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VOL. 10, No. 2. SEPTEMBER 1970

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THE JAFFNA MEDICAL JOURNAL

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CONTENTS

Editorial . . . .

The Need For Journals

THIS is the 23rd journal published by the Jaffna Medical Association and its predecessor The Jaffna Clinical Society. Recently there has been a spate of journals in Ceylon, both the emergence of new ones and the revival of old ones. About eight journals at least are being published in Ceylon at the moment. Questions have been asked as to whether all these journals are necessary and whether it would not be better to have fewer journals of a higher standard rather than several journals of uneven quality.

Even in a small country such as ours, patterns of disease vary in the different parts and certain problems encountered in one area are very uncommon in another.[1] For instance "Folidal" (organophosphorus) poisoning is very common in Jaffna but most doctors are dangerously ignorant of its management until they have worked in the North. Doctors specially in the government sector are liable to be transferred from one area to another at intervals and it is obviously desirable therefore to have data regarding the peculiar problems of the area documented as fully as possible for reference by subsequent workers in that area.

A journal also serves as a means of communication among its members. A General Practitioner working in an area would be more interested in knowing the type of work that is done in the area, than in research centres abroad. He would probably like to know the results of mitral valvotomies in the hospital of the area, the bacteriology of the epidemic diarrhoeas, the incidence of cerebrovascular disease, the management of snake bites, or the antibiotic sensitivity of the gonococcus, in preference to the long term results of heart transplants carried out in a reasearch centre.

A busy doctor wishing to know the recent development on any particular topic has to wade through a mass of literature before gathering a few points Members with specialised knowledge on that particular subject could help by presenting a condensed easily assimilable account—a Review Article.

However the most important aim of having more and more journals should be to encourage medical journalism among the doctors in Ceylon. It is only when one attempts to write a case report or article, and often only then, that one realises the great deficiencies in the history, investigations, management etc. Thus writing articles not only produces a record for future reference but also makes one approach any problem critically.

It is very heartening to note that in this issue of our journal one General Practitioner, a medical officer in a Peripheral Unit and two house officers too have contributed papers.

The difficulties confronting members who wish to write are considerable and have been commented on earlier[2]. At present we probably cannot do much more than carefully record and collect cases of clinical interest. Such papers may not be acceptable to international journals due to the paucity of investigations etc. Acute

cardiac failure during an influenzal epidemic in a previously healthy young girl may be considered as due to a viral myocarditis, but in certain circles this diagnosis would be considered proven only if the virus was isolated from the myocardium which showed an inflammatory reaction. We are confident that these difficulties will gradually be overcome if not immediately at least in the near future.

The paucity of research by doctors in Ceylon is often commented on. Even the Advisory Committee to the Ministry of Health has done so and has adduced serveral reasons for this. We feel that encouragement of the writing habit is an important step to rectify this. For this purpose we welcome more and more journals. So convinced are we of the need for journals that our association has gone to the extent of drawing on of its meagre funds to subsidise the journal in the last few years.

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NEUROLOGICAL COMPLICATIONS IN INFECTIVE HEPATITIS

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INVOLVEMENT of the nervous system occurs not infrequently as a complication in non-fatal infective hepatitis, but has received little attention in medical literature. Cameron [1] noted two cases with temporary paresis of accomodation in a study of 170 cases with infective hepatitis. In a hospital series of 787 cases seen over a period of five years Nagaratnam and Sikkander [2] had recorded two cases with neurological complications.

It is the purpose of this paper to present two cases of infective hepatitis with neurological manifestations together with brief reference to two other cases described earlier.[2] Thereafter a survey of neurological manifestations which are seen in infective hepatitis will be given.

CASE REPORTS

Case 1.

A male (J. A. N. S. 15770) was transferred from his local hospital on 7-6-69. He had been sedated with paraldehyde as he had been boisterous. On admission, a history of fever and headache of 3 days duration and restlessness going on to delirium of one day duration was recorded.

The patient was unconscious (under sedation) and responded only to painful stimuli. A doubtful icterus of the sclerae was seen. Examination of the heart and lungs revealed no abnormality. The liver was just palpable below the right costal margin. Examination of the nervous system revealed increased tone in all four limbs, hyper-reflexia and flexor plantar responses. There was no neck stiffness and Kernig's sign was negative. On the 2nd day of admission he was more alert but irritable, lying in a curled up position in bed and resenting examination. There was neck stiffness now and Kernig's sign was positive. There was weakness of his left upper limb and he had an extensor plantar response on the right side. Examination of the ocular fundi revealed congestion of the veins and pink discs. A lumbar puncture done at this stage revealed a clear fluid but under tension.

Investigations:

URINE: Bile + at the time of admission.

C. S. F.: Occasional lymphocytes.
Proteins 50 mgm%.
Sugar++ (qualitative). No organisms were seen.

W. B. C.: 10,800/ cmm.
N 60%. L 34%. E 2%. M 4%.

Serological tests for Leptospirosis were negative.

Liver Function Tests: Serum bilirubin 4.2 mgm%. Zinc turbidity 15 units. Thymol turbidity 8 units. Alkaline phosphatase 9 K. A. units. Cephalin Cholesterol 4+.

On 12-6-69. (5th day of admission) Serum bilirubin 1.4 mgm%. Zinc sulphate turbidity 15 units. Cephalin Cholesterol 3+. S. G. O. T. 252 units. S. G. P. T. 197 units.

Course and Management :

He remained semi-conscious and restless till the 4th day when he regained consciousness and was able to speak. From then onwards he continued to improve and left hospital on 18-6-69. He was treated with intravenous glucose, vitamins and steroids. He attended the Out-Patients' Clinic a week later when he complained of blurred vision. He was referred to the Eye Surgeon and when seen by him 4 days later he had no abnormality and his visual acuity was normal.

Comment :

This patient's illness lasted about 5 days. He was never severely jaundiced. He had both generalised and focal signs of the nervous system.

Case 2.

A boy (E P G 17669) aged 8 years was admitted on 28-6-69, with a history of generalised convulsion of sudden onset and he was said to have passed dark-coloured urine for 2 days previously. There had been no previous history of febrile convulsions

While examining, the patient had another generalised convulsion, was unconscious and febrile. There was no detectable icterus. He had crepitations in both lungs. The abdomen was distended and he had a liver which was palpable 2 finger-breadths below the right costal margin. Examination of the nervous system revealed fixed and dilated pupils. Ocular fundi were within normal limits. The reflexes were normal and plantars flexor. There was no neck rigidity and Kernig's sign was negative.

Investigations :

URINE: Bile nil on the 2nd day.
Bile + on the 3rd day.

E. S. R. 50 mm.

Serological tests for Leptospirosis were negative.

Liver Function Tests: Serum bilirubin 2.8 mgm%. Zinc sulphate turbidity 28 units. Thymol turbidity 8 units. Alkaline phosphatase 29 K. A. units. Cephalin Cholesterol 4+. S.G.O.T. 380 units. S.G.P.T. 450 units

Course and Management :

Though the child did not have any more fits he was restless in spite of sedation. On the following day he regained consciousness and was alert and rational. Now, he had mild icterus of his sclerae. Icterus disappeared on the 5th day. He was treated with intravenous glucose and steroids.

Comment

The boy was never deeply jaundiced. The duration of illness was short, lasting three days. He had an illness simulating encephalitis.

Tables I and II summarises the clinical and laboratory data in both these cases and of Cases III and IV.

Case	Age	Sex	Mode of Onset	Icterus	Liver	Duration of illness	Head-ache	Disordered consciousness	Fits	Vision	Menin-geal	Fundi	Misc.
I	20 yrs.	M	Fever Headache Restlessnes	slight	1 f	5 days	+	+	—	blurred	+	congestion of veins	weakness limb, ↑ Plantar (R
II	8 yrs.	F	Generalised Convulsions Dark urine		2 f	3 days	0	+	+	0	0	0	0
III	8 yrs.	F	Vomiting Restlessness		just palpable	5 days	0	+	0	0	0	0	0
IV	10 yrs.	M	Fever Vomiting Drowsiness		0	5 days	0	+	(unilateral) + pupils dilated fixed	0	0	0	↑ Plantar (R

TABLE I Summarises the Symptomatology.

Case	Day of illness	Serum bilirubin	$ZnSO_4$ turb.	Thy turb.	Alk. Phos.	Ceph. Chol.	SGOT	SGPT	Serological tests for Leptospirosis
		mgm%	units	units	KA units	units	0	units	
I	4	4.2	15	8	9	4+	—	—	—ve
	6	1.4	15	7	16	3+	252	297	
II	3	2.8	28	8	29	4+	380	450	—ve
III	4	4.6	8	8	29	4+	400	552	—ve
IV	10	1.6	24	—	32	—	—	—	—ve

TABLE II Summarises some of the Laboratory Data.

Clinical Profile

They were all relatively young. Noticeable icterus was seen only in one and in the same patient bile was present in the urine at the time of examination. The liver was palpable in three. Duration of illness was short, lasting 3 to 5 days. All of them made full recovery without any lasting sequelae.

Neurological manifestations: Headache was present in one. Restlessness and irritability in all going on to semi or total loss of consciousness. Generalised convulsions occurred in one, unilateral fits in another. Meningeal signs in one and congestion of the retinal veins in the same patient. Pupils were fixed and dilated in another, weakness of limb in one and unilateral extensor plantar response in two. One complained of temporary blurring of vision during convalescence. Cerebrospinal fluid examination done in one showed no abnormality.

Discussion

Leibowitz and Gorman [3] studied the neuro-psychiatric features of infectious hepatitis with special reference to the psychiatric complications. It is worthy that this paper be studied alongside the earlier and detailed papers. They grouped these complications under two headings. In one there is structural involvement of the central or peripheral nervous system and in the other mental changes without proved disease in the nervous system. Meningitis, encephalitis, disturbances of vision, myelitis and polyneuritis have been described. Table III summarises the neurological complications described by some workers.

Severe Headache Paraesthesiae in limbs	Newman J. L. [8]
Unilateral Convulsions Hemiplegia Mild Polyneuritis	Brain W. R. [7]
Temporary paresis of accomodation	Cameron J. D. A. [1]
Meningitis Generalised polyneuritis	Lescher F. G. [4]
Blurring of vision Meningitis Peripheral neuritis Myelitis	Byrne E. A. J. and Taylor G. F. [5]
Meningeal reaction Blurring of vision	Weinstein L. and Davison W. T. [12]
Irritability Headache Convulsions	Harris M. J. and Beveridge J. [9]
Unilateral convulsions Dilated fixed pupils Extensor plantar response	Nagaratnam N. and Sikkander [3]
Generalised convulsions Meningeal irritation Weakness of limb Congestion of retinal veins Blurred vision	Nagaratnam N. S. Ariaratnam and T. Kariyawasam (present series)

TABLE III Neurological manifestations in infective hepatitis reported by different writers.

NEUROLOGICAL MANIFESTATIONS

Meningeal

Lescher [4] mentioned 3 cases of meningitis and describes 2 in detail. Leibowitz and Gorman [3] in an analysis of 6 communications found 15 cases who had neck rigidity together with or without cerebro-spinal fluid changes. The C. S. F. was either normal, under increased tension or showed pleocytosis. Four of the five cases described by Byrne and Taylor [5] had signs of mild meningitis. Flukes [6] described a girl of 13 months who was admitted as a case of cerebro-spinal fever and on admission was found to be irritable with a stiff neck and a palpable liver. She also had broncho-pneumonia. Though jaundice was absent during life, at autopsy an enlarged, engorged and yellow liver was found and histologically showed generalised necrosis. Case I in this paper had neck rigidity and a positive Kernig's sign.

Encephalitis :

Two cases described by Nagaratnam and Sikkander [3] had disordered sensorium and vomiting. One of them had unilateral convulsions, fixed dilated pupils and an extensor plantar response. One of the two cases described here presented with generalised convulsions. Brain [7] described one patient with unilateral convulsions and hemiplegia before the onset of jaundice. Transient weakness of ocular accomodation was seen in two patients by Cameron. [1] Temporary blurring of vision occurred in three of the five patients described by Byrne and Taylor. [5] Temporary blurring of vision occured in one of our cases during convalescence.

Polyneuritis :

Leibowitz and Gorman [3] cite 10 cases by 6 observers with polyneuritis. Newman [8] refers to occasional occurrence of parasthesiae of limbs.

Myelitis :

This has been known to occur. [5]

General Considerations :

These complications usually occurred early in the course of the illness before the onset of jaundice. In the two cases described and in the two others referred to here in this paper they occurred from 1—3 days of the onset of illness. As a rule they occurred in the pre-icteric stage or within 3 days of onset of jaundice, though Lescher [4] described a case of a 24 year old man who developed hemiplegia two months after an attack of infective hepatitis. Leibowitz and Gorman [3] quote two group of workers, one group described the appearance of polyneuritis in a girl during a relapse one month after the onset of acute jaundice and the other described a patient who developed a typical Guillan-Barre syndrome during the fourth week of illness.

Neurological Sequelae

All our patients mentioned here recovered fully without any permanent sequelae. Unusual neurological sequelae occurred in some patients. One of the cases described by Byrne and Taylor [5] when seen 3 months after the onset of the illness had weakness with numbness of his legs, hyper-reflexia in all four limbs sensory deficit and a spastic gait. One other described by them had flaccid paraplegia (myelitis) who two months later had exaggerated reflexes in his lower limbs.

Diagnosis :

Leibowitz and Gorman [3] emphasised the importance of demarcating these patients who recover from those with fulminant hepatitis who may die as early as

several days after the onset. Neuropsychiatric symptoms and signs occur in both groups. In both they may develop at any time during the course of the illness and may occur before the appearance of jaundice. Among the mental symptoms, frank mania or fits of screaming tend to occur in the younger age group while drowsiness and nightmares in the older. Neurological signs include increased reflexes, ankle clonus and extensor plantar responses. It is difficult to distinguish between the two groups, however, mental symptoms appear to be more common with fulminant hepatitis whereas neurological signs both generalised and focal in the other. The presence of a small liver, flapping tremor and foetor hepaticus may suggest liver cell failure. Electro-encephalographic changes have been described in hepatic coma. According to Davidson and Summeskill [8] they are based on the presence of bilaterally synchronous, symmetrical high voltage, slow waves in the theta and delta ranges. In two children described by Harris and Beveridge [9] with convulsions and jaundice, EEG showed no abnormality.

It is important to distinguish between these two groups for prognosis differs. In those with fulminant hepatitis it is poor. In the other the prognosis is good and duration of illness short. Leptospirosis where meningeal symptoms can occur may closely simulate this illness. However muscle tenderness is marked and serological tests are positive.

Aetiology

The question of causation of the neurological syndromes in viral hepatitis is still uncertain. Infectious hepatitis is now considered a generalised disease and manifestations of tissues other than the liver have been studied by several workers. Myocarditis and pancreatitis has been demonstrated on autopsy material of patients dying of acute fulminant hepatitis. [10] Changes have been demonstrated in the mucosa of the stomach and small intestine. [11] They have also observed anaemia due to haemolysis. The patients in this series were all young. The disease tends to get localised as age advances. Leibowitz and Gorman [3] proposed three mechanisms whereby the nervous system could be involved by the virus hepatitis. (1) the virus may become neurotrophic and attack the nervous system, (2) the liver cells that are autolysed may produced a toxin which may affect the nervous system and (3) toxins from the gut may affect the nervous tissue. Though neurotophism is the most likely cause, Byrne and Taylor [6] argue that if we take into consideration the widespread distribution of infective hepatitis and the extreme rarity of the neurological complications, it is doubtful if the first mechanism is likely.

Acknowledgements :

We wish to thank Dr. D. T. D. Bulugahapitiya for the use of the clinical record of Case II and the Superintendent of Health Services, Colombo for permission to publish this paper.

SUMMARY

Two cases of infective hepatitis with neurological features are described and two others referred to briefly. Involvement of the nervous system in infective hepatitis though uncommon is not rare. Sequelae are infrequent and duration of illness short.

The neurological features that may occur have been described and the available literature surveyed.

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THE DIMINISHING SENSITIVITY OF THE GONOCOCCUS TO PENICILLIN

WITH SPECIAL REFERENCE TO TREATMENT FAILURES IN CEYLON

BY

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WHEN penicillin was introduced in the treatment of gonorrhoea over 25 years ago it was never thought that the drug would ever lose its efficacy. A dose of 150,000 units was all that was required to eradicate the gonococcus. Susceptibility studies from 1945 to 1954 showed that only less than 1% of strains of gonococci needed more 0.05 units per ml of penicillin to inhibit their growth in vitro.[1] However after about a decade reports from several countries began to show that the gonococcus was progressively getting less susceptible to penicillin. Treatment failures increased and laboratory evidence for the increasing numbers of less sensitive strains was forthcoming. The correlation between strains of gonocci less sensitive to penicillin in vitro and treatment failures was also demonstrated.[2] Today some strains require more than 2 or 3 units per ml of penicillin for inhibition.

The incidence of less sensitive strains in many countries has been reported periodically, in London 37.3% (1966);[3] in Denmark about 50% (1961/62);[4] in Australia 44% (1966);[5] in Greenland 86% (1963);[6] 54% (1964/65), [7] 19% (1966/67);[7] in U. S. A. 86% (1959);[1] in Czechoslovakia 22% (1965/67)[8] and in Ceylon 35% (1961.[9].

However these figures cannot be compared as (i) no standard method was used for the determination of sensitivity, the methods in use are the plate dilution, tube dilution, tablet or diffusion and impregnated disc methods, and (ii) The criterion employed to decide "less sensitivity" has not been fixed, sometimes even in the same country, e g. in London it was a minimum inhibitory concentration (m.i.c) $\geq$ 0.125 units per ml[3] in one study and $\geq$ 0.1 ug per ml = 0.166 units per ml[3] in another; in U. S. A. a m.i c. $\geq$ 0.1 units per ml;[1] in Denmark a 50% inhibitory concentration or IC_{50} $\geq$ 0.053 ug = 0.088 units per ml.[10] Nevertheless the figures clearly indicate the large proportion of strains showing increased resistance to this antibiotic. This resistance however has still not been shown to be absolute in that no strain has yet been isolated whose m. i. c. cannot be reached and sustained in the blood and tissues. But it has been found that a strain less sensitive to penicillin is almost always completely resistant to streptomycin.

To counter the increasing number of treatment failures there are 2 methods open; to increase the dosage of penicillin avoiding the depot preparations or to use an alternative antibiotic. The first method has been adopted widely using progressively increasing doses of the shorter acting preparations of penicillin, but this only had a temporary effect in reducing the failure rate which began to rise again after a time. In any case it did not succeed in preventing

the increasing incidence of the partially resistant strains. In U. K., dosages of 800,000 units, 1.2 mega units and 2.4 mega units of aqueous procaine penicillin have been used; in U. S. A. the recommended dose today is 2.4 mega units for males and 4.8 mega units for females, while in Denmark and Greenland 5 mega units of sodium penicillin G has been given. The failure rates that have been reported very between 8.5%[11] and 14%[12] with 1.2 mega units of aqueous progaine penicillin; between 25%[13] and 5.8%[11] with 2.4 mega units of the same preparation; while with 5 mega units of sodium penicillin G the rate has been almost nil.[7] The limiting factors to the use of increasing doses of penicillin have been the cost and the tolerance of the patient to the volume of injectable substance. These together with the possible anaphylactic reactions have led to the search for alternate antibiotics. Almost all known ones have been experimented with and the results with many of them have proved satisfactory, but here again the high cost of some of them to be used routinely and the fear that their wide use particularly if the doseage is inadequate may eventually lead to the emergence of resistant strains, have diminished the initial promise it appeared to hold out. With the cost of tetracycline now much lower it has been chosen as the routine treatment in many countries with failure rate ranging from nil [14] to 6.2%.[15]

In Ceylon the occurrence of less sensitive strains had been noticed in 1961 but no problem ensued from this. In a W.H.O. survery conducted in 1961, of 25 strains from Ceylon 35% were found less sensitive.[9] This situation however caused no concern as the routine treatment carried out at that time of procaine penicillin in oil with 2% monostearate (P. A M.) 600,000 units proved quite adequate with only occasional failures. It was not until 1968 that the change in the sensitivity of the gonococcus was felt. As facilities for sensitivity determination are not available at the Laboratory Service of the Anti – V. D. Campaign this change became apparent on the clinical results. There was than noticed an unusual number of treatment failures with the routine one dose treatment of P. A. M. 600,000 units.

Investigation

It was therefore decided to undertake a study of the response of cases of gonorrhoea to penicillin with a view to finding the most effective dose for the one dose treatment of the disease.

Method

The study was commenced with cases attending the Central and Port VD Clinics, Colombo and continued at the VD Clinic, Jaffna. The period of the study was between July 1968 and June 1970. Only males with acute urethritis were included in the study for in the absence of routine culture facilities, tests for cure in the female were not adequate.

Those with positive smears (gram stain) were given the treatment indicated below. They were then followed up on the 3rd, 10th, 17th, and 24th day and thereafter once a month for three months. At each visit the cases were examined for urethral discharge and the two glass test with urine carried out and smear examination done even if minimal signs were present. Serological follow up was done to detect any coincident syphilis.

The preparations and dosages of penicillin studied were procaine penicillin in oil with 2% aluminium monostearate(P.A.M) 600,000 units, fortified procaine 400,000 units, 800,000 units, 1.2 mega units and 1.6 mega units, in that order.

RESULTS OF DIFFERENT SCHEDULES OF TREATMENT

TREATMENT	Number of cases assessed	Number of failures	Number reinfected	Percentage failures
P. A. M. 600,000 units	91	48	1	53
Fort. procaine penicillin 400,000 units	51	19	1	37
Fort. procaine penicillin 800,000 units	83	23	4	28
Fort. procaine penicillin 1.2 mega units	48	14	0	27
Fort. procaine penicillin 1.6 mega units	29	2	3	7

* Fort procaine penicillin contains 300 000 u, procaine penicillin G and 100 000 u, Sodium penicillin G in 1 ml.

RESULTS

Of the cases treated, only those who returned for a minimum follow up were assessed, the first visit being within five days and another within fourteen days. The number of failures included those who showed no change with treatment and those who relapsed within fourteen days. The distinction between relapse and reinfection has always been difficult. In this study a negative history of contact following treatment was relied upon. If those who defaulted follow up were presumed to have been cured the failure rates would have been lower.

Discussion

The above study was commenced at two VD clinics in Colombo and continued at the VD clinic in Jaffna 250 miles away. The sensitivity patterns of the strains of Neisseria gonorrhoeae in the two towns were not expected to be so much different on the basis of topographical and social factors, as to influence the results of the study. The treatment at the clinics in those two areas prior to the study was also identical for several years and could have thus not altered the sensitivity pattern of any one alone. It is also likely that any exotic strain that may have been introduced through the Port of Colombo would have soon worked its way throughout Ceylon. Further at the annual conference of Medical Officers of the Anti V.D. Campaign in 1968 it became known that the inadequancy of P.A.M. 600,000 units was being felt all over Ceylon alike.

Though facilities for sensitivity determinations are not available at the V.D. Laboratory Service, the clinical results with increasing doses of penicillin is used in the study, disclosed a dimunition in the sensitivity of the gonococcus. This increased resistance though it made its clinical appearance relatively late in Ceylon, has reached a level now which could only be

satisfactorily dealt with using 1.6 mega units of fort. procaine peniciliin in the male. It will be noted that the calculated failure rate with 1.2 mega units in Ceylon is 2—3 times that found in U. K. using aqueous procaine penicillin in the same dosage, indicating a possible higher resistance of the local strains. It is also known that certain strains from the Far East have so far proved the most resistant, a failure rate of 20—30% with 2.4 mega units of procaine penicillin having been noted.[14]

Therefore the failure rate of 7% achieved with 1.6 mega units of penicillin which is the recommended routine treatment in males with acute uncomplicated gonorrhoea, appears quite satisfactory at the present time but experience has shown that such reductions in failure rates have not been long lasting and also that a progressive increase in dose of penicillin has not succeeded in preventing the gradual increase in the number of less sensitive strains. Thus a further increase in the dose of penicillin in the near future cannot be considered a remote possibility.

However, the cost and patient acceptance of large doses are certainly going to be the limiting factors to further increases in dosage. Already the routine dose for females is 2.4 mega units or 6 ml of procaine penicillin.

The cost of 1.6 mega units of fort procaine penicillin today is 60 cents while the cost of 1.5 G tetracycline in one oral dose which is the routine treatment in certain foreign clinics is 33 cents. This lowered cost of tetracycline today and the ease of administration, dispensing with syringes and needles and the increasing incidence of anaphylactic reactions with penicillin could well make tetracycline the drug of choice in the treatment of gonorrhoea.

Summary

(1) The decline in the efficacy of penicillin in the treatment of gonorrhoea and the rise in the incidence of less sensitive strains of N. gonorrhoeae over the years in many countries are described.

(2) The effect of the increasing number of less sensitive strains was much more delayed in Ceylon but the level of resistance reached appears to be relatively high.

(3) A small study employing different methods of treatment with penicillin was conducted and the failure rates noted to range between 7 and 53 per cent. The calculated failure rate of 7% with 1.6 mega unit of fort. procaine penicillin for acute uncomplicated gonorrhoea in males is considered satisfactory at the present time.

(4) The position with regard to the future and the need to investigate alternate antibiotics in the treatment of gonorrhoea is discussed.

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THE FAMILY OF MAN AND THE PILL

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MAN, whether primitive or civilised, has always enabled his woman to bear children in some form of security, by the creation of protective patterns of behaviour — from tribal taboos — to marriage laws. Prolific and continued breeding has been, and in parts of the world nowadays, still is, influenced by the desire to raise a family in the face of a high infant mortality rate. But the impact of modern medical care and and education in the developed society, including our own which is cynical to the extreme towards anything, has lessened this need.

No longer is procreation the sole contribution that woman can make to the community, no longer is it necessary to have seven pregnancies to ensure that two children will survive to maturity, and no longer is woman merely a 'retort for the distillation of her husband's children'. Perhaps one of the greatest steps man has taken in the long history of the development of his family, has been securing fertility control as the modern right of the modern woman.

The unwanted pregnancy

All gynaecologists are aware of the magnitude of genuine gynaecological illness that is caused by the fear of further unwanted and possibly dangerous pregnancies. There is mounting evidence to show that woman has a deep emotional as well as economic need to control her fertility.[1,2] It is not possible to ascertain how many of the 63,000,000 people added to the world population each year[3] are born as a result of planned pregnancies, but among low-income groups the unwanted pregnancy rate has been estimated at 54 per cent.[4] The unwanted pregnancy leads to illegal abortion, child–neglect, the 'battered baby' syndrome and many more subtle community problems. For the individual woman it leads to despair emotional insecurity and perhaps financial disaster. For the family it leads to over-crowding and the over-straining of an already limited economy, whilst for the nation its cost is measured in the expensive provisions of the social services. The indices of social pathology such as suicide, crime, family instablity and many forms of mental disorder are highest in the most over-crowded portions of large cities. The problem families, uncontrolled fertility, and poverty, are directly associated.[5]

Quality of marriage and family relationship

As we become more capable of lowering mortality rates, neonates, infants and adults, so it is inevitable that we are becoming more concerned with the quality of life. In particular, during the next decades we shall be exploring means improving the quality of our marriage and family relationships, since a stable and happy home is the key factor in any child's development. So it should be possible for men and women everywhere to have babies when they want them, and not

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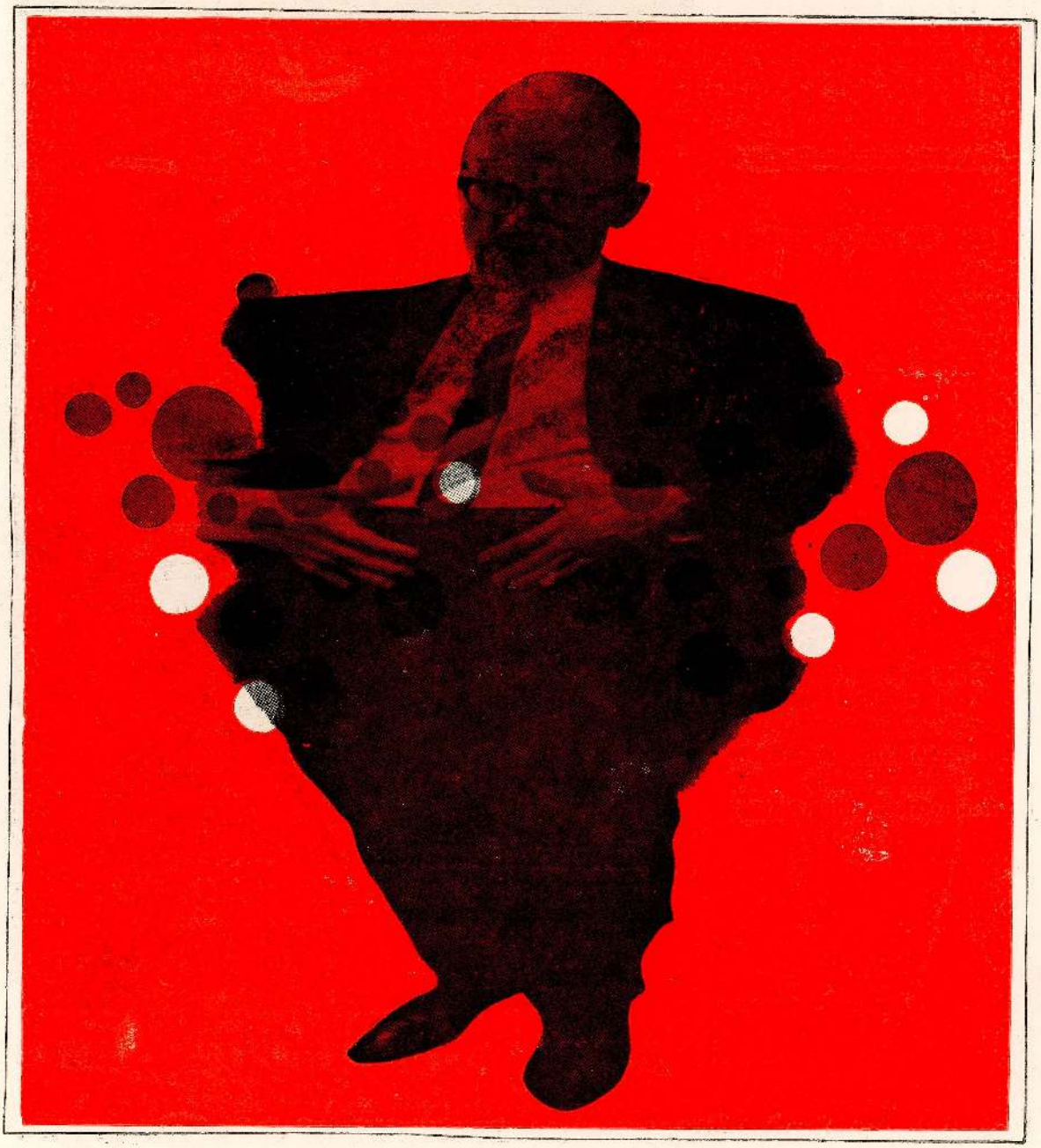

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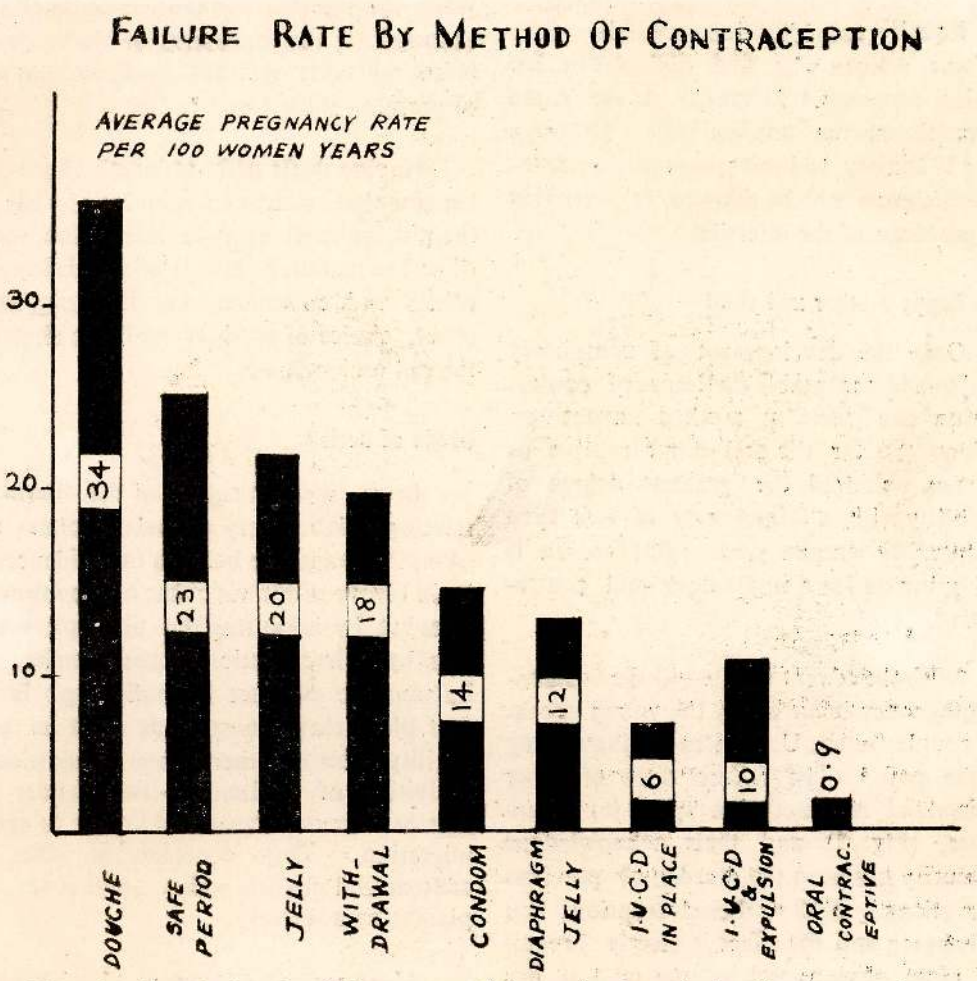

FIG. 1 Graph showing failure rates of the various methods of contraception.

through ignorance or because of accident. Is it really too ambitious to look forward to the time when the accidental pregnancy and the unwanted baby are as rare as the plague?

Equally, consideration should be given to those women who find difficulty in becoming pregnant. Infertility is the cause of much marital unhappiness. Although there is anxiety to limit population explosion this must not be allowed to over-ride the problems of the infertile.

The happy mother and child

Only the development of completely reliable and acceptable methods of contraception can have a marked impact on society. So far the oral contraceptive or pill has achieved the greatest degree of reliability with a failure rate of less than one per 100 woman years. But search is still going on for a single dose oral contraceptive.

With the advent of the pill the accidental pregnancy incurred by the young working couples in the U. K. is becoming a thing of the past.[6] The failure rates of other methods of contraception speak for themselves, (Fig. 1) and their acknowledged insecurity has been the burden of previous generations. With oral contraception, this is changing and the effect is slowly becoming more obvious and in the west it has proved its merit. In one survey, investigating the emotional responses of women receving oral contraception, it was reported that 53 per cent. found improved coital satisfaction and libido was markedly increased.[7] In another survey, which reviewed the situation from that of a family doctor, it was noted that the families who were using oral contraceptive showed a considerable drop in their consultation needs, from 8.24 to 3.16 average annual surgery attendances with a great reduction in their manifestations of latent anxiety.[8] When the interval between pregnancies is extended to the optimum of three years, infant mortality decreases and the hazards of prematurity reduced.[9]

Having dealt with at length about the benefits that accrue to man by the use of the pill, we must now look into the mode of action metabolic effects acceptability side effects and complications, the long term effect, choice of product and the effect of the pill on lactation.

Mode of action

In an excellant review of the literature relating to laboratory animals, Holmes and Mandl[10] found the balance of evidence to be in favour of the view that oral contraceptives act by inhibiting the pituitary rather than by a direct action on the ovaries. In humans the evidence is conflicting: in the first place these compounds exert an antifertility effect by other means in addition to inhibition of ovulation — they render the cervical mucus viscous and hostile to sperm migration. They considerably alter the endometrial picture which could effect implantation adversely.

More recently, Taymour,[11] with newer assay methods suggested that orai contraceptives abolish the mid-cycle peak of L. H. (luteinising hormone) secretion with little effect on the output of F. S. H. (follicle stimulating hormone so that at present the most likely mode of action is a supressive effect on the synthesis and / or release of pituitary L. H.

Metabolic effects

Administration of oestrogen and progestogen alone and in combination have some effect on various metabolic processes. They have been shown to cause an increase in protein-bound iodine and in plasma cortisol and an alteration in aldosterone secretion. These abnormalities are without any clinical significance. Carbohydrate metabolism has been affected only in those patients who already had a pre-diabetic condition.

One of the early anxieties raised was the possibility of an increased risk of carcinogenesis, despite the fact that the balance of these tablets is progestogenic and progestogens are known to be anti-cancerous. Bishop[12] in a review of the literature found nothing to indicate that cancer of the breast or uterus in humans has ever been induced by exogenously administered oestrogen or progestogen.

A hypothetical hazard, apparently without clinical importance, is possibility of virilisation of a female foetus. This arose partly because the 19-norsteroids show some androgenic activity in laboratory animals and partly because of an increase in the incidence of foetal masculinisation following the use of large doses (10mg or more) of these progestogens in pregnancy.[13] There is no evidence that the much smaller doses now used for oral contraception have ever had this effect.

Acceptability

For the first time we have a method which is virtually 100% effective and one which is taken orally without relation to individual coital acts. It is cycle by cycle contraception and has proved to be acceptable to many couples who have found conventional methods quite unacceptable; this is true of sophisticated women and equally true of women from problem families who would not contemplate the use of methods involving genital manipulation at the time of coitus. Although the number of patients withdrawing from trials normally gives an index of acceptability, the number of withdrawals and the percentage of patients complaining of side-effects is higher when the method is first introduced in a new area and seems to reflect the anxieties of both patient and doctor. Withdrawal rate also depends on newspaper publicity and other factors outside the control of the doctor.

Side-effects and Complications

The side-effects are related to the oestrogen/progestogen balance of the product. High oestrogen content can cause nausea, premenstrual tension, irritability, oedema, increase in weight, menorrhagia, mucorrhoea and cervical erosion. High-progestogen content can cause breast fullness and discomfort, premenstrual acne, greasy hair and skin, cramp-like pain in legs and abdomen (venous effect of progestogen), dry vagina, premenstrual leucorrhoea and mental depression.[14]

Though nausea was a disturbing feature in the early days of oral contraception, it is certainly less common now that the dosage is reduced and the method more widely accepted. The most troublesome side-effect found with every pill was headache which tended to occur in the gap after stopping the pills. This was explained as being due to migrainous in nature. With the low dose preparations even this side-effect is seldom reported.

Thrombo - embolic disease is now accepted as a possible complication. Evidence has been accumulating that oestrogens given alone increase the risk of thrombosis. This is due to the increase in the clotting factors including factor X which is involved in the intrinsic clotting mechanism. Platelet aggregation time has also been found to be significantly accelerated. This has been found to occur even with the low dose oestrogen preparations. Only preparations containing chlormadinone alone were free of this effect.[15]

At the present moment, the effect on mood of oestrogen / progestogen mixtures is displacing thrombo-embolic episodes as the focus of disquiet about oral contraceptives. High rates of depression appear to be associated with pills with high progestogen content. But it is said that the pill can precipitate depression in predisposed women of child-bearing age. This disturbance is attributed to an aberration in tryptophan metabolism and there is also evidence that few cases of 'pill' induced depression have responded to pyridoxine.[14] A contraceptive pill incorporating pyridoxine has already been marketed in Spain.

Contra-indications

There is no known absolute contra-indication in normal women, and no harmful effects have been proved to occur when the pills have been administered to women with a normal menstrual history in whom pelvic and breast examination has been satisfactory. Obviously, oral contraceptives should not be given if there is an existing breast cancer in a young woman and on physiological grounds, they should not be given to young girls who are not yet physically mature.

Recently, oral contraceptives have been used in the United Kingdom for patients who suffer from illnesses such as tuberculosis, diabetes mellitus, cardio-vascular disorders, epilepsy and migraine. In all these conditions oral contraceptive pills, in common with some other medicaments, are occasionally responsible for aggravating these disorders, particularly those with an allergic basis; but it is well worth giving them a trial for a patient with any of these illnesses, as there is a good chance that she will be much improved and even if the condition is aggravated, it will return to normal as soon as medication is stopped.[16] But one has to be careful when considering whether to give oral contraceptives to patients with a previous history of thromboembolic disease, a clear cut history of depression and recent catarrhal jaundice. We should also keep in mind that apart from sterilisation, this is the most effective method of contraception and that possible side effects should be assessed in relation to whether pregnancy may represent danger to the life or health of the mother.

The long term effect

Holmes and Mandl[10] found evidence of pituitary enlargement (mainly of increased chromophobe tissue) in adult rats treated over long periods with norethynodrel. But, clinical experience of about twelve years with oral contraceptives has provided no cases of pituitary tumour. Furthermore, as soon as therapy is discontinued, even after long-term treatment, there is an almost immediate return to a normal output of gonadotrophic hormones. The higher conception rate and successful maintenance of pregnancies to term following oral contraceptive therapy, which investigators report from all over the world, demonstrate clearly that pituitary gonadotrophic secretion, ovulation, endocrine activity and end-organ tissue responses remain intact.

CHART 1

Groups of Contraceptive Pills

Gr. A Pincus Pill.

They are taken for 20, 21 or 22 days of the cycle.

	Oestrogen / Progestogen content.		Trade name
1.	Norethisterone acetate Ethinyl Oestradiol	4 mg. 0.05 mg.	Anovlar
2.	Norethisterone acetate Ethinyl Oestradiol	3 mg. 0.05 mg.	Gynovlar
3.	Norethisterone acetate Ethinyl Oestradiol	2.5 mg. 0.05 mg.	Norlestrin
4.	Norethisterone acetate Ethinyl Oestradiol	1 mg. 0.05 mg.	Minovlar
5.	Norethisterone Mestranol	1 mg. 0.05 mg.	Norinyl—1
6.	Norethisterone Mestranol	2 mg. 0.05 mg.	Norinyl—2
7.	Norethisterone Mestranol	1 mg. 80 mcg.	Ortho-Novin 1/80
8.	Norethisterone Mestranol	2 mg. 100 mcg.	Ortho-Novin 2
9.	Megestrol acetate Ethinyl Oestradiol	4 mg. 0.05 mg.	Volidan
10.	Megestrol acetate Ethinyl Oestradiol	2 mg. 0.1 mg.	Nuvacon
11.	Lynestranol Mestranol	5 mg. 0.15 mg.	Lyndiol
12.	Lynestranol Mestranol	2.5 mg. 0.075 mg.	Lyndiol 2.5
13.	Ethinodiol diacetate Mestranol	1 mg. 0.1 mg.	Ovulen
14.	Ethinodiol diacetate Ethinyl Oestradiol	1 mg. 50 mcg.	Ovulen 50
15.	Norethynodrel Mestranol	5 mg. 0.075 mg.	Conovid
16.	Norethynodrel Mestranol	2.5 mg. 0.1 mg.	Conovid—E

Gr. B. Pincus pill continuous.

As above ; but the pack contains seven inert tablets.

1.	Norethisterone acetate 1 mg. and ethinyl oestradiol 0.05 mg.	— 21 tablets	
	Inert lactose tablete	— 7	Orlest 28

Gr. C. Sequential Pill

1.	Mestranol	0.1 mg.	16 pink tablets	
	Mestranol 0.1 mg. and Norethynodrel 2.5 mg.		5 white tablets	Feminor 21
2.	Mestranol	0.1 mg.	14 yellow tablets	
	Mestranol 0.1 mg. and Chlormadinone 1.5 mg.		7 pink tablets	C-quens 21
3.	Mestranol	100 mcg.	14 white tablets	
	Mestranol 100 mcg. and Norethisterone 2 mg.		7 blue tablets	Ortho-Novin SQ
4.	Mestranol	80 mcg.	15 white tablets	
	Mestranol 80 mcg. and Chlormadinone 2 mg.		5 peach tablets	Sequens

Gr. D. Sequential continuous

One tablet daily commencing initially on day 5 with the oestrogen, followed by the combination, followed by inert lactose tablets which is then followed by the oestrogen.

1.	Ethinyl oestradiol	0.1 mg.	16 red tablets	
	Ethinyl oestradiol 0.1 mg. and Megestrol acetate 1 mg.		5 white tablets	
	Lactose tablets		7 blue tablets	Serial 28

Gr. E. continuous progestogen

A low dose progestogen alone in each tablet. One tablet is taken every day without any interruption even during menstruation.

1.	Chlormadinone acetate	0.5 mg.	Normenon

Choice of product (Chart I)

With mounting criticism in the lay press with regard to the potential dangers of the pill such as thrombo-embolic disease, there has been intensive research to cut down side-effects and possible complications. One aspect of this research was the reduction in the amount of oestrogen, the amount of progestogen and the amount of both in the pill. When pills containing low dose of oestrogens are used, the possible risk of pregnancy should be kept in mind. As 50 mcg. of oestrogen may stimulate ovulation or cause delayed ovulation, it seems in changing from a high dose oestrogen product to a low dose oestrogen product, there is a risk of delayed ovulation in the first cycle. Unless the woman is changed to a strongly progestogenic pill such as Anovlar, other precautions should be taken for six weeks. The two weeks recommended by the Family Planning Association of Britain are not long enough to cover this possibility. [16]

The other aspect of the research is the introduction of sequential regime. In this regime there are two kinds of tablets — one type containing an oestrogen alone which is taken for the first 15 or 16 days and this is followed by a combination tablet containing oestrogen and progestogen to complete a course. Early experience has suggested that the sequential regime was a less efficient one. Mears [17] has found most sequential formulations so far less effective, break through ovulation occasionally occurring in later cycles, and that the more normal endometrium found with sequential therapy makes implantation and pregnancy possible.

Continuous regime through menstruation with inert tablets has been and is being used to prevent patient failures. Continuous progestogen regime with chlormadinone has proved successful with some limitation. When chlormadinone acetate 0.5mg. was used ovulation occurred in 40% of cycles. The endometrial effect is that of a weak oestrogen / weak progestogen, with a high break- through bleeding incidence of 23% of cycles. [15] The oestrogen effect is due to the endogenous oestrogen. Normal cycles also occur, so that fertility control possibly depends on cervical mucus changes. Thus, there is little margin for error on missed tablets and reported pregnancy rates with chlormadinone acetate 0.5mg. vary from 1 to 12 per cent. [15] Hence if chlormadinone alone is used, it should be given to someone who does not mind a possible pregnancy.

Effect on lactation

The effect of oral contraceptives on lactation is as yet not properly understood. The original Enavid 10mg. or 5mg. tablets certainly cause a decrease in breast milk, but there are indications that this may not be so with the smaller dose tablet now being used. The patient who wants to continue lactating should wait until weaning has begun so as to avoid any risk of decreasing the milk.

Conclusion

This article is based on studies of patients in the United Kingdom. The importance of family planning, when it is extremely necessary, with the most effective contraceptive method is discussed. The pill as the most effective contraceptive method apart from sterilisation, is shown. The various pills available are grouped according to their mode of use and steroid content. The limitations of the low dose oestrogen pill, the sequential regime and the continuous low progestogen (chlormadinone) regime are pointed out.

Acknowledgement

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INTRA-UTERINE CONTRACEPTION

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THE problem of today all over the world is undoubtedly the question of "Planned Parenthood" to prevent or control the "Population Explosion". The doctors, the politicians, economists and the planning administrators all are haunted and perturbed by the thought of this impending "population explosion" in years to come. In practice, some form of contraception is necessary for family planning though it is vital to be clearly understood that family planning does not mean mere prevention of conception.

Many methods are available for contraception and they can be listed as follows:—

1. The rhythm method or safe period
2. Coitus interruptus
3. Use of condom or the sheath
4. Use of spermicides
5. Use of douches and sponges
6. The cap and chemicals
7. Oral contraceptive tablets
8. Injectable long term contraceptive agents
9. Intra-uterine contraceptive devices (I. U. C. D.)
10. Sterilisation of either the male or female

The first six of the above methods did not have the expected degree of safety, acceptability and convenience and thus the oral contraceptives and the intra-uterine devices came into prominence. Of these the oral contraceptives were found to be virtually one hundred percent effective, very convenient and proved to be acceptable to many. Thus, this method is widely used all over the world. Inspite of this extensive use there had been some degree of fear in the minds of doctors and research workers as to the long term effects of oral contraceptives — especially the metabolic effects and the risk of cancer. Further in recent times there has been some publicity that complications such as thrombosis and embolism, liver damage and glucose intolerance may occur as a result of the use of oral contraceptives. Some experts on human metabolism feel that oral contraceptives alter the normal processes of metabolic pathways and this leads to emotional or psychological side effects such as headache, tension, depression, irritability, frigidity, tiredness and some unspecified mental disorders. They feel that within the next few years the oral contraceptives will be out of use. In such an event the intra-uterine contraceptive devices will receive more prominence and as such a clear understanding of the types of devices, their mode of action, and the technique of insertion, complications of and contraindications for their use is very necessary.

"Stoning the camel" was a practice that dates back to the ancient Egyptians who introduced a smooth oval stone in the uterine cavity of the female camels to prevent them from becoming pregnant if they were to be used for long journeys across the desert.

Very much later Pust — a German gynaecologist designed a number of cervical stem pessaries made of glass, combination

of metals and silk worm and used to treat dysmenorrhoea when associated with acutely anteflexed or retroflexed uterus. It was observed that these pessaries acted as contraceptives. Another German gynaecologist Ernst Grafenberg eliminated that part of the appliance that lay in the cervical canal and produced his now well known ring made of coiled silverwire. If left in for long, the rings were found to burrow through the uterine wall and pass into the peritoneal cavity the process now called transmigration.

Subsequently many workers from various parts of the world for instance United States, Eygpt, Israel, England and Japan continued to try out various materials to make intra-uterine devices of various shapes and sizes. The Japanese were the first to make and use plastic devices and the popular one was Oto ring. The drawback with this device was that the cervix had to be dilated up to 6 Hegars before inserting this ring. Further as the plastic mix was without any radio-opaque element in it, the ring could not be detected by X-rays.

Once the idea was given, many other workers started moulding plastic into shapes and sizes and impregnated the plastic with barium or bismuth so that the devices would be radio-opaque. Thus Margulies spiral (1962) Birenberg bow and Lippes loop (1962) came into existence. Another plastic device called the 'Saf-T-Coil' was produced in 1965.

Bacteriological Studies

It is reasonable to assume that one could expect bacterial contamination of the uterine cavity to be an inevitable sequel to the insertion of the intra-uterine contraceptive devices, especially with those where the stem or the nylon thread of the device reaches the vagina through the cervical canal. But Mishell and his colleagues after a careful study[1] confirm that the bacterial flora of the uterine cavity is not altered by the presence of an I. U. C. D.

Histological Changes

The effects of the I. U. C. D. on the endometrium have been well studied in human beings. There is an imprint of the device in the endometrial surface. The portion beneath the device is compressed and those which bulge between the loops of the device are oedematous with patchy hyperaemic areas. The most obvious changes are:

1. An increase in the number and size of vascular channels.
2. Diffuse or patchy subsurface stromal haemorrhage.
3. Changes in the amount and distribution of fluid in the endometrial stroma.

Mode of action

The mode of action of oral contraceptives is well known to be by inhibiting ovulation. But how does the I. U. C. D. act? Is it really a contraceptive or is it an abortifacient? The exact way in which these devices protect against pregnancy is not clearly known.

There is evidence that the I. U. C. D. does not inhibit ovulation in human beings as it does in cows and water buffaloes. This is evident by the changes in the endometrial glands which can occur only by the action of varying amounts of oestrogen and progesterone thus proving that ovulation has occurred.

It was suggested by some workers that an I. U C. D. alters the tubal function in that the peristaltic action is accentuated so that there is rapid transference of ova

through the tubes. This may prevent fertilisation or if this should occur the fertilised ovum is made to reach the uterine cavity before the endometrium becomes receptive for implantation. This theory has not been proved yet.

Most probably an I. U. C. D. alters the intra-uterine environment into a state that is unsuitable for the survival and/or the implantation of the blastocyst. This may be due to changes in myometrial activity or changes in the endometrium. The activity of the myometrium was proved to be increased in rat uterus containing a foregin body, by Marcus, Marcus and Wilson.[2] But there is no evidence that this happens in the human uterus. Rozin, Schwartz and Schenker[3] could not demonstrate any increase in the myometrial activity while Lippes loops C and D were in the uterine cavities. They postulated that an I. U. C. D. transforms a potential uterine cavity into an actual one. As a result the blastocyst which would normally be held in the uterine cavity by the approximation of the anterior and posterior endometrial surfaces, loses its support and so is lost.

Complication of I. U. C. D.

1. PAIN

Pain deep in the pelvis is experienced by most women after insertion of I. U. C. D. It is cramp-like, varying from mild to severe degree, but usually transient. Cramps are more common in nulliparous women than in multiparae. This is probably due to the fact that the uterus in a multipara is larger. It is important that a smaller device should be used in nulliparous women or they may be pretreated with oestrogens and progesterones for three or four cycles with a view to enlarge the uterus. Usually the pain can be controlled by local heat and mild analgesics but in a few, one may have to remove the device because of this complication.

2. BACKACHE AND DYSMENORRHOEA

At least half the number of women fitted with I. U. C. D. complain of low backache and of these in about fifty percent the backache is fairly severe. Such people also complain of dysmenorrhoea of varying degree. Tejuja and Malkani[4] of the All India Institute of Medical Sciences in New Delhi measured uterine cavities using planimeter-hysterogram technique and found that the size of the uterine cavity was not related to age, parity or body surface area. By measuring the inter-cornual distance and the fundus to anatomical internal os distance, they found that the area of uterine cavities ranged between 4.2 and 9.2 cm.[2] In most women who complained of backache, uterine cramps and dysmenorrhoea the area of the uterine cavity was less than 6 cm[2]. Based on these findings they suggested that the frequency of the above side effects may be related to the disparity between the size of the uterine cavity and that of the device. This further stresses the point that selection of the correct size of the device is as important as the selection of women suitable for I. U. C. D. insertion.

3. BLEEDING

After insertion of the I. U. C. D. there may be some bleeding for one to two days. The usual pattern is for these women to have increased flow during the next two to three menstrual periods. In a few there may be some intermenstrual bleeding for some months. The intermenstrual bleeding

usually cannot be satisfactorily controlled by any oral contraceptive agents, oestrogens, progesterones or oxytocics. If the intermenstrual bleeding should cause any alarm then the loop should be removed and a curettage considered. The loop can be reinserted after two to three cycles.

4. SEPSIS

Because of the fact that the nylon thread or the plastic stem protrudes through the cervical canal it may be thought that an I. U. C. D. may predispose to ascending infection but experience proves that this is not the case. As long as pelvic infection is excluded before insertion of the device and careful aseptic technique is employed there is found to be no increased incidence of pelvic or uterine infection as a result of the I. U. C. D.

5. TRANSMIGRATION

This has been reported to be a definite complication though the risk is small. Does this really occur or could it be that the uterus is perforated at the time of insertion and the device is placed partly or wholely into the peritoneal cavity ? If the uterine size, its position and consistency of the uterine wall are preassessed and the correct size of the device selected, and inserted with care, the risk of perforation or transmigration can be avoided.

If an I. U. C. D. is found to have transmigrated into the peritoneal cavity it should be removed to prevent the risk of intestinal obstruction in case of a bow or ring and perforation in case of a loop or spiral.

6. RISK OF CANCER

Quite rightly both patients and doctors are concerned over this question There is no evidence yet to suggest that presence of an I. U. C. D. increases the risk of cancer of the cervix or the body of the uterus. This problem certainly needs further study.

7. RISK OF PREGNANCY

The risk of pregnancy is found to be higher in women fitted with I.U.C.D than in the pill-users, but definitely less than that reported for general use of most conventional methods. The main cause of pregnancy occuring in women with I. U. C. D. is expulsion of the device. Many report to the clinic with the device in their hands or handbags, but some are not aware that the device had fallen off. Careful clinical examination, probing of the uterine cavity and radiography of the pelvis show no device and obviously expulsion had taken place without the woman's knowledge. Pregnancy can occur with the device in the uterus. Most of these reach term without any problems even though some may have intermittent antepartum haemorrhage. The foetus is not affected in any way and the process of labour is not altered. The device is commonly found to be expelled with the placenta, lying on its maternal aspect. There is no necessity to attempt removal of the device during pregnancy. In fact this will be hazardous. The risk of pregnancy is fairly high with the bows and reasonably low with double coils. The risk is reported to be in the region of 2% with Lippes loop but is definitely lower with the 'Saf-T-Coil.' In the author's experience the Safe-T-Coil has given maximum protection against pregnancy with low expulsion rate.

The use of an I. U. C. D. does not impair fertility and most fertile

women conceive promptly afer removal or expulsion of the device.

The women to be fitted with an I. U. C. D. should be carefully selected. This matter should be discussed with the husband and he must be adequately reassured that this does not in any way interfere with sexual functions or enjoyment. Both husband and wife should be made aware of the risk of pregnancy with this method. Further the correct size of device should be selected based on the size of the uterine cavity.

Contra-indications for the use of I. U. C. D.

1. PELVIC INFECTION

Any form of pelvic infection-salpingitis, salpingo-oophoritis, endometritis and even cervicitis should be adequately treated before a device is fitted. A recent septic abortion is also a contra-indication till the infection is eradicated.

2. UTERINE FIBROIDS

Submucous fibroids especially, will enlarge and/or distort the uterine cavity. The device cannot cover the endometrial surface and this leads to inadequate protection against pregnancy.

3. ABNORMAL BLEEDING

Unless and until the cause of this is ascertained and treated, an I.U.C.D. should not be inserted.

4. MALIGNANCY OF THE GENITAL TRACT

Usually, the treatment of the condition ends fertility in the woman, and the question of contraception does not arise. But in the case of carcinoma in situ of the cervix, treated either by conization or partial amputation of the cervix, I. U. C. D. can be fitted. But of course the usual follow up of the carcinoma in situ should be conducted regularly.

Time and Method of Insertion

The best time for the insertion of an I. U. C. D. is during the tail end of a menstrual period. One can be certain that she is not pregnant and the already open cervical canal facilitates introduction of the device.

During the post-partum period, London and Anderson[5] inserted I. U. C. Ds during the first week after delivery when the patient is ready to be discharged. This definitely affords protection against pregnancy but expulsion rate is high and so is the risk of perforation of the uterus during this period. As long as the mother can be provided with another form of contraception till then-the best time for the I. U. C. D. is at the post-natal examination, six weeks after delivery.

Insertion of an I. U. C. D. should be regarded as a surgical procedure. The device and the instrument should be sterile. The plastic device cannot be heat-sterilised. It would suffice if the device and the introducer are immersed in 1 in 2000 aqueous iodine for five minutes.

It is essential to do a pelvic examination to assess the size and position of the uterus. A cervical smear is taken for cytological examination. Now the vagina is cleaned. The anterior lip of the cervix is drawn down with a vullsellum to straighten the cervico-uterine canal. The depth of the uterus is assessed with a uterine sound. There is no need for the cervix to be dilated for the insertion of a loop or spiral or the 'Saf-T-Coil.' After straightening the device within the introducer, this is inserted into uterine cavity through the cervical canal. The tip of the introducer should be above the internal os but definitely well below the fundus. If the introducer is pushed further it may easily perforate the

fundus and enter the peritoneal cavity. This is the reason that the introducers have a shelf a little more than one inch from the tip so that it cannot be pushed further than necessary. When the shelf is held at the external os the tip is above the internal os. As the device is pushed, the introducer is withdrawn. The nylon thread from the distal end of the device protrudes through the cervical canal into the vagina. This facilitates removal of the device when necessary, in addition to helping to confirm that the device is in place. It is best to check the presence of the device three months after the insertion and later at six monthly intervals. Many women have worn I. U. C. Ds for years without any discomfort. But it is best to remove and replace it with a new one once in two to three years.

Recent Developments

Clinical trials in the United States have proved the efficacy as a contraceptive, of a vaginal ring impregnated with progestogens. It is easy for this to be inserted and removed like a diaphragm. From a woman's point of view it appears to be very satisfactory. It is also well tolerated by the husband and wife during coitus. The vaginal ring is made of silicone rubber with the drug 100mg of medroxyprogesterone acetate added at the time of moulding of the device. The drug is absorbed through the vaginal mucosa and the contraceptive effect is found to be by suppressing ovulation. Dr. Daniel R. Mishell[6] of Los Angeles County Harbor General Hospital in California who did the clinical trial is also carrying out studies with various doses of progestogens to assess the lowest dosage that will provide the maximum contraceptive effect.

At Michael Reese Hospital and Medical Center in Chicago[7], investigators are combining drug-filled silastic capsules containing 10–30 mg of milled progesterone crystals to modified Lippes loops. It is presumed that by altering the physiology of the endometrial receptor this combination device may increase the effectiveness of the I. U. C. Ds and avoid systemic effects of the pill. It is also presumed that the progestogens might decrease the expulsion rate of the I. U. C. D. and bleeding problems in its use. Investigations on the I. U. C. D. capsule are not yet complete to draw any conclusion.

Summary

There is no doubt that "planned parenthood" has become essential to every country in the world. To achieve this, it is inevitable that some form of contraceptive method should be adopted. Though the protection afforded by the intra-uterine contraceptive devices is somewhat less than that given by oral contraceptives it seems that complications can be reduced to the minimum by proper and careful selection of patients, the correct choice of the type and size of the devices and proper timing and careful aseptic technique of insertion.

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IMPLANTATION ADENOCARCINOMA OF THE ANUS

BY

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CARCINOMA of the anus is a comparatively rare disease and accounts according to Gabriel[1] for 3.4% of all carcinomata of the rectum, anal canal and anus. Goligher[2] holds the view that half the cases of carcinomata presenting at the anus are adenocarcinomata extending down from the rectum. True carcinoma of the anus is squamous cell in type with the exception of exceptionally rare basal cell carcinoma which Morson[3] found to have an incidence of less than 0.3%.

Adenocarcinoma of the anus not arising as an extension of a rectal carcinoma is a surgical curiosity of curiosities and the case to be described is one where no other explanation but that of implantation can account for the situation that was discovered.

Case Report

J. D. J., a 58 year old married female from Bamunugama was admitted to the University Surgical Unit in the General Hospital, Colombo on April 14th 1969 for the investigation and treatment of rectal bleeding of 18 months duration.

The patient's symptoms dated back to August 1967 when she noticed bleeding at defaecation, the blood being mixed with the faeces and some time later much mucus in addition to blood. The frequency of her bowel evacuations increased progressively (up to about 10 motions per day) and some six months after the onset of her symptoms, blood and mucus were evacuated with faeces as well as without faeces.

She first sought Ayurvedic treatment and since there was no relief, Western treatment at the local Government Dispensary. Ten months later she was no better and hence she reported to the Base Hospital of her area where she was admitted, a rectal examination was done, a diagnosis of haemorrhoids was made and haemorrhoidectomy carried out in July 1968. A fortnight after surgery and a few days after she returned home her old symptoms recurred with about the same intensity as before.

She reported back to her Base Hospital where she was treated with tablets and injections on two occasions. Since there was no appreciable improvement she had recourse to various other forms of treatment with no greater success. When she finally decided to report to the General Hospital, Colombo she found that she had lost weight considerably and was feeling faint, dizzy and breathless on exertion.

At the General Hospital, Colombo she was referred to the Rectal Clinic where proctoscopy was attempted but abandoned owing to the resultant profuse haemorrhage. The patient was advised admission but was unable to enter immediately and when she ultimately warded herself she complained of another symptom which she had noted for the past four months - a painful lump a the anus.

Examination revealed an emaciated and moderately anaemic elderly female with poor oral hygiene and clinically normal cardiovascular and respiratory systems. The abdomen was soft, undistended, with the liver and spleen impalpable and no masses or free fluid detectable. There was neither jaundice nor lymphadenopathy.

Local examination, in view of the past history and the painful anal complaint, was postponed to the next earliest operation day when it could be done under sedation and more ideal conditions. This revealed (on April 18, 1969) an indurated, tender, craggy mass about 2 cm. in diameter at about the 3 o'clock position just above the anal verge and bleeding on contact. A fleshy proliferative sessile growth of restricted mobility was also palpable in the anterior rectal wall at 7 cm. from the anus. Blood and mucus were found on the examining finger. A biopsy was taken from the rectal mass.

The microscopic report on the rectal growth was returned as "well differentiated adenocarcinoma."

After adequate preparation the abdomen was explored through a left lower paramedian incision under general anaesthesia on May 2, 1969. Multiple secondary deposits of the size of table tennis balls were discovered in both lobes of the liver. The rectal growth which was at the level of the pouch of Douglas was found to have infiltrated the uterus but was sufficiently mobile as one mass.

A palliative abdominoperineal resection of the rectum together with the involved uterus was carried out.

Examination of the resected specimen showed a clear separation between the rectal and anal masses (Fig. 1) by about

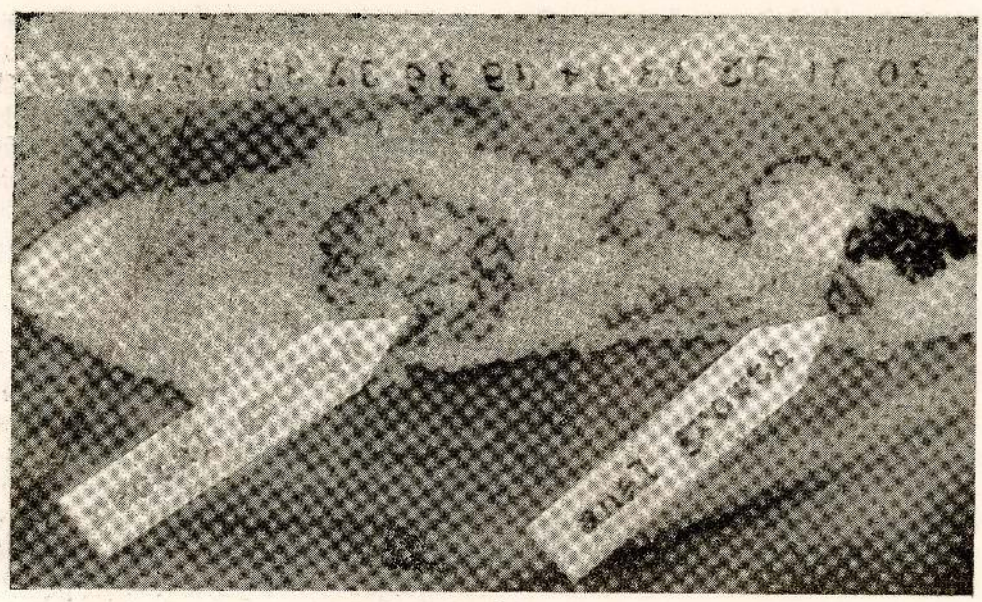

FIG. 1. Resected specimen showing the two growths.

6 cm. and this intervening area was found to be macroscopically and microscopically free of carcinoma. A representative portion of the anal mass was submitted to histology and reported as "well differentiated adenocarcinoma."

The patient's postoperative convalescence was complicated by infection and partial dehiscence of the perineal wound. About the 6th week after surgery this wound was almost healed, the colostomy working satisfactorily and the patient's general condition much improved. At this stage, on the advice of the Radiotherapist of the General Hospital, Colombo (Dr. H. K. T. Fernando) the patient was given cytotoxic drug therapy -60 mg. of Mitomycin were administered intravenously in divided doses over a period of three weeks under prednisolone and pyridoxine 'cover'. She was discharged home in a reasonable state of health on August 16, 1969.

The patient was lost to follow up in that she did not appear monthly at the Outpatient Surgical Clinic as instructed. Inquiry by post some three months after her dicharge, brought forth the news from her husband that one month after she returned home she began to deteriorate and expired on October 6, 1969.

Comment

The facts that the patient's original symptoms (which were not characteristic of those of primary haemorrhoids) recurred soon after haemorrhoidectomy, the anal lump that appeared subsequent to haemorrhoidectomy at the site of the surgical wound of the left lateral pile mass, the identical histological reports on both growths together with the neoplasm free area intervening between the two masses are considered sufficiently incontrovertible to pinpoint the anal mass as an implantation one from the rectal lesion which was missed before haemorrhoidectomy and unfortunately continued to be missed afterwards. It is considered superfluous to point out the axiom or moral exemplified by this case.

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DESENSITISATION AS A METHOD OF TREATMENT OF ASTHMA

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BRONCHIAL asthma consists of periodic attacks of breathlessness due to constriction of the air-ways of the lungs principally by bronchial spasm or oedema of the bronchial mucosa, caused by the response of an unduly sensitive bronchial tree to specific allergens and or non-specific irritative stimuli. The attack is characterised by expiratory dyspnoea, cough, wheezing and rhonchi.

Less than 10% of the population are allergic (atopic), i.e., they are liable to develop allergic or hypersensitivity reactions in various parts of the body which are referred to as "shock organs", when exposed to substances to which they are sensitive. The two principal shock organs are the skin and the respiratory system, the possible sites of reaction in the latter being the nose the accessory nasal sinuses, the trachea, bronchi and the bronchioles and the pulmonary blood vessels. The allergic response consists of an antigen-antibody reaction. The commoner allergens consist of pollens, dusts, foods, drugs, and bacteria which may be introduced by inhalation, ingestion or injection. They stimulate the reticulo-endothelial system to form globulins which pass into the blood stream and are deposited in the shock organs. Subsequently exposure of the organs to a similar antigen causes a specific antibody-antigen reaction and the development of histamine-like response with increased capillary permeability, oedema, the outpouring of eosinophil cells and spasm of the smooth muscles. Hence there is narrowing of the airway in asthma due to bronchial and bronchiolar muscular spasm together with oedema of the mucosa and excessive secretions.

In the Jaffna peninsula and presumably the rest of Ceylon approximately half the cases of bronchial asthma result from allergy to external allergens, most often dusts suspended in the inhaled air including bacteria, but occasionally ingested foods or drugs. This type of asthma is usually classified as "extrinsic asthma." The remainder in which no evidence of hypersensitivity to specific allergens is found by skin tests is classified as "intrinsic asthma". Most of these types can be shown to result from infections of the respiratory system. In a certain percentage of cases a combination of infection and allergy to inhaled allergens operate and here the symptoms may be seasonal, itnermittent and chronic. The symptoms in extrinsic asthma are usually seasonal or perennial.

The allergens causing extrinsic asthma are the same as those causing allergic rhinitis. By far the most important ones are the inhaled organic dusts such as pollens, mould spores, animal danders, feathers, insecticides, glue and lint from fabrics. House dust contains in addition to obvious constituents, other allergens apparently arising from the disintegration of fibres or from contamination with moulds and bacteria. For practical purposes an extract of a mixture of dusts from several houses may be used as if it were a single antigen. Grain dusts, flour, spices and

such vegetable seeds like cotton seeds, castor and beans are important causes in persons exposed to them by nature of their occupation. Practically any food may occasionally be a cause. Among those most active as antigens are eggs, fish, crabs, prawns, lobsters, cuttle-fish, nuts, spices and chocolate. In general, the antigens are proteins of somewhat lower molecular weight. Certain synthetic drugs like aspirin and penicillin may cause severe asthma presumably through acting as haptens. Quite recently it has been claimed that purification of ampicillin with respect to protein impurities has reduced the incidence of rashes and allergic reactions in treated patients. This has been confirmed by animal experiments where the injection of isolated protein impurity caused the formation of circulating IgG antibodies and skin sensitisation antibodies.

The infections of the respiratory tract causing asthma are the recurring infections of the bronchi, often secondary to chronic infections of the paranasal sinuses, tonsils, or adenoids. The sinusitis is usually of the chronic hyper plastic type with purulent secretions only during the more acute phases. It is often accompanied by mucous polyps in the nasal cavity or within the sinuses. Cultures of the respiratory system usually show a mixed growth with pneumococcus, staphylococcus viridans and haemolyticus, Neisseria catarrhalis, kliebsella pneumoniae, haemophilus influenzae, staphylococcus and bacillus pyocyaneus. It is very seldom that the aetiological importance of a single organism could be established.

The role of allergy in infective asthma due to respiratory infection is less obvious than in extrinsic asthma, but there is considerable evidence that infected asthma results from specific hypersensitivity to the bacteria present. The asthma may continue severe at times when the infection is in a relatively quiescent chronic stage. The symptoms and clinical findings are similar in infective and extrinsic asthma, including the abundance of eosinophils in blood and sputum.

Although the distinction between extrinsic and infective asthma is useful in the discussion of diagnosis and treatment, it is important to remember that many if not all asthmatic patients are affected by both extrinsic allergens and infective factors. Studies of aetiology of a case of asthma should attempt an evaluation of the importance of both extrinsic and infective causes rather than simply classifying them into one group or the other. Table 1.

Once the asthmatic pattern of reaction has developed through allergy to extrinsic agents or infection, paroxysms of asthma may be precipitated by many factors unrelated to the original cause. Such secondary factors include emotional stress, changes of humidity and temperature, irritating fumes or smoke, strong odours and physical exertion. These factors may be the obvious precipitating causes of individual attacks. Their recognition and control play an important part in therapy and occasionally the underlying infective or allergic basis is obscure and resistant to treatment and may constitute the main approach.

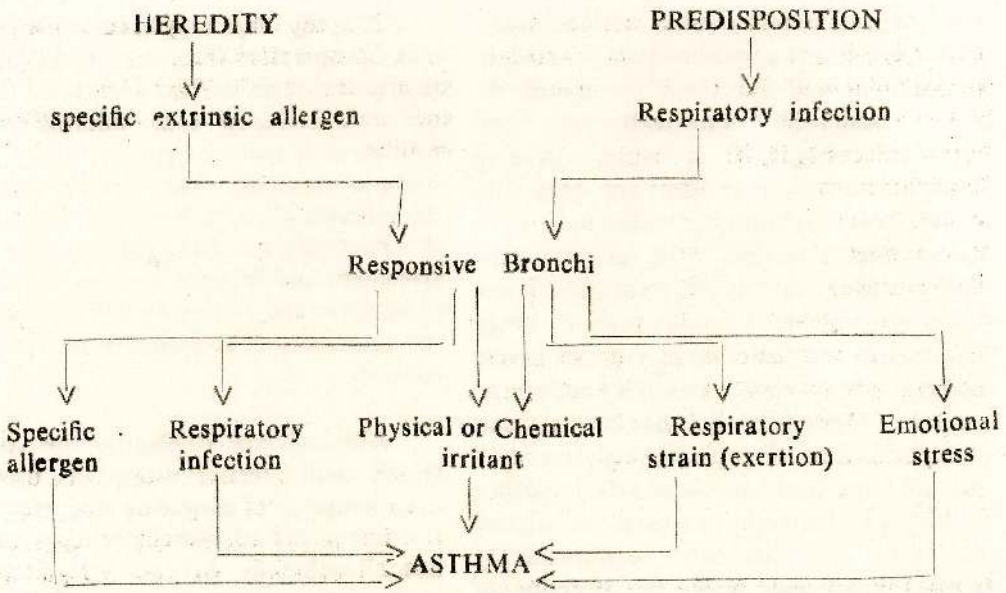

Table 1. Showing the part played by different factors in the causation of asthma.

Management

The successful management of a case of bronchial asthma depends largely on the intricate details obtained during history taking. More often than not it consists of much more than prescribing ever-increasing dose of antispasmodics and advice regarding the future progress of the disease. Very often children grow out of it at puberty. During history-taking the following details have to be looked into.

1. Allergy — the identification of specific allergens, subsequent avoidance and or desensitation.
2. Infection
3. Psychological aspects.
4. Drug therapy
5. Physiotherapy
6. Complications — the management of complications such as status asthmaticus, bronchopneumonia, heart failure and eosinophilic pulmonary infiltration.

This paper is mainly concerned with the management of allergic and infective types. The rapid advances made in the field of research on allergy makes it incumbent on the general practitioner to utilise such knowledge for the treatment of these unfortunate patients. In the treatment of the allergic and infective types there cannot be any denial of the fact that the identification of the specific allergens and subsequent avoidance and or desensitisation should be the main concern of the general practitioner. Unfortunately our laboratory facilities lag behind so much that the treatment of asthmatics by these procedures is beyond our reach. The next best we can do for our patients is to desensitise them to the common allergens — mainly bacteria and their body proteins by a common procedure.

The Swiss Serum and Vaccine Institute, Berne has put out a vaccine called 'Vaccine Antiasthmatnique Berne' the composition of which is as follows:

Pneumococcus I, II, III	20 millions	Per ml. of vaccine
Staphylococcus	400 ,,	
M. catarrhalis	40 ,,	
M. tetragenes	40 ,,	
B. pyocyaneus	500 ,,	
Preservative (phenol)	0.4%	

This vaccine was used along with autohaemotherapy to treat patients. This was done in order to desensitise the patients to

(a) the patient's own body proteins

(b) the protein content of the body of organisms.

In addition the body is induced to produce antibodies against the invasion and the subsequent infection by these organisms.

Material and methods

Strict antiseptic and aseptic measures are adopted almost rigidly. A vial of the vaccine is mixed with the patient's own venous blood whose volume is gradually increased from 2 ml. to 10 ml. and injected into the patient's gluteal regiom. A series of of ten such injections are given every third day. The course is repeated after six weeks and again after three months.

The patients are not selected on any particular basis. Every asthmatic is advised to take the injection and those voluntarily agreeing to take the injections are given the course of injections. All young adults not showing any damage to the lungs such as emphysema are persuaded to have the course of injections

Of a total of 875 cases of bronchial asthma and bronchiolitis seen during the years 1968 and 1969, 55 cases were given the course of auto-blood and anti-asthmatic vaccine. in my dispensary and 6 cases treated at Co-operative Hospital, Moolai, by me are also included in this review. The age and sex distribution of these patients is in given below.

Age group	Male	Female
10—15 yrs.	2	1
21—30 yrs.	9	10
31—40 yrs.	6	11
41—50 yrs.	12	5
51—60 yrs.	2	3

Of these 61 cases, only 15 cases had taken all three courses of the injections of the vaccnie and auto-blood. Patients who have completed only one course of the injections and who are yet to take or are taking the other two courses are not included in this review.

Results

The 15 patients who had all three courses of injections were patients who had been having asthma almost all the time and had been taking not less than one or two injections of adrenaline and intravennous aminophylline daily. 7 of these patients are living quite healthily without recourse to any drugs. The remaining 8 patients are maintaining themselves free on one or two tablets of promethazine.

All the 46 patients who did not take all three courses, took two courses of injections of vaccine and auto-blood. 31 of these patients are symptom free and able to manage without recourse to injections but only on aminophylline tablets and promethazine or chlorpheniramine tablets. The remaining 15 patients are free of symptoms and therefore are not taking any drugs. In fact as a result they are reluctant to receive the third course of injections. Continued

observation of all the 61 cases has not been possible, as 17 patients did not report either because they were quite well or they were disgusted with the whole procedure because of the accompanying pain with the deep intramuscular injections. Two patients admitted this as the cause. Table 2.

6 were cases observed over a period of 5 years, and these patients had all three courses. The results here are encouraging as they were quite free of all symptoms and needed drugs only when they had an upper respiratory infection or bronchitis. Even then the attacks were mild.

Conclusions

Desensitisation of patients against bacterial invasion, the body protein of bacteria, and their own body proteins is the treatment in cases of bronchial asthma. If the desensitisation procedures are all done against the specific allergens of individual patients the treatment will be complete and successful. If recurrent, desensitisation of the patient over a period of years must be aimed at owing to the variation of the environment to which the patient is exposed. This is more desirable than prescribing ever increasing dose of antispasmodics.

Acknowledgements

My sincere thanks are due to Dr. W. K. M. de Silva former Radiologist, General Hospital Jaffna, for valuable guidance and constantly urging me to prepare this paper. I acknowledge my great indebtedness to Dr. K.E. de S. Karunaratne and Dr. T. Parameswaran for having guided me in preparation if this paper. My sincere thanks are also due to my wife for having sat through with me to prepare this manuscript. All the statistics in this paper were compiled by my three assistants in the dispensary which I gratefully acknowledge. This paper would not have been possible but for their able assistance.

No. of course of injections	Age Group	Sex Males	Females	Treatment before course of injections	Treatment after the course of injections	Cases Not needing treatment
3	10 — 15 yrs.	2	1	Aminophylline 1 tab or 2 tabs t.d.s Mepyramine 50 mg. b. d. Mist Pot. Iodide	Nil	All three cases
3	20 — 60 yrs.	8	4	Aminophylline 3—6 tabs Prednisolone 1—6 tabs Adrenaline injections Aminophylline I. V. during attacks Mist Pot. Iodide	8 cases take aminophylline tablets 1 b.d., and or promethazine 25 mg. nocte.	7 cases needed no treatment except when having an upper respirattrac infection
2	20 — 50 yrs.	28	18	Aminophylline 2—6 tabs Prednisolone 1—6 tabs Adrenaline injcetions Aminophylline I. V. during attacks	31 cases maintained on aminophylline 1 tab. t. d. s, and chlorpheniramine 1 b. d., or promethazine 1 tab nocte.	15 cases either requirep no treatment, or did not wish to attend and hence were not seen

Table 2. Shows the results of the courses of injections on 61 patients who had auto-haemotherapy and the vaccine.

BEDSIDE ESTIMATION OF CHOLINE-ESTERASE IN ORGANO-PHOSPHORUS POISONING

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PATIENTS with organo-phosphorus poisoning are often admitted to the Medical wards of the General Hospital, Jaffna. These admissions are commonest during the early months of the year, when there is widespread spraying of crops with organophosphorus compounds such 'Folidol', and 5—10 admissions per day is the rule. In addition throughout the year there are cases admitted with a history of attempted suicide by drinking the pure substance.

The organo-phosphorus compounds act by inhibiting cholinesterase and the clinical features are due to the accumulation of excess acetyl choline. The treatment given is Pyridine-2-aldoxime, (P_2 AM) and atropine. The P_2 AM acts by reactivating the cholinesterase, and atropine acts at the post-ganglionic nerve parasympathetic endings. Both these patients, the folidol sprayers and the attempted suicides are usually clinically normal in a day or two and leave hospital.

However it is well known that even after clinical recovery a patient may have a markedly decreased serum cholinesterase and that this may take some weeks to return to normal. There is considerable individual variation in the time interval. It is important to estimate the cholinesterase levels of these patients before discharge, especially the sprayers who may return to spraying early with a very low cholinesterase level. This may be dangerous as a very slight exposure may be fatal. The ordinary laboratory methods of estimating the cholinesterase level are time-consuming and tedious and are a burden to an over-worked pathological laboratory. A simple bedside method would be very valuable and such a method was used in the three cases reported here.

The method (ACHOLEST) utilises a specially prepared test paper. The cholinesterase in the plasma hydrolyses the substrate in the paper liberating acetic acid, which changes the colour of the indicator in the paper from dark green to a yellow-green. The amount of cholinesterase activity is measured by the time taken for the colour to reach and match the colour of the control paper.

The test is done as follows: About 2ml of blood is withdrawn in to a sterile dry syringe and the serum separated off either by centrifugation or by natural coagulation in a dry test tube. There should be no haemolysis and the serum should be erythrocyte free and separated from the blood clot as soon as possible. The test should be carried out within 48 hours. The serum may be kept in a refrigerator upto 4 days and the test done after allowing it to attain room temperature.

Apply a drop of the serum to the centre of each of the two halves of a clean glass slide. The acholest strip is placed on one drop and the control strip on the other. The control strip turns greenish yellow, and the acholest strip turns dark green or light green. A cover slip or another glass slide is placed over the papers with gentle pres-

sure to ensure equal distribution of the fluids but seeing that the two fluids do not mix with each other. With time the acholest strip becomes lighter and attains the colour of the control and becomes yellow later. Acholest time is the time elapsing between the contact of the serum and the appear ance of the identical colour in both strips.

The relation of acholest time to cholinesterase activity is as follows :—

Acholest time	Serum Cholinesterase activity
5 mins.	Increased
6-18 mins.	Normal
20-30 mins.	Decreased
35-150 mins. & over	Strongly decreased

Case Report

Case 1. S. M. 23 year old male was admitted on 26-6-70 to General Hospital Jaffna, with a history of having drunk the contents of about 2 bottles of an insecticide 'Runbug' (containing 25% Malathion). He was conscious and complained of giddiness. The physical signs present were sweating, secretions in the throat, crepitations in the lung and half dilated pupils which became constricted within a few minutes. He was treated with P_2 AM 0.5 gm., Frusemide 20 mg. and atropine 12 mg. intravenously. He made a rapid recovery and on 29-6-70 he was discharged from hospital. At this time he was quite normal clinically, apart from a complaint of increased salivation. His pupils were slightly more dilated than normal. The serum cholinesterase activity as determined by the above method was found to be strongly decreased the Acholest time being 40 mins. The patient was re-examined on 9-7-70 and was found to be quite normal apart from some difficulty in reading small letters. The pupils were normal in size. The serum cholinesterase was repeated and found to be normal— Acholest time being 17 mins.

Case 2. V. M. female aged 44 years was admitted with a history of of having drunk 'Folidol' on 15-7-70. She was given 2 gm. P_2 AM 90 mg. atropine and 40 mg. of Frusemide by intravenous injection. Her serum cholinesterase activity by the Acholest method was done later, the serial estimations done gave the results shown in Table 1.

Date of collection	Time of colletion	Acholest time
15-7-70	7-00 p. m.	150 mins.
	9-00 p. m.	185 ,,
	11-00 p. m.	100 ,,
16-7-70	8-00 a. m.	120 ,,
	12-00 noon	100 ,,
	6-00 p. m.	85 ,,
17-7-70	9-45 a. m.	60 ,,
18-7-70	9-45 a. m.	50 ,,
19-7-70	10-00 a. m.	35 ,,
20-7-70	10-00 a. m.	25 ,,
22-7-70	10-00 a. m.	30 ,,
23-7-70	2-00 p. m.	15 ,,

Table 1. Cholinesterase activity in a patient recovering from organo-phosphorus poisoning.

Case 3. I. S. a 20 year old male was admitted on 21-7-70 with a history of having ingested 'Folidol'. A sample of blood taken before commencement of treatment showed normal cholinesterase a activity—Acholest time 10 mins.

Comments

This method was first described in 1959 by Sailler and Braunsteiner. In the past five years this method has been used very widely in several European countries and also in Senegal, Nigeria, Israel and El Salvador. In comparison to other methods, electrometric and spectrophotometric. The corelation both for normal and decreased cholinesterase activity is very good. The advantages of the method are the extreme simplicity and relative rapidity. The disadvantages are that the plasma has to be separated before the assay, and that it is necessary to wait for the colour to reach that of the control, instead of reading it at a fixed time. Personal factors such as colour vision defects are also involved.

For the rational management of patients admitted with organophosphorus poisoning, serial determinations of their cholinesterase activity is important. Case 1 described was not severely poisoned by clinical standards and he recovered quickly. Yet three days later when he was clinically quite normal his cholinesterase activity was strongly decreased. There is no doubt that many patients after organophesphorus will be having strongly decreased enzyme levels. Such persons should have their cholinesterase levels checked at regular intervals and be allowed to resume spraying Folidol only when their level has come back to normal. Further those spraying Folidol should take all precautions while spraying and in addition have their cholinesterase levels checked frequently. Regulations should be drawn up to enforce these safety measures. In the long run this would be a considerable saving in both time and money as a large amount of time is spent in treating patients with accidental Folidol poisoning in the medical wards.

In case 1 it took thirteen days for the patient to recover completely, whereas case 2 took nine days to regain normal enzyme activity. The sudden improvement in the cholinesterase activity that occurred in case 2 between 9-00 p.m., and 11-00 p.m., (Table 1) could be due to the intravenous injection of 1.0 gm. of P_2 AM given at 9-00 p. m.

Case 3 illustrates another use of the Acholest. In this patient the normal cholinesterase indicated that the patient had not ingested Folidol as alleged. Thus he was not given the large doses of atropine normally given thereby preventing the occurence of atropine poisoning in him. Further this eliminated the need for intensive care and thereby relieved the work load in the already overcrowded ward.

Summary

A simple bedside test of cholinesterase activity is described and three different cases are described to illustrated its different uses.

Acknowledgements

We thank the manufacturers of "Acholest" Osterreichische Stickstosswerke A.G., Llnd Austria for generous samples of Acholest papers given for these tests. (A pack of material for 30 tests costs approximately 2 $ U. S.)

SNAKE BITES IN KILINOCHCHI HOSPITAL 1969—1970

BY

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THE problems of management of the patient admitted with a history of snake bite to a small hospital are rather different from those encountered in a Provincial Hospital. This paper deals with these problems as seen in 34 patients who attended Kilinochchi Hospital from 1-1-69 to 30-6-70 with a history of snake bite. The records of 7 other patients who presented with a similar history during this period could not be traced.

There is a widespread belief, prevalent even now among the public, and some Medical Officers and Assistant Medical Practitioners, that Western Medicine has little to offer the patient who is bitten by a poisonous snake and that the treatment of choice is some form of Ayurvedic treatment. However, the fact that many seriously poisoned patients are helped by the treatment given in Government Hospitals is gradually being acknowledged. This is reflected to some extent in the number of admissions to Kilinochchi Hospital during the past 18 months. (Table. 1)

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1969	0	1	2	0	0	0	0	0	0	3	3	3
1970	5	12	3	0	1	1	—	—	—	—	—	—

Table 1. shows the number of cases admitted for snake bite to Kilinochchi Hospital.

Some tentative conclusions can be drawn from these figures. Perhaps snake bites are relatively uncommon in the dry months, i.e. April to August, and commoner during wet season. There is an increase in the admissions in the first few months in 1970. This may be because the first few months of 1970 have seen very frequent showers. Another possibility is that in 1969 a number of patients with signs of systemic poisoning were treated successfully in Kilinochchi Hospital, so that there may have been a greater tendency to come to Kilinochchi Hospital in 1970.

A consideration of the time of the bite also reveals some interesting facts.

Time of Bite	No. of Cases 1969	1970
6 a. m. — 6 p. m.	9	18
6 p. m. — 6 a. m.	2	1
Not known	1	3

The majority of snake bites that came to hospital occurred during the day. This may be due to fact that most of these patients were farmers who worked in their

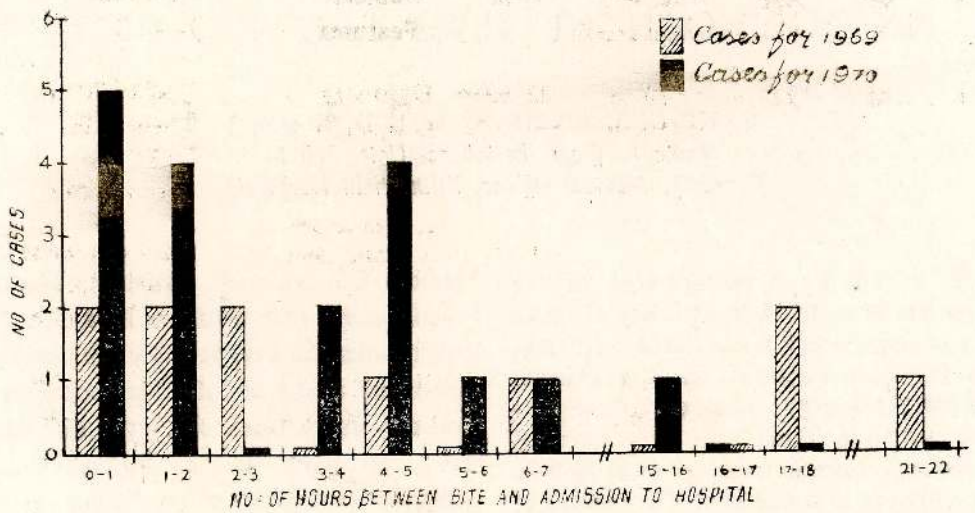

FIG. 1 Shows the time elapsed between time of bite and the time of admission.

fields during the day. This is rather different from the findings of Visuvaratnam et al. where the majority of bites occurred at night.

Patients also seem to be coming in earlier to hospital than before. Fig. 1 gives the approximate delay in hours between the bite and seeking treatment in hospital.

Of the 12 patients seen in 1969, 4 had definite clinical evidence of systemic poisoning. The clinical details of these patients are as follows.

BHT	Sex	Age	Date Admitted / Discharged	Delay	Clinical Features	Treatment
1530	M	35	19-3-69 / 24-3-69	7 hours	Bite mark Reaction CT over 65 mins. Diplopia Oliguria Red urine	Penicillin ATS Hy 100 mg. ASV 20 ml.
1563	M	38	21-3-69 / 24-3-69	2 hours	Bite Mark CT 25 min. (9-50 p.m.) CT 10 min. (4-00 am) Giddiness Drowsiness	Hy 100 mg. ASV 10 ml. 10 p.m. ASV 10 ml. 2 am. ATS Penicillin

BHT	Sex	Age	Date Admitted / Discharged	Delay	Clinical Features	Treatment
1536	M	22	17-10-69 / 18-10-69	22 hours	Dyspnoea Dysphagia Ptosis Haematuria Lungs creps Allergic rash	ASV 20 ml. Penicillin ATS Hy 100 mg. Antihistamine Adrenaline Prednisolone
7177	M	25	4-12-69 / 14-12-69	3 hours	Bite mark Swelling L leg Ptosis CT 6 mins. Red urine (7/12) Reaction to ASV	ASV 10 ml. ASV 10 ml. Penicillin ATS Hy 100 mg. ASV 10 ml. Antihistamine Prednisolone

C. T. Clotting Time

Penicillin—1,000,000 IM bd
ASV —Antisnake Venom
ATS —Antitenanus Serum
Hy —Hydrocortisone 100 mg IV

Of the other 8 patients, 6 had evidence of snake bite. There was a local reaction round a bite mark, but no definite signs of systemic poisoning. The other 2 patients had no signs at all. All these patients were treated alike, with antivenom 10 ml; Hydrocortisone 100 mg. IV; penicillin 1,000,000 units IM b.d; ATS and antihistamines. It is not really possible to evaluate the treatment in this group. They may have recovered in any case if left to themselves.

22 patients were admitted to Kilinochchi Hospital during the period 1-1-70 to 30-6-70 with a history of snake bite. However no antivenom was available in 1970. 13 of these 22 patients were transferred to Jaffna Hospital as these patients showed signs suggestive of systemic poisoning and it was considered safer to transfer them to Jaffna. Of the remainder, 4 were removed home by the relatives as the condition was bad. The balance 5 patients were observed and treated at Kilinochchi Hospital. They showed local oedema, but no signs of systemic poisoning. They were treated with penicillin and antihistamines and were discharged home in a few days. It is likely that these patients too would have recovered by themselves.

Comments

One of the problems of management of snake bites is that the snake is hardly ever seen and definitely identified. Only once was the snake captured and brought for identification. Very often the history is not at all clear whether it was a snake, an

insect, or something else that bit the patient. This problem is all the more pressing now that more patients are coming to the Governmant Hospitals early, before systemic signs have appeared. In all these cases careful examination and observation are required to determine a line of treatment.

A recent review has recomended that any bite which is followed by swelling of the region be treated with antivenom. This may not always be necessary. Some of our patients in 1970 showed local swelling only, and no evidence of systemic poisoning. They were treated with antibiotics and antihistamines only and recovered satisfactorily.

The dose of antivenom recommended in recent papers is of the order of 100 ml IV to be repeated if necessary. In 1969 4 cases were treated in Kilinochchi Hospital with antivenom 20 ml—30 ml (total dose). These patients showed evidence of systemic poisoning. They recovered and were fit for discharge in a few days This does not necessarily mean that small doses will always be adequate. It has been reported that 80—85% of those bitten by venomous snakes have recovered without any antivenom. Much depends on how much venom has been injected into the body at the time of the bite, and this is governed by many factors.

It is not possible to predict with certainty the future behaviour of patients bitten by snakes. Perhaps knowing that antivenom is no longer available at Kilinochchi Hospital they will once more go to the local snake bite specialist, till the next quota of antivenom arrives. In any case it is well worthwhile for Medical Officers manning the smaller hospitals to lay by a good stock of antivenom especially during the rainy months On the other hand if stocks are low, it may be reasonable to try out the effect of a small dose first and see the response. This of course is not wise if the patient's condition is serious—in such a case full doses should be given. If the patient's condition does not show a marked improvement, the patient should be transferred immediately to an institution where ample antivenom is available. If possible this should be ascertained before transfer.

Finally, it seems hardly economical for the Department of Health Services to transfer a patient from one hospital to another for the sake of antivenom. This should be readily available in all hospitals in areas where snake bites are common, and if stocks run low they should be immediately replenished.

Acknowledgements

I wish to thank Dr. T. Shanmuganathan former D. M. O. Kilinochchi and Dr. T. Gnanasuntheram for allowing access to the case records of these patients and Dr. K. E. de S. Karunaratne for the help and guidance in preparing this paper.

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SNAKE BITE POISONING

EXPERIENCES IN GENERAL HOSPITAL JAFFNA.

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Introduction

Poisonous snakes fall into two large groups — the cobras including the kraits; and the vipers. With cobra bites the classical effects are neurological, while with viper bites haemorrhagic manifestations predominate. However as seen in Ceylon the haemorrhagic and neurological effects are both present together, and the snake concerned is hardly ever definitely identified. The literature has been reviewed by Visuvaratnam [1] who described 15 cases of snake bite poisoning in Jaffna, in 12 of whom there were neurological, haemorrhagic and haemolytic features.

Material

This paper sets out experiences with 14 patients with evidence of systemic poisoning following snake bite, admitted to one Medical Unit during the period November 1969 to June 1970. During this period 6 other patients were admitted with a history of snake bite, but did not show any evidence of systemic poisoning. They are not included in this study.

Results

Clinically, these patients could be separated into 3 main groups.

GROUP—A. There were 9 patients in this group. They all had signs of a neurological lesion, as well as a prolonged clotting time. The commonest neurological sign observed was ptosis, which was present in 7 of these patients. Other clinical features were dysphagia, dysarthria, dyspnoea, drowsiness and giddiness. The clotting time was grossly prolonged, sometimes the blood did not clot for several hours or even days. These patients are summarised in Table 1.

GROUP—B. There were 3 patients in this group. These patients also had non-clotting blood, but there were no symptoms and signs of involvement of nervous system. This is the clinical picture classically with associated with viper bites.

These patients are summarised in Table 2.

GROUP—C. One patient in this group showed the features of cobra bites in that there were neurological signs, but no prolongation of clotting time.

Firally there was one patient who was brought to hospital with a history of snake bite 5 days previously, and anuria of 4 days. He was said to have had ptosis earlier, but there were no neurological signs on admission. The clotting time was normal. The blood urea was 282 mg/100 ml. He was advised transfer to Colombo for peritoneal dialysis as facilities for this were not satisfactory in this hospital at that time. He was removed by his relatives.

Renal Failure

This occurred in 3 patients. They were all treated conservatively with a modified 'Bull Regime'. The water loss via the skin and lungs was estimated as being about 1000 ml/24 hours in Jaffna.

Table 4 summarises the progress of these three patients.

BHT	Sex	Age	Time of bite	Delay in reaching hospital	Clinical Features	Maximum Blood urea	Days in hospital
1956	M	55	5-30 p.m.	5 hrs.	Dyspnoea Dysarthria Abdominal pain Giddiness	51	3
3213	M	16	3-00 p.m.	7 hrs.	Ptosis Dysphagia	51	3
6163	M	19	8-00 a.m.	10 hrs.	Ptosis Dysphagia Red urine	42	12
6176	F	29	3-00 p.m.	7½ hrs.	Ptosis Dysarthria Red urine 3/12 Amenorrhoea and bleeding per vaginam	430	12 Died
6181	M	12	3-00 p.m.	10 hrs.	Ptosis Drowsiness	280	16
9011	F	16	4-00 a.m.	½ hr.	Ptosis	107	13
13995	M	20	8-00 p.m.	10 hrs.	Ptosis Red urine	50	Removed by relatives
20366	F	20	11-00 a.m.	6 hrs.	Ptosis	33	7
16913	M	18	9-00 a.m.	28 hrs.	Ptosis Dysphagia	500	30

TABLE I. Details of the 9 patients in Group A.

BHT	Sex	Age	Time of bite	Delay in reaching hospital	Clinical Features	Maximum Blood urea	Days in hospital
5246	M	50	11-00 a.m.	9 hrs.	Abdominal pain	57	4
11285	F	21	6-00 p.m.	5½ hrs.	Drowsiness Giddiness	28	8
6174	M	16	7-00 p.m.	3 hrs.	Chest pain	44	3

TABLE 2. Details of the 3 patients in Group B.

BHT	Sex	Age	Time of bite	Delay in reaching hospital	Clinical Features	Blood urea maximum	Days in hospital
8013	M	33	11-00 a.m.	7 hrs.	Ptosis	68	7

TABLE 3. Details of the 1 patient in Group C.

The plasma fibrinogen was estimated in two patients. The fibrinogen content and the dose of antivenom given is as follows:—

BHT No. 16913

Date	Antivenom	Plasma Fibrinogen mg %
31-5-70	150 ml	—
1-6-70	50 ml	—
2-6-70	—	< 100 mg
3-6-70	70 ml	—
6-6-70	—	> 500 mg
7-6-70	—	> 700 mg
8-6-70	—	800 mg
10-6-70		500 mg

Thus even after 200 ml of antivenom the plasma fibrinogen was less than 100 mg% (Normal 150—450 mg / 100 ml). After further antivenom there was a hyperfibrinogenaemia. Rebound hyperfibrinogenaemia after hypofibrinogenaemia is well known However this does appear to have been commented on in other series of snake bite.

BHT No. 20366

Date	Antivenom	Plasma Fibrinogen mg %
28-6-70	50 ml	—
29-6-70	50 ml	—
30-6-70	—	550
1-7-70	50 ml	600
2-7-70	—	700
5-7-70	—	500

Here again hyperfibrinogenaemia is seen, perhaps a rebound phenomenon after hypofibrinogenaemia.

Discussion

The number of admissions of serious snake bite poisoning to this hospital seem to be increasing. Visuvaratnam [1] reported 15 cases of venomous snake bites admitted

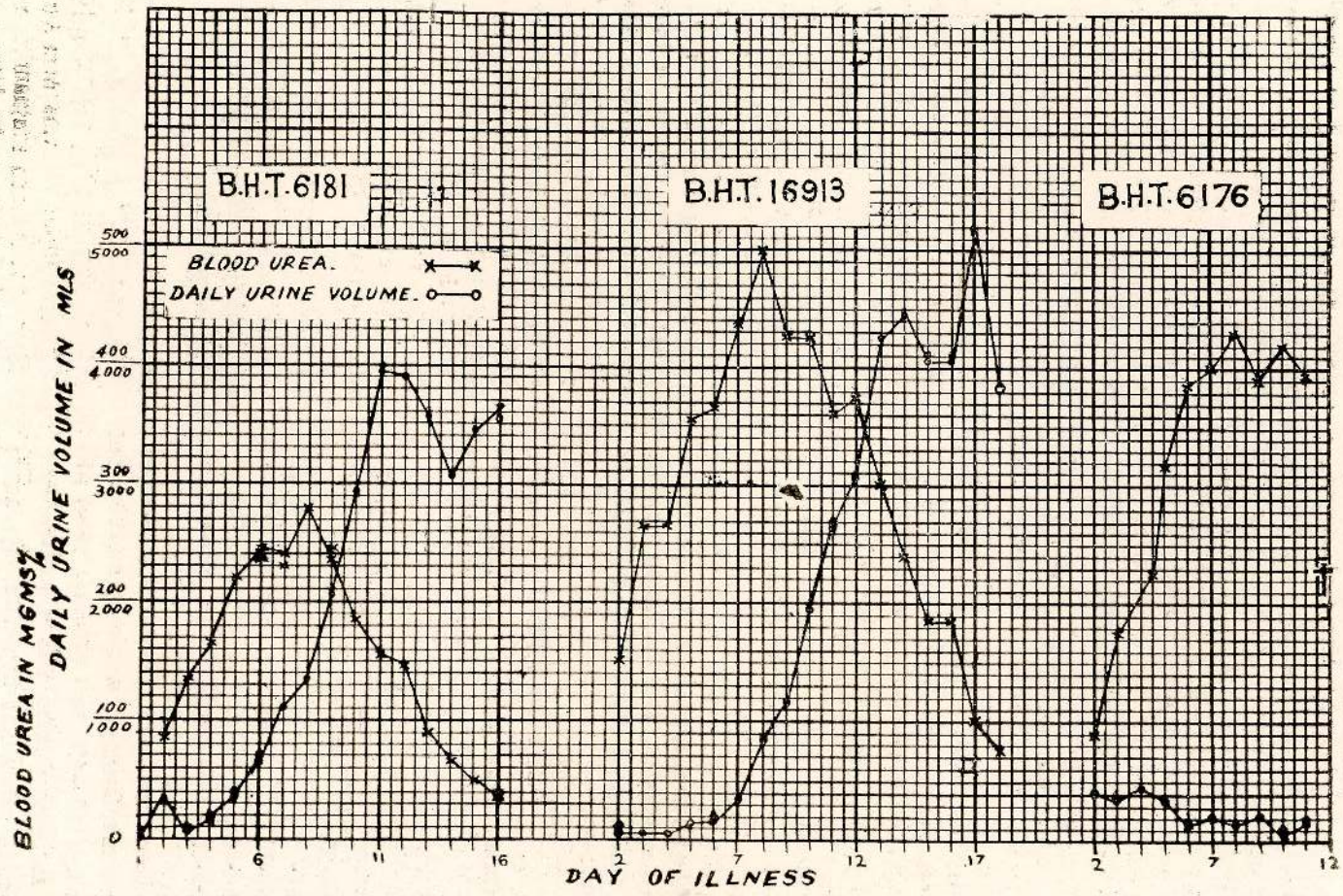

TABLE 4. Summary of the blood urea level and total daily urine output in the three patients who had renal failure.

to this hospital during the period 1-12-66 to 30-11-67. In the present series 14 cases were seen in one Medical Unit during a period of 7 months. There may be several reasons for this increase. 8 of these patients were transfered from Kilinochchi hospital, 40 miles away, as there was a shortage of a antivenom in that institution. With increasing colonisation and clearing up of the jungles, there may be even more cases of poisonous snake bites in the future. Also it is very likely that the general public is becoming aware that the Government Hospitals have something effective to offer these cases. Indeed in recent years it has been noticed that many patients are being advised admission to Government Hospitals by the Ayurvedic Snake Bite Specialists themselves. This generally occurs when ptosis, drowsiness, the passage of red urine and anuria develop.

The incidence of systemic poisoning is very high in this series— 70% (i e. 14 out of 20). This probably means that the majority of cases of snake bite with mild, minimal, or no poisoning are being treated by the snake bite specialist. In Reid's series[2] of 47 cases of cobra bites seen in Malaya between 1958—1963, only 6 had neurotoxic effects (13%). Similarly in another series[3] of 250 cases of bites of the Malayan Pit Viper seen between April 1960—April 61, moderate systemic poisoning (non-clotting of blood) was seen in 32 i.e. 13%; and a haemorrhagic syndrome in 37 patients i e. 15%.

Unfortunately in the present series none of the snakes were captured and definitely identified. It is likely that many of these bites were due to the Russell's viper. Viper venom has an action on the blood clotting mechanism. In a study of he coagulant properties of the Malayan Pit viper venom (Ancistrodon Rhodostoma) it was found that this venom could convert fibrinogen to fibrin in the absence of other clotting factors [4]. The venom of the Saw-scaled viper (Echus Carinatax is also coagulant, but this effect is due to the activation of prothrombin to thrombin and not due to any action on fibrinogen [5]. The hypofibrinogenmia and the possible rebound hyperfibrinogenemia noted in the two patients mentioned earlier, seem to point to viper venom.

Renal failure sometimes occurs after snake bite in Ceylon. It is not clear how common it is in other parts of the world, and it is not referred to in a recent review of the subject of snake bites in the tropics. It can occur in the absence of blood loss and oligaemic shock. Tubular necrosis due to haemolysis and haemoglobinuria, intravascular fibrinogen deposition, or a nephrotoxin, may be responsible. There is no convincing evidence regarding this. In the present series 3 patients developed renal failure; they were all treated conservatively and two recovered, one died. Peritoneal dialysis, diuresis with mannitol, and exchange transfusions were not done. The blood urea may remain elevated for long periods, but as long as the patient is passing reasonable amounts of urine, there is no cause for alarm, On the other hand, if the urine volume remains low after 8 or 9 days, dialysis may be considered.

There is no doubt about the efficacy of antivenom in the treatment of snake bite poisoning. The recommended dose by authorities on the subject [6] is 100 ml IV, to be repeated as required The neurological features are rapidly reversed by antivenom, often in a matter of hours. Sometimes there may be residual ptosis, which clears up by itself in about 48—72 hours. In the present series antivenom was given till the clotting time was within 10 minutes, irrespective of

the clinical state of the patient. These patients therefore received quite large doses of antivenom. It is difficult to say whether such large doses are useful, as there are so many variables involved. Most of the patients in this series who did not have renal failure were able to leave the hospital in a few days—average 6 days—even though some of these patients were admitted acutely ill. In Visuvaratnam's series [1] the highest dose of antivenom used was 110 ml. and the patients left hospital after 14 days on an average. No firm conclusions can be drawn from these data as there are so many variables — how much venom was injected, how soon the patients arrived in hospital, the presence of other complications which made it necessary for the patients to remain in hospital.

Antivenom should be given only if there is evidence of systemic poisoning, and not if there is local reaction only [7].

There were no serious reactions to antivenom. The occasional reactions that occurred were easily controlled by steroids.

Steroids were not used as a primary therapeutic measure, though they have been used as such by other workers. Benyattu et al[8] describe 60 cases of viper bite in Thailand where they used cortisone 300 mgm/day, or prednisolone orally or IM.

There are different snakes in different parts of the world, and it may even be that the venom of the same species is different in different countries. Therefore it may not be helpful to adopt completely the lines of treatment advised by workers in Malaya or Thailand. It is most important to study the snakes and their venoms in this part of the world, and also the clinical effects of snake bite poisoning, so that reasonable measures may be evolved to prevent and treat snake bite poisoning.

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TUBERCULOSIS OF THE CERVIX UTERII — CASE REPORT

BY

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Mrs. P. M. admitted on 10-4-70.

Age–35 – married 14 years–4 living chidren' Last child 10 months old.

L. M. P. – 1 week agc–Periods regular, not heavy

Complaint: White discharge per vaginum on and off for several years, but has become worse during the last few months. No pruritus vulvae.

On Examination: A brownish white discharge was noted.

Speculum examination revealed a cervical erosion readily bleeding to touch with the speculum.

The uterus was found to be normal in size, anteverted and the fornices showed no evidence of any masses or tenderness.

Blood Hb % = 50%

Urine — alb — nil.
sugar — nil.
deposits — nil.

An early carcinoma of the cervix was suspected and the patient was submitted to biopsy of the cervix.

The patient developed a temperature the following day (101 'F) and inspite of treatment with tetracycline for 4 days and Chloramphenicol for a further 5 days, the temperature did not settle.

At this stage the biopsy report was received.

Biopsy — 15-4-70

A small piece of tissue was received. On histological examination it was found to be a portion of the cervix uterii lined in part by stratified squamcus epithelium extending into an area lined by a simple layer of columnar cells. In the sub-epithelial tissue were found several tubercles composed of epithelioid cells and giant cells surrounded by lymphocytes.

The appearances were those of Tuberculosis of the Cervix Uterii.

On receving this report the patient was sent to the Pannai Chest Clinic for examination to exclude Pulmonary Tuberculosis.

The M. O. Chest clinic sent the following report.

X'Ray, Lungs clear.

Sputum — T. B. Nil.

The patient was started on routine antituberculosis treatment and the temperature settled in a few days time. The patient is still continuing her treatment as an outdoor patient.

On closer questioning of her husband it was found that he had had treatment for T. B. epididymo-orchitis in 1958.

On physical examination of husband it was found that his left testis had been removed, but his right testis appeared to be quite normal and free of disease.

A rectal examination revealed no abnormalities of the seminal vesicles. A prostatic massage was performed and the prostatic secretions examined microscopically. No evidence of disease was found in the prostatic fluid.

His E. S. R. was

1st hour — 10 min.

2nd hour — 20 min.

Urine for Full Report

alb. — nil.

sugar — nil.

deposits — pus cells — nil.

Comment

Tuberculous cervicitis is a rare condition, but may be seen at times as late secondary manifestation of genital tuberculosis of primary tubal type. In rarer cases it appears to be primary and introduced by a male partner with genito urinary disease. It produces in the cervix an ulcerative and at times a hypertrophic lesion which may simulate carcinoma quite perfectly. The distinction between the two is made readily enough by biopsy and microscopic examination, but before the days of routine biopsy confirmation, the mistake was more than once made of subjecting these patients to radical cancer operation or radiotherapy.[1]

The case under discussion is rare enough as it is, but the question arises as to whether the cervix was involved secondarily to tubal involvement or primarily due to sexual contact.

In this patient though there is no direct evidence that tuberculous disease is absent in the tubes and endometrium (the endometrial curettings were not submitted for histology or guinea pig innoculation. (At the time of the biopsy and curettage. tuberculosis was not suspected and as additional investigations would have cost the patient extra money these were not done at that time.) Yet circumstantial evidence suggests that the lesion here is a primary tuberculous lesion of the cervix.

This patient has been very fertile the last child being only 10 months old, which makes it unlikely that the tubes are involved in which case fertility would have been affected and also the fact that the husband had suffered from tuberculous epididymitis suggest the likelihood of direct infection at sexual intercourse.

Duration of the Disease:

If we accept that the lesion is from direct contact from the husband, then the disease must have contacted several years ago, as he had treatment 12 years ago and he is now found to be entirely free of the disease. Genital tuberculosis active but silent for several years is not unknown and cases have been followed for 10 yrs. or more at the Oxford Gynaecologic Department before the days when chemotherapy was available.

Fertility

It is well known that tuberculosis of the tubes and endometrium contributes to sterility in the female. However in primary tuberculosis of the cervix fertilisation and conception may not be affected at all.

Treatment

After excluding tuberculous lesions at other sites, e. g. : lung, kidney, etc. antituberculosis drug therapy should be commenced even if the lesion appears to be

silent and not producing constitutional symptoms as the lesion may extend locally or generally at any time, often for no apparent reason. A possibility of reinfection of the husband's remaining testis has also to be kept in mind and avoidance of intercourse till the lesion is healed should be advised. In the alternative the use of a condom may be advocated.

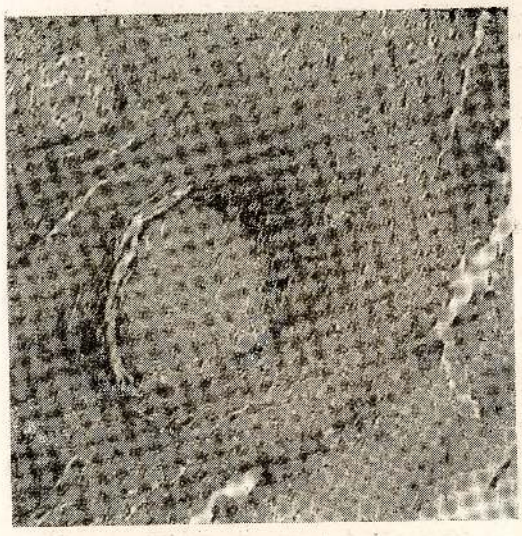

FIG. 1 Histological appearances of the cervix showing tubercles.

Acknowledgement:

My sincere thanks are due to Dr. W. D. Ratnavale M. D,, M. R. C. P., M. C. P., D. P. H., for the report on the histology of the specimen and the photomicrograph.

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PULMONARY TUBERCULOSIS

PROCEEDINGS OF A SYMPOSIUM HELD BY THE JAFFNA MEDICAL ASSOCIATION

A Symposium on Pulmonary Tuberculosis was held on 7-8-70 in the N. T. S. Hall. The panel consisted of

DR. T. VAMADEVA, M. B. B. S. (CEY.) M. R. C. P., (EDIN.), D. C. T. D. (WALES)
Physician, Chest Clinic, Jaffna.

DR. (MRS.) B. S. WILSON, M. B. B. S. (MADRAS), D. Obst. R. C. O. G. (LOND.), D. C. H. (ENG.), M. R. C. P. (LOND.)
Physician, Green Memorial Hospital, Manipay.

DR. C. INDRARAJA, M. B. B. S. (CEY.), D. C. T. D. (WALES)
Physician, Chest Hospital, Kankesanturai.

DR. N. GANESHANANTHAN, M. B. B. S. (CEY.), F. R. C. S. (ENG.)
Thoracic Surgeon, General Hospital, Jaffna.

DR. T. VAMADEVA, opened the discussion dealing with CASE FINDING PROCEDURES

From the general practitioner's point of view involving a doctor-patient relationship, a case of tuberculosis would be when that patient needs anti-tuberculous treatment. The decision is made after a total clinical examination with other diagnostic aids such as Mantoux, X-rays, sputum examinations etc. This would be dealt with adequately by the next speaker, and varies according to the different views of each individual doctor.

From the point of view of those involved with the control of tuberculosis in a community, the definition would also vary with the facilities available on a community wide basis in each particular country, and also the prevalence of the disease in each country.

The object of case-finding in a control program is to find out those who are transmitting the disease to the non-infected population in the early stages of the control program and only when this is done, to seek out those who in future may be an infective source. The degree of infectivity of a patient would be in the following order:

(1) These who are sputum positive on direct smear on the first examination, i.e., disseminating bacilli in large quantities almost all the time. These form the most important group.

(2) Those positive on direct smear after repeated examinations.

(3) Those positive on culture only.

(4) Those who are suspect. There is X-ray evidence of active disease but not bacteriologically confirmed.

(5) Those who are inactive on X-ray.

Groups 4 and 5 have about the same degree of infectivity. The variation in the infectivity has been confirmed by the studies on the contacts of the different groups. (Tables 1, 2 & 3.)

When planning out a control program priorities must be established and standardised procedures laid down so as to detect the largest number of patients at a reasonable cost. The part played by variations in the manifestation of the disease in out of the ordinary groups of individuals are over-looked. Only a small lattitude is allowed for the individual doctor in diagnosis, allowing for problems of social and humanitarian points of view.

In this country the priority has been set at discovering the first three groups i. e., those who are bacteriologically confirmed, especially by direct smear.

The procedure used as a screening tool i.e. as the first examination to which a group of people coming for examination are subjected to, had been the X-ray of the chest by miniature radiography. There is no clinical examination of the patient, and all those found to have a suspicious shadow are further examined with a large film and sputum examinations.

X-ray is a very sensitive tool but its specificity is low. It is very rare to miss a patient with significant tuberculosis. But over-diagnosis is a constant danger even in the hands of experienced clinicians. There is always a temptation to label as tuberculosis those patients for whom no other label could be found. About 15 years ago it was found that a considerable number of cases in the chest hospitals had non-tuberculous diseases and had been subjected to prolonged treatment and inconvenience. Yet the X-ray is a useful tool in case-finding, provided every effort is made to isolate the bacillus before treatment is begun. It has been shown that a delay of 6 weeks to 2 months (time taken for culture) does not materially alter the ultimate progress. It is a very convenient tool from the point of the doctor but not necessarily so for the patient who may have to travel long distances to the X-ray set up.

The other tool for screening patients now being introduced in some parts of the island is the examination of the sputum by direct microscopy. All presenting themselves for examination are requested to give a specimen of sputum. No X-ray need be taken. It is repeated if there is clinical evidence. The aim is to detect all cases that are of high epidemiological significance. The specificity of this method is very high. It is only in very rare circumstances that one finds a false positive.

How efficient or sensitive is this method, which is usually considered low? From April this year all patients who came for diagnostic reasons i.e., excluding those who came for mandatory X-rays for medical examination and routine X-rays for teachers etc., were asked to give a specimen of sputum before they were X-rayed. The sputum was examined by direct smear and culture. The average daily attendance was 25-35.

	April — July entire period of study		June — July (2nd half of period of study)	
Notified cases of adult Pulm. Tub	87		37	
No. direct smear +ve on 1st visit	49	(56%)	26	(69%)
No. „ „ +ve after repeated examinations	21	(24%)	7	(18%)
No. —ve on culture only				
X—ray suspect not confirmed	17	(20%)	5	(13%)

Table 4. Results of sputum examinations on the notified cases of Pulmonary Tuberculosis at Chest Clinic Jaffna for the period April—July 1970.

Age Group	Household with Bacillary case Children infected		Household with X-ray case Children infected		Household without case Children infected		Total study Population infected
	No.	%	No.	%	No.	%	%
0—14	189	41	604	19	9186	12	13

Table 1 Incidence of tuberculous infection in children (0—14 years) in different households. (Raj Narain et al. Bull. Hlth Org. (1966) **35**, 639–654.)

Contact Group	Total tested age group 10—4	Reactors	
		No.	%
Direct smear +ve	375	244	65.2
Culture +ve	288	61	26.6
Culture—ve diagnosed on X-ray	221	39	17.6
Non-contact group	709	157	22.1

Table 2 Incidence of Mantoux reactive children (0—14 yrs.) in the different contact groups. (Shaw, J. Brian & Williams, Whyn, Am. Rev. of Tub (1954) **69**, 724—732)

	Index Cases with		
	Direct Smear +ve	Culture +ve	Culture —ve
No. of contacts examined	539	396	181
No. with active tuberculosis	35	5	2
% with active tuberculosis	6.5	1.3	1.1

Table 3 Incidence of active tuberculosis in the different contact groups. (Graybowsky, S., et al. Am. Rev. Resp. Dis. (1964) **90**, 707—720)

From the above it would appear that the part played by highly skilled and expensive officers and costly sophisticated equipment in community wide programmes has been over emphasised. It leads to the sobering thought that of all the notified cases of adult pulmonary tuberculosis, 56% could be diagnosed on the first visit and 80% if all suspects were subjected to 3 examinations, without the two medical officers, the X ray plant and the necessary personnel to man it. The main advantage of this method is that the patient need not travel long distances to go to the institution where the X-ray facilities are available. But can get this done close to his home.

The standardised procedure is for the patient to go to the nearest peripheral institution where, if he has one of the following symptoms, sputum is collected for examination.

(a) Cough of over a month (2 weeks if the patient is over 40 years.)

(b) Cough with fever of shorter duration

(c) Haemoptysis

(d) Fever of over a month's duration.

A correct specimen of sputum is collected from the patient, a smear is made, and the slide posted to the central chest clinic where it is stained and examined. In some countries the entire specimen is posted to the centre where a culture could also be made. But inspite of the good results seen here and abroad this has not been proved to be a success in actual practice. In the trials conducted in the North Western Province in Ceylon the results had been poor. Of the cases notified as bacteriologically positive on direct smear in 1970, only 54 were diagnosed by this method as compared to 155 by the conventional method of X-ray followed by sputum examination of those with relevant shadows. Why this is so is still being studied.

At the Chest Clinic, Jaffna there is an M. L. T., a subassistant, and a laboratory orderly doing about 30-35 direct smears and cultures a day. A lot of care is taken to see that a proper specimen is taken from the patient and a smear made from the correct portions. The fault may be in this aspect of the work, when the smears are done in the periphery. Or it may be that at the clinic there is a higher degree of selection of patients, those likely to have pulmonary tuberculosis by-passing the peripheral units and prefering to go to the prestigeous chest clinics.

Until this problem is solved one has to continue with conventional methods. But it is useful to know the efficiency of sputum examinations and its value in places far removed from the centre. Yet this is possible only if those involved believe in its efficacy.

DR. (MRS.) WILSON followed next talking on

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS

It is my priveledge today to continue this Seminar on the Diagnosis and Differential Diagnosis of Tuberculosis. Unfortunately tuberculosis still remains a problem in the developing countries. Sir William Osler one morning met Sir Robert Phillip and said 'If you know all about typhoid fever you know all about Medicine.' But Sir Robert interrupted and said 'If you had said the same about tuberculosis I would have agreed with you.'

When tuberculosis presents itself with the typical symptoms of cough, haemoptysis, evening pyrexia and loss of weight accompained by radiological shadows and a positive sputum then the diagnosis of tuberculosis is simple.

But unfortunately, it must be remembered that acute and progressive pulmonary tuberculosis may fail to produce symptoms and signs. Occasionally it may produce symptoms not related to the chest. e.g. A patient presented with generalised aches and pains and the chest X-Ray, revealed active pulmonary tuberculosis. In another case, a patient presented with abdominal discomfort and the chest X-Ray revealed miliary tuberculosis.

Nevertheless one must not forget the common symptoms of pulmonary tuberculosis.

1. Cough with or without purulant sputum or Haemoptysis.
2. Pain in the chest.
3. Loss of weight and appetite.
4. Unexplained fever.
5. Shortness of breath.

Signs of tuberculosis may be very misleading at times.

There may be no physical signs, a few physical signs or a combination of many physical signs.

A few physical signs that are of importance are:—

1. Post-tussive crepitations in the upper zone.
2. Signs of cavitation.
3. Or it may present with signs of consolidation, effusion, collapse, bronchiectasis or rarely even a pneumothorax.

DIAGNOSIS:

The diagnostic tools we have in tuberculosis are: —

1. Mantoux Test: This is read in 72 hrs. and induration of 6 m. m. or more is taken as positive.

A negative test is useful in excluding tuberculosis, except in certain situations.

a. Improper technique or use of old vaccine.
b. In overwhelming disease — miliary tuberculosis, meningeal tuberculosis.
c. It may be negative in the first few weeks after infection.
d. State of anergy may develop in sarcoidosis.
e. Certain exanthemantions states. e. g. measles.
f. Certain people fail to react positively even with active tuberculous infection.

A positive test is useful is a child under the age of 2 years or a recent tuberculin converter.

2. Bacteriology:

Examination of sputum, gastric lavage or in certain cases bronchial secretion. This is one of the most important tools. Proper collection of samples is easential. Sputum and not saliva is required. In the case of gastric lavage—use sterile water and not tap water, as the saprophytic bacteria in the tap water may yield false positive results. Occasionally when the diagnosis of tuberculosis is considered and the patient is unable to expectorate, bronchscopy and bronchial aspiration of secretion is done.

The success of sputum examination depends on a good laboratory.

A positive smear must always be supported by a positive culture. Unfortunately, cultures take 6 weeks unless one has the facilities of using special media which speed up the growth of the tubercle bacilli.

At this stage I would like to mention the group of anonymous or opportunist Mycobacteria which closely resemble the Mycobacteria tuberculosis. They produce disease which is very similar except for a few radiological differences, i. e. disease with more cavitation and less fibrosis.

They however differ in their bacteriological characters. They grow more rapidly and are resistant to the first line drugs.

3. X-ray:

Another diagnostic tool that we relay on in chest disease is radiology, but it does not indicate with reliability the nature of the disease.

(At this stage several X-rays were shown to demonstrate the following:—

1. Upper lobe consolidation.
2. Lung abscess.
3. Pleural effusion.
4. Solitary round shadow.
5. Miliary mottling.
6. Primary complex.

She explained that most of them could have been non-tuberculous in aetiology.)

Finally I would like to stress that tuberculosis can present itself at any age. It can occur in the infant, child, adult and even the elderly. In fact the grandfather or grandmother who is coughing and spluttering at home is often forgotten, and may well be the source of infection.

Tuberculosis is a treacherous disease, as it fails to produce symptoms. It still continues to claim its victims in civilised health conscious communities.

DR. C. INDRARAJAH than dealt with DRUG THERAPY IN TUBERCULOSIS

There were no anti-tuberculosis drugs prior to 1948. In Ceylon anti-tuberculosis drugs were introduced in 1951. The first-line drugs namely Streptomycin, Para-Amino Salicyclic Acid (PAS) and Isoniazid (INAH) were given as Triple Regimen for the first three months and later the patients were placed on PAS & INAH. The Triple Regimen (presently called the intensive treatment) was given in hospitals. I will now mention, chiefly, the type of treatment given at the Chest Hospital, Kankesanturai. All patients new or old when hospitalizid are placed on Triple Regimen for three months. The main assessment of treatment done is sputum examination—Direct Smear test monthly and culture for T. B bacilli initially and at the end of three months. The E. S. R. and monthly X-ray of chest are of no value.

FIRST LINE DRUGS

Streptomycin Sulphate is given intramuscularly daily (inclusive of Poya Day or Sunday) 1 Gm. if under 40 yrs of age and ¾ Gm. for those over. Streptomycin is bacteriostatic and bactericidal, less powerful than INAH, diffuses into the body tissues and into the C. S. F. when the meninges are inflamed.

Toxic Effects are chiefly, effects on the eighth nerve causing giddiness. Yet patients adopt successfully and with time the giddiness disappears. In the elderly it is more difficult. However if the serum level is maintained below 2 microgramme / ml no complications arise.

One other important feature is that streptomycin is almost entirely excreted in the kidneys, therefore the blood urea level should be determined when necessary and the dose of streptomycin scaled down. The excreted streptomycin reduces Benedict's solution to some extent and thus mimics glycosuria.

Tingling sensation round the mouth, occurs in a few cases during the first few weeks of treatment.

In pregnant mothers it is wise to avoid streptomycin, since the drug crosses the placental barrier and deafness in the infant may result.

Dihydrostreptomycin causes increased incidence of permanent deafness and therefore is not used.

Isoniazid (INAH) is the most potent drug available. It is cheap, easy to swallow, has little toxicity and can be taken as a single dose. It is bactericidal and diffuses readily throughout the body tissues and enters the C. S. F. in therapeutic concentrations. It also enters the macrophage cells and kills the bacilli within these cells.

The daily dose is 300 mg. or 1.5 mg. / kg. body weight.

Toxic Effects are uncommon. The common one experienced is peripheral neuropathy manifested usually by a burning sensation in the limbs. To overcome this pyridoxine (vitamin B 6) not exceeding 20 mg. a day can be given. An amount higher than 20 mg. a day may affect the therapeutic effectiveness of isonizid.

Rare side effects are insomnia, difficulty in micturition, tremor, restlessness, psychosis and epileptic fits.

Para-Aminosalicylic Acid (PAS) is less powerful than INAH and streptomycin.

It is usually orally administered and is chiefly bacteriostatic. PAS is available as the Sodium or Calcium Salt. The sodium salt is preferred. It however should not be given to patients taking treatment for congestive cardiac failure. The daily dose is 10 grams or 300 mg. per kg. which is given in two divided doses.

Toxic Effects. The commonly encountered ones are, diarrhoea and passing of the tablets "entire" in the faeces. To prevent this patients can take the tablets with milk or magnesium trisilicate. If the diarrhoea is severe opiates may be given. Severe vomiting is rare.

PAS also causes prolonged prothrombin-time therefore this should be taken into account when the patient is on anticoagulent therapy.

The effect on the liver is a hypersensitive reaction, the drug can be started after the jaundice subsides.

HYPERSENSITIVITY REACTIONS occur within a few weeks of treatment. This is clinically manifested by an unexplained fever or rash and if not recognised leads to exfoliative dermatitis.

Hypersensitivity reactions occuring much later in treatment, usually after 3 months in the elderly group, appear as a chronic, very irritating eczematous rash affecting the limbs. This reaction is due to streptomycin. Witholding the drug for two weeks, produces a remarkable cure.

The other reported reactions are hepatitis with clinical jaundice, enlarged cervical lymph glands, anaphylaxis diffuse pulmonary opacities in chest X-ray and acute myocarditis.

Management of Hypersensitivity Reactoni

All drugs should be stopped immediately and the patient admitted to hospital. Application of Lotio Calamine and the administration of anti-histamines is usually sufficient.

If the patient is severely ill Corticosteroids should be given.

Once the symptoms of hypersensitivity have subsided the offending drug should be sought. The patient is later desensitized. I am not giving you the methods involved due to lack of time.

Most of the patients after three months of triple regimen show sputum conversion. These patients are then referred to other medical institutions where bi-weekly treatment with streptomycin 1 g/ a day, INAH. 700 mg. (14 mg/kg body weight) and vitamin B6, 20 mg. is given. Trained medical personnel give the injections, the tablets are put into the mouth of patient, water added and the patient told to swallow in the presence of the Medical Staff. This ensures that the patients actually take, the drugs. This method of treatment is continued for one year and nine months, thus completing two years of Anti-Tuberculosis Chemotherapy. Once in three months the patient comes to the Chest Clinic for direct smear of sputum test.

FAILURE OF CHEMOTHERAPY

(1) If the patient has had a combination of penicillin & streptomycin for twelve days without the other two anti-tuberculosis drugs, his organisms develop resistance to streptomycin. This is called secondary resistance. Similarly the patient who reduces the number of tablets prescribed develops secondary resistance to that particular drug.

(2) A patient infected with "opportunist mycobacteria" (atypical mycobateria) does not respond to second line drugs. The Bovine Bacillus is naturally resistant to PAS.

(3) Intermittancy of treatment is not so dangerous as reducing the number of prescribed tablets. Of course the disease shows much advance if the patient has not taken treatment for about three months, yet his organisms can be killed by the first line drugs. Therefore the first line drugs can be repeated. But for a patient who has reduced the number of tablets the first line drugs will not be of value since his organisms will be resistant by them. (X-rays of a patient were shown to illustrate this.)

(4) Primary resistance is due to initial infection with resistant organisms which is fortunately not a problem here.

By-Weekly treatment was introduced in 1960 at the Madras Chemotherapy Centre after conducting several trials assisted by the W.H O. Several important observations were made in the trials. The most noticeable feature was that fresh air, sunlight, extra food and good housing are not necessary factors to aid in the healing of the disease. Further in the administration of drugs, Gangadaran showed that what is more important is the peak level of the drugs intermittently attained rather than the continuous level of the drugs in the serum, attained by regular administration of drugs. Other forms of Bi-Weekly treatment were tried—Ethionamide & Cycloserine, Ethionamide & Kanamycin, Ethionamide & Viomycin. The results were not satisfactory. At the Chest Hospital as all patients request hospitalization initially, initial bi-weekly treatment is not instituted.

SECOND LINE DRUGS. These are less powerful, more toxic, expensive and no one knows the duration for which the drug should be continued. These drugs are useful when the bacteria are resistant to the first line drugs, reflected by persistent absence of sputum conversion even after the sixth month of treatment.

Ethionamide is the most powerful drug. It rapidly diffuses into the body tissues and crosses the blood-brain barrier. The bovine and opportunist mycobacteria are susceptible to it. The drug should be combined with INAH and pyrazinamide.

The usual dose is 1 gr. daily in two divided doses. However it can be reduced to 0.5 gr. and given last thing at night if the patient has unpleasant symptoms. The results are good as shown by these X-rays. (X-rays were shown to demonstrate this.)

The main side effects are nausea, vomiting and a metallic taste in the mouth. Other side effects which may arise are hepatits and peripheral neuropathy. In experimental studies it has been found to be teratogenic and therefore this drug is not given to pregnant mothers.

Pyrazinamide is moderately powerful and acts only against the human type. The drug should be given with companion drugs. The dose is 1 gr. a day in two divided doses. The chief toxic effect is on the liver. The Serum Glutamic oxaloacetic Transaminase (SGOT) is estimated fortnightly. If the level rises above 90 units the drug should be withdrawn.

The drug causes less urinary excretion of uric acid, thus the elevated serum uric acid causes symptoms similar to gout.

Cycloserine is a weak drug, seldom used. It should be given with companion drugs. The dosage is 1 gr. daily in two divided doses.

The side effects are personality changes, aggressive behaviour and tremor. Any suicidal threats mentioned by the patients should be taken seriously. The personality changes, are very remarkable as shown in

one of our cases when the patient repeatedly saluted the Medical Officers and indicated that he will be dead.

Kanamycin is useful against streptomycin - resistant organisms but its total duration of use should not exceed 6 weeks. The usual dose is 1 gr. a day. The drug causes permanent deafness.

Thiacetazone is cheap and is taken as a single dose of 150 mg. daily. This is very convenient for the patient. However due to its side effects, chiefly liver damage and skin rashes, it is not commonly used in Ceylon. In certain parts of Africa it has been well tolerated but not in India. It also causes depression of the bone marrow. Thiacetazone is included as one of the first-line group of drugs when combined with INAH.

Ethambutol is a very powerful drug. It is useful against opportunist mycobacteria too. Absorption is rapid when administered orally. The usual dose is 25 mg. per kg. The main toxic effect is narrowing of the field of vision.

DR. N. GANESHANANTHAN concluded speaking on SURGERY IN TUBERCULOSIS

I shall first deal briefly with the surgica methods used in the

(a) **Diagnosis** of pulmonary tuberculosis.

1. **Lymph node biopsy**: When a lung lesion of obscure pathology is asociated with pathologically enlarged lymph nodes, biopsy of such of node is usually diagnostic. Cervical nodes are most commonly removed. Axillary and intercostal nodes have also been biopsied. Scalene node biopsy is a particular form and is resorted to even when no lymph nodes are palpable. Intrathoracic malignancy can often be differentiated from pulmonary tuberculosis by this means.

2. **Bronchoscopy**: In addition to observing the naked-eye appearances mucosa can be obtained for histology, swabs taken for bacteriological studies and washings for cytological examination.

3. **Aspiration of pleural fluid**: Cytology, culture and guinea pig innoculation can be carried out.

4. **Pleural biopsy**: We have had to resort to this in a number of cases. Needle-biopsy is simpler than open biopsy but due to the lack of the special needle we have performed open biopsies, sometimes under local anaesthesia.

5. **Lung biopsy**: This can be done through a small incision with little disturbance to the patient's condition.

6. **Resection of lung tissue**: In some cases excision of a segment or a lobe is necessary to establish the diagnosis.

(b) In the **surgical therapy**, of pulmonary tuberculosis, minor procedures such as aspiration of effusions, pus or air are commonly resorted to. If this fails, intercostal drainage, with or without removal of a segment of rib is done. Artificial pneumothorax, once used extensively in collapse-therapy is performed only rarely now. It may be tried in cases of severe haemoptysis, where facilities for thoracotomy are not available.

Major surgical measures in the treatment of pulmonary tuberculosis have undergone various changes over the years. It is interesting that this condition has provided a potent stimulus to the development of

thoracic anaesthesia and surgery During the first few years of this century, Von Mickulicz, a surgeon from Breslau, told his assistant that "hundreds of thousands of people are succumbing to tuberculosis, because as yet no one has been able to operate in the thorax. Sauerbruch, the young assistant to whom these remarks were addressed and many others like him, devised methods by which intra-thoracic surgery could be performed. But till 19 2, when positive pressure respiration with endotracheal anaesthesia and muscle-relaxants became a reality, surgery for pulmonary tuberculosis was hazardous.

The next era was from 1942 to the time of effective chemotherapy in the treatment of tuberculosis. Although streptomycin was introduced in 1947, it was not till 1952 that chemotherapy was established on sound lines. This decade was the hey-day of surgery for pulmonary tuberculosis.

For about 10 years after the beginning of effective chemotherapy there was much controversy and individual variation in the extent to which patients with pulmonary tuberculosis were submitted to surgery. The general trend was that less and less number of cases were operated upon.

Lastly we come to the present situation when the indications are less controversial and the number of patients submitted for surgery has stabilized itself at a low level.

1. Number of cases, treated surgically in Ceylon. The first Thoracic Unit was established in Colobmo in 1952. In 1959, Paul and Uragoda reviewed 250 cases treated surgically over the 6-year period 1952—1957. This works out to 42.5 cases per year. Uragoda in 1968 compared this with the number of cases from Chest Clinic Kandy treated surgically in Ratnapura. The period reviewed was 1962—1966 (Table 1). Table 2 shows the number subjected to surgery, in the Thoracic Unit Jaffna for 1968—1969 and the first half of 1970. Although the three series may not be comparable in every detail, they show that surgery is used less commonly compared with the early 1950's. The latter two series are very similar, suggesting a consolidation in the position over the last decade.

YEAR	No. of Newly Diagnosed Cases	No. of Cases Treated Surgically
1962	558	4
1963	487	3
1964	449	6
1965	489	2
1966	546	8
Total	2529	23
Annual average	505.8	4.6

Table 1 Surgically treated cases of pulmonary tuberculosis, in relation to newly diagnosed cases in the Kandy series of Dr. C. G. Uragoda quoted in text (from Uragoda, C. G. (1968) Ceylon Medical Journal 13 p 9.)

YEAR	No. of Newly Diagnosed Cases	No. of Cases Treated Surgically
1968	410	1
1969	410	7
1970 (first half)	200	2
Total	1020	10
Annual average	408	4.6

Table 2 Number of cases treated surgically and number of new cases of pulmonary tuberculosis in Jaffna over the last 2½ years.

INDICATION	Kandy		Jaffna	
	No.	%	No.	%
Persistent positive sputum	7	31	–	—
Recurrent haemoptysis	6	26	4	40
Pyopneumothorax	3	13	3	30
Occupational consideration	3	13	~~3~~	~~30~~
Tension cavity	1	4	–	—
Thickened pleura	1	4	–	—
Undiagnosed pre-operatively	2	9	1	10
Destroyed lung	–	—	2	20
Total	23	100	10	100

Table 3 Indications for surgery in the Kandy and Jaffna series (adapted from Uragoda, C. G., (1968), Ceylon Medical Journal 13 p. 9)

2 **Indications:** Table 3 shows the indications for surgery in the Kandy series and in our series in Jaffna. It is interesting to compare this with a mnemonic I learnt, around 1959 as a medical student. This listed the indications in alphabetical order of their first letters

'A' was for 'Adenoma which stood for **Tuberculoma**. This is a radiological concept used to describe a discrete, spherical, usually solitary lesion of tuberculous actiology. The exact nature of the lesion could be one of many things an area of caseous pneumonia, blocked cavity, etc., This has ceased to be an indication, except where it poses diagnostic difficulties.

'B' was for **Bronchiectasis:** Caseous bronchiectasis usually of the upper lobes, can now be made non-infective with chemotherapy. But the residual dilatation of bronchi may give symptoms of cough and expectoration. This is rarely an indication for surgery, as such upper lobe bronchi drain satisfactorily. Another form of bronchiectasis in tuberculosis is that produced by enlarged lymph nodes constricting the bronchus. This frequently occurs with the middle lobe bronchus. Such bronchiectasis may persist even after the enlargement of lymph nodes has subsided with chemotherapy and may require surgery. Fig 1. shows the bronchogram of such a patient. Even these usually do well with conservative measures. Permanent bronchial stenosis, either following constriction by lymph nodes or due to endobronchial tuberculosis may need surgical treatment. The only type of bronchiectasis which needed surgical treatment (in the absence of haemoptysis) in the two series in Table 2 is the 'Destroyed Lung.' This is a unilateral lesion of the entire lung, which is small and functionless due to a combination of bronchiectasis, fibrosis and cavitation.

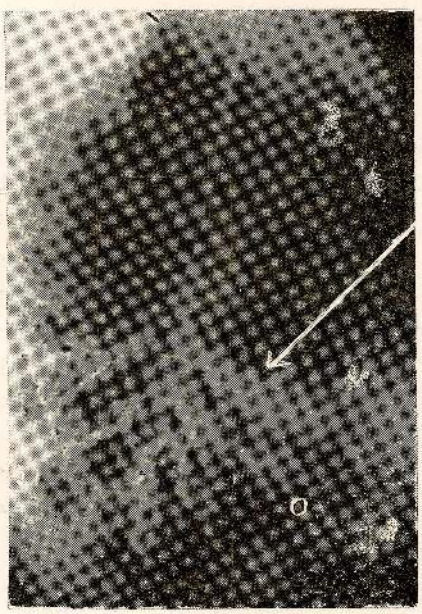


Fig. 1 Bronchogram (lateral view) of a patient treated for a sputum-positive upper lobe tuberculous lesion. The arrow indicates residual bronchiectasis of the middle lobe.

Cavities: In the case of cavities the indications for surgery now are haemoptysis and 'Tension Cavity' (Increase in size of a cavity due to the valvular nature of the bronchus leading to it). 3 of the 4 cases operated on for haemoptysis had bleeding from cavities. The remaining case bled from an upper lobe affected by bronchiectasis and cavitation. Cavities of the apical segment of the lower lobe figured twice in our series, giving rise to haemoptysis in one case and empyema in the other.

During this period three lobectomies were done in Jaffna for Tension Cavities, These were not proved as tuberculous on histology and are therefore not included in this series.

Diagnostic problems Lung resections as a mode of diagnosis has been mentioned earlier. It is resorted to mostly when a neoplasm cannot be ruled out. Also included under this heading are patients operated upon after a wrong diagnosis had been made. In these cases the tuberculous aetiology was not suspected till after resection. One such case included in our series was a young man, 28 years old who had a lung abscess of the lingula. He had sustained a fracture of the neck of femur 8 months prior to this and had general anaesthesia on several occasions. He had also been in a recumbent position for a long time. A diagnosis of pyogenic abscess was made. As this did not heal quickly enough to enable a further operation on his lower limb, a lobectomy was done. Although the sputum had been repeatedly negative for tubercle bacilli, tuberculosis was diagnosed on sectioning the specimen.

Empyema : 30% of the Jaffna series and 26% of the Kandy cases had pyopneumothorax as the indication for surgery. Intercostal drainage very often fails to control the leak and decortication and resection become necessary. Thickened pleura by itself is not an indication if the lung expansion on the affected side is reasonably good. It has been shown that lung function tests are not markedly affected by decortication in such patients.

Failed Treatment : This was mainly due to emergence of drug-resistant strains in the early days of chemotherapy. In the Colombo series of 1952-1957 reported by Paul and Uragoda persistent positive sputum was the cause of surgery in 53% of cases. In the Kandy series, this indication dropped to 31%, while in the Jaffna series there were no such cases. Combination of drugs, regular therapy, the introduction of twice-weekly treatment and the availability of 'second-line drugs' have reduced this indication to a minimum.

Incorrigible defaulters and alcoholics may pose problems for chemotherapys Doctors were at one time considered poor long-term drug-takers! We did not resort to surgery for this reason alone, though two of the patients with haemoptysis and one with empyema admitted that they had been irregular in taking drugs.

General : This included occupational considerations, and generalised diseases. Diabetes was considered an indication for surgery at one time. Two of the ten cases in our series, one with haemoptysis and one with empyema had diabetes, but the diabetes per se was not considered an indication. At one time people who came into contact with children, like teachers, were advised surgery to shorten the infective period. Persons who wanted to get back to work early were also recommended surgery. Present drug regimes have done away with these indications.

Haemoptysis Large, repeated attacks of haemoptysis are an indication for surgery. 40% of our series and 26% of the Kandy series were for this indication.

Type of operation	Colombo 1952—1957 No.	%	Kandy 1962— 966 No.	%	Jaffna 1968—1970 (1st half) No.	%
Thoracoplasty	116	49	—	—	—	—
Plombage	3	1	—	—	—	—
Segmental resection lobectomy or both	96	38	13	57	5	50
Pneumonectomy	30	12	9	39	2	20
Decortication	3	1	1	4	2	20
Decortication with pneumonectomy	—	—	—	—	2	20
Others	2	0.8	—	—	—	—
Total	250	100	23	100	10	100

Table 4 Comparison of the type of operation for the three series (Adapted from Paul, A. T. S., and Uragoda, C. G., (1959) Tubercle, **40**, 93 and Uragoda, C. G., (1969) Ceylon Medical Journal, **13**, 9.

3. **Nature of operation.** Table 4 shows the relative incidence of the type of operations done in the 3 series quoted. Collapse operations of thoracoplasty and plombage made up 47% of the earliest series from Colombo. These operations were favoured at that time as many patients had bilateral disease or active tuberculosis at the time of surgery. The risks of spread of disease to healthy lung tissue, post-operative stump leaks and respiratory insufficiency prevented the extensive use of lung resections in preference to collapse operations. Now, with adequate pre-operative chemotherapy, these dangers are minimal. Thoracoplasty, which produces deformity of the chest, and plombage with the high incidence of infection, have now been almost given up in favour of resections. Thoracoplasty still provides the answer to the desperate problem of severe haemoptysis in patients with bilateral disease. Fig. 2 shows the

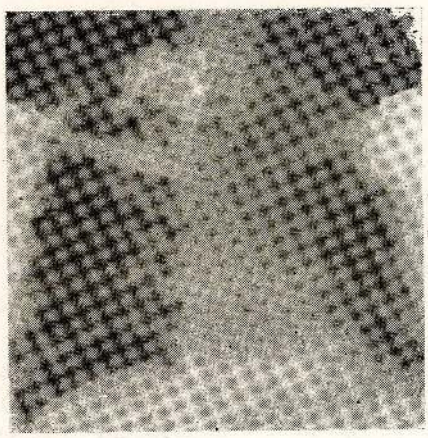


Fig. 2 Chest X-ray (P. A view) of a patient with bilateral disease and haemoptysis. (See text for details.)

chest X-ray of such a patient. Resection of the left upper lobe, which had the bleeding cavity was not considered possible as the patient had poor pulmonary reserve. Thoracoplasty was contemplated but the bleeding subsided after some time. Thoracoplasty is also used in cases of resistant pleural cavity infection after resection.

Considering lung resection in tuberclosis the tendency now is to resect the minimum amount of tissue—segmentectomy rather than lobectomy and lobectomy rather than pneumonectomy.

4. **Contra indication for surgery**

These are poor respiratory function, bilateral tuberculous disease, active endobronchial tuberculosis or severe cardiovascular, renal or hepatic disease. A minimum of 3—4 months of active chemotherapy is considered essential before surgery.

A discussion then followed:

Dr. Benjamin: Could you enlarge on how surgery became gradually less and less important in pulmonary tuberculosis.

Dr. Ganeshananthan: After about 1952, follow up studies were done after adequate anti-tuberculous chemotherapy. Some conditions in which surgery was earlier thought necessary, were seen to do well with chemotherapy alone. A case in point is residual cavities. The 'Open negative syndrome" is now recognised. This is a condition of the patient who has had an excellent response to chemotherapy and is sputum free, but is left with a walled cavity. Such patients have been found to do well.

Dr. Mrs. Ganeshananthan: It was also shown that even when surgery was practised extensively the death rate did not drop markedly. It did so only with the advent of chemotherapy.

Dr. Vamadevan:— Awareness of the very high efficacy of proper chemotherapy, in the freshly diagnosed cases and the discovery of powerful second line drugs for the treatment of failures, has resulted in the narrowing of the indications for surgery in pulmonary tuberculosis and accounts for the reduction in the amount of surgery for pulmonary tuberculosis during the last few years.

The two main indications now would be Empyema and Diagnostic purposes.

Haemoptysis would rarely be an indication now. Those who die of haemoptysis are invariably dead by the time the medical officer arrives at the scene. Sudden profuse haemoptysis results in the drowning of the patient in the aspirated blood. The majority of the patients who have persisting haemoptysis lasting for weeks ultimately recover, when treated conservatively with sedation and occasionally may need transfusions. The number of patients among this lot who will ultimately succumb to a fatal attack is very small and cannot be predicted on clinical grounds. It is also rare for these patients to have a localised lesion and bronchoscopy is not always correct in determining the site of the lesion.

The main problem in the cases of destroyed lung is that they are subjected to repeated attacks of secondary infection on the destroyed lung and sometimes haemoptysis. When an entire lung is destroyed as an end result of tuberculosis it is very rare for the other lung to have escaped without a damage to a relevant portion, due to the

primary disease process. The removal of a lung at this stage would seriously affect the function of the other lung tissue when subjected to compensatory emphysema. The long term end result of pneumonectomy in Pulmonary tuberculosis would not therefore be satisfactory from a functional point of view. The repeated infections that harass these patients could be satisfactorily treated with antibiotics and physiotherapy.

Dr. Ganeshananthan: I agree with Dr. Vamadevan but I still feel that there is a place for surgery in haemoptysis and the destroyed lung. Taking haemoptysis, patients are sent to us from other institutions, mainly the Chest Hospital K.K.S., by the time they reach us they have had several or one big bleed. 15 such cases were seen by us during the last 2½ years. All were given blood transfusions and observed. 4 patients continued to bleed and had to be operated on. Of these one was a diabetic, who died after a month of uncontrollable pleural cavity infection. 7 others recovered with conservative treatment. The remaining two are significant. They died of severe haemoptysis within a few hours of admission while being prepared for surgery. These two patients could well have been saved if the operation was done earlier. So I feel surgery has a place particularly with the restricted blood transfusion facilities that we have.

Regarding the destroyed lung, we always try conservative measures such as control of infection and physiotherapy first. Operation is resorted to only when symptoms are intolerable. This was so in one of our two cases, who had copious sputum and severe halitosis, which made life miserable. He had a very satisfactory result after pneumenectomy and is completely asymptomatic now. The other case (Fig. 3) was a patient

Fig. 3 X-ray of chest after Ba-swallow showing a "destroyed lung" on the left and a carcinoma of the oesophagus.

with a destroyed lung on the left side, with carcinoma of the oesophagus. The latter condition necessitated surgery. If the damaged lung was left behind, the post-operative lung complications would have been unmanageable. So we performed a left pneumonectomy and oesophagectomy at the same time. The patient made an excellent recovery.

Dr. Sivaganavel: In any disease rest, good food, and fresh air have an important part to play. As such it is not correct to dismiss these as non-essential in the treatment of pulmonary tuberculosis.

Dr. P. Arulanandam: In Madras it has definitely been shown that a sanatorium regime referred to, makes no difference at all to prognosis as long as effective drug treatment is maintained under reasonable home conditions.

ASSOCIATION NEWS

HALF YEARLY REPORT

(MARCH 1970 TO SEPTEMBER 1970)

THE Annual General Meeting was held on 21st March 1970. At this meeting, a new category of members, called Out-Station Members, was created by the passing of a resolution. Such members were to be those normally resident outside the Jaffna peninsula. The subscription payable by them is Rs. 12/- per year.

16 Scientific Meetings were held. In April a team of eminent French doctors visited us. They were Professor Bilski-Pasquier, Professor Philippe Seringe, Dr. Bernard Guy-Grand and Dr. Jean-Pierre Caron. The other guest speakers during this term were: Dr. S. J. Stephen, Mr. Mailoo Jayaratnam B. Sc. (Cey), M. Sc. (Strath) LLB (London), F.R.I.C., Assistant Govt. Analyst, Dr. Darrel Weinman, Dr. C. Vivekananthan, Dr. S. Ramachandran, Dr. J. St. George and Dr. N. Kodagoda. We thank all of them for the trouble taken. We are also grateful to the French Embassy and the Department of Health Services for arranging the visit of the the French Medical team. Panel discussions and presentation of clinical cases were each held roughly once a month.

Three dinners were sponsored by the association during this six months.

Dr. W. J. K. M. de Silva, one of the editors of the Journal, left us. We thank him for his services to the Association. Dr. T. Parameswaran was elected in his place.

Dr. S. Narendran
Dr. N. Ganeshananthan
(Honorary Joint Secretaries)

Lectures

Lectures Summary of Scientific Meetings

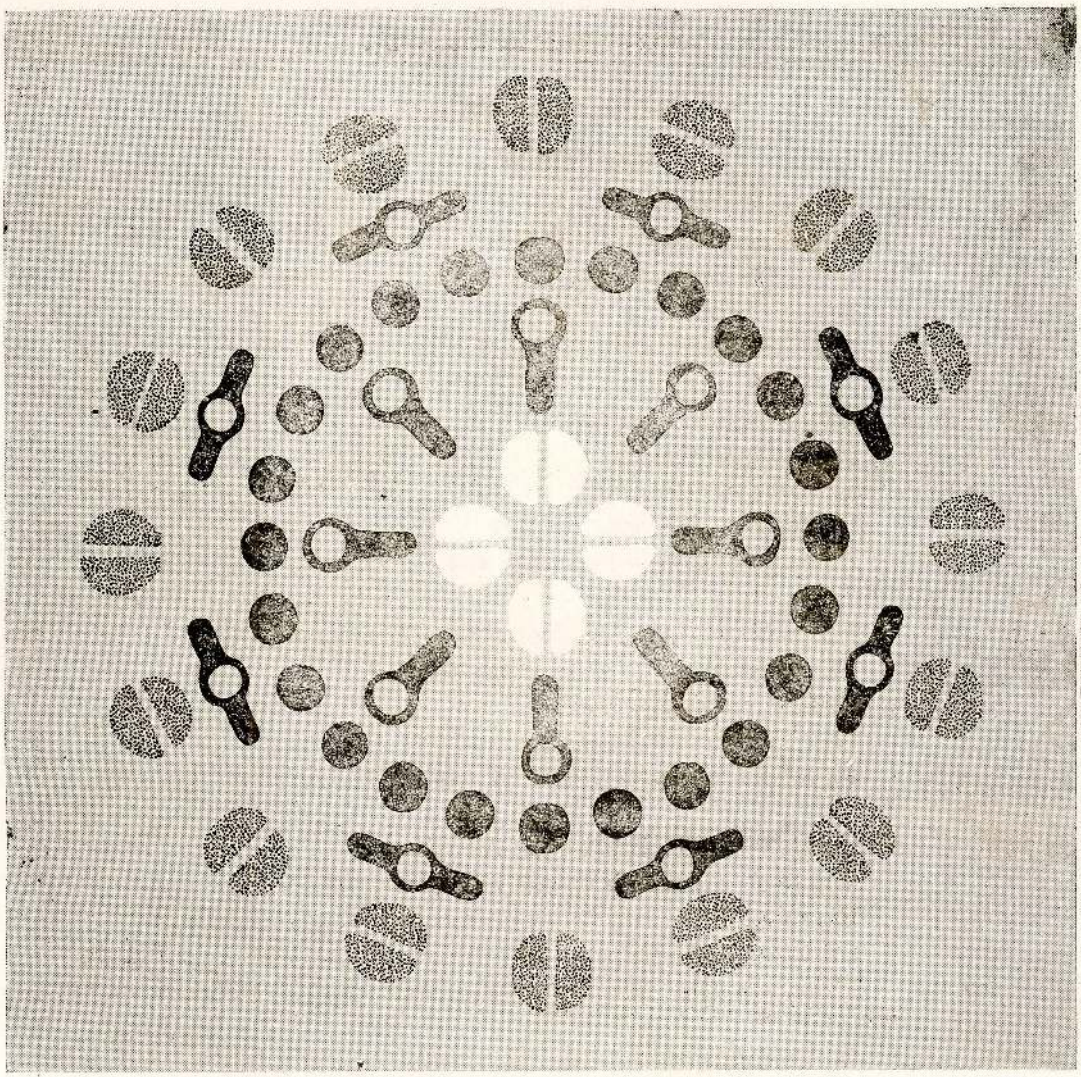
Date	Lecturer	Subject
4-4-70	Dr. S. J. Stephen, M.S., F.R.C.S., Thoracic Surgeon G. H. Ratnapura.	Mitral Stenosis (Short Paper)
20-4-70	Dr. Darrel Weinman, F.R.C.S., F.R.C.S.E. Neuro—Surgeon G. H. C.	Headache.
14-5-70	Prof. Jean-Pierre Caron, Professor of Neurology and Neurosurgery Paris.	Surgery in Cardio—Vascular lesions.
	Prof. Phillippe Seringe, Professor of Paediatrics, Paris.	Rickets.
9-7-70	Dr. C. Vivekananthan, F.R.C.S., Senior Registrar, The United Sheffield Hospitals.	Some aspects of Plastic Surgery.
23-7-70	Dr. J. Balachandran. L.M.S. General Practitioner, (formerly of the Diabetic Clinic G. H. Jaffna)	Juvenile Diabeties (Short Paper)
28-8-70	Dr. S. Ramachandran, M.D. (Ceylon) M.R.C.P., M.R.C.P.E., Physician, Base Hospital, Negombo.	Some aspects of Renal failure Haemodialysis and Transplantation.
10-2-70	Dr. J. St. George, M.B.B.S., F.R.C.S., F.R.C.O.G. Senior Lecturer in Obstetrics and Gynaecology, University of Trinidad.	Preparation for Breast feeding.
26-9-70	Dr. N. Kodagoda, M.D. (Ceylon) M.R.C.P. Senior Lecturer in Forensic Medicnie, University of Ceylon, Colombo.	Nature of Interstitial Pneumonitis.

Panel Discussions

Date	Subject	Members on Panel
15-4-70	Poisoning by Agricultural Pesticides	Mr. Mailoo Jayaratnam Dr. A. V. A. Vethanayagam
11-6-70	Family Planning	Dr. K. Sivagnanaratnam Dr. E. Kankesu Dr. R. Ramalingam
1-7-70	Jaundice	Dr. (Mrs.) R. Abeyasuria Dr. K. Puvanendran Dr. K. Arumugam
7-8-70	Pulmonary Tuberculosis	Dr. T. Vamadevan Dr. (Mrs.) B. S. Wilson Dr. C. Indrarajah Dr. N. Ganeshananthan
20-9-70	Extra-Pulmonary Tuberculosis	Dr. (Mrs.) R. Kanagasundaram Dr. S. Selvendran Dr. T. Parameswaran Dr. J. L. Amarasingham Dr. A. E. D. Navaratnam

Clinical Demonstrations

Date	Cases shown
4-4-70	Ovarian ectopic pregnancy.
	Secondary abdominal pregnancy.
	Idiopathic thrombocytopenic purpura complicating pregnancy.
	Bell's palsy.
	Mononeuropathy of the 3rd cranial nerve.
3-5-70	Atlanto-axial dislocation.
	Idiopathic cavo varus.
	Fractures of capitellum.
	Marble Bone Disease.
	Hare-lip occuring in more than one family.
2-6-70	Idiopathic epilepsy and effect of dilantin sodium overdose.
	Idiopathic thrombocytopenic purpura.
	Hirs chsprung's disease.
	Primary myocardial disease.
	Thyrotoxicosis—comparison of medical and surgical treatment.
23-7-70	Pseudohypertrophic Muscular Atrophy.
	Von Recklinghausen's disease with quadriparesis.
	Hypeprarathyroidism presenting as a tumour of the rib.
	Pulmonary tuberculosis diagnosed on lung biopsy.
	Blalock-Taussig shunt performed on a patient with Fallot's tetralogy.
21-8-70	Common skin conditions: Ringworm, Scabies. Psoriasis, Lichen planus. Leprosy etc.
	Carcinoma of rectum with multiple polyposis.
	Diverticulosis of bladder.



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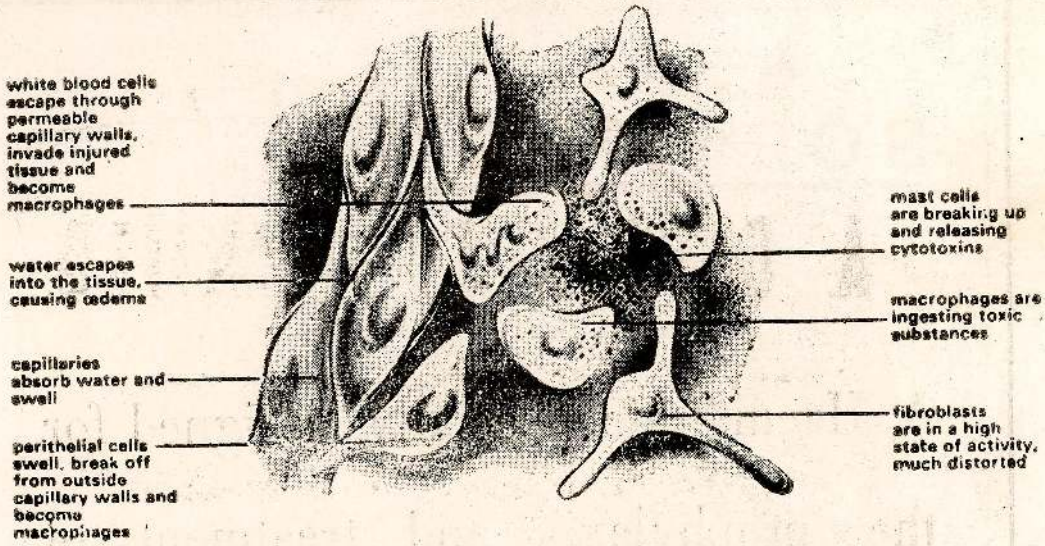

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