of death		
	1967	1968	1969
Pre-eclampsia	2	0	2
Eclampsia	19	25	20
Post-partum Eclampsia	10	4	7
	31	29	29

Inspite of the fact that deaths from toxaemia are preventable and that by careful antenatal treatment a reduction can be achieved, the deaths due to toxaemia have remained as 31 in 1967, 29 in 1968 and 29 in 1969. The answer to this problem would be early hospital admission in cases of excessive weight gain, elevation of blood pressure or proteinuria, but this poses problems for the rural patient as she is reluctant to be admitted to hospital for treatment. Socio-economic and cultural factors are responsible for her desire to want domiciliary delivery and only seek hospital treatment when there is an obstetric complication like eclampsia.

Table V
Infections

Type	Number		
	1967	1968	1969
Puerperal sepsis	9	10	11
Puerperal pyrexia	3	10	1
Thrombophlebitis	0	2	0
	12	22	12

Inspite of antibiotics, infections have remained a problem in the rural areas, especially in cases of premature rupture of the membranes. In such cases because of the delay in seeking treatment in hospitals, the patient presents with signs of septicaemia.

Other complications of pregnancy, childbirth and puerperium

Table II shows that this group accounted for 22.5% in 1967, 21.9% in 1968 and 30.8% in 1969.

The main causes of maternal deaths were the obstructed and neglected labours due to cephalopelvic disproportion, abnormal lie, presentation and ruptured uterus referred from the rural areas to the hospitals. The majority of patients in this group had their pregnancy labour or puerperium managed by an untrained kampong midwife and by the time the patients were referred to the hospital, the maternal conditions were very critical and inspite of resuscitation and treatment in the hospitals, the maternal morbidity and mortality was high.

Table VI
Associated Causes of Maternal Mortality

Cause	Number		
	1967	1968	1969
Anaemia	2	3	2
Hypertension	9	10	9
Vascular (pulmonary embolism)	6	3	3
Urinary tract infection — pyelitis and acute pyelonephritis	3	0	0

Table VI shows that hypertension was the most important cause in the associated maternal diseases. Anaemia is a major problem in the rural areas, but by itself it only accounted for 2 deaths in 1967, 3 in 1968 and 2 in 1969, but anaemia in combination with haemorrhage was the most important cause of maternal mortality in West Malaysia. With the introduction of antibiotics, deaths due to acute pyelonephritis were reduced from 3 in 1967 to 0 in 1968 and 1969.

Comments

Maternal mortality, like perinatal mortality in any community, is influenced by not only biological and social factors like physique, age parity, socio-economic status, cultural factors like child-bearing

habits, early marriage, spacing, activity, work level of education, housing, economic conditions but also influenced by the availability of the obstetric care and the utilisation of medical services. In Malaysia, the government has taken steps to reduce the maternal mortality, as shown below:

1. The Second Malaysia Plan is aimed at eradicating rural poverty and raising the standard of living of the rural people.

2. There is an excellent infrastructure of health units so that ultimately every 50,000 of rural population is covered by a health unit consisting of main health centres, with 4 sub-centres and 20 resident midwife-cum-clinics at the periphery to serve about 2,000 of the population.

3. A training programme has been started so that midwives, both trained as well as the untrained kampong midwives from the rural areas, are given refresher courses.

4. There is a plan to integrate the family planning services with the health services so that with family planning and population control the hazards of pregnancy and repeated child-bearing is minimised.

5. Applied nutritional projects are being carried out to eliminate malnutrition and anaemia in the rural areas.

6. The authors have suggested that since 60% of the births are conducted in the rural areas by trained or untrained midwives, there should be a standardised method for the management of the third stage of labour. The authors feel that by active management of the third stage of labour, i.e. intra-muscular syntometrine with controlled cord traction, the problem of post-partum haemorrhage can be eliminated thus reducing maternal deaths due to post-partum haemorrhage which at present accounts for 35.6% of the total maternal deaths.

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Mortality in hyaline membrane disease

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HYALINE MEMBRANE DISEASE (HMD) or the respiratory distress syndrome (RDS) is an acute condition, affecting predominantly, premature infants shortly after birth and is characterised by tachypnoea, cyanosis, inspiratory retraction of the chest wall, and expiratory grunting. Investigators in many parts of the world consider it to be the leading cause of death of premature infants[1] and despite almost three decades of intensive research, there seems to be no appreciable decline in the mortality from this disease. The pathophysiology of the condition remains imperfectly understood and its aetiology is unknown.[2,3] This predicament, should, no doubt, be a cause for distress amongst eminent students of the disorder.

A definite diagnosis of HMD can only be made by histological examination of the lungs,[4] and therefore until an unequivocal test is devised to identify the disease in life, autopsy studies will provide the only reliable means of determining its real incidence. A search of the literature in 1959 showed that HMD had not been reported outside the United States and Europe. In 1960, a study of pulmonary lesions of the newborn in Singapore revealed that HMD was the commonest cause of infants dying within the first week of life and it was demonstrated that epidemiological and ethnic factors were of little significance in its aetiology and incidence.[5] There have been other careful studies since then, [6,7,8] drawing attention to the worldwide prevalence of HMD, and also reports from this region.

The purpose of this paper is to analyse the trends in mortality from HMD in this region.

Material and Methods

The material is derived from five separate series of study, the first four being based almost exclusively on autopsies at the Kandang Kerbau Hospital (KKH) Singapore and the final series from autopsies at the University Hospital, Kuala Lumpur.

Series 1. This is based on a 1-year investigation of neonatal deaths ending in June 1960. During this period, there were 38,114 live-births, which includes a small number of births before arrival. There were 555 early neonatal (first week) deaths of which 423 were autopsied. The 'autopsy index' (per cent of early neonatal deaths autopsied) was 76.2%.

Series 2. This is a survey of stillbirths and neonatal deaths[9] over a period of 6 months, ending in December 1962. During this period there were 19,566 livebirths and 345 neonatal deaths. Autopsies were performed on 274, and of these 259 were early neonatal deaths which accounted for 75.1% of the neonatal deaths that were autopsied.

Series 3. This is derived from a perinatal mortality survey over a period of 1 year ending in March 1965.[10] There were 38,667 livebirths during this period and 618 early neonatal deaths of which 485 or 78.5% were autopsied.

Series 4. This is an analysis of neonatal mortality in KKH.[11] This is a 1-year study ending December 1966. There were 38,547 livebirths and 596 neonatal deaths, including 546 early neonatal deaths of which 399 or 73.1% were autopsied.

Series 5. This is an investigation of neonatal deaths at the University Hospital, Kuala Lumpur from January 1970 — December 1971. During this period there were 4,761 livebirths and 95 early neonatal deaths, of which 68 or 71.5% were autopsied.

The autopsies and histological examination of the lungs for the first three series were performed by three different pathologists from the Department of Pathology, University of Singapore.

Table I
Summary of the material by years

Series Concluding	1	2	3	4	5
Year of study	1960	1962	1965	1966	1971
Autopsy index	76.2%	75.1%	78.5%	73.1%	71.5%
Autopsies	423	259	485	399	68
Deaths	555	345*	618	546	95
Live births	38,114	19,566**	38,667	38,547	4,761

* Refers to all neonatal deaths
** Six months only.

In Series 1 and Series 5 of this study, the lungs were fixed in buffered formaldehyde solution (10% formalin). Representative or whole lung, paraffin embedded sections, stained with haematoxylin-eosin were then examined by the present investigator. Lungs showing varying degrees of collapse, not necessarily complete cohesion of the alveolar septa, together with the presence of eosinophilic membranes lining the alveolar ducts and/or the alveoli were diagnosed as cases of HMD. The hyaline membranes varied in thickness and length, and were diffusely distributed. Hyaline membranes were associated with focal haemorrhages, or neutrophil leucocytes within the alveoli, in a small proportion of cases.

Results

The mortality from HMD confirmed by autopsy in the five series of autopsies are compared in Table II. The number of premature infant (birth weight of 5 lbs or less) deaths, and their percentages of the total number autopsied for the same periods are also compared.

Table II
Comparison of autopsy incidence of HMD by years

Series	1	2	3	4	5
Year *	1960	1962	1965	1966	1971
HMD % Autopsies	29.8	18.2	28.4	35.8	32.3
No HMD cases confirmed	126	47	138	144	22
Prem. % Autopsies	82.2	81.9	80.7	73.4	70.5
Premature deaths	348	239	499	401	48

* Year study concluded

In addition to the data given in Table II, other findings which are considered relevant to the discussion below are:—

Series 1. Intracranial haemorrhage was the cause of death in 75 (17.7%) infants and this did not include 20 (4.7%) deaths with intraventricular, intracranial haemorrhage. Atelectasis with no hyaline membrane was found in 29 (6.3%) premature infants.

Series 2. Intracranial haemorrhage was the cause of death in 92 (35.5%) early neonatal deaths and included 37 (14.2%) cases of intraventricular haemorrhage. In 17 (6.6%) infants, the cause of death was attributed to prematurity itself.

Series 3 & 4. Intracranial haemorrhages accounted for 25.0% and 14.3% of deaths respectively; prematurity itself was the cause of death in 3.7% and 2.0% respectively in each of these series.

Discussion

An analysis of the results shows a decline in mortality from HMD in 1962 as shown in Table II and an increased mortality in 1966. An increase has also been a cause for comment in the past elsewhere.[12]

The changes in the lungs in an infant who develops RDS consist of progressive collapse of the air sacs leading to atelectasis, and this has been confirmed by radiologic studies.[18] The hyaline membranes are rarely found if the baby dies before within 7 or 8 hours,[14, 15] and the classical appearance of the lungs is seen only in infants dying after 8 to 10 hours.[16] It is unlikely that a diagnosis of HMD in the absence of pulmonary hyaline

membranes was made by any of the pathologists connected with these series. There is no doubt that different investigators might show minor differences in pathologic criteria, (Avery 1968) and also when haemorrhages or inflammatory changes are present, strands of fibrin may resemble hyaline membranes, presenting difficulties in diagnosis and classification.

Fig 1

Decline in premature infant mortality from 1962-70 (except 1963) in Kandang Kerbau Maternity Hospital

The increasing survival of premature infants at KKH[17], except for an inexplicable rise in 1964, is shown in Fig. 1. Apart from reduction of deaths due to infection, increased survival is probably attributable to improving standards of paediatric and nursing care, themselves consequences of better understanding of the problems of the premature newborn, more rational and improved methods of oxygen administration, and thermal protection in incubators. In 1970, there were only 120 deaths per 1,000 premature livebirths at the KKH. This improvement is highly suggestive of at least longer survival of ill-fated infants with RDS, allowing time for hyaline membranes to form, and this most probably accounts for the apparent increase in deaths from HMD in 1966.

It will also be noted in Table II, that, throughout the period 1960 to 1966, there has been a steady decline in the proportion of premature infants examined post-mortem. At the University Hospital, Kuala Lumpur the figure was 70.5%. There are also reasons to believe that in spite of the lack of any established specific therapy for RDS, general supportive measures enable a greater proportion of infants who develop the condition to survive.

Intraventricular haemorrhage is due to anoxia and this has recently been emphasised again.[18] HMD was found in 42% of babies with intraventricular haemorrhage in a perinatal survey.[19] When hyaline membrane is present in a lesser degree, it will be a matter of opinion whether the case should be so classified,[20] and it is therefore reasonable to presume that many infants in Series 2 died of HMD rather than intraventricular haemorrhage which is one of the complications of the disease. An unexpectedly low mortality from HMD in Series 2 may be due to some extent at least to accepting intraventricular haemorrhage instead of HMD as a primary cause of death in 14.2% of cases. Furthermore, in Series 2 prematurity itself has been attributed as a cause of death in 6.6% compared to 3.7% and 2.0% in Series 3 & 4. In premature infants that are autopsied, there will be a substantial number of cases of atelectasis, 6.3% in Series 1, and a few of these would be due to RDS in its early phase.

Summary and Conclusion

1. An analysis of 5 separate series of consecutive autopsies on newborn infants, with special reference to hyaline membrane disease is presented.
2. Despite the improved survival of premature infants as shown in Fig. 1, no comparable reduction in mortality from HMD as disclosed at autopsy was noted.
3. Nevertheless, it is very likely, that in these series, where the presence of hyaline membranes at autopsy was the main criterion used, the comparable reduction to be expected was not disclosed.
4. To some extent this finding may be due to the fact that hyaline membrane formation does not occur unless the infant lives for 8 hours or more.

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Prostaglandin F_2 alpha for induction of labour

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PROSTAGLANDINS ARE a group of active biological compounds found widely distributed in mammalian tissues. They are lipid soluble unsaturated 20-carbon hydroxy acids with a cyclopentane side ring and have been divided into four major groups called the E,F,A and B series.

Recently prostaglandins were subjected to intensive investigations. Bygdeman (1964) demonstrated that the prostaglandin F_2 alpha (PGF_2 alpha) had a potent stimulatory effect on pregnant myometrial strips. Embrey and Morrison (1968) found PGF_2 alpha to have a selective spasmogenic effect on the upper segment of the myometrium and relatively inactive on lower uterine segment strips. At the same time, the identification of PGF_2 alpha in amniotic fluid and in the maternal venous blood during labour were reported (Karim & Devlin, 1967; Karim, 1968). This was followed by the first successful clinical trial of PGF_2 alpha for the induction of labour administered via a continuous intravenous infusion. (Karim et al, 1969a).

In the University Hospital, a study of the use of PGF_2 alpha for the induction of labour was undertaken. The chief aim was to test the efficacy of the drug in our local population and to gain experience in the use of prostaglandins, particularly with regards to its side effects, if any, on the mother or foetus.

Materials and Methods

When this study was commenced, all patients requiring induction of labour were put on the trial, till our sample of PGF_2 alpha was exhausted. Altogether we had 17 cases.

Table I: Results of PGF2alpha infusion for Induction of Labour

Case No.	Age	Parity	Gestational Age	Indication for Induction	Cx at start of Infusion Length (cm.)	Cx at start of Infusion Dilatation (cm.)	Total Dose Infused (ug)	Induction — Uterine activity interval	Induction — delivery interval
1	23	2	Term+2 days	PET	2	3	3500	13 minutes	14 hrs. 43 mins.
2	24	3	Term+10 days	Postmaturity	2	2	4000	5 minutes	24 hrs. (failed)
3	37	6	Term+13 days	Postmaturity	3	1	500	12 minutes	5 hrs. 30 mins.
4	33	6	Term+11 days	Postmaturity	3	2	1000	30 minutes	7 hrs.
5	26	0	Term+14 days	Postmaturity	2	1	1100	10 minutes	9 hrs. 30 mins.
6	27	2	Term−3 days	PET	3	1	1000	15 minutes	7 hrs.
7	32	11	Term+7 days	Postmaturity	2	2	4300	5hrs. 30 mins.	22 hrs. (failed)
8	26	1	Term−7 days	PET	2	3	5000	50 minutes	23 hrs. (failed)
9	22	1	Term+11 days	Postmaturity	1	2	500	15 minutes	6 hrs. 15 mins.
10	27	2	Term+18 days	Postmaturity	1	2	1000	45 minutes	11 hrs. 45 mins.
11	33	2	Term+14 days	Postmaturity	2	1	2000	45 minutes	8 hrs. (failed)
12	20	2	Term+14 days	Postmaturity	2	1	500	40 minutes	5 hrs. 35 mins.
13	24	1	Term+10 days	Postmaturity	1	2	3350	1hr. 40 mins.	20 hrs. 10 mins.
14	19	1	Term+20 days	Postmaturity	2	1	1350	3 hrs.	14 hrs. (failed)
15	29	4	Term−2 days	PET	2	1	500	10 minutes	6 hrs. 5 mins.
16	25	1	Term+12 days	Postmaturity	1	2	1000	1 hr. 20 mins.	9 hrs. 40 mins.
17	30	2	Term−1 day	PET	2	1	4000	50 minutes	22 hrs. 40 mins.

Table II: Details of the Cases of Failures

Case No.	PGF_2 alpha Infusion Rate Minimum ug/min.	Maximum ug/min.	Total Dose	Hours of Infusion	Cx Dilatation achieved (cm.)	Uterine Activity Achieved: Frequency	Duration	Resting Tone	Strength	Subsequent Delivery
2	2	6	1000	24	2	1 in 7	60 secs.	8 cm.	50 cm.	Delivered vaginally with Pitocin Drip in 6 hours
7	2	4	4300	22	4	1 in 6	50 sec.	6 cm.	40 cm.	LSCS for Prolapsed Hand 10 hours later
8	2	4	5000	23	5	Irregular	30-60 sec.	14 cm.	12-80 cm.	Delivered with Pitocin Drip in 3 hours
11	2	2	2000	8	3	1 in 2	45 sec.	13 cm.	80 cm.	Delivered with Pitocin Drip 8 hours later
14	2	2	1350	14	4	1 in 3	60 sec.	15 cm.	70 cm.	Delivered with Pitocin Drip 5 hours later

The patients were first examined by one of us and basal recordings obtained in respect of maternal pulse, blood pressure, respiratory rate, foetal heart rate, cervical length and dilatation and station of the presentating part. Uterine tone and contractions were monitored prior to and during the induction process with a twin-channelled external tocograph.

In all cases, amniotomy was performed prior to the commencement of PGF_2 alpha infusions. Continuous tocographic recordings were made for the first four cases, but it was later felt sufficient to make half-hourly recordings of ten-minute durations each time, complemented by clinical palpations for uterine contractions. All other vital data, such as maternal blood pressure, pulse, foetal heart rate, were taken at half-hourly intervals. Vaginal examination was performed when indicated or at six-hourly intervals to assess progress of labour.

The ampoules of PGF_2 alpha supplied (1,000 ug/ml) were first diluted in 500 ml. of 5% Dextrose to give a concentration of 2 ug/per ml. Infusion of the PGF_2 alpha was then commenced at the rate of 2 ug per minute and gradually stepped up at hourly intervals to 6 ug per minute depending on response.

The third stage of labour in all cases were managed as routinely performed in the unit, comprising intra-muscular injection of syntometrine at crowning of the foetal head and employing controlled cord traction when the uterus was well contracted.

Results

The efficacy of PGF_2 alpha in the induction of labour is shown in Tables I and II. Twelve

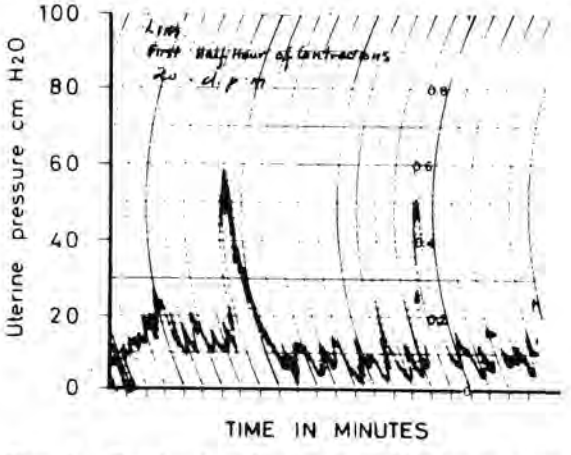

Fig. 1. Typical uterine activity seen within half-hour of infusion

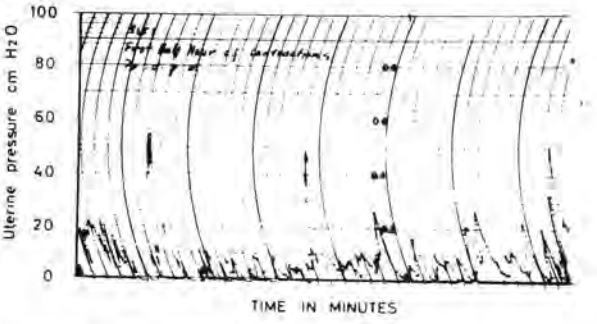

Fig. 2. Another typical recording of early uterine activity.

out of the 17 patients studied were successfully induced, the time taken varied from 5 hours to 24 hours; 9 patients delivering within 12 hours, 1 patient delivering in 15 hours and 2 patients between 20 to 24 hours. All deliveries did not require assistance except for an episiotomy where indicated.

Uterine Activity

Uterine activity was recorded in 8 patients within half an hour of PGF_2 alpha infusion, within one hour in 4 patients, within 2 hours in 2 patients and in $5\frac{1}{2}$ hours in the last patient. Figures 1 and 2 show examples of the type of uterine activity obtained within the first half hour of PGF_2 alpha infusion. There was no correlation between the time taken to initiate uterine contractions and successful induction.

Pattern of uterine contractions

The pattern of uterine contractions, however, differ markedly in the later stage between those who deliver successfully and those who fail. Figure 3 is typical of a case successfully induced, where there was increasing intensity of uterine contractions at regular intervals. In this case, there was also complete uterine relaxation between contraction. Figures 5 and 6 are recordings obtained in a case which failed to deliver under PGF_2 alpha stimulation; in this case it was obvious uterine contractions were ineffectual, occurring at irregular intervals and of varying intensity.

Uterine tone

An increase in uterine tone in-between contractions (Figs, 4, 5 & 6) has been found in 12 of the cases studied. This represents failure of the uterus to relax completely between contractions and the residual pressure recorded varied from 5 to 15 cms of water. During the second stage,

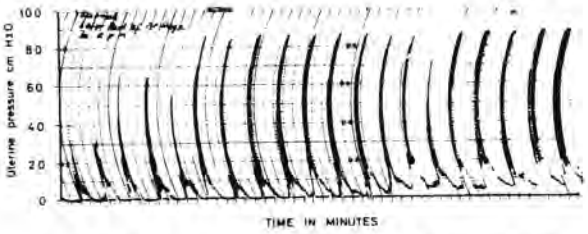

Fig. 3. Regular uterine contractions in a successful case.

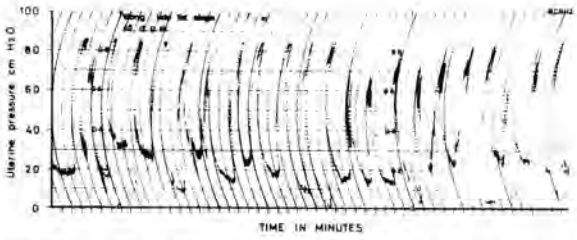

Fig. 4. Regular uterine contractions with raised uterine tone between contractions in a successful case.

uterine tone was maximal at about 20 cms of water. There was no case of summation of uterine tone leading to tetanic contraction observed.

General effects on the Mother and Foetus

The blood pressure, pulse, respiration, micturition and general condition of all the patients monitored remained normal throughout labour. None of the patients had diarrhoea. All babies born had good apgar score of at least 7 and above taken at one and at 5 minutes after delivery. In the post-natal period, they had remained normal. In the 5 patients who desired to breast-feed, there was no failure of lactation encountered. The others had lactation suppressed successfully as required.

Complications

One patient had excessive sweating and complained of hotness (but afebrile) after half an hour of the start of PGF_2 alpha infusion at the rate of 2 ug/minute. This, however, subsided in the following hour when the infusion was persisted and the excessive perspiration did not recur. She was delivered successfully in 14 hours 43 minutes. (Case No. 1)

Another patient began to vomit excessively (six times) when the infusion was continued for 22 hours and a total dose of 5,000 ug was reached, the infusion rate at which time was 6 ug/minute. This case (No. 8) was considered a failure and the PGF_2 alpha infusion stopped as the cervical dilatation was then at 5 cms with poor uterine contractions coming at intervals of about 1 in 4 to 5 minutes, each lasting for about 40 seconds. She, however, delivered vaginally, without complications within the next 6 hours 20 minutes when the infusion was changed over to a syntocinon drip.

There were 2 patients who developed mark phlebitis, at the site of infusion. These occurred after 15 hours and 19 hours of the infusion when total doses of 1100 ug and 2400 ug were infused respectively. No other cases were observed to have developed phlebitis in the puerperium. The phlebitis, however, resolved completely within the next six days with symptomatic treatment.

Post-partum haemorrhage was encountered in two patients. In one case, it occurred three hours after delivery with a blood loss of 600 ml. This was due to uterine relaxation and was effectively treated with intra-muscular injection of syntometrine and a syntocinon drip. No blood transfusion was deemed necessary and the patient recovered and was discharged well on the 5th post-partum day. In another patient, 400 ml. of blood loss occurred 2 hours after delivery also due to uterine relaxation; she was similarly treated, and discharged well.

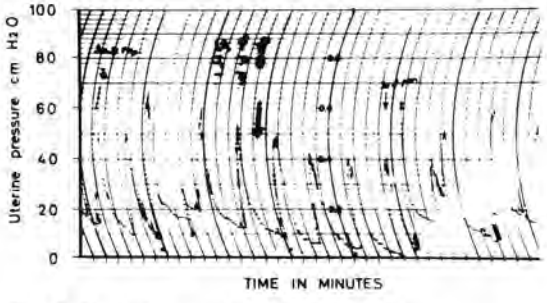

Fig. 5. Irregular contractions with raised uterine tone in an unsuccessful case.

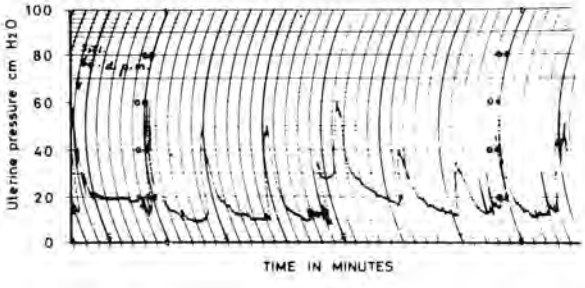

Fig. 6. Same case as in Fig. 5. at a later stage.

Failures

Five patients failed to deliver with the PGF_2 alpha infusion and their details are given in Table II.

In all these patients, uterine activity were found to be erratic, being irregular and weak. Resting tone was also generally high between contractions in the range of 10 to 15 cms of water. Cervical dilatations achieved were less than 5 cms. in all these cases. The duration of the infusion varied from 8 hours to 24 hours. No correlation was found between the failures and gestational age of the pregnancy, parity of the patient and the time taken for the PGF_2 alpha to initiate uterine activity.

It is interesting to note that 4 of these patients were subsequently delivered between 3 hours and 8 hours when the infusion was changed over to syntocinon.

Discussion

Prostaglandin F_2 alpha is effective for the induction of labour at term. The results obtained in our present series of 17 patients, however, did not reflect the high success rate as reported in other clinical trials. Karim (1969) using a continuous intravenous infusion at the rate of 0.05 ug/kg/min. was successful in 33 out of 35 women, who delivered normal babies except when prior foetal death had occurred; Kinoshita et al (1971) were successful in all the 30 women they studied using an infusion rate of PGF_2 alpha ranging from 0.02 - 0.18 ug/kg/min. Lately, Gerald et al (1972) in a comparative study on the efficacy of PGF_2 alpha, PGE_2 and synthetic oxytocin for induction of labour in 100 cases reported an overall success rate of 76 per cent for PGF_2 alpha. They also noted an added advantage of a shortened infusion-delivery interval for PGF_2 alpha.

In all our cases, amniotomy was performed prior to PGF_2 alpha infusion. This is in keeping with the current practice of inducing labour wherein amniotomy is always performed when possible in conjunction with an oxytocin infusion. We felt amniotomy should be performed in our series as it would also facilitate the early recognition of foetal distress by noting meconium staining of liquor and allow foetal-scalp blood sampling to be performed where indicated.

In our study, uterine activity was initiated in a variable period of time varying from 5 mins. to 5 hours 30 mins. No correlation was found between the time taken for the initiation of uterine activity and gestational age of the pregnancy, parity and eventual success of the induction. Embry (1969) using a dose range 2 - 8 ug/min. reported uterine stimulation within 15-30 minutes after the starting of infusion in all his 5 cases. Karim (1969) using a continuous low dose 0.05 ug/kg/min reported that the first uterine contractions were usually recorded within 15-20 minutes after starting the PGF_2 alpha infusion, and this was also the experience of Kinoshita et al (1971) in his series of 30 women. An apparently longer latent interval is found in our series. Whether this could be due to racial and ethnic differences will require to be further explored. This latent interval supports the theory that prostaglandin may be acting on the uterus via a metabolite or by a release of an intermediate substance.

The pattern of uterine contractions in all those who delivered were similar to that occuring in normal labour as obtained in studies by Caldeyro et al (1950).

However, 12 of our cases had increased uterine tone in between contractions, 4 of which occurred in those who failed to deliver with PGF_2 alpha infusion. This high incidence of increased uterine tone is again not found in other clinical trials, where hypertonicity was reported as a rare occurence in occasional cases. Occasional increase in intra-uterine tone is said to occur transiently in normal labour which could be alleviated by altering the position of the patient (Caldeyro-Barcia et al 1960). In our 12 cases, the increase in tone persisted almost throughout the entire course of the induced labour, and this disappeared when the PGF_2 alpha infusion was stopped. This is an unsatisfactory feature as increase in tone between uterine contractions can compromise the well-being of the foetus due to diminished placental perfusion. There was, however, no incidence of any tetanic uterine contractions.

Complications arising from PGF_2 alpha infusions include vomiting, diarrhoea, hyperventilation and severe phlebitis. With the dosage used so far in clinical trials, there has not been any case of tetanic uterine contractions, ruptured uterus, maternal or foetal death. Karim et al (1969b) in their investigation into the safety of PGF_2 alpha infusions at rates of 2 ug/kg/min (40-80 times higher than the dose used for induction of labour) in male and non-pregnant female volunteers reported that there was no significant effect on the heart rate, blood pressure, respiration rate or on the electrocardiogram. Hillier and Embrey (1972) using high doses of PGF_2 alpha (25 ug/min — 200 ug/min) for termination of mid-trimester pregnancy did not find any significant change in blood urea, S.G.O.T., total bilirubin and alkaline phosphatase, but toxic

effects such as vomiting and diarrhoea were common. There appear so far no evidence that PGF_2 alpha affects the blood sugar or creatinine, but these were not studied in our present series.

Chemical phlebitis as seen in our two cases is a serious limiting factor to continual intravenous infusion. The effect manifests itself as an area of erythema and tenderness overlying the infused vein and collateral circulation. The patients complained bitterly about the pain as the infusion was continued and the area affected was variable. However, over a period of six days these resolved completely with symptomatic treatment and no residual thrombosis or venous thickening were observed. This tissue reaction is either an apparent individual sensitivity or perhaps there had been a local extravasation of the infusion. It is not strictly dose related or dependent on the length of time the infusion is carried out. There is increasing evidence that prostaglandins are important agents in the "inflammatory reaction" of tissue trauma and infection. Perhaps local extravasation at the site of infusion is responsible for the phlebitis seen.

Post-partum haemorrhage due to subsequent uterine relaxation was also encountered in two patients. The practice of immediately removing the PGF_2 alpha infusion on delivery could have been contributory.

An interesting feature was noted by us in the 5 cases who failed to deliver. Except for one case who required Caesarean section for dystocia associated with a prolapsed hand, all the other four patients responded readily to syntocinon infusion and delivered normally within 3 to 8 hours. The suggestion is made that PGF_2 alpha could either sensitise or enhance the action of subsequent oxytocin infusion. This pharmacological phenomenon has been recently reported by Gillespie (1972) and the clinical advantage if it could be further explored appears very promising, as it would then allow smaller doses of prostaglandin and/or oxytocin to be used in combination for induction of labour, thereby not only increasing their effectiveness but also perhaps reducing the troublesome side effects of either agent when used alone.

Conclusion

1. A prelimary study of the use of PGF_2 alpha for induction of labour was carried out in 17 cases and there were 5 failures.
2. Minor complications of vomiting, hyperventilation and chemical phlebitis were encountered and there were two cases of post-partum haemorrhage.
3. Our results have shown that though PGF_2 alpha is effective for inducing labour, perhaps greater familiarity with the use of the drug and dosage regime may be required to obtain a success rate comparable to those reported in other clinical trials.
4. The incidental finding of enhancement of uterine response to oxytocin by prior PGF_2 alpha infusion appears to be of promising clinical value.

Acknowledgements

The writers are very grateful to May & Baker Ltd. for the supply of PGF_2 alpha which were manufactured by ONO Pharmaceuticals, Japan; Professor T.A. Sinnathuray for his encouragement; the Medical Illustration Department and the Nursing Staff of the Labour Ward University Hospital for all their help; and Miss C.Y. Kwan for secretarial services.

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An unusual cause of hypothyroidism (following excision of lingual thyroid) in a Chinese boy

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THE FREQUENCY OF lingual thyroid is very uncommon (Means, De Groot and Stanbury, 1963; Cheah et al., 1969). Lahey (1923) reported 2 cases in 7,800 cases treated surgically for thyroid diseases while Ulrich (1932) found only one in 4,000. In 70% of patients with lingual thyroid, the normally placed thyroid in the neck is absent (Montgomery, 1935 and 1936); in such instances, removal of the lingual thyroid would result in hypothyroidism. In this paper we report a Chinese boy who developed hypothyroidism following the excision of his lingual thyroid.

Case Report

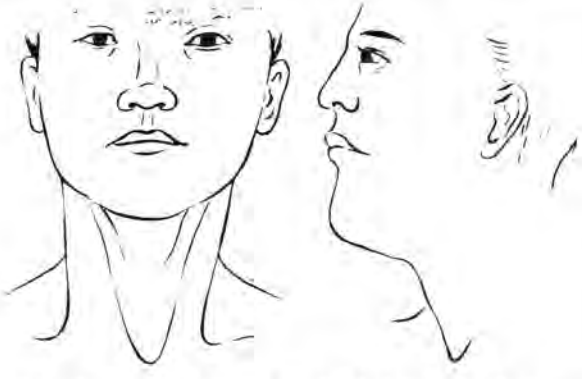
This patient, O.P., a 17-year-old Chinese boy, was referred to us when he underwent a routine medical examination for National Service and was found to be stunted in growth and had no secondary sexual development. He is the sixth child in a family of 3 boys and 5 girls. His brothers attained puberty at about the age of 14 years. He left school at the age of 10 years because he did not do well in school.

In 1967, he was seen in hospital because of

irritation at the back of his throat. This was found to be due to a mass at the base of his tongue. This mass was removed and histology showed it was a lingual thyroid. He defaulted from follow up after the operation.

Clinical examination showed that his height was 57 inches (below the 3rd percentile) and his weight was 85 pounds (at the 25th percentile). Clinically, he was hypothyroid (dry and coarse skin, pulse rate of 60 per minute, delayed ankle jerks). There was early sexual development of the external genitalia but there was no axillary or pubic hair. He was of average intelligence and his blood pressure was 90/65 mm Hg. The other systems were normal.

Investigations showed that his basal metabolic rate (Dubois) was minus 36% (normal: ± 15%); the serum protein-bound iodine was 3.4 ug% (normal: 4 to 8 ug%); the resin uptake of triiodothyronine was 74% (normal: 75 to 115%); the serum total thyroxine was 1.4 ug% (normal: 3 to 7 ug%) and the free thyroxine index was 104 (normal: 225 to 805). A thyroid scintiscan showed that there was some uptake of radioiodine over the base of the tongue but none over the neck (see figure). this showed that there was some thyroid tissue at the base of the tongue and there was no thyroid at its usual site over the neck. The uptake of radioiodine over the tongue was 9.2% at 4 hours, 14.6% at 24 hours and 12.3% at 72 hours (normal: 15 to 50%). Thyroid antibodies (antithyroglobulin and antimicrosomal) were absent. The ankle reflex time (tap to half-relaxation) was 320 msecs. (normal: 230 to 310 msecs.). The electrocardiogram showed typical features of hypothyroidism. The bone age was 14 years. The chest X-ray was normal while X-ray of the skull showed that the pituitary fossa was on the large side of normality.



Anterior-posterior and lateral scintiscan showing concentration of radioiodine (131I) at the base of the tongue. Note the absence of the thyroid gland in the neck.

The patient was started on thyroxine replacement therapy (0.1 mg thrice daily) and he has progressed well.

Discussion

The usual causes of childhood and juvenile hypothyroidism include dysgenesis of the thyroid gland, deficiency of iodine, dyshormongenesis, ingestion of goitrogens, primary thyroid diseases and pituitary disorders (Hutchinson, 1969; Means, De Groot and Stanbury, 1963). Juvenile hypothyroidism due to excision of a lingual thyroid as is seen in our patient is very rare as there are about 200 cases of lingual thyroid reported in the literature (Cheah et al., 1969).

In our patient, like 70% of patients with lingual thyroid, the normally placed thyroid is absent (Montgomery, 1935, 1936). In such instances, as this patient illustrates, removal of the lingual thyroid results in hypothyroidism. In 15% of cases of lingual thyroid, spontaneous hypothyroidism has been reported (Goetsch, 1948). This suggests that the function of an ectopically placed thyroid gland is not as efficient as the normally placed gland.

Our patient has retarded physical, gonadal and skeletal growth. These are the hallmarks of hypothyroidism in children (Hubble, 1956). Although delayed puberty is often found in hypothyroidism as in our patient, precocious puberty has also been reported (Hubble, 1969).

Thyroid antibodies are absent in this patient as was in the case previously reported (Cheah et al., 1969). The occurrence of thyroid antibodies in lingual thyroids has not been previously reported (Means, De Groot and Stanbury, 1963; Cheah et al., 1969).

Like other thyroid disorders, lingual thyroid is commoner in females; about 75% of cases occur in females (Schilling et al, 1950). Our first patient was also a female (Cheah et al., 1969); the present patient is a male.

Irritation of the throat was the symptom that brought the present patient to have his lingual thyroid detected and removed. The symptomatology and treatment of lingual thyroid have been discussed in detail previously (Cheah et al., 1969).

Summary

A 17-year-old Chinese boy with hypothyroidism due to excision of a lingual thyroid five years previously is described. He has delayed physical,

gonadal and skeletal growth. There is still some thyroid tissue in the tongue but there is no thyroid tissue in the neck. The clinical features and treatment of lingual thyroid are discussed. The literature on lingual thyroid is briefly reviewed.

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Hypersecretion of growth hormone in an acromegalic of 25 years' duration

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ACROMEGALY IS A rare disorder occurring in about 1 in 3,000 to 10,000 hospital admissions (Gershberg, Heinemann and Stumpf, 1957). In 1886, Pierre Marie described 2 patients with this disorder and coined the term acromegaly to emphasise the enlargement of the extremities which is a prominent feature in this disorder. Before the introduction of an accurate method of measuring growth hormone, it was believed that the disorder would burn itself out after some years. However, since the advent of radioimmunoassay, it has been found that untreated cases of acromegaly of many years duration have high growth hormone levels (Linfoot et al., 1970). In this paper, we report a patient who had acromegaly untreated for 25 years with marked elevation of serum growth hormone.

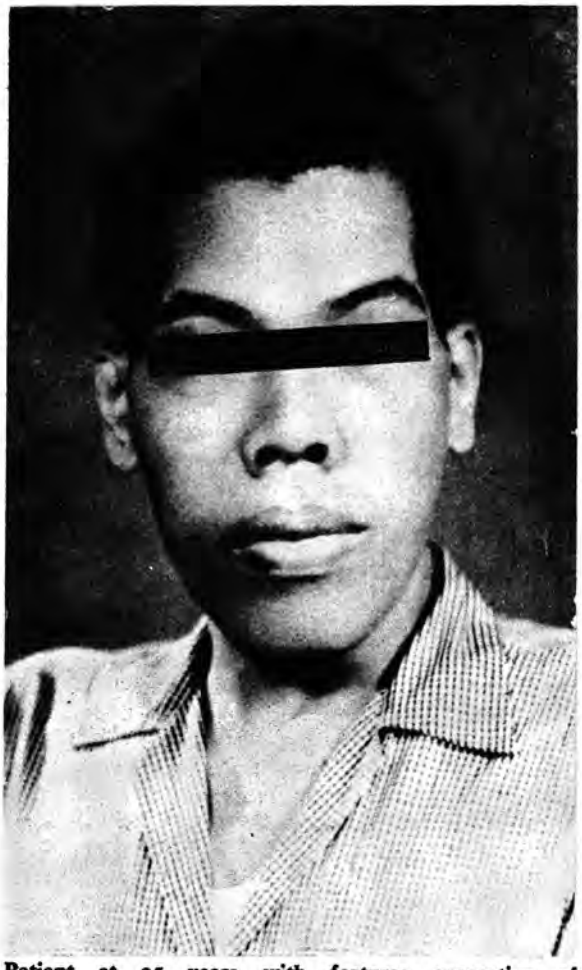
Clinical Record

This patient, L.T., was first seen in 1967 when he was 46 years old for pulmonary tuberculosis and diabetes mellitus. He was also found to have acromegaly. A photograph when he was 25 years old showed features suggestive of acromegaly (Fig. 1).

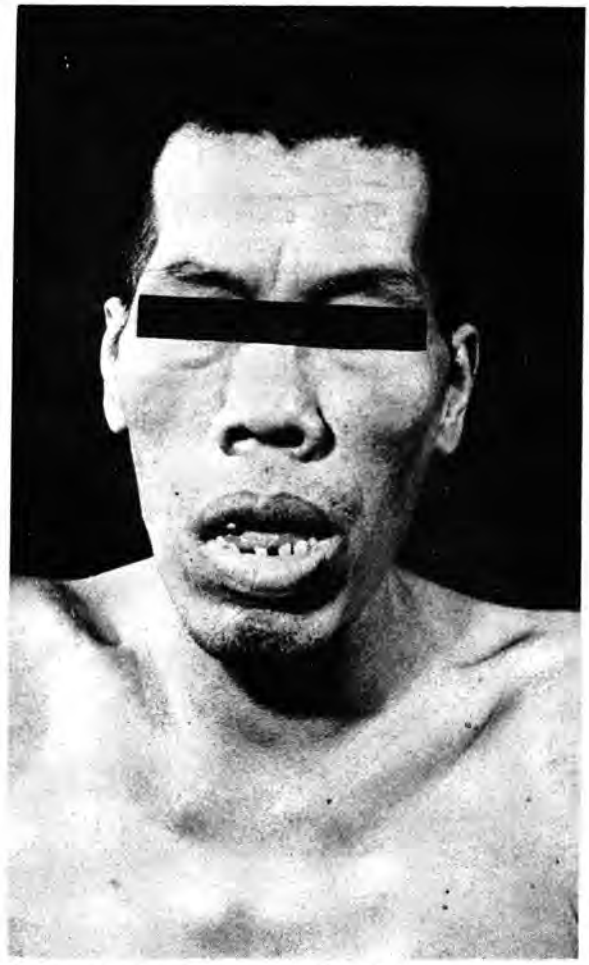
His last admission was in July 1971. His diabetes and pulmonary tuberculosis had not been well controlled as he was a frequent defaulter. He had the characteristic features of acromegaly; this was more marked than 25 years ago (Fig. 2). His height was 194 cm. (6ft. 4½in.) and his weight was 103 kg. (226 lbs). The blood pressure was 130/80 mm.Hg. Varicose veins were present on the legs. The testes were small. The fundi and visual fields were normal.

X-ray of the skull showed an enlarged pituitary fossa. The changes in the rest of the skeletal system were typical of acromegaly; these have been described in detail elsewhere (Cheah, 1970). He had also renal calculi.

He had hypercalcuria (512 mg/day; normal:



Patient at 25 years with features suggestive of acromegaly.



Patient at 50 years; acromegalic features are marked.

less than 270 mg/day). The urinary 17-ketosteroids was 7.5 mg/day (normal: 9-24 mg/day). The serum calcium, phosphate and alkaline phosphatase were normal. Thyroid and adrenal function tests were normal.

Serum growth hormone was measured by a solid-phase radioimmunoassay (Catt and Tregear, 1967) using the Abbott human growth hormone immunoassay kit. The fasting serum growth hormone was 50 ng/ml (normal less than 10 ng/ml); the 2-hour level after an oral 50g glucose load was 79 ng/ml (normal less than 5 ng/ml).

He was given injection streptomycin, para-aminosalicylic acid and isoniazid tablets for his pulmonary tuberculosis; because of resistance to Isoniazid, he was later given pyrazinamide and ethambutol tablets in addition to para-aminosalicylic acid. He was given tolbutamide 0.5g thrice daily for his diabetes. While in the ward, he suddenly collapsed and died; the cause of death was uncertain and permission for necropsy was refused.

Discussion

The fundamental defect in acromegaly is a hypersecretion of growth hormone by the pituitary acidophilic cells. Acidophilic adenoma of the pituitary is found in 75% or more of cases at autopsy (Christy, 1963). However, mixed acidophilic and chromophobe adenoma may occur in a higher percentage (Gordon, Hill and Ezrin, 1962; Young, Bahn and Randall, 1965).

Human growth hormone is now measured with great accuracy by radioimmunoassay. An increase of basal plasma growth hormone above 10 ng/ml and a failure to fall below 5 ng/ml 2 hours after an oral glucose load substantiate a diagnosis of

acromegaly. In our patient, the basal serum growth hormone was 50 ng/ml and its value 2 hours after glucose administration was 79 ng/ml. This paradoxical rise in the serum growth hormone after a glucose load is quite typical of acromegaly (Burger and Catt, 1969; Lawrence, Goldfine and Kirsteins, 1970).

In the past, it was considered that in some acromegalics the disease would burn itself out with time. This concept of a "burnt-out" acromegalic has been found to be fallacious. There is little evidence to show that growth hormone levels can decline spontaneously (Linfoot et al., 1970). Wright et al., (1970b) have shown in a retrospective mortality study of 194 patients that acromegalics have a shortened life expectancy. Death tends to occur in the fifth and sixth decades; the chief causes of death were cardiovascular and respiratory diseases in males and cerebrovascular and respiratory diseases in females. The presence of hypertension and diabetes mellitus were associated with a higher mortality. Our patient had diabetes mellitus and his sudden death at age 50 illustrates in a most vivid manner the need for treatment. All acromegalics should be treated as long as the serum growth hormone is elevated.

Treatment is by hypophysectomy or radiotherapy. If the tumour is large and visual field defect is present, hypophysectomy is desirable. In the other cases, yttrium implantation, heavy particle irradiation, cryohypophysectomy or ultrasonic ablation may be used (Fraser, 1970; Linfoot et al., 1970; Wright et al., 1970a). A satisfactory response to treatment results in clinical improvement and the growth hormone levels return to normal or near normal. If the growth hormone remains elevated, repeated treatment may be required.

Summary

A 50-year-old Chinese male with untreated acromegaly of 25 years' duration is described. His serum growth hormone is markedly elevated and is not suppressed by a glucose load. This hypersecretion of growth hormone contradicts the concept that acromegaly "burns" out after a number of years. This patient also had diabetes mellitus, pulmonary tuberculosis, hypogonadism, osteoporosis, osteoarthritis, hypercalcuria and renal calculi. His death at the age of 50 emphasises the fact that acromegalics have a shortened life span and all acromegalics should be treated when detected.

Acknowledgements

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Endodermal sinus tumour of Teilum

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WHILE ENDODERMAL SINUS TUMOUR of Teilum generally originates from the germ cells in the gonads or in certain extragonadal sites, we have no knowledge of any case originating in the umbilical region and hence consider it worthwhile placing the following report of a case on record.

Case Report

The patient, a three-year-old Chinese male child was asymptomatic until two months before his admission to the General Hospital, Penang. The mother had noticed a gradually enlarging abdominal lump with an accompanying loss in weight and decrease in appetite. Examination of the abdomen revealed a firm, mobile lump over the umbilical area with distension of the overlying superficial cutaneous veins.

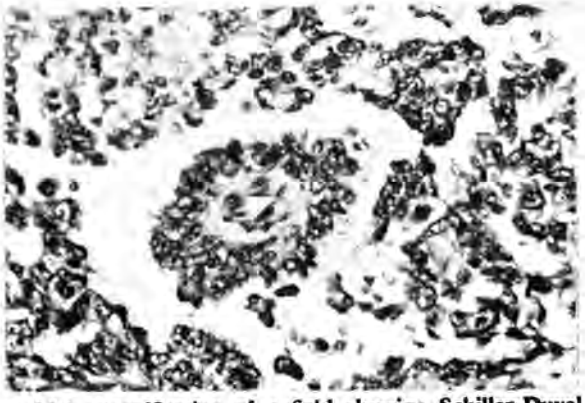
An abdominal X-ray taken revealed a soft tissue mass in the centre part of the abdomen which on lateral view, appeared to be situated anteriorly.

At laparotomy, a fleshy, friable, grey growth of about 7.5 cms size with central areas of necrosis and haemorrhage was found. It was seen arising from the umbilical region and was adherent to the adjoining small intestine, omentum and peritoneum. The testes were free from the tumour as were the lungs, kidney, liver and adrenals. The tumour was excised from the umbilicus after separating it from the surrounding structures.

The patient was lost to follow-up and presumably died shortly after being seen.

Histopathology

The sections from the tumour showed a variable appearance with solid and cystic areas. The epithelial cells were undifferentiated and arranged in solid aggregates in some areas: in other areas, there were papillary and glandular alveolar patterns. The tumour stroma showed fibromyxoid change. In the more vascular parts, the appearance was angioblastic. Epithelial vascular mantling was common. Also conspicuous were peculiar structural units with glomerular-like invaginations (Schiller-Duval bodies). In addition, there were areas of haemorrhage, necrosis and cystic degeneration.



A high magnification of a field showing Schiller-Duval body.

All these findings corresponded well to the description of endodermal sinus tumour of Teilum (1959) or Yolk sac tumour (Huntington 1970).

The endodermal sinus tumour of Teilum has been given a variety of names. In the ovary, Schiller (1939) called it a mesonephroma, supposing that it arose from misplaced foetal remnants of the mesonephros and he described a glomerular-like unit as its distinguishing feature. Kazancigil et al (1940) failed to find evidence of its derivation from remnants of the primitive mesonephros and regarded it as papillo-endothelioma. Other names suggested were mesoblastoma and embryonal cell carcinoma. In the testis, it has been called embryonal carcinoma, clear cell carcinoma and distinctive carcinoma. At extragonadal sites it has been reported as teratoma, ependymoma and choroidal teratoma.

Thus, it would appear that the microscopic pattern is easily recognised, although the histogenesis has been controversial. There are many arguments as to the origin of this tumour but Teilum's concept seems most acceptable.

In 1959, Teilum presented an excellent study of the morphogenesis of the mesonephroma ovarii and compared it to extraembryonic structures of the rat's placenta. He presented convincing evidence that the pattern of this tumour reproduces characteristic stages in the phylogenetic development of such extraembryonic structures as the allantois and yolk sac. He identified the so-called glomerular-like units of Schiller's "mesonephroma" and found these to compare in every detail with the specific intraplacental, perivascular structures in the rat's placenta, i.e. endodermal sinuses of Duval. He also suggested that the irregular communicating vascular channels reflected the supporting vascular mesoderm of the labyrinthine placenta. He named this entity an endodermal sinus tumour.

The tumour is rare and generally occurs in the ovaries and testes and has been reported also at extragonadal sites such as the anterior mediastinum, the region of the pineal gland, the sacrococcygeal region and the vagina in infants. It may occur in either sex and is seen most commonly in the first two decades of life. One case has been described by Huntington, on the first day of life. The patients most commonly present with a history of pain or an enlarged abdominal mass. Generally the tumours vary in size, and are friable, haemorrhagic and necrotic. The salient histological features in the recognition of this tumour are:

(1) Schiller-Duval body, i.e. the glomerular-like unit which is a projection containing a blood vessel surrounded by loose connective tissue and covered by undifferentiated cuboidal or columnar malignant cells.

(2) A cavity lined by endothelial cells.

(3) In other areas, the tissue may appear angiomatoid, fibrous, or myxoid.

The prognosis of these cases is poorly treated or untreated; and the longevity is a few months. Radiation and chemotherapy have produced discouraging results.

Acknowledgement

I would like to thank Prof. G. Teilum of the Copenhagen University, Institute of Pathology for having confirmed the histological diagnosis, and Prof. G. Montogomery of the University of Malaya, for his encouragement. I am also grateful to Dr. R. Bhagwan Singh, Director, Institute for Medical Research, for approval to publish this case.

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Effects of sublethal concentrations of dieldrin on *Culex pipiens fatigans*

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Introduction

IN ROUTINE CONTROL PROGRAMMES, it is possible that aquatic stages of mosquitoes in breeding grounds are exposed for prolonged periods of time to sublethal concentrations of various insecticides, including dieldrin. Information on the effects of such prolonged exposure of *Culex pipiens fatigans* larvae to sublethal concentrations of dieldrin, on their susceptibility or tolerance to dieldrin, on duration of their larval life and on reproductive potential of the adults which emerge from these larvae, is not available. This information is of great practical importance.

In comparison to the large proportion of research work on the development of resistance by insecticide selection, on the physiology of resistance and on the mode of inheritance of insecticide resistance, very little work has been done on the effects of sublethal concentrations of dieldrin on larvae of *C. p. fatigens*. The only work of this kind on *Culex pipiens* is that of Zaghloul and Brown (1968) on the effects of sublethal doses of DDT on the reproduction and susceptibility of this species. They have exposed one-day-old adults of three strains of *C. pipiens* to sublethal doses of DDT for one, two or 8 hours through 6 to 7 generations.

No such work has been done with any insecticide on the larvae or adults of *C.p. fatigans* in Malaysia although it is the most important vector of urban strain of *Wuchereria bancrofti* and the chief nuisance mosquito. This work, therefore, was undertaken to study the various effects of sublethal

Fig. 1

DOSAGE MORTALITY REGRESSION LINES FOR EARLY FOURTH-INSTAR LARVAE OF CULEX PIPIERS FATIGANS REARED IN SUBLETHAL CONCENTRATIONS OF DIELDRIN FOR 10 GENERATIONS TO DIELDRIN

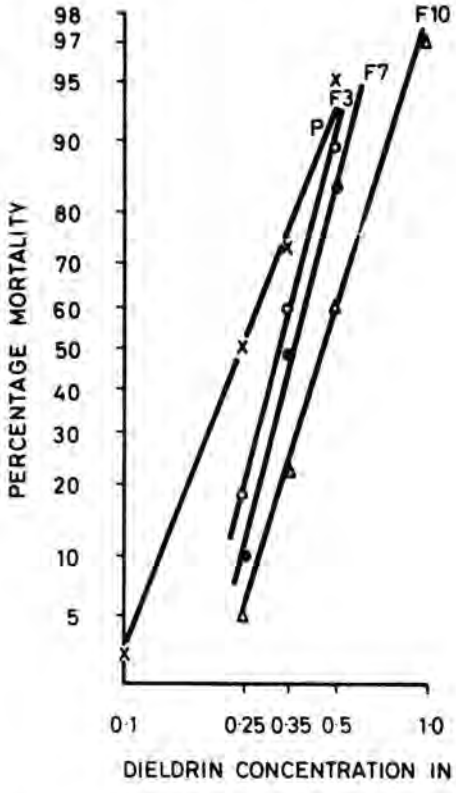
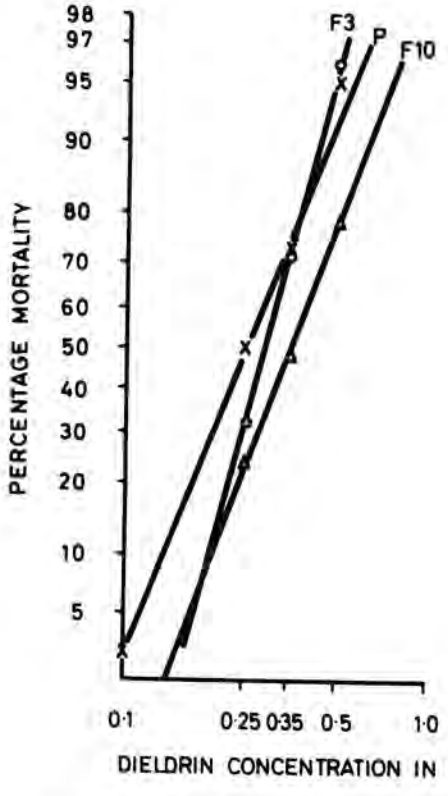


Fig. 2

DOSAGE MORTALITY REGRESSION LINES FOR EARLY FOURTH-INSTAR LARVAE OF CULEX PIPIERS FATIGANS FROM CONTROL SUBCOLONY TO DIELDRIN



doses of dieldrin on development of resistance, duration of larval life and fecundity of the adults when larvae were reared in truly sublethal concentrations of dieldrin.

Materials and Methods

Insecticide — Dieldrin

Dieldrin, which was used in these series, was obtained as standard solutions from the Vector Biology and Control Unit of the World Health Organisation, Geneva. Any intermediate strengths of insecticides needed were prepared from higher doses.

The term "sublethal" has been used to cover all concentrations of dieldrin which did not cause larval mortalities higher than those noticed among larvae in control cultures. As the effects of insecticides were thought to be proportional to the concentrations, it was necessary to keep the sublethal concentrations at the highest level. In order to do so, the concentrations used in older instars of larvae were progressively increased. The concentrations were also increased for some later generations. The concentrations used in these experiments varied from 0.004 ppm to 0.05 ppm dieldrin.

Mosquitoes

Larvae from a single colony of *Culex pipiens fatigans* were used for all experiments. Over 200 egg-rafts were collected from a natural breeding ground in Kuala Lumpur and these were put together for hatching. When the eggs hatched,

TABLE I
Effects of rearing larvae of Culex Pipiens Fatigans larvae in sublethal concentrations of Dieldrin

No. Pupated In		Percentage Pupation		Egg No/Raft For 20 Rafts					
				Control Culture			Sublethal Culture		
Culture Control	Sublethal Culture	Control Culture	Sublethal Culture	Minimum	Maximum	Mean	Minimum	Maximum	Mean
547	555	91·2	92·5	85	193	141·3	91	198	142·5
680	704	85·0	88·0	102	175	138·8	99	185	141·1
285	287	95	95·7	96	186	142·1	95	191	141·7
750	775	93·8	96·8	95	156	126·0	91	187	132·5
422	420	88·8	88·4	102	197	148·1	87	202	147·2
712	717	89	89·6	75	188	132·4	81	189	137·3
176	185	88	92·5	96	201	142·3	93	198	145·7
678	757	84·8	84·6	107	193	143·6	98	195	144·1
672	686	84	85·7	95	189	140·3	101	187	141·7
314	322	73·9	75·8	98	177	139·4	97	182	142·3
—	—	—	—	—	—	—	—	—	—

F5, F7 and F9 generations were 0.33 ppm, 0.36 ppm, 0.37 ppm and 0.43 ppm respectively compared to 0.29 ppm, 0.25 ppm, 0.34 ppm, and 0.34 ppm for control larvae in the same generations. In F10 the LC50 values for experimental larvae were 0.46 ppm as compared to that of 0.35 ppm for control larvae. This level was 1.8 times higher than that found for parents. Throughout this series of experiments, larvae from the sublethal cultures always showed a higher level of tolerance than those from the control cultures. In addition, there were some slight fluctuations in LC50 levels over 10 generations. A certain degree of fluctuations in LC50 levels to insecticides are common in *Culex pipiens fatigans*. Similar variations in LC50 levels among larvae of various generations of a laboratory colony of *C.p. fatigans* submitted to DDT-selection pressure has been observed (Thomas, 1966). These results show that rearing the larvae of *C.p. fatigans*, in sublethal concentrations of the insecticide, did not develop any significant degree of resistance. However, the larvae exhibited some increase in tolerance (1.8 times) levels. A lesser degree of increase in LC50 levels (1.4 times) was observed for larvae from control cultures also although these larvae have never been exposed to dieldrin. These slight variations and increase may then be a normal character and brought about by the optimum rearing conditions rather than by development of true resistance.

The results obtained in this series of experiments were very similar to those which have been noticed in a DDT-resistant and a DDT-tolerant strains of *Culex pipiens* which failed to show any material increase in resistance levels to this insecticide after sublethal exposure to DDT over 6 generations (Zaghloul and Brown, 1968). Similar results were obtained by Harrison (1952) who was unable to induce resistance in a housefly strain frequently exposed to very small doses of DDT. On the other hand, a susceptible strain of *C. pipiens* has developed a considerable degree of DDT-resistance when the adults were exposed to sublethal doses of DDT for 6-7 generations (Zaghloul and Brown, 1968). They concluded that the increase in resistance in this strain was due to hidden selection of eggs in ovary and of females which failed to oviposit. Lineva (1962) noticed that when houseflies were exposed to sublethal doses of DDT for successive generations, they became slightly more susceptible to DDT for the first four generations. In the subsequent 4 generations, the houseflies became steadily DDT-resistant. She also noticed disturbances in oogenesis in the first 4 generations which later disappeared.

Duration of larval life and larval mortality in sublethal cultures.

Subjection of larvae throughout their life to sublethal doses of dieldrin did not prolong the:

TABLE I
Effects of rearing larvae of Culex Pipiens Fatigans larvae in sublethal concentrations of Dieldrin

Generation	No. Of Larvae Reared In		Concentration Of Dieldrin (P.P.M.)		No. Larvae Used For LC 50 Tests From		No. Of Larvae Died In Cultures		Duration Of Larval Life In Days In	
	Control Culture	Sublethal Culture	Control Culture	Sublethal Culture	Control Culture	Sublethal Culture	Control Culture	Sublethal Culture	Control Culture	Sublethal Culture
F1	800	800	NONE	0·004 to 0.05 ppm	200	200	53	45	7-10	7-12
F2	800	800	"	"	—	—	120	96	6-11	6-11
F3	600	600	"	"	300	300	15	13	6-10	7-11
F4	800	800	"	"	—	—	50	25	6-10	6.10
F5	850	850	"	"	375	375	53	55·	6-12	7-12
F6	800	800	"	0·01 to 0.05 ppm	—	—	88	83	7-12	6-11
F7	400	400	"	"	200	200	24	+5	7-12	6-10
F8	800	800	"	"	—	—	123	43	6-14	6-13
F9	800	800	"	"	—	—	128	114	6-10	6-10
F10	800	800	"	"	375	375	111	103	7-11	—
F11	400	400	"	0·02 ppm	Heavy mortality in sublethal culture				—	—

larvae were allowed to remain together for a few hours for thorough mixing. Later, sufficient numbers of larvae were picked up and reared under normal laboratory conditions. The adults which emerged from these were kept as the stock colony (P). When females of this colony laid eggs (F1), the egg-rafts were all put together for hatching. A few hours after hatching, 2 sets of 800 larvae were picked up and were reared in two batches in measured quantities of water. One set of 800 larvae was reared normally without any insecticide (control subcolony) whereas the second batch of larvae was reared in weak solutions of dieldrin (sublethal subcolony).

In subsequent generations, newly-hatched out (3-5 hours old) larvae from experimental cultures were reared in sublethal concentrations of dieldrin. Larvae from the control subcolony were never exposed to dieldrin. The larvae from the sublethal subcolony were exposed throughout larval life to doses which were found to be sublethal to the entire population using modification of WHO method (1963). One cc of insecticide solution in absolute alcohol was added under water surface for every 250 cc of water. Twenty-five mosquito larvae were then reared in that amount of water. When larger numbers of larvae were reared, the same proportions (i.e. 10 cc water/larvae and 1 cc of dieldrin solution/250 cc of water) were used. The room temperature varied from 27°C to 29°C. The larvae in the sublethal cultures and those in the control cultures were fed daily on well-grounded farex, dried liver and yeast in a 3:1:1 ratio. The water in these cultures were changed twice during the larval life. When water in the sublethal cultures were changed, appropriate amount of dieldrin solution was added before the larvae were introduced. Mortality, if any, duration of larval life, number and percentage of pupation, etc., in both the sublethal and control cultures were recorded. LC50 levels of larvae were measured in various generations. Number of eggs per raft for 20 rafts collected in each generation were counted for both subcolonies.

Results and Discussion

Development of dieldrin tolerance in larvae

The number of first-instar larvae reared in sublethal and control cultures, the concentrations of dieldrin used, the larval mortalities in these cultures and the number and percentage of pupation are given in Table I. The LC50 levels of the larvae in alternate generations of control and sublethal subcolonies are given in Table II, and shown in Figures I and II.

The LC50 levels of the parent colony were 0.25 ppm (Table II, Figs. I & II). The LC50 values for larvae from the sublethal cultures were 0.35 ppm in F1 compared to that of 0.26 ppm for larvae from the control cultures. The LC50 levels for larvae from sublethal cultures in F3,

Table II:
Mortality Rates and LC 50 Values for Larvae of Culex Pipiens Fatigans from Control and Sublethal Subcolonies to Dieldrin.

Colony	Generation	Corrected percentage of larval mortality after 24 hrs. exposure to varying concentrations of dieldrin (p.p.m.)					
		0.1	0.25	0.35	0.5	1.00	LC50 (p.p.m.)
—	P	3	50	73	95	100	0.25
Control	F1	2	48	82	94	100	0.26
Sublethal		0	21	52	73	100	0.35
Control	F3	0	32	71	96	100	0.29
Sublethal		0	18	59	89	100	0.33
Control	F5	0	49	81	97	100	0.25
Sublethal		0	25	51	70	98	0.36
Control	F7	0	29	56	76	100	0.34
Sublethal		0	10	48	84	100	0.37
Control	F9	0	22	52	84	100	0.34
Sublethal		0	7	32	64	100	0.43
Control	F10	0	24	48	78	100	0.35
Sublethal		0	5	22	60	97	0.46

larval life (Table I). In most generations, larvae from both sublethal and control cultures which hatched out on the same day pupated on the same day. The larvae from control cultures pupated within 6 to 14 days and those from sublethal cultures pupated within 6 to 13 days (Table I). It was noticed, that in F10 generation, there were five or six larvae in experimental cultures, which remained as second stage larvae, while all other larvae pupated. Since this number was insignificant, these larvae were thrown off. These experiments clearly showed that true sublethal concentrations of dieldrin did not prolong the larval period of *Culex pipiens fatigens* or delayed the pupation. These concentrations did not have any apparent adverse effects on larvae or pupation.

The mortality rates in sublethal larval cultures were negligible in the first 10 generations (Table I). Number and percentage of pupation were very similar to those in control cultures. In F11 generation, the concentration of dieldrin used on first instar larvae was raised to 0.02 ppm from 0.01 ppm which was used on first instar larvae of F10 larvae and on larvae of a few other earlier generations (Table I). There was heavy mortality among first instar larvae of this generation. This was considered as selection rather than sublethal exposure and the experiments were discontinued.

These experiments showed that continuous exposure of all stages of larvae to truly sublethal concentrations of dieldrin for 10 generations did not increase the normal mortality rates of the larvae, pupae or adults which emerged from these larvae. Adults fed normally on pigeon and laid egg-rafts normally without any hesitation.

Effects of Sublethal Concentration of Dieldrin on Fecundity of Adults.

The mean numbers of eggs per raft for 20 rafts collected at random from adults which have emerged from sublethal and control cultures for 10 generations are given in Table I. In all generations except F3 and F5, the adults emerged from experimental cultures gave slightly larger rafts. In F1 generation, the mean number of eggs of control subcolony was 141.3 compared to that of 142.5 from experimental subcolony. In F3 and F5, the mean numbers of egg-rafts from adults of sublethal colony (141.7 and 147.2) were slightly fewer than those from adults of control colony (142.1 and 148.1) in corresponding generations. In all other generations, adults from experimental culture gave larger rafts. In F10 generation, the mean number of eggs from control females was 139.4 compared with the mean of 142.3 for adults from sublethal cultures. Thus the exposure of larvae of *Culex*

pipiens fatigans throughout their life to true sublethal concentrations of dieldrin did not reduce the fecundity of the adults. On the other hand, the adults laid on the average slightly larger eggs. The increase in the mean number of eggs varied from less than 1 per cent in F1 adults to about 5 per cent in F4 adults. It is doubtful whether this increase in the mean number showed any significant increase in the reproductive potential of the adults as the minimum-maximum range of egg numbers for 20 rafts has always been within the normal range of variations.

Increase in egg production has been reported in adult insects which as larvae have been subjected to sublethal doses of insecticides. Ouye and Knutson (1957) reported that adults from melathion-treated housefly larvae produced 12% more potential offspring, as a result of increased egg production and larval development rate. The adults of *Ae. aegypti* which emerged from larvae treated with sublethal concentrations of DDT developed 9 per cent more basal egg follicles (Sutherland, Bean and Gupta, 1967). Zaghloul and Brown (1968) noticed a 16-19 per cent increase in the basal follicles of adults which as larvae were reared for 24 hours in sublethal concentrations of DDT. When a normal housefly strain was exposed to DDT for successive generations, marked disturbances in oogenesis was induced for the first 4 generations (Lineva, 1962). Sublethal exposure of larvae of *Ae. aegypti* to DDT did not produce any significant overall effect upon the reproductive potential of this species (Havertz and Curtin 1967). All known effects of sublethal concentrations/doses of insecticides on larvae and adult mosquitoes, houseflies and other insects are reviewed by Brown and Pal (1971).

Summary

A colony of *Culex pipiens fatigans* was established in the laboratory from more than 200 egg-rafts collected from a natural breeding ground in Kuala Lumpur. The susceptibility level of the larvae (P) which hatched out from these egg-rafts to dieldrin was 0.25 ppm. In the F1 generation, the larvae were divided into control and sublethal subcultures. The larvae from control cultures were never exposed to dieldrin whereas those from sublethal cultures were exposed to true concentrations of dieldrin which varied from 0.004 to 0.05 ppm on various instars of larvae in different generations. The larvae from this subculture was exposed throughout their life for 10 generations. The LC50 levels of the larvae from these subcolonies were measured in different generations. There was a slight fluctuating increase in tolerance of about 1.8 times in the larvae of sublethal colony to dieldrin as compared to that of 1.4 times in the larvae from control culture during 10 generations.

Sublethal rearing of larvae did not cause any high mortality rates among larvae, pupae or adults. The duration of larval life has not increased or pupation delayed due to sublethal exposure throughout the life of larvae in 10 generations.

There was a slight increase in the mean fecundity rate of adults (except in F3 and F5) which emerged from larvae exposed to true sublethal concentrations of dieldrin. The rate of increase in mean number varied from less than 1 per cent in F1 adults to about 5 per cent in F4 adults, as compared to those in the control subcolony.

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All the illustrations were done by the Department of Medical Illustration, Faculty of Medicine, University of Malaya.

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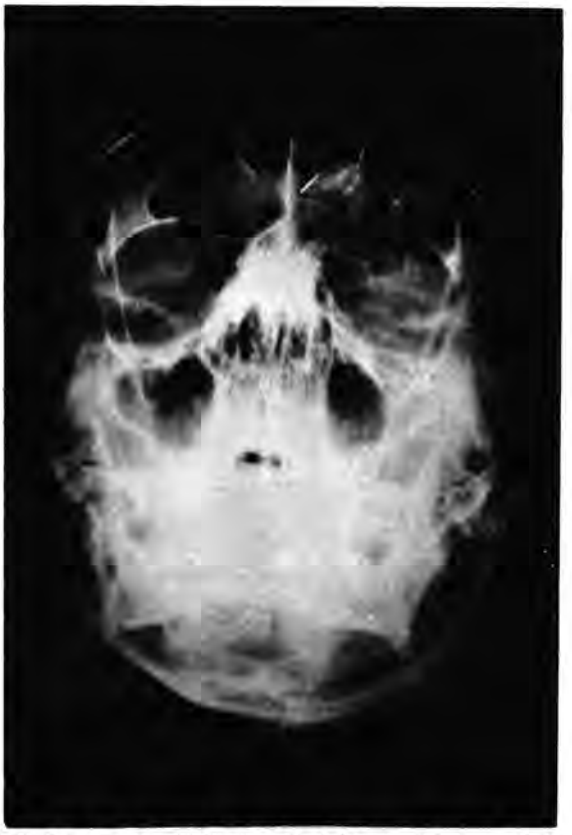
Correspondence



S. b B., 40-year-old Malay. Occipito-mental view of the skull showing a fairly typical pattern of insertion of 'charm needles' in the face. Three were placed in the forehead, centrally and above the eyebrows and a pair into each cheek.

'CHARM NEEDLES'

Dear Sir,

I was interested to read the article entitled "Some radiological observations on the practice of insertion of 'charm needles'" (Soo and Singh, 1972), which appeared in the September 1972 issue.

The practice of inserting 'charm needles' is quite widespread in Singapore and in one year alone (1970), I made a personal collection of 42 cases from casualty subjects on whom skull radiographs were taken. The analysis of these subjects in terms of age, sex and race is presented below, bearing in mind, of course, that the number studied was small.

The practice was found to be curiously commoner in the males, seen only in adults and mainly in those in the fourth and fifth decades. Malays resorted to this practice more frequently than other ethnic groups if these figures are viewed on a proportionate racial basis.

Contrary to what Drs. Soo and Singh reported, there appeared to be a pattern of needle insertion in the face. One, two or three needles were usually introduced in the forehead, either centrally and/or above each eyebrow. Commonly, there were two needles, one in either cheek. There was also one at the point of the mandible; in its place or in combination, there was a needle on each side of the lower jaw. (Fig. 1).

On the average, 3 or 4 needles were inserted in the face but the number ranged from 1 to 47 (Fig. 2). There were in fact 14 cases with a single needle. The needles used were usually fine ones though there was an occasional case in which the needles were thick and resembled gramophone needles.

This was a purely radiological study made when I was attached to the Outram Road General Hospital. The subjects in the series were not interviewed. However, I subscribe to the view of Drs. Soo and Singh that the practice was carried out for beautification purposes or in the belief that the needles conferred a curative effect on certain ailments.

Yours faithfully,

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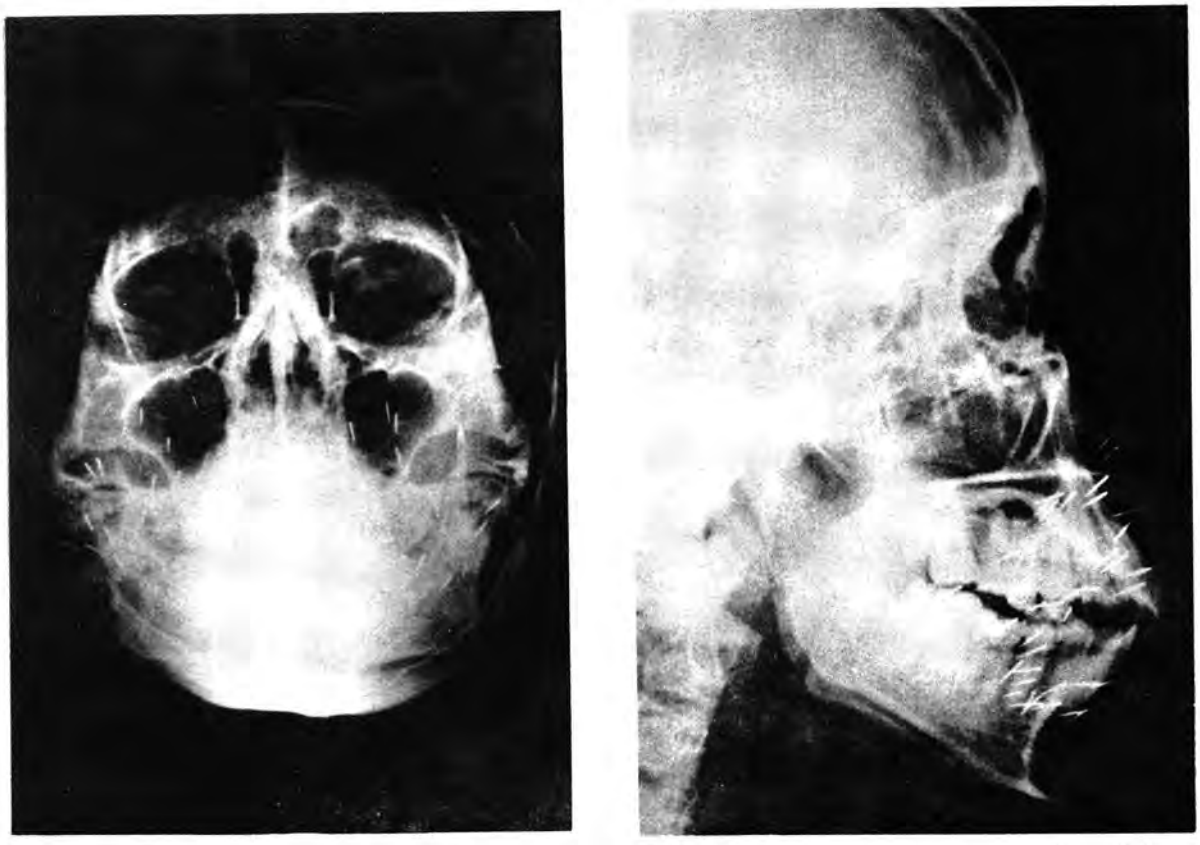

C.S.H., 21-year-old female Chinese. P.A. and lateral views of the face showing an extreme example of needle insertion. A total of 47 needles was implanted in both cheeks by a sinseh for treatment of typhoid.

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Age, Sex and Racial Distribution

Years	21-30	31-40	41-50	51-60
No.	7	18	14	3

Males	28
Females	14
Chinese	25
Males	14
Indians	3

CORRIGENDUM

In the article "An outbreak of rabies in West Malaysia in 1970 with unusual laboratory observations" by Dora S.K. Tan et al in the December 1972 issue (Vol. XXVII No. 2), some of the pages were wrongly numbered. The pages of the article should have been:

First page	=	Page 107
Second page	=	Page 112 not 108
Third page	=	Page 113 not 109
Fourth page	=	Page 110
Fifth page	=	Page 111
Sixth page	=	Page 108 not 112
Seventh page	=	Page 109 not 113
Eighth page	=	Page 114