



The Medical Journal of Malaya

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Ten years of the Malayan Medical Association

by A.A. Sandosham

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I HAVE BEEN assigned the task of reviewing the work of the Malayan Medical Association since its inception ten years ago. A decade seems a relatively short period but both our Association and the Singapore Medical Association have been built on the foundations of the Malaya Branch of the British Medical Association and the Alumni Association of King Edward VII College of Medicine and Faculty of Medicine, University of Malaya, Singapore. Attempts were made to form a joint medical association to include the states of East Malaysia and Singapore but the requirements of the Registrars of Societies, differences in the Medical Registration Ordinance and Ethical Code, combined with long distances that have to be covered, made that impossible. Despite this, close liaison exists between the Singapore, Sarawak and the Malayan Medical Associations which are affiliated to one another, while some of the doctors in Sabah and Brunei are our members.

CONSTITUTION

The M.M.A. Constitution was approved at a special meeting held on 24 Oct 1959 and subsequently accepted by the Registrar of Societies. It is a democratic organisation with the management vested in a Council composed of a President, a President-Elect, the Immediate Past President, an Hon. General Secretary, an Hon. Deputy Secretary, an Hon. General Treasurer, an Hon. Editor and four representatives elected by each of the three Branches. An

Executive Committee, composed of Council Members with the exception that the Branches are represented only by its Chairman or a single nominee, manages the day-to-day affairs of the Association.

OFFICIALS OF THE ASSOCIATION

The Trustees of the Association are Dr. S.G. Rajahram, Dr. P.T. Arasu and Dr. Chong Yew Chong.

The Presidents of the Association, starting from 1960, have been Dr. S. G. Rajahram, Tan Sri (Dr.) Mohamed Din bin Ahmad, Dato (Dr.) S.M.A. Alhady, Dr. Abdullah bin Ahmad, Dato (Dr.) R. Sathiah, Dr. A.W.E. Moreira, Dr. R.F. D'Costa, Dr. Tan Chee Khoon, Dr. J.B.A. Peter and Dr. Lim Kee Jin.

During this period, we have had four Honorary General Secretaries, namely Dr. T. Visvanathan, Dato (Dr.) Keshmahinder Singh, Dr. F.R. Bhupalan and Dr. S. Param Palam, the last named having officiated for more than six years and continuously for the last three years.

By having a President-Elect appointed to the Council a year ahead of his assuming office as the highest ranking official of the Association, he acquires experience and knowledge of the Association's problems and responsibilities. By his continuing to serve another year as the Immediate Past President, he provides continuity and guidance to the new Council. This system has worked very well while at the same time, by arranging for the President-Elect to be nominated by each of the Branches in rotation,

the net is cast widely for the selection of suitable candidates and the honours are distributed evenly. This avoids the concentration of power in one individual as it might well happen if the same officer holds such a high executive office in an organisation continuously for too long a period.

OBJECTS OF THE ASSOCIATION

The main objects of the Association have been to represent the profession in the country, to maintain a high standard of medical ethics and conduct, to promote social, cultural and professional activities, to enlighten and direct public opinion on problems of health and to express the views of the profession to Government and other bodies.

MEMBERSHIP

The total membership has risen from 539 in 1960 to 1,249 in 1970, of whom 40 are Life Members and 85 contributing towards Life Membership. We regret that some of the doctors have not yet seen fit to become members for reasons of their own but the increasing membership list augurs well for the future. We have recently opened our doors to scientists in the para-medical fields to enable them to join us as Associate Members.

Dr. (Miss) Soo Kim Lan, Dr. Teh Lian Swee and Dato (Dr.) Cheah Toon Lock, are our Honorary Members.

AFFILIATIONS

The M.M.A. is a member of the Commonwealth Medical Association and the Confederation of Medical Associations in Asia and Oceania. Professor A.A. Sandosham has been elected to serve on the Council of the Confederation of Medical Associations in Asia and Oceania for the next four years. We are affiliated to the British Medical Association, the Singapore Medical Association, the Sarawak Medical Association and the Australian Medical Association.

Our delegates or representatives have attended the General Meetings of the British Medical Association, Singapore Medical Association, Australian Conference of General Practitioners and Commonwealth Medical Association. In August this year, the M.M.A. and the Singapore Medical Association will have the honour of acting as joint hosts for the first time to the biannual General Meeting of the Council of the Commonwealth Medical Association and it has been agreed that Professor A.A. Sandosham and Dr. Gwee Ah Leng will be Joint Presidents of the Commonwealth Medical Association for the next two years.

MEDICAL JOURNAL OF MALAYA

This, the official organ of the M.M.A., had its origin 34 years ago as the quarterly publication of the British Medical Association (Malaya Branch). It has been taken over with the formation of M.M.A. in 1960 and is under the charge of an Editorial Board, Mr. H.M. McGladdery having been Hon. Editor from 1960 to 1964 and Professor A.A. Sandosham since then. It is a scientific journal and has made its appearance regularly and finds its way into the Medical Libraries of many parts of the world and its contents are quoted and abstracted extensively. The editorial columns often reflect the Association's views and attitude towards medical problems of the country which receive publicity in the local press. All members receive a free copy of the Journal and it is also distributed on a reciprocal basis to the members of the Singapore Medical Association.

M.M.A. NEWSLETTER

There has long been felt the need for a regular publication, like the Newsletter, giving information to members scattered throughout the country regarding the activities of the Association, especially the Council, encouraging a healthy participation by members. It is intended to give members the opportunity to express their views about medical, social and related problems so that fellow members, the public and even Government may become aware of them. It has been published since the foundation of the M.M.A. somewhat irregularly and whenever there has been sufficient material to justify one. During the last year, four issues have appeared at 2-monthly intervals, largely through the efforts and enthusiasm of Dr. Lim Kee Jin and his Johore colleagues. It has been well received and whether it will endure or not will depend on the support in the way of contributions it receives from members.

THE ETHICAL COMMITTEE

As becomes a noble profession, it is necessary that its members maintain the highest standards of professional conduct. His first consideration should be his patient's health and he should not be unduly motivated by gains and profits. His behavior towards the fellow members of his profession should be above reproach. For instance, self-advertisement, enticing of patients from his colleagues, etc., are considered unethical. There are laws which can bring a miscreant to book but in practice, these laws are difficult to enforce. The Association, therefore, tries to enforce

the correct behaviour by showing its disapproval of unethical conduct on the part of the members of the profession, and by giving sound advice on what should be done.

The Association has drawn up a set of Ethical Rules to try and get acceptance of the Ethical Code of Behaviour. The Ethical Committee of the M.M.A. Council listens to complaints and impresses on the medical practitioners the need for maintaining a high standard in the practice of the profession. The Ethical Committee, under the chairmanship of Dr. S.G. Rajahram (except for one year when Dr. A.W.E. Moreira took charge), has done a splendid job answering numerous questions for clarification and interpretation of the Code and by appeals, impressing on those (fortunately few) who try to achieve fame and fortune by unethical methods. The Ethical Committee has achieved a measure of success and it is now considered that the time has come for Government to legislate and allow a small amount of punitive powers for minor offences rather like in New Zealand.

RELATIONS WITH GOVERNMENT

We have always tried to maintain cordial relations with the Ministry of Health and have made representations to Government on matters affecting the health of the people and the profession. Recently, an ex-Minister of Health had this to say: "Well, going back to the days when I was the Minister of Health, which I can assure you was a very pleasant one, I recall the cooperation and assistance given to the Ministry by the M.M.A. A number of schemes, now being put into operation, were as a result of discussions held with the chiefs of the M.M.A. who, as you know, were very generous with their comments or suggestions."

We have submitted memoranda to Government on numerous subjects, including undergraduate and post-graduate medical education in the country, and offered the voluntary services of our private practitioner members during national emergency, to help to run a School Health Service, to assist in the Government Hospitals which are proverbially understaffed, etc.

Our Association is represented on numerous Statutory Boards, like the Poisons Board, National Family Planning Board, Kedah Health Board, Estate Hospitals Board and Malaria Advisory Board, to mention only a few.

Our members serve on numerous Government and

non-Government Committees, such as the Medical Legislation Standing Committees on Employees' Provident Fund Ordinance, Workmen's Compensation Ordinance, Registration of Estate Dressers and Social Security. We have our nominees on the National Health Council, National Research Council, Malaysian Red Cross Society Council, Pharmacopoeas Advisory Committee and Committees on Communicable Diseases, Hospital Facilities, Public Health Education, Malayan Association for Prevention of Tuberculosis, Post-Graduate Medical Studies, Private Charitable Hospitals, Medical and Health Planning, Maternal and Child Health and others.

Our members have always readily come forward to the help of the people during periods of stress and strain. Both Tun Razak and the Minister of Health, Tan Sri Sardon, have singled out the medical profession for the yeoman service rendered during the recent emergency.

M.M.A. COMMITTEES

We have set up numerous Committees from time to time to study special problems like accident prevention, effects of smoking, medical legislation, sale of drugs and poisons by unqualified persons, dental health education, school health service, cholera epidemic, postgraduate medical education and others.

M.M.A. SOCIETIES

To facilitate professional advancement, we have been organising scientific and clinical meetings in all the Branches, lectures by various visiting and local specialists, film shows, refresher courses, conferences, and discussion panels, both for members and the public.

To cater for sectional interests and enhance their professional status in their respective specialities, we have organised the Public Health Society, Paediatric Society, Neuropsychiatric Society and Ophthalmology Society. These Societies organise Conferences, Panels and Scientific Meetings of their own and the Public Health Society publishes a Bulletin annually. There was a Private Practitioners' Section and the Association is presently considering the feasibility of setting up a College of General Practitioners to maintain high academic standards on the lines of the Australian College of General Practitioners.

OTHER BENEFITS FOR MEMBERS

We have entered into an agreement with the Medical Defence Union of London to provide M.M.A.

members with medical defence in cases where proceedings involving questions of professional principle or otherwise are brought against them.

We have established a Medical Benevolent Fund for the benefit of members and arrangements have been made to enable members to take out insurance policies under favourable terms.

We have issued car badges with the M.M.A. Crest for the exclusive use of members and car stickers and identity cards for use during emergencies.

We have published a Directory of Information on Medical Practitioners in West Malaysia giving details of qualifications, honours bestowed and other relevant data of our members.

We run competitions in tennis and golf in connection with the Annual General Meetings for trophies presented by Dr. S.G. Rajahram and Dr. Teh Lian Swee respectively.

M.M.A. HOUSE

Ambitious plans have been drawn up and piles have been driven for the building of a National Centre for the medical profession of this country. The M.M.A. House Committee in charge of this project is under the chairmanship of Dr. P.T. Arasu. The Association has obtained from the Selangor State Government a piece of land measuring 26,800 square feet in front of the General Hospital, Kuala Lumpur, on 99 years' lease at nominal cost. This is conveniently situated in close proximity to the General Hospital, Maternity Hospital, Institute for Medical Research and the T.B. Clinic and when ready, it will provide facilities for members to meet and more effectively carry out the objects of the Association. It will house the M.M.A. office and have accommodation in flats for use of outstation members.

THE FUTURE OF OUR MEDICAL SERVICES

We are far from achieving the U.N. goal for W.H.O. of "attaining the highest possible level of health for all people regardless of colour, race or economic level." Many modern countries have come a long way from the fee-for-service system wherein the rich got the cream of the medical service while the poor got the crumbs, if that. No longer should the poor depend on the traditional charitable disposition of the doctor or the community. Instead, the idea must be generally accepted that every individual has the right to health and that the Government is responsible for providing a total comprehensive medical service.

Even in the most enlightened and wealthy

countries, the changes have come about gradually, fighting reactionary elements. To start with, voluntary private health insurance plans catered for special groups. Small groups of workers, through their trade unions, obtained medical care for their workers, the doctor-patient relationship being maintained by the panel system. Gradually, a comprehensive programme was introduced financed by compulsory health insurance, social security, general taxation, etc., the doctors becoming full-time salaried officers, or through a capitation system or by Government reimbursing the patient for medical fees paid to the doctor, the practice of medicine changing from competitive business to a social service.

Medicine has come to be recognised as a social welfare institution in many modern countries. We like to know what system we should adopt, in what direction we should go and how soon should we start. It seems futile to go along haphazardly trying to meet the problems as they arise and hope for the best. We need people, with knowledge of the various systems including their good and bad points, to study the whole question of the future of our medical and health services and make recommendations on the direction we should take, having in mind the past and the present state of development, the conditions likely to prevail in Malaysia in the foreseeable future. The Association has made repeated attempts to get Government to set up a Royal Commission of Enquiry to study the whole problem, so far without any results.

CONCLUSION

In this rapid survey of the work of our Association in the last ten years of its existence, I have tried to show that ours is a democratic organisation representing the profession as a whole in the country. We have tried to maintain high ethical and professional standards among our members, have tried to serve the public and Government by being represented on numerous Boards and Committees at considerable sacrifice of time and energy on the part of members and by submitting our views on problems of health in numerous memoranda and publications. Though not a Trade Union, we have endeavoured to help our members, both in the private and public sectors, to improve their lot.

We look forward with confidence to the future, when our M.M.A. House is ready and when the Association will have better facilities to serve the members and the people of the country even more effectively and efficiently than in the past.

Cholera in the Kedah River area

by Paul C.Y. Chen

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INTRODUCTION

DURING the months of December 1963 to April 1964, an outbreak of El Tor cholera occurred in the state of Kedah, West Malaysia. During this period, a total of 83 cases, including 11 deaths and 60 carriers, were reported. Seventy-five of these cases, including the 11 deaths and 56 of the carriers, were reported from the Kedah River area, this being defined as the area within two miles of the Kedah River, its tributaries and irrigation canals with connection to these waters. It is the purpose of this paper to consider some of the epidemiological and ecological observations made in relation to the outbreak in the Kedah River area.

THE KEDAH RIVER AREA

The Kedah River flows through the low-lying Kedah plain and has two main tributaries, the Sungei Besar in the north and the Sungei Tajar in the south. For the purpose of this report, the area served by any of the canals or tributaries with connection to the western bank of the Sungei Besar will be designated as area "A". The eastern bank and eastern tributaries of the Sungei Besar will be designated as area "B", while the area drained by the Sungei Tajar and its tributaries will be designated as area "C", as depicted in Maps 1 and 2.

On the basis of such a division, area "B" would contain Alor Star town in the south and Kepala Batas airport in the north. It is a relatively densely-populated area with good roads, piped water, electricity and telephones. Economically, it is the most developed of the three areas under consideration. The majority of houses have private connections to the water mains. In addition to this, a total of 57 standpipes were available at the outset of the outbreak.

Area "C", on the other hand, is the least developed of all the three areas. It consists of villages arranged in a linear fashion on both banks of rivers and canals. Beyond these villages stretch the padi-fields. These rivers and canals serve as waterways, for fishing, for washing and bathing, as a source of drinking water, especially when the dry season arrives and the wells dry up, and also as a means of excreta disposal. No water main exists in this area and the main sources of drinking water are wells and the river especially when the drought affects well water supplies. Figure 1 depicts a cross-section through a small river showing the arrangement of padi-fields, houses and surrounding fruit trees, waterways and overhung latrines.

Area "A" is intermediate between the last two areas in that although it resembles area "C" in most

aspects, it has a water main from which 26 standpipes supplied some of the more fortunate villagers at the outset of the outbreak. In the north of area "A" stretches a network of irrigation canals. At some points, these canals have connections to the Kedah River, but throughout the duration of the cholera outbreak these connections were kept closed.



Fig. 1: A diagrammatic representation of a cross-section of a small river showing padi-fields, houses surrounded by fruit trees, and overhung latrines.

EPIDEMIOLOGICAL OBSERVATIONS

1. The occurrence of cholera cases and carriers

(a) The initial phase of the outbreak

The first case that occurred in the Kedah River area, occurred in Kampong Elir, on the upper reaches of the Gunong tributary of the Kedah River. This was a 26-year-old Malay labourer employed at a granite quarry at Gunong. He was stricken with cholera and died at home on December 7, 1963. Diagnosis was based on a positive culture obtained by post-mortem rectal swabbing. At the time of his death, a new coastal road linking Perlis to Alor Star that ran past Gunong was under construction, and was opened only to Public Works Department lorries. The first case of cholera in Perlis occurred along this road on November 26, 1963. Investigations revealed that the dead man had disappeared for about two days some two weeks before his death, and that two days before his death, another labourer from the same area had been admitted into hospital with diarrhoea and vomiting but had been discharged the following day after improving. No rectal swab had been obtained and it is not known whether he was suffering from cholera. The possibility that the case was linked to the outbreak in Perlis will be discussed later.

The second case occurred 18 days later on December 25, 1963, and involved a 59-year-old Malay man who died some 8½ hours after admission into hospital. Prior to his death, he had been visited by one of his daughters accompanied by her three children, all of whom lived in the same village as the

granite quarry labourer. Further, this woman had attended the funeral of that labourer.

This was followed by a lull of one month when on January 26, 1964, a 31-year-old Malay woman, who lived a little downstream of the granite quarry labourer, developed cholera. She had a habit of bathing in the river and of drinking from it. A member of her household contacts was found to be a carrier. Thus, during the period December and January, three cases (of which two were deaths), and one carrier were reported in the Kedah River area, all occurring in the northern part of area "A". The location of the three cases are marked as black triangles in Map 1.

(b) The massive phase of the outbreak

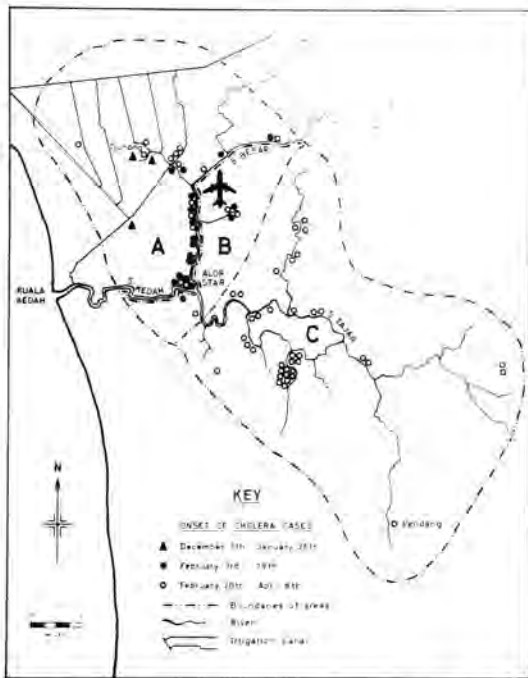
On February 3, 1964, the outbreak moved downstream and the first case occurred in the southern part of area "A" at Seberang Terus, just outside the Alor Star Town Council area. On February 8, a further case occurred and this was followed by a series of cases so that between February 3 and 19, there was a total of 18 cases and 20 carriers. These 18 cases are marked in Map 1 as black spots and are confined to areas "A" and "B" on both banks of the Sungei Besar. Of these 18 cases and 20 carriers, only three cases and two carriers were reported in area "B". This disproportionate distribution of cases and carriers between the two areas will be discussed later. Thus up to February 19, the Sungei Tajar area, area "C", had not been involved.

On February 20, the first case occurred in area "C". In the meanwhile, the outbreak had begun to decline in areas "A" and "B". On March 6, the last case and carrier occurred in these areas, bringing the total reported cases and carriers in the massive phase for area "A" to 29 cases and 24 carriers, and that for area "B" to six cases and two carriers. Meanwhile, the outbreak continued in area "C" and reached its peak on March 7. Thereafter, the incidence began to drop and by April 8, when the last case occurred, there was a total of 37 cases and 29 carriers in area "C". The geographical distribution of cases is summarised in Map 1, where the initial three cases are marked as black triangles, the 18 cases occurring between February 3 and 19, by black spots, and the remaining 54 cases occurring thereafter by white spots. The daily occurrence of cases and carriers in areas "A" and "B", and in area "C" during the massive phase of the outbreak is summarised in Figure 2.

(c) The origin of the outbreak

The first case of cholera in Perlis occurred on

CHOLERA IN THE KEDAH RIVER AREA



MAP 1: Map showing the division of the Kedah River area into areas "A", "B" and "C", and the distribution of cholera cases therein.

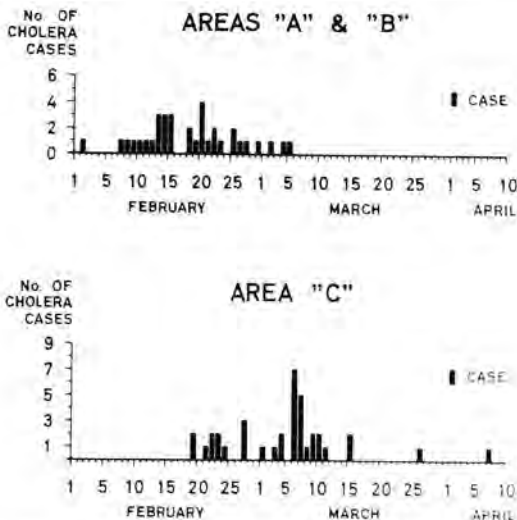


Fig. 2: The daily incidence of cholera cases during the massive phase of the outbreak in the Kedah River area in February, March and April 1964.

November 26, 1963, 11 days prior to the onset of the outbreak in the Kedah River area, and involved a 65-year-old Malay woman. She lived next door to her daughter who was the second wife of a Thai Malay. This man possessed a border pass and constantly shuttled between southern Thailand and Perlis. His last visit to Thailand had been to Songkhla between November 3 and 10, 1963. Since July 24, 1963, the province of Songkhla in southern Thailand bordering on Perlis and Kedah, had been from time to time reporting the occurrence of cholera cases. In the week November 3 to 9, no cases were reported from Songkhla, but in the following week, November 10 and 16, 22 cases and six deaths were reported. In all probability, the Thai Malay was at that time a healthy carrier and might have been the source of infection of his mother-in-law, who lived 5½ miles from Kangar along the new coastal road linking Kangar to Alor Star via Gunong. As has been pointed out, the first case in the Kedah River area lived along this same road at the Gunong end. Although no direct link between these two cases was established, the possibility that the outbreak in the Kedah River area might have been linked to the one in Perlis cannot be discounted.

2. Age and Sex Distribution

Of the 75 cases reported, there were 38 males and 37 females, including six deaths among the males and five deaths among the females. Among the 56 carriers detected, there were 27 males and 29 females, there being statistically no significant difference in the distribution between the sexes.

The mean age of the cases and of the carriers for both sexes, as computed from the original data available from investigation sheets, is summarised in Table I. For comparison, the mean age for both sexes for the general population of Kedah, from the census of 1957, is included. The age distribution by five-year age intervals for the two sexes for both cholera cases and carriers, is shown in Figures 3 and 4.

The standard error of the difference for the data in Table I is 4.5 years, the difference between the mean ages of the cholera carriers and of the general population, Kedah, for both sexes being statistically not significant. However, the difference between the mean ages of the cholera cases and of the general population for both sexes is statistically highly significant, $p = 0.00003$.

Thus, it would appear that cholera cases were relatively more commonly reported in the older groups than the age distribution of the general population would suggest. On the other hand, the

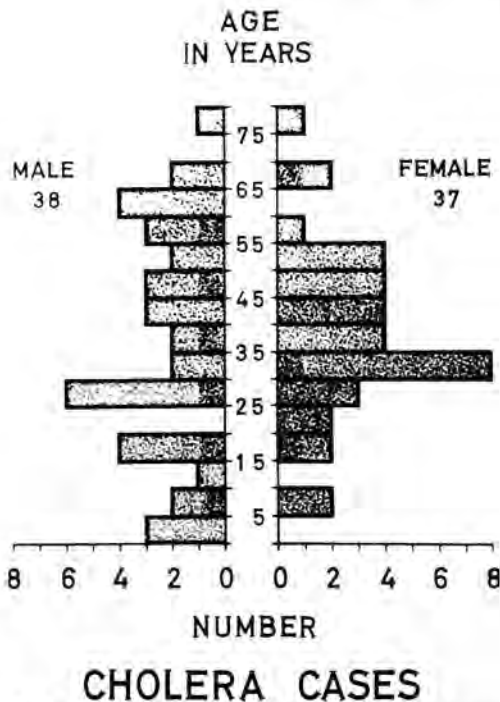


Fig. 3 Age distribution of cholera cases by five-year age intervals.

distribution of carriers followed that of the general population. This is similar to the findings in Taiwan (Yen, 1964). Dizon et al. (1965), studying an outbreak in the Philippines, noted that "the attack rate among those of 20 years of age and older was more than twice that of the population under 20 years of age. The noted higher attack rates is similar to past El Tor outbreaks in Sulawesi and is also characteristic of Asian cholera." Tamayo et al. (1965) suggested that there were factors, more common in adults, that predisposed to the manifestation or recognition of the disease. Further investigation is certainly indicated in this field.

TABLE I

Mean age in years of cholera cases, carriers, and the general population of Kedah by sex.

Group	Sex	Mean age in years
Cholera cases	Male	36.6
	Female	36.1
Cholera carriers	Male	18.5
	Female	18.5
Kedah population*	Male	17.7
	Female	17.3

*Census of 1957

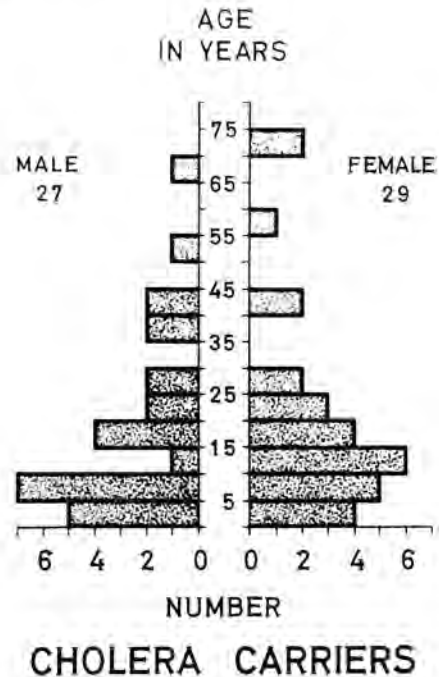


Fig. 4: Age distribution of cholera carriers by five-year age intervals.

3. Ratio of carriers to cases

When the carrier-case ratios are compared for various age groups as summarised in Table II, a very striking feature stands out, namely that although the overall ratio of carriers to cases for all age groups is approximately 0.7:1, the ratio is 3.5:1 for the age group 0-14 years and only 0.2:1 for the age group 45-79 years, indicating a preponderance of carriers over frank cases among subjects below the age of 15 years and a preponderance of frank cases over carriers in the higher age groups. Fairly similar findings were reported by Yen (1964) from Taiwan.

4. Household cases

The 75 cases were studied to determine the frequency of households with multiple recorded cases. Examination revealed that there were six households (9%) out of a total of 67 in which there were multiple cases. In four of these six households, the household cases occurred on the same date as the index case. In the remaining two households (3%), the secondary cases occurred later, namely five and seven days after their respective index cases.

The occurrence of the household cases on the same date as the relevant index case in the four households seems to suggest that household cases,

CHOLERA IN THE KEDAH RIVER AREA

TABLE II
Cholera carrier-cases ratios by age

Age-group (Years)	No. of carriers	No. of cases	Carrier-case ratio
0 - 14	28	8	3.5 : 1
15 - 24	13	8	1.6 : 1
25 - 44	10	32	0.3 : 1
45 - 79	5	27	0.2 : 1
TOTAL	56	75	0.7 : 1

and the index case for each of the households, showed a common source or a common contact. On the other hand, the remaining two household cases, occurring five and seven days after their respective index cases, would be consistent with a secondary spread from index case to household case. Nevertheless, what is apparent is that the majority of cases (91%) occurred as the only case in the household.

Dizon et al. (1965) found that 3.6% of households contained multiple cases. They also noted that this was characteristic of the El Tor outbreaks in Sulawesi and suggested that either the infection, once introduced into a community or household, did not spread easily or that infection caused significant disease on rare occasions only. Van de Linde and Forbes (1965) noted that "in Hongkong in three years, no direct household contact was established between two cases at any time. In fact, the occurrence of one case seemed like a talisman protecting the remainder of the household from disease."

5. Inoculation status

The inoculation status of cholera cases and of their household contacts, at the time of the reporting of each individual case, was investigated. The investigations included a rectal swab for culture of *Vibrio cholerae*, investigations into the inoculation status of all contacts, and the collection of other relevant epidemiological information. A total of 320 household contacts were thus investigated in the Kedah River area, of whom 56 were found to be carriers.

Inoculation status has been summarised into two categories, "valid" and "non-valid/nil". A "valid" inoculation, on the same basis as international requirements, is defined as one given six or more days but not longer than six months prior to the onset of symptoms in the cholera case in question or in the index case of that contact in question. A "non-valid/nil" inoculation, on the converse, is defined as one given within six days or longer than six months prior to the onset of symptoms in the cholera case in

question or in the index case of that contact in question, and includes the unvaccinated. The inoculation status of the 75 cases, 56 carriers and 264 negative contacts is summarised in Table III.

Comparison of the distribution of "valid" and "non-valid/nil" inoculations among the three groups of individuals by the chi-square test showed that there was no significant difference in the distribution among them ($p = \text{greater than } 0.1$). It would therefore appear that anti-cholera inoculation conferred little if any protection during the outbreak in the Kedah River area. The Philippines Cholera Committee (1968), carrying out a controlled field trial, noted that the cholera El Tor vaccine used conferred more than 50% protection for a period of at least six months against El Tor infection. Mosley et al. (1969) noted in their field trial in East Pakistan that "a single injection of cholera vaccine reduced the cholera case rate by 46% while the 2-injection schedule had an effectiveness of 64%". They also noted that "a significant level of protection was maintained for only about three months." In the Kedah River area, many different preparations from various sources were used.

ECOLOGICAL FACTORS

1. Pollution of the Kedah River

In the early stages of the outbreak, the whole of the Kedah River area was dotted with hundreds of overhung latrines. Typically, these consist of a simple makeshift arrangement of a few boards secured together as a squatting platform built upon piles driven into the shallows of the river or canal running past the house, the structure being discreetly located among bushes or surrounded by some cover to provide some degree of privacy. A photograph of an example is shown in Figure 5. Not only did these overhung latrines abound in the remoter areas, but several existed within the Alor Star Town Council area.

A second method of excreta disposal fairly common in the Kedah River area is indiscriminate depositing on to soil around nearby bushes - soil which often drains into adjacent streams, canals or padi-fields. A few pit-latrines existed in the area. Many more were added as a result of the cholera control programme.

During the period March 8 to April 5, 1964, a total of 30 samples of raw river water were obtained and cultured for the cholera vibrio. Twenty-one of these samples were taken from the headworks of the Bukit Pinang Water Works while the remaining nine

TABLE III
Inoculation status of cholera cases, carriers and negative contacts

Group	Inoculation status				Total
	"valid"		"non-valid/Nil"		
	NO.	%	No.	%	
Cases	30	40.0	45	60.0	75
Carriers	21	37.5	35	62.5	56
Negative contacts	131	49.6	133	50.4	264
TOTAL	182	46.1	213	53.9	395

samples were taken from other stretches of the Kedah River. Only one sample, taken at low tide on March 8 at Limbong in area "C", yielded a positive culture of *Vibrio cholerae* (Ogawa type). The position of this site is shown on Map 2 as a spot within a circle.

The Institute for Medical Research (1915) observed that "cholera vibrios inoculated into water drawn from the river at Alor Star could be recovered from it as long as 80 days thereafter and that . . . similar numbers of cholera vibrios inoculated into

similar quantities of Kuala Lumpur tap water were dead in less than 24 hours in nearly every case." It was suggested that this was due to the inorganic salt content rather than to the organic content of the waters.

2. Rainfall

The onset of the cholera outbreak coincided with the beginning of the dry season and was at its height during the driest month of the season, February



Fig. 5: In the foreground is an overhung latrine, while in the background can be seen a house surrounded by fruit trees.

CHOLERA IN THE KEDAH RIVER AREA

1964. This relationship between the outbreak and rainfall is summarised in Figure 6 where the monthly incidence of cholera cases is plotted along with the monthly rainfall as recorded at the meteorological station at Kepala Batas Airport, Alor Star. The dry season of January, February and March 1964 was a particularly dry one. The average monthly rainfall during those three months for that year was much lower than during corresponding months for the previous years of 1961, 1962 and 1963, as shown in Table IV. During this particularly severe season, many wells that usually survived the dry season were affected.

3. Water supplies

The people of the Kedah River area obtain their water supplies from three main sources, namely tap water, well water and river.

(a) Tap Water Supplies

The main source of tap water is from the Bukit Pinang Water Works. The Sungei Besar tributary of the Kedah River is tapped at Bukit Pinang, filtered, chlorinated and stored at two reservoirs from which the supply is distributed mainly to area "B", the town of Kuala Kedah at the mouth of the Kedah River, and along the trunk road south. In area "B", a total of 57 standpipes and a large number of individual house connections existed at the time of the outbreak. A second source of tap water is from the Bukit Wang Water Works. Water is tapped from a catchment area in Kubang Pasu District and the only form of treatment rendered is chlorination. Apart from supplying those living in Kubang Pasu District, a main flows along into area "A", in which a total of 26 standpipes existed at the outset of the outbreak. Few individual house connections existed then.

(b) Well water

A number of unprotected earth wells exist in the area, especially in areas "A" and "C". A few semi-protected wells, constructed under the Rural Development programme, also exist. However, as the dry season in early 1964 was a particularly severe one, most of the wells dried up and were of little use.

(c) River water

Except for area "B" where tap water is readily available to most people, river water formed the main source of water for bathing, cooking, drinking and personal ablution for most of the people, as was indicated by the investigations. Although there was a water main from the Bukit Wang Water Works

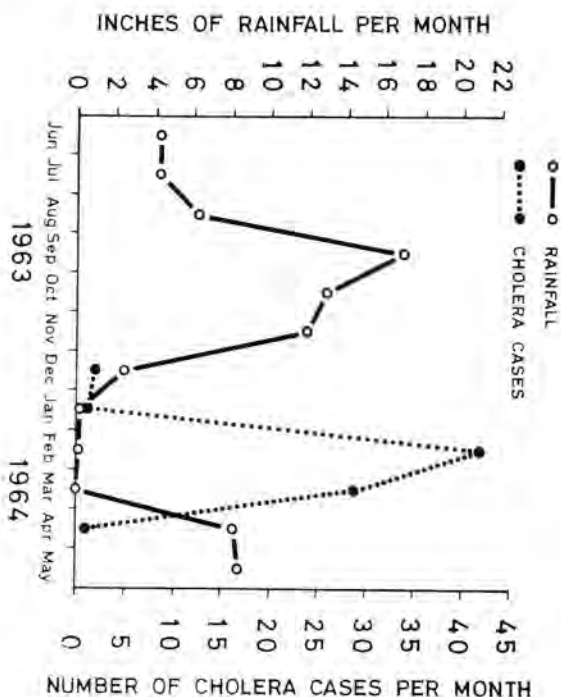


Fig. 6: The incidence of cholera cases in relation to rainfall.

TABLE IV
Average monthly rainfall for the years
1961 - 63 and 1964

Month	Average monthly rainfall (in inches)	
	1961 - 63	1964
January	1.37	0.14
February	1.01	0.11
March	3.81	0.03

running into area "A", few houses had connections since the cost of connection was beyond the means of the majority. In area "C", no water main existed. Further, due to the unusually dry period, the majority of wells dried up. Thus, during the initial part of the dry season, the majority of the people in both areas "A" and "C" were using the river as a source of water. One of the control measures, and probably the most important one, was the provision of potable water to the affected areas. The villagers were warned that the rivers and canals were polluted and dangerous. Approximately 90 standpipes were installed along existing water mains during February and March. In addition, a temporary water main was

brought across the Kedah River to Seberang Nonya, where six cholera cases and seven carriers were reported. In early March, water was supplied by lorries and boats to various affected areas. Approximately one million gallons of water each day was supplied in this manner to these areas, during that period.

It should be pointed out that the tides affected the Kedah River and its effects could be felt several miles upstream, particularly since the water level in the river had dropped unusually low as a result of the severe drought. As a result the river water was used mainly when the tide was low and the salinity at its lowest. Nevertheless, the water remained palatable along most tributaries of the Kedah River. However, where salinity remained high, particularly towards the mouth of the river at Kuala Kedah, the water was not used.

4. The distribution of cholera cases and the salinity of the Kedah River

The salinity of the river water was tested at 15 different sites along the Kedah River and its related irrigation canals. A total of 85 samples, taken at these various points between March 2 and 11, were sent to the Department of Chemistry in Penang for analysis. Salinity values were reported in terms of parts of thousand (o/oo) values below 0.1 o/oo being reported as "insignificant." The 15 sites at which the

samples were drawn are marked in Map 2. Those with salinity values of 0.1 o/oo or more at any time are marked with black squares, while those where salinity was consistently "insignificant" are marked as white squares. The results of the salinity tests are summarised in Table V and in Map 2.

Read et al. (1939) established, in the course of their investigations, that "in the absence of salt, multiplication did not occur in any peptone concentration and in no case did survival reach 24 hours." They also noted that multiplication of *Vibrio cholerae* was observed in the case of 1/500 peptone water at a salt concentration as low as 0.075 o/oo.

It will be noted that, with the exception of six cases occurring in the Gunong and the related irrigation canal areas and one occurring in the Pendang area, all other cases, totalling 68, occurred in proximity to areas of the Kedah River where salinity exceeded 0.1 o/oo. Further, it should be noted that the Gunong and related irrigation canal areas have a population excess of that for the remaining parts of area "A". Where salinity was sufficiently high to make the river water unpalatable, as at Kuala Kedah, no cholera cases were reported.

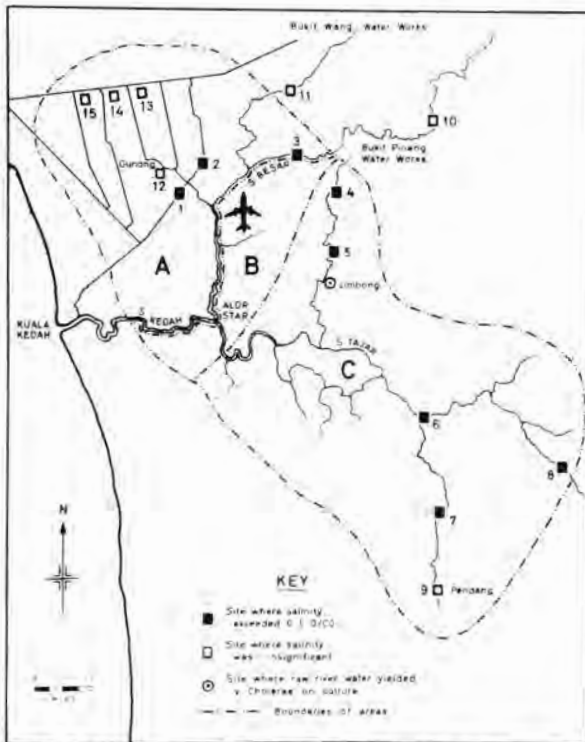
DISCUSSION

It would appear that in the initial phase of the cholera outbreak during the months of December and January in which three cases and one carrier were

TABLE V
Salinity of water samples taken from
15 sites in the Kedah River area
between March 2 and 11, 1964

Site Number	Site of Sampling	Number of samples	Range of salinity in parts per thousand
1	Sg. Baru Bridge	10	1.83 to 24.17
2	Sg. Baru A. Melintang	10	1.83 to 24.13
3	Kepala Batas Bridge	10	0.21 to 5.32
4	Sg. Langgar, Masjid Lama	5	1.41 to 1.63
5	Sg. Langgar Bridge	10	1.41 to 2.10
6	Titi Haji Idris	3	1.82 to 1.97
7	Pekan Tanah Merah	10	0.15 to 1.82
8	Kg. Paya Rawa, Sg. Rambai	5	Insignificant to 0.26
9	Pendang	5	Insignificant
10	Kg. Lubok Batu	4	Insignificant
11	Sg. Tg. Pauh, Kg. Chegar	5	Insignificant
12	Gunong Keriang	2	Insignificant
13)			
14)	Jalan Sanglang,	6	Insignificant
15)	Canals 1, 2 and 3		
Total Number of Samples		85	

CHOLERA IN THE KEDAH RIVER AREA



MAP 2: Comparison of this map with Map 1 shows that the majority of cases occurred in areas of high salinity, from which also was obtained the only sample positive for *Vibrio cholerae*.

reported, the infection was carrier-borne. The three cases were separated in time by 18 and 32 days from one another. They occurred during the early phase of the dry season and in an area with "insignificant" salinity. On the other hand, the subsequent phase was characterised by the massiveness and speed associated with a common source of infection, such as a polluted communal water supply. With the exception of the last two cases, occurring on March 27 and April 8, the interval between cases was very short and in no case longer than five days. The peak of the outbreak in areas "A" and "B" occurred 11 days after the onset of the massive phase of the outbreak, while that in area "C" occurred ten days after the first case occurred in this area.

It appears that it was a combination of many factors that led to the massive phase of the outbreak. They may be classified into two groups — the predisposing factors and the precipitating factors.

(a) Predisposing Factors:

Chief among these was the excremental pollution of the rivers via overhung latrines. The second predisposing factor was the use of river water for

drinking, unboiled, by people who were not aware of the danger involved.

(b) Precipitating Factors:

Primarily there was the importation of cholera vibrios from Perlis by a human carrier into the Kedah River area. The second precipitating factor was the pollution of the river water by a carrier and/or frank case during the period of the drought as borne out by the recovery of cholera vibrios therefrom. The presence of the drought itself was the third and final determinant which further aggravated and perpetuated the second in the following manner. Firstly, the drought dried up a great many wells which led to the more frequent use of river water for domestic purposes. Secondly, the drought diminished the volume and flow of the river leading to a greater concentration of vibrios, and to their longer life on account of increased river water salinity. The increase of river water salinity was due to the lowering of the level of outgoing freshwater flow, so that the incoming tidal flow was greater in volume and ascended to higher reaches. Nevertheless, the degree of salinity was not enough to make the water undrinkable in the populated areas above Kuala Kedah.

The waterborne aetiology of the massive phase of the outbreak is proved by the following features. Firstly, the geographical distribution of the cases, which were most numerous in the areas where river water was most used. Secondly, the decline of the outbreak as soon as piped water was supplied, either through pipes or by lorries, as for example in area "A" where the outbreak rapidly declined upon the provision of standpipes linked to the existing water mains. Likewise, as soon as potable water was ferried into the affected regions of area "C" via water trucks and water boats, the outbreak in this region declined. Thirdly, the waterborne aetiology is proved by the decline of the outbreak when the drought ended. The occurrence of the outbreak during the dry season in Kedah is in contrast to the findings of Macnamara (1876) that "cholera is at its height . . . every year in March and April and again in September and October, and these are the very months in which we get heavy downpours of rain, washing the surface soil and its contents into wells and tanks from which we procure our drinking water." On the other hand, Pollitzer (1959) noted that "cholera manifestations, if they arise after or during periods of exceptional drought, often become particularly dangerous . . . at such times, the people are forced to make use of the scanty water supplies remaining available, however unsuitable or even repulsive they may be."

Other possible sources of the massive phase of the outbreak could have been the piped water, which would surely have produced many more cases; or one or more polluted wells, when there would have been a higher incidence of cases in families using the wells; or carriers at a focal point such as a restaurant, in which event, the distribution of cases would have been less extensive than it was. It would thus appear that the river was undoubtedly the source of the massive phase of the outbreak. Nevertheless, it could not have been heavily polluted, otherwise there would have been many more cases, and this is borne out by the recovery of vibrios from only one out of the nine samples taken from likely areas of the river.

SUMMARY

The cholera outbreak in the Kedah River area of West Malaysia between December 1963 and April 1964 involved 75 cases and 56 carriers. It appears that the outbreak had two phases, an initial carrier-borne phase and a later massive waterborne phase. The massive water-borne phase itself may be distinguished into the component affecting areas "A" and "B", and that affecting area "C". The spread was from area "A" downstream to "B", and thence to area "C".

Of the 75 cases and 56 carriers reported, no significant difference was found in the distribution between the two sexes. However, it was noted that the mean age of cases for both sexes (males 36.6 years and females 36.1 years) differed significantly from that of the general population of Kedah (males 17.7 years and females 17.3 years). On the other hand, the mean age of carriers for both sexes (males 18.5 years and females 18.5 years) did not differ significantly from that for the general population of Kedah. The ratio of carriers to cases for the age group 0-14 years is 3.5:1 and that for the age group 45-79 years 0.2:1, indicating a preponderance of carriers over frank cases among subjects below the age of 15 years, and a preponderance of frank cases over carriers in the higher age groups.

Analysis of households for multiple cases showed that only six (9%) out of the total of 67 households had multiple cases. This feature of a preponderance of single cases in households has also been noted in similar outbreaks in the Philippines, Hongkong and Sulawesi.

Comparison of the distribution of "valid" and "non-valid/nil" anti-cholera inoculations among the frank cases, carriers and negative contacts, showed no significant difference and suggests that inoculations

conferred little if any protection during the outbreak in the Kedah River area.

The aetiological factors of the massive phase of this outbreak include the predisposing factors, namely, river pollution by human excreta via overhung latrines and the use of this river water for drinking, unboiled, by people not aware of the danger involved. The precipitating factors include first the importation of cholera vibrios by a carrier from the neighbouring state of Perlis, and second the pollution of river water in the Kedah River area during a drought which diminished the volume of river water, increased the volume of incoming tidal water and thus increased the salinity of the estuaries in the area of the outbreak.

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Ventricular septal defect — autopsy study of 46 cases

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THERE WERE 46 autopsy cases of ventricular septal defect collected from the Paediatric Department, University of Singapore, over a period of three-and-a-half years, from January 1964 to June 1967.

Mortality Rate:

There is a high mortality in infants with large ventricular septal defect and the age distribution of death is as shown in Figure 1.

There are 22 males and 24 females showing no sex bias. The number of cases that died before the age of six months is 33 (72.0%) and before the age of one year, 40 (87.0%). Therefore, the mortality in ventricular septal defect is highest during infancy.

Muir's series of 95 cases (1960)¹ showed that 54 were males and 40 females, one with no sex stated. In this series, 23% died under the age of one month, compared with the present series of 22%; and 62% between one month and one year, compared with the present series of 65% as shown in Table IV.

There is a remarkable uniformity in these two series collected in the same hospital although the

Age Distribution of 46 Deaths due to VSD Confirmed by Autopsy Jan. 1964-June 1967.
(Paediatric Unit West)

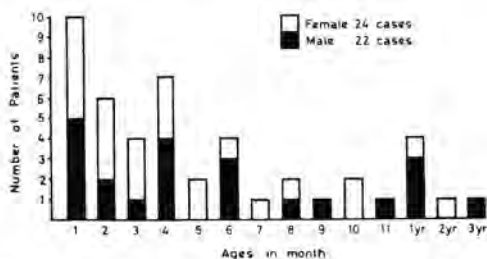


Figure 1 shows death due to ventricular septal defect at various ages. The black area denotes male and the blank female.

present series was collected ten years later. This reflects the fact that there has not been any change in the method of management as the incidence of death has remained the same for the last 20 years.

The ages of four cases listed at one year old were one year six weeks, one year two months, one year, and one year two months respectively, giving the

	Muir, 1948-57	Dept. of Paediatrics, University of S'pore (1964 - mid 1967)
V.S.D.	95	46
Male	54	22
Female	40	24
Death under 1/12	22 (23%)	10 (22%)
Death between 1 month & 1 year	59 (62%)	30 (65%)

Table IV shows the comparison of the two series of ventricular septal defect confirmed by autopsy.

total of 40 cases dying before the age of 14 months. 87% of the total mortality occurs before the age of 14 months. It would appear that the first 14 months of life are the most critical period for patients with ventricular septal defect. Engle (1954)² and Edward (1954)³ have produced evidence that the most critical period of life in ventricular septal defect is the first 18 months. Keith⁴, in reviewing 92 cases from the literature plus 19 of his own series, found that 34% died before the age of one year. Nagayama (1965)¹¹ collected reliable statistical data from the Japanese Pathological Association, showing a mortality rate of 59% in infants with V.S.D. The higher mortality rate in Singapore may be a reflection on the standard of care and availability of surgical treatment.

Size of Defect

In post-mortem patients, the pathologist measured all defects, the distribution of which is as shown in Table V.

More than 1.0 cm in diameter	= 13 cases
Between 0.5 cm to 1.0 cm in diameter	= 26 cases
Less than 0.5 cm in diameter	= 7 cases

Table V shows the size of ventricular septal defect measured by the pathologist.

Selzer (1949)⁵ reviewed the literature in ventricular septal defect and emphasised that size of the defect rather than the site is the major determinant of haemodynamic status. Becu (1956)⁶, from a similar survey of 50 patients, shared Selzer's opinion on the relative importance of the size of the defect. If the defect is less than 1.0 cm in diameter (or less than half the diameter of its aorta), the magnitude of left-to-right shunt is from small to moderate. If the defect is larger than 1.0 cm in diameter (or greater than half the diameter of its aorta), pressures in the two ventricles are virtually equal (Gorlin 1952)⁷.

The size of the shunt is determined by the relative peripheral resistance in the pulmonary and systemic circuits. Left-to-right shunt predominates if the pulmonary vascular resistance is low. Bidirectional shunt or even right-to-left shunt as found in Eisenmenger - V.S.D. occurs if the pulmonary vascular resistance is equal or greater than systemic. It should be emphasised that the size of the defect should not be considered alone; it should have relation to the age of the patient and the size of the heart. For example, a defect of 0.5 cm diameter, which is considered small for an adult patient, is tremendously large for a small infant. Selzer (1954)⁸ suggested that the size of the defect should be compared with the diameter of its aorta to be of significance. This has been generally accepted, especially in measuring the defect in open heart repair.

Unfortunately, in the present series of 46 cases, no measurement of the size of the aorta was made at autopsy. The criticism in post-mortem measurement in general is the slight underestimation of the size of the defect compared with that in vivo because of the contracted state of the specimen after death. Be this as it may, a defect more than 0.5 cm in diameter is considered large in the present study because 37 (80%) of them were below the age of one year. Therefore, 39 cases (85%) had defects measuring more than 0.5 cm in diameter.

All the defects were of the membranous type situated posteroinferior to the crista supraventricularis involving the outflow portion of the ventricular septum. This is the commonest site of involvement and it occurred in 80% of Becu's series (1965)⁶. Ward (1957)⁹ reported the incidence of 85% in their 84 operated cases. However, the site of the defect is the least important compared with other factors, such as the size of the defect, the pulmonary vascular resistance and the associated lesions. (Veasy 1960).¹⁰

VENTRICULAR SEPTAL DEFECT

Chest Roentgenology

The importance of chest X-ray investigation in small infants with ventricular septal defect cannot be over-emphasised. The cardiac lesion in more than half (26 cases) of this autopsy series was only suspected after chest X-ray was done because cardiac murmur was not apparent on admission. This could probably be due to tachycardia and cardiac failure with balanced pressures in both ventricles, as in most of them, cardiac murmur appeared a few days after treatment.

It is almost impossible to assess cardiac enlargement clinically in small infants and one has to rely on chest X-ray appearance. Unfortunately, not all chest X-rays were done on full inspiration which requires full co-operation of the patient. Therefore, the apparent size on measurement may not reflect the true heart size.

The cardio-thoracic ratio from a plain chest X-ray is used as an index of heart size the distribution of which is as shown in Table VI.

Cardio-thoracic Ratio	Heart Enlargement	No. of cases
More than 0.60	Severe	20
0.55 - 0.60	Moderate	18
Less than 0.55	Slight	5
No chest X-ray	—	3

Table VI shows the assessment of cardiac enlargement from the cardio-thoracic ratio in a plain chest X-ray

Thirty-eight cases (83%) had roentgenographic cardiac enlargement ranging from moderate to severe. The degree of plethora was difficult to assess because of added pulmonary consolidation as all the patients were admitted with chest infections. It was equally difficult to differentiate which chamber was enlarged. The roots of the great vessels were not well shown in the majority of chest X-rays because of prominent thymic shadow.

Electrocardiography

Not all the patients had electrocardiograms done because cardiac lesions were not suspected in some of them. Electrocardiograms were done in 31 patients and analysis shows that 17 patients (55%) had a mean QRS axis of more than $+90^\circ$ as illustrated in Figure 2.

The diagnosis of ventricular hypertrophy is based on the criteria laid down by Sodi-Pallares and associates (1958)¹² and Guntheroth (1965).¹³ The distribution of various ventricular hypertrophies is as shown in Table VII.

All the electrocardiograms were abnormal for the respective ages except one. Isolated right ventricular

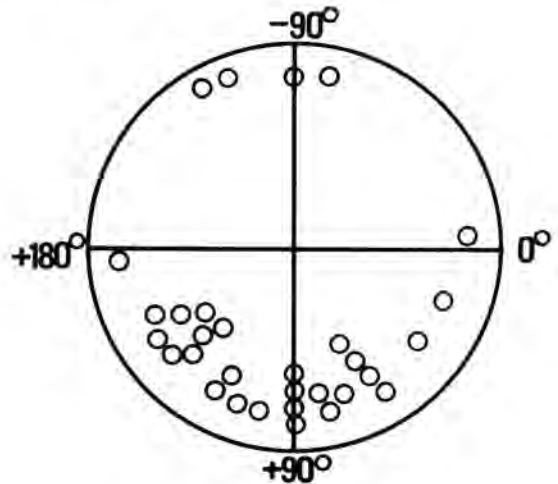


Figure 2 shows the distribution of the mean electrical QRS axis in electrocardiograms done on 31 patients who died of ventricular septal defect.

Normal	LVH	LVH + RVH	RVH
1	6 (19%)	9 (29%)	15 (48%)

Table VII shows the numbers of various ventricular hypertrophies

overload pattern occurred in 15 cases (48%), left ventricular hypertrophy alone in nine cases (19%) and combined ventricular hypertrophy in nine cases (29%). Eighteen cases had an upright T wave in right precordial leads (V_4R and V_1) which was abnormal for the age and is characteristic of severe right ventricular hypertrophy. The deep q wave of more than 4mm and tall T wave in left precordial leads (V_5 and V_6) denoting left ventricular diastolic overload pattern were only present in four cases. Therefore, electrocardiogram obtained in this series was abnormal in 96% of the cases.

Mongolism	10
Edward trisomy	4
Cleft palate	3
PDA (probed)	6
ASD (small)	3
Twins	2
Endocardial Fibroelastosis	1
Congenital Laryngeal stenosis	1
Hydrourerter	1
Intersex	1
Microcephaly	1

Table VIII shows a list of various malformations associated with ventricular septal defects with autopsy.

Associated Malformations

In this series of 46 autopsy cases of ventricular septal defect, there was a high incidence of associated malformations. The different types of abnormalities are listed as shown in Table VIII.

The presence of associated abnormalities plays an important part in contributing to the high mortality rate. Chromosomal anomalies like Mongolism and Edward trisomy were associated in 14 cases (30%) and these anomalies are noted for their high mortality in infancy and early childhood.

Summary

Forty-six cases of ventricular septal defect confirmed by autopsy are analysed and discussed in some detail. The high mortality rate seems to be confined to the first 14 months of life. Most of these cases have large defects measured at autopsy. Chest roentgenology and electrocardiography further confirm the severity of the lesions. Associated malformations are common and they play an important role in contributing to the high mortality rate.

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Leptospirosis in rural West Malaysia

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(Lecture given at the Seminar of the Malaysian Society of Parasitology & Tropical Medicine on 24th January, 1970.)

LEPTOSPIROSIS is one of the most important zoonotic diseases known to man. The main reservoir host is the rodent species although some serotypes are most commonly found in dogs, pigs or cattle. A high incidence of this disease may therefore be expected among the rural population and people who frequent areas likely to be contaminated with infected animal urine.

In West Malaysia, a serological survey of 4,819 afebrile individuals throughout the country, during the period of September 1960 to December 1961, revealed an overall antibody prevalence ratio of 11.8%. The test employed was the Sensitized-Erythrocyte-Lysis (SEL) test described by Chang et al. (1957) and recently evaluated as an epidemiology tool for human leptospirosis serological surveys (Tan, 1969). Among the localities surveyed were seven types of rural areas comprising one oil palm estate in Bukit Jelutong, Selangor; five rubber estates in various parts of W. Malaysia, five rice fields in Kelantan, one forest village in Ulu Langat, Selangor; one tin-mining village in Sungai Lembing, Pahang; and

scattered farms and aborigine settlements.

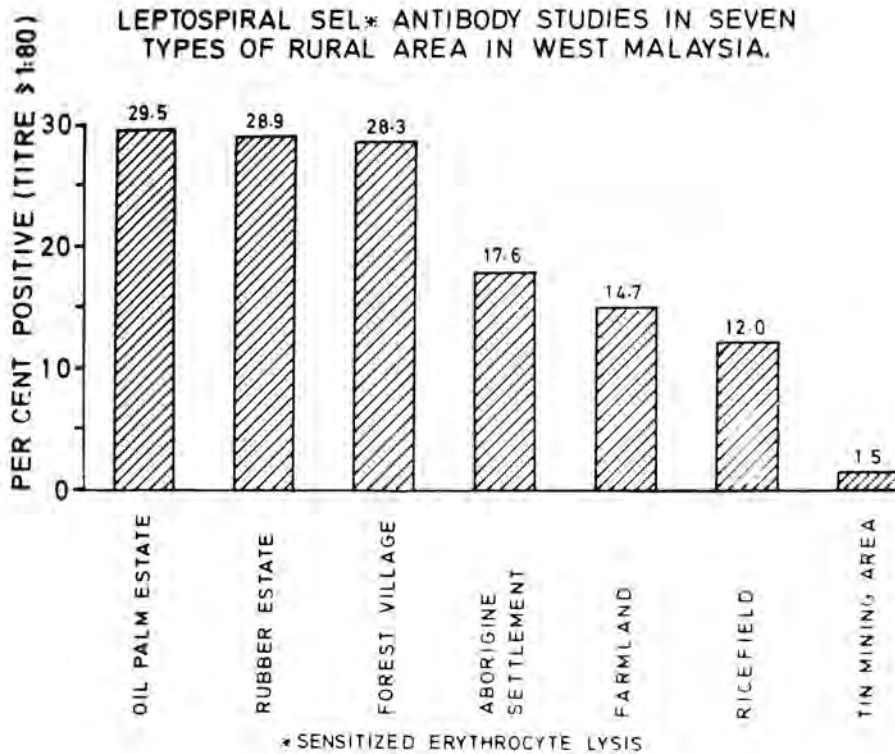
A ten-year clinical appraisal of leptospirosis in W. Malaysia was also carried out, the full results of which will be published elsewhere (Tan, in press)

RESULTS

Serological Survey

The following figure summarises the results of the serological survey in rural areas of W. Malaysia:

The highest incidence of leptospirosis was found in oil palm workers (29.5% or 18/61), rubber estate workers (28.9% or 4/221) and the Ulu Langat forest residents (28.3% or 17/60). The aborigines (most of whom have been re-settled in villages along forest fringes) with 17.6% or 27/153, farmers with 14.7% or 30/204 and padi planters in Kelantan with 12.0% or 31/259 form the second most highly infected group. Villagers living and working in the tin-mining area of Sg. Lembing, Pahang showed a very low incidence of 1.5% or 2/136. The total number of rural residents examined was 1,154 out of which 189 (16.4%) were found positive.



Tables 1 and 2 give the detailed results of the survey on the five rubber estates and the five Kelantan ricefields, respectively.

A very distinct and significant difference in the antibody prevalence ratios between the first three estates (42.6% – 45.9%) and the last two estates (0% – 3.3%) listed in Table 1 may be observed. On the other hand, the five Kelantan ricefields yielded less contrasting individual results (Table 2).

By comparison, Table 3 shows leptospiral antibody ratios in the main state capitals of West Malaysia, which, of course, represent the urban setting of the country. A total of 2,388 town residents was examined of which 134 (5.6%) were positive. The ratios ranged between 0% in Johore Bahru to 12% in Georgetown, Penang.

Clinical appraisal

Out of 1,993 suspected cases of leptospirosis, 559 (28%) were confirmed positive. The highest number of cases occurred among males, 20 – 40 years old, and of the three main racial groups, Malay,

Chinese and Indian, the Indian community was most frequently affected, based on estimated population. This finding bore a direct relationship to the distribution of cases by occupation, where the general labourers (they deal with sewage, drainage, forestry, town-cleaning or anti-malarial work.) and rubber estate workers, who are mainly of Indian origin, headed the list in the order of case frequency (Table 4).

Padi planters, tin miners, farmers and veterinary workers were comparatively free of clinical leptospirosis. Similarly, the number of clinical cases in aborigines was so small that it had to be included with the "other races" in the distribution by racial group (Tan, in press). The oil palm estate worker has, apparently, also escaped the severe effects of leptospirosis.

DISCUSSION

The very high incidence of leptospirosis in the oil palm estate workers and forest residents may be attributed to the fact that rats, the main reservoir

LEPTOSPIROSIS IN RURAL WEST MALAYSIA

TABLE 1

LEPTOSPIRAL SEL + ANTIBODY STUDIES IN
FIVE RUBBER STATES IN W. MALAYSIA

LOCALITY	STATE	No. EXAMINED	POSITIVE	PER CENT
GUA MUSANG	KELANTAN	37	17	45.9
PUCHONG	SELANGOR	50	22	44.0
TANGKAK	JOHORE	54	23	42.6
SUNGEI CHOH	SELANGOR	60	2	3.3
BATU TIGA	SELANGOR	80	0	0
TOTAL		281	64	22.8

+ SENSITIZED ERYTHROCYTE LYSIS

TABLE 2

LEPTOSPIRAL SEL + ANTIBODY STUDIES IN
FIVE RICEFIELDS IN KELANTAN,
W. MALAYSIA.

Locality	No. Examined	Positive	Per cent
Pasir Puteh	51	10	19.6
Pasir Mas	53	7	13.2
Tanah Merah	49	6	12.2
Bachok	53	4	7.5
Tumpat	53	4	7.5
TOTAL	259	31	12.0

+ SENSITIZED ERYTHROCYTE LYSIS

TABLE 3

LEPTOSPIROSIS – SEROLOGICAL SURVEY OF STATE
CAPITALS (URBAN) IN W. MALAYSIA.

Capital	State	No. Examined	Positive	Per cent
Georgetown	Penang	224	27	12.0
Seremban	Negri Sembilan	277	20	7.2
Kuantan	Pahang	45	3	6.6
Kuala Lumpur	Selangor	527	33	6.3
Malacca Town	Malacca	398	19	4.8
Butterworth	Province Wellesley	320	14	4.4
Alor Star	Kedah	94	4	4.3
Kota Bharu	Kelantan	199	8	4.0
Ipoh	Perak	35	1	2.8
Kuala Trengganu	Trengganu	203	5	2.5
Johore Bharu	Johore	66	0	0
TOTAL		2,388	134	5.6

TABLE 4

**DISTRIBUTION OF 559 CASES OF LEPTOSPIROSIS
ACCORDING TO OCCUPATION
(1958 - 1968)**

Occupation	No. of cases	Per cent of total positive
General labourers	94	16.8
Rubber estate workers	53	9.5
School children	37	6.6
Army personnel (mainly Caucasian)	28	5.0
Housewives	23	4.1
Police	16	2.9
Business	12	2.2
Padi Planters	8	1.4
Tin miners	7	1.2
Office workers	7	1.2
Farmers	7	1.2
Field research workers	6	1.1
Medical	6	1.1
Veterinary workers	1	0.2
Miscellaneous	2	0.4
Total	307	54.9
Unknown/Unemployed	252	45.1
Grand total	559	100.0

host, abound in the areas in which these people live and work. The main rat species in oil palm estates is the *R. jalorensis* rat which is normally arboreal in habitat. However, being strongly attracted to the oil palm fruit, they are very numerous not only on tree tops but also at ground level when the fruit is cut down and stored. Although the incidence of leptospirosis in this rat species was found to be only 3% (Smith et al., 1961), their sheer abundance in numbers in these estates more than facilitates transmission of leptospirosis to the workers, the majority of whom live, as well as work there.

In the forest areas, the predominant rodent species are the three forest giant rats, *R. bowersi*, *R. mulleri* and *R. sabanus*, in which the overall incidence of leptospirosis was found to be 17%. These are ground rats and are numerous especially where man has made his settlement. Transmission of leptospirosis to the forest residents is therefore very feasible.

The five rubber estates examined showed very high antibody ratios in three of them and very low in the remaining two (Table 1). Here, the main rat species is also *R. jalorensis* but unlike the conditions in the oil palm estates, these tree rats are not

attracted to ground level by the products of the rubber tree in the same way as they are by the oil palm fruit and are therefore not expected to be an important source of leptospirosis to the rubber estate workers. The extremely high infection rates found in the above-mentioned three estates must therefore be attributed to factors other than those directly related to the rubber industry.

Many rubber estates, especially the small ones, are closely adjacent to forest areas and are likely to be invaded by the highly-infected rats from them. Most of the workers, in the course of their daily duties, trudge through the estate bare-footed. After a period of rainfall, the water on the ground, if previously contaminated with infected rat urine, may well serve as an effective vehicle for the transmission of leptospirosis through the worker's feet, the skin of which is often far from intact. This situation is, in fact, true of the three estates which showed high antibody prevalence ratios. Secondary forests are, indeed, situated near or around these estates, whereas the last two estates, with extremely low antibody ratios, stretch for miles across the country with hardly a secondary forest in sight.

LEPTOSPIROSIS IN RURAL WEST MALAYSIA

Another possible means of infection is through infected house rats, *R. r. diardi* (incidence: 3%) or *R. norvegicus* (incidence: 34%). In addition, the scrub or grassland rat, *R. exulans* (incidence: 7%) commonly enters homes from its normal habitat. The homes of the estate workers, situated in the estates themselves, are usually in the form of "labour lines" which consists of about 10 – 12 small brick housing units attached to one another to form a "line". These units are often overcrowded and it would be surprising if one does not find most of them infested with commensal rats. Infection in this case is by contact with food and utensils contaminated with rat urine.

The aborigines, originally from the jungles of West Malaysia, are gradually being re-settled in farms and villagers. Their leptospiral antibody ratio (17.6%) did not vary much from those of farmers (14.7%) and padi planters (12%). The tin-mining village sampled was conspicuously low in incidence (1.5%) which supports Baker's unpublished findings that most mining pools in West Malaysia were very infrequently contaminated with leptospires, especially during the dry seasons.

The presence of specific antibody against a disease in an individual merely indicates that he has been previously infected by that particular disease. Whether the outcome of the infection is a latent, mild or severe disease depends mainly on the level of acquired immunity, the virulence and dose of the infecting organism.

In West Malaysia, the number of clinical cases severe enough to be hospitalised, (and eventually laboratory-confirmed as leptospirosis) has been small

compared to the number of infected persons, detected by antibody surveys. SEL antibodies are acquired as early as four to six years of age, especially by children in rural areas. As these antibodies have been found to last for about two years only (Tan, 1969) the persistence of antibody prevalence ratios throughout the older age-groups at much the same levels indicates constant re-infection throughout life even up to 60 years and above (Table 5). This pattern confirms the endemicity of leptospirosis in this country and supports the observation that no severe epidemics of leptospirosis have been experienced in West Malaysia so far.

Frank clinical leptospirosis was uncommonly encountered among the oil palm estate workers, aborigines, forest residents, padi planters and tin miners (Table 4). It is possible, of course, that most of the clinical cases were mild and often did not require medical treatment, much less hospitalisation. In those groups with antibodies, acquired immunity due to constant exposure to infection might account for the relatively small number of clinical cases, whereas in the case of the tin miners this was presumably due to comparatively infrequent or low degree of exposure to the disease.

Although the rodent host species most frequently found in ricefields, viz. *R. argentiventer*, had a high leptospiral (*L. javanica*) excretion rate (Smith et al., 1961) and contamination of the ricefields was expected to be serious; when the inlet and outlet water of a ricefield was checked for leptospires during a 5½-month period of observation, the outlet water yielded only half the number of isolates as the inlet water

TABLE 5

LEPTOSPINAL SEL + ANTIBODY RATIOS IN DIFFERENT AGE GROUPS

Age groups	No. Examined	Positive	Per cent
0 – 10	193	19	9.8
11 – 20	781	99	12.7
21 – 30	1,571	191	12.2
31 – 40	1,080	111	10.3
41 – 50	673	90	13.4
51 – 60	331	42	12.7
60 or more	190	16	8.4
Total	4,819	568	11.8

+ SENSITIZED ERYTHROCYTE LYSIS

(Baker, unpublished findings). Analysis of water and soil samples taken from the Kelantan ricefields by the author showed very low pH values in both (mean pH of water: 5.9; mean pH of soil: 5.2) and *L. javanica* survives for very short periods below pH 6.0. Moreover, the soil types were reported by the Malaysian Department of Agriculture to include sandy loam, montmorillonite clay loam and peat and Smith & Turner (1961) have disclosed that leptospire were readily absorbed by bentonite clay which is similar to the montmorillonite clay of the ricefields. The small number of clinical cases among the padi planters may therefore be attributed not only to acquired immunity from constant exposure to leptospirosis but also to reduced virulence and dose of the leptospire due to the unfavourable growth conditions for the leptospire in the ricefields.

Why rubber estate workers are so highly susceptible to clinical leptospirosis is not clearly understood. Since those with very high antibody ratios are expected to be immune from the ill effects of leptospirosis, the workers who fall ill and land in hospital are presumably from estates which are normally "leptospirosis-free" and therefore have had no opportunity to develop immunity from constant exposure. An incidental infection through contact with infected rats from nearby forest or through swimming in contaminated forest streams which happen to flow past the estates can, therefore, cause illness in the non-immune victim. In order to substantiate this theory, it is necessary (1) to carry out more surveys to verify the existence of "leptospirosis-free" rubber estates, and (2) to show that the majority of susceptible rubber estate workers do actually come from such estates, if any.

SUMMARY

A serological survey for leptospiral antibodies employing the Sensitized-Erythrocyte-Lysis (SEL) test was performed in West Malaysia during the

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period of September 1960 to December 1961. Of 4,819 afebrile individuals studied, 11.8% were positive. Among the localities surveyed were seven types of rural areas, comprising one oil palm estate in Selangor, five rubber estates in various parts of West Malaysia, five ricefields in Kelantan, one forest village in Selangor, one tin-mining village in Pahang and scattered farms and aborigine settlements.

The highest incidence of leptospirosis was found in oil palm estate workers, rubber estate workers and in forest residents (28.3% to 29.5%). The aborigines, farmers and padi planters had moderately high antibody ratios (12% to 17.6%) while the villagers in the tin-mining area showed a very low incidence of 1.5%. Of the five rubber estates surveyed, three revealed extremely high antibody ratios (42.6% to 45.9%) while the remaining two gave ratios of 0% and 3.3%, respectively. The possible connection between these results and environmental factors was discussed.

Of the 1,154 residents examined, 16.4% were positive. On the other hand, only 5.6% of 2,388 town residents surveyed had significant antibodies.

The number of clinical cases severe enough to be hospitalised was small compared to the number of infected persons, detected by antibody surveys. Immunity was acquired as early as four to six years of age, especially among rural children. In the above groups of persons studied, except for rubber estate workers, a very low proportion suffered from the ill-effects of leptospirosis. Possible reasons for these were given and further studies were recommended.

ACKNOWLEDGEMENT

The author wishes to thank Dr. B. Freeman, of the Sg. Lembing tin-mining estate, all the Health Officers, Health Inspectors and Estate Managers for collecting or assisting in the collection of sera specimens for the survey. She is also indebted to Mr. Mohamed Omar and Mr. Johan Haji Adam for their technical assistance.

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Tuberculous pericardial disease

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THE PERICARDIUM may be involved in a wide spectrum of diseases. A diagnosis of pericarditis is often incomplete until the aetiological cause is established, although this may not be always possible. Some of the important causes of pericarditis are: rheumatic, bacterial (including tuberculosis), viral, malignant, collagen diseases, metabolic diseases and myocardial infarction.

In Singapore to-day, tuberculosis is still one of the most important causes of pericarditis, although the incidence of tuberculosis is decreasing as a whole.

Tuberculous pericarditis can present in a wide variety of ways. We report here five cases seen at Tan Tock Seng Hospital, Singapore, between the years 1968 to 1969, illustrating the wide clinical spectrum of T.B. pericardial disease and the problems encountered in its diagnosis and management.

CASE REPORTS

Case No. 1.

C.M.C., a 68-year-old Chinese male, was seen at T.T.S.H. in March 1968, for cough and breathlessness on exertion for two weeks. On physical examination, a right pleural effusion was found. There were no signs of heart failure or cardiac tamponade, but a distinct pericardial rub was heard over a wide area of the praecordium. A chest X-ray (Fig. 1) confirmed



Fig. 1. Right pleural effusion, extensive bilateral pulmonary tuberculosis and pericardial effusion.

the right pleural effusion and showed extensive tuberculous lesions over both lungs; and an enlarged heart probably because of a pericardial effusion. Sputum for Acid Fast Bacilli (A.F.B.) was positive on direct microscopy and cultures. Right pleural aspiration yielded 500 mls. of hemorrhagic fluid.

He was treated with injection Streptomycin and Tabs. Paraaminosalicylic Acid and Isoniazid (Tabs. PAS. & INH.) and made good progress. After four months in hospital, he was discharged, and his chest X-ray then showed marked clearing of the pulmonary lesions, together with a normal-sized heart. When reviewed recently as an outpatient, he had no abnormal physical findings.

Case No. 2.

S.F., a 56-year-old Indian male, was first admitted to a psychiatric hospital in 1963 for schizophrenia. He was found to have minimal pulmonary tuberculosis and received chemotherapy consisting of Streptomycin, PAS. & INH. On completing the course of Streptomycin, PAS. & INH. were continued for two years. He was re-admitted in May 1969, for a relapse of schizophrenia and was found to be in heart failure. On physical examination, the patient was dyspnoeic and ill with a blood pressure of 80/50 mm. Hg. and a pulse rate of 120/min. The jugular venous pressure was grossly elevated. The apex beat was not palpable and the heart sounds on auscultation were normal. Bilateral pleural effusions were found, and the liver was five cm. enlarged with no splenomegaly and no ascites. Moderate oedema of both legs were present. A chest X-ray showed a very large heart consistent with a pericardial effusion, together with bilateral pleural effusions and tuberculosis lesions over the upper zone of both lungs.

He was then transferred in July 1969 to Tan Tock Seng Hospital where his sputum was found to be positive for A.F.B. on direct microscopy and culture. A pericardial tap done via the xiphisternal route yielded 375 mls. of hemorrhagic fluid. Air injected into the pericardial cavity after aspiration revealed that the parietal pericardium was thickened (Fig. 2). The pericardial fluid was negative for A.F.B. on direct microscopy but was positive on culture. An E.C.G. done showed non-specific ST segment depression over the praecordial leads. He was treated with digitalis and diuretics, and a second course of anti-tuberculous therapy, consisting of Streptomycin, PAS. & INH. together with prednisolone, was given. While in the ward, pericardial aspiration was repeated twice because of cardiac tamponade.



Fig. 2. Injection of air after pericardial aspiration demonstrating thickened parietal pericardium.



Fig. 3. Normal-sized heart.



Fig. 4. Large pericardial effusion.



Fig. 5. Normal-sized heart and right pleural effusion.

He improved remarkably and the signs of cardiac tamponade gradually disappeared. In November 1969, there were no abnormal physical findings and his chest X-ray showed a normal-sized heart (Fig. 3).

Case No. 3.

C.L., a 68-year-old Chinese female, was admitted to another hospital in April 1969, for breathlessness on exertion and swelling of legs for three months. She was found to have a large pericardial effusion (Fig. 4) and a diagnostic pericardial tap yielded hemorrhagic fluid which grew A.F.B. on culture. She was treated for heart failure and transferred to Tan Tock Seng Hospital where anti-tuberculous therapy (Streptomycin, PAS. & INH.) together with Prednisolone was started.

Repeated chest X-rays showed her cardiac silhouette growing progressively smaller. In September 1969, a right pleural effusion developed (Fig 5) with signs of cardiac tamponade. The jugular venous pressure was elevated to the angle of the jaw and showed a steep 'Y' descent consistent with constrictive heart disease. Blood pressure and radial pulse were normal; pulsus paradoxus was not present. The apex beat was easily felt in the 5th left intercostal space within the left mid-clavicular line. On auscultation, the heart sounds were normal. The liver was six cm. enlarged with a two cm. enlarged spleen; moderate ascites and ankle oedema were present. Sputum was negative for A.F.B.; and an electrocardiogram showed inverted 'T' waves in leads III & AVF.

A total pericardiectomy was done in November 1969. The lateral portion of the right pleura was found to be thickened and the heart encased by thickened pericardium. Histology revealed a thickened, fibrotic pericardium, but no A.F.B. were seen. She made good progress and when reviewed recently showed no signs of cardiac tamponade.

Case No. 4.

L.S.N., a 34-year-old Chinese female, was first admitted to Tan Tock Seng Hospital in July 1968 for breathlessness. She had been unwell for ten years prior to this, having been admitted to Outram Road General Hospital several times for heart failure. There was no past history of tuberculosis or rheumatic fever. On physical examination, her jugular venous pressure was elevated to the angle of the jaw, with prominent 'V' waves. The heart was in atrial fibrillation at 100/min. with a blood pressure of 100/70. The apex beat was heaving in type and felt at the 6th

left intercostal space at the anterior axillary line. A left parasternal heave denoting right ventricular hypertrophy was present. On auscultation, a pansystolic murmur, grade III, was heard at the mitral area radiating to the axilla, together with a short mid-diastolic flow murmur. A pansystolic murmur was also present at the tricuspid area, and the liver was seven cm. enlarged and pulsatile. The spleen was two cm. enlarged and moderate ascites was present. A chest X-ray (Fig. 6) showed an enormous cardiac shadow occupying almost the entire chest and an electrocardiogram showed atrial fibrillation with tall 'R' waves in V5 and V6, suggesting left ventricular hypertrophy. A diagnosis of mitral and tricuspid incompetence with a possible pericardial effusion was made. She was put on a heart failure regime and discharged in August, 1968, but subsequently had two further admissions for heart failure. On her fourth admission in July 1969, a diagnostic pericardial aspiration was attempted via the xiphisternal route and 800 mls. of straw-coloured fluid were obtained. Air injected after aspiration revealed an enlarged hair-line thin pericardial sac (Fig. 7). The fluid was positive for A.F.B. on direct microscopy, but negative on culture. Pericardial aspiration was later repeated twice and a total of 2,000 ml. of fluid withdrawn. Repeat chest X-rays still showed a very large heart due to the mitral and tricuspid incompetence. She was started on Streptomycin, PAS. & INH, and was relatively well on discharge in December 1969.



Fig. 6. Grossly enlarged heart due to pericardial effusion.

Case No. 5.

C.N.N., a 15-year-old Chinese girl, was first admitted to T.T.S.H. in December 1967 for exertional dyspnoea with swelling of the legs for one year. There was no previous history of pulmonary tuberculosis. Physical examination & chest X-ray revealed a pleural effusion in the right chest (Fig. 8). The pulse and blood pressure were normal, and the apex beat was in the 5th left intercostal space within the mid-clavicular line. A third heart sound was heard at the mitral area. The liver was seven cm. and the spleen two cm. enlarged, and there was ascites and leg oedema. A right pleural aspiration showed that the effusion was a transudate, and sputum and pleural fluid were both negative for A.F.B. on direct microscopy and culture. A tuberculin test of one T.U. was two m.m. The hemoglobin, total white and sedimentation rate were normal. Blood for L.E. cells and rheumatoid factor were repeatedly negative; and viral studies of the blood and stools were also negative. Liver function



Fig. 7. Hairline thin, pericardial sac (inked and arrowed) demonstrated after pericardiocentesis and injection of air.

TUBERCULOUS PERICARDIAL DISEASE

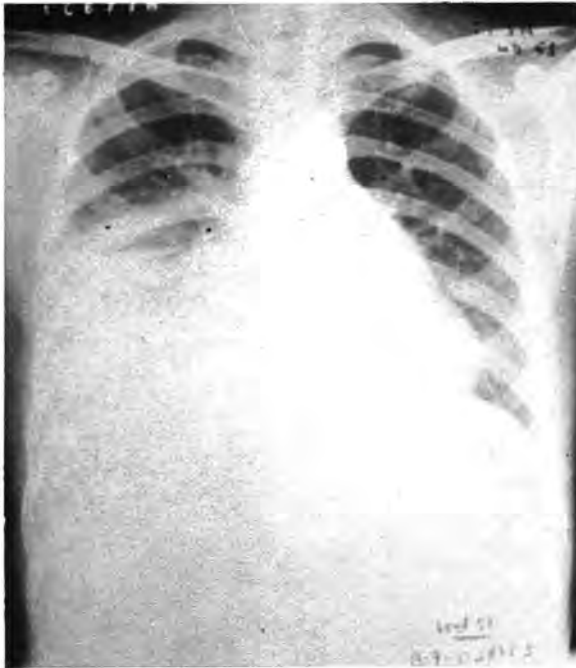


Fig. 8. Right pleural effusion.

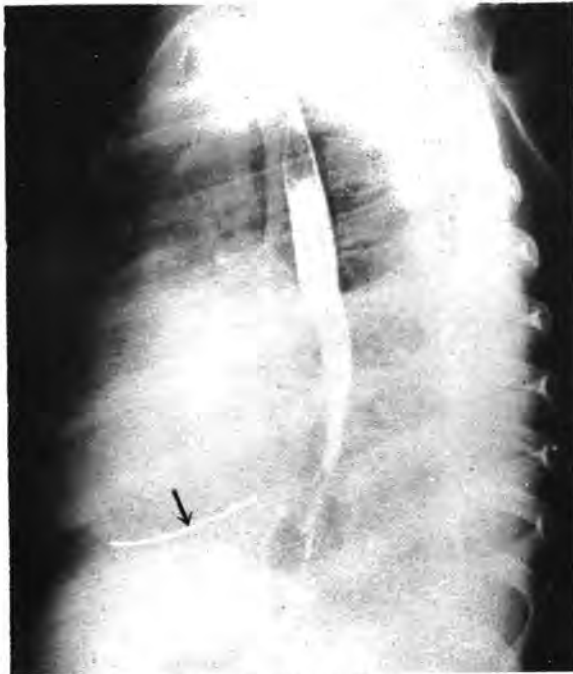


Fig. 9. Barium swallow showing calcified pericardium (inked and arrowed).

tests were all normal, and a liver biopsy revealed fatty change only.

She was discharged in February 1968, with little improvement, and was re-admitted in March 1968, with more severe breathlessness and leg oedema. This time, the jugular veins were markedly distended and elevated to the angle of the jaw. Pulsus paradoxus was not present. Further chest X-ray and a barium swallow showed a distinct calcified pericardium (Fig. 9), and an electrocardiogram showed widespread 'T' wave inversion with bifid 'P' waves in leads II & III.

Subtotal pericardiectomy was done in June 1968. At operation, adhesions between the pericardium and heart with calcifications at the atrio-ventricular grooves and between the interventricular grooves were found. Histology revealed collagenous fibrous connective tissue consistent with a much thickened fibrotic pericardium. Post-operatively, she did very well, as the signs of cardiac tamponade gradually diminished and a chest X-ray (Fig. 10) in March 1969, showed a normal-sized heart with no pleural effusion. When last seen in October 1969, she was perfectly well with no abnormal findings.

DISCUSSION

Schrire, (1967) in one of the largest series of pericardial diseases, reported on a total of 382 patients seen in the Groote Schuur Hospital in Cape Town, South Africa. Forty per cent of these were definitely tuberculous, 40 per cent were most likely

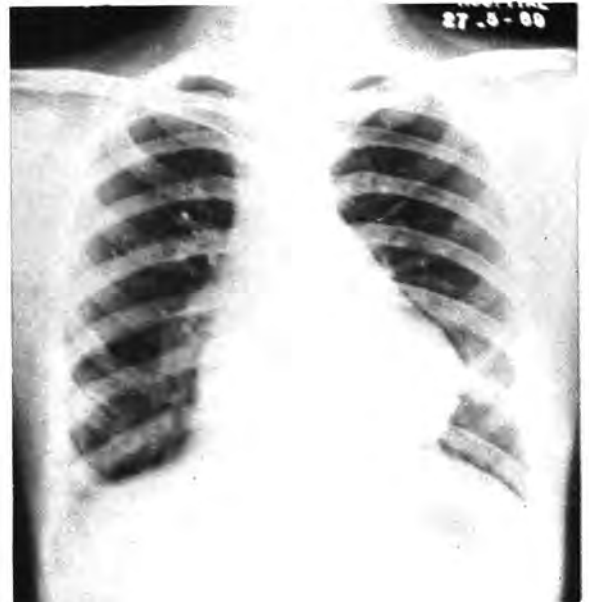


Fig. 10. Normal-sized heart.

tuberculous, whilst 12 per cent were idiopathic, and six per cent pyogenic, with two per cent miscellaneous.

The criteria for making the diagnosis of tuberculous pericarditis in Schrire's series were based on the presence of any of the three following conditions, and their respective incidence in his series were:

- (i) A.F.B. detected in the pericardial fluid ... 18%
- (ii) Histological finding of T.B. in the pericardium ... 44%
- (iii) Organ involvement (Lungs, glands etc.) ... 38%

In three of our cases (Cases Nos. 2, 3, 4), A.F.B. were found in the pericardial fluid. In Case No. 1, A.F.B. were found in the sputum. Case No. 5 presented some problem in diagnosis, as histology of her pericardium showed fibrous connective tissue only, with no definite evidence of tuberculosis. This patient presented with constrictive pericarditis, and as all other causes of this disease were excluded, it was most likely tuberculosis in origin.

A histological finding of tuberculosis was found in only 44% of the definite tuberculosis pericarditis in Schrire's series, and he commented that anti-tuberculous treatment can prevent histological evidence of T.B. from developing. This fact is further supported by Case No. 3 where the pericardium obtained at operation after seven months of anti-tuberculous treatment showed only fibrous connective tissue.

T.B. pericarditis can present as three distinct syndromes — dry (fibrinous) pericarditis, pericardial effusion and constrictive pericarditis. Dry (fibrinous) T.B. pericarditis presenting with chest pain, pericardial rub, and a normal-sized heart is uncommon, and was seen in only 12 of the 382 cases in Schrire's series.

Four of our five patients presented with pericardial effusion. Case No. 4 was a great diagnostic problem because, in addition to the pericardial effusion, she also had mitral and tricuspid incompetence, most likely of rheumatic origin; hence pericardial effusion was confirmed only after a diagnostic pericardial aspiration. Sometimes, the differentiation between pericardial effusion and cardiomyopathy may be impossible to resolve and in such cases a right heart catheterization, with or without the injection of radio-opaque dye or carbon dioxide, could be of immense value. Where the diagnosis is in doubt, pericardial aspiration could be dangerous

because of the possibility of piercing the cardiac muscle, but the development of the pericardial electrode needle (Bishop et alia, 1965) has reduced considerably the danger of aspiration in such cases.

The patient who presents with T.B. constrictive pericarditis de novo sometimes poses a special diagnostic problem. Although the classical signs of constrictive heart disease are well known to all, the diagnosis is sometimes not made because the jugular venous pressure may be so grossly elevated that the venous pulsations are missed. Such patients present with pleural effusion, hepatomegaly and ascites and hence liver cirrhosis is often mistakenly diagnosed. Other forms of heart disease, e.g. Amyloidosis, may mimic constrictive pericarditis but the presence of pericardial calcification as in Case No. 5, is extremely helpful in the diagnosis.

In the management of pericardial effusion, it is important to remember that the effusion may resolve completely without giving rise to constriction as exemplified by Case No. 1 and 2. In the patients who develop constrictive disease following pericardial effusion, surgery can safely be deferred up to six months, because the constrictive phase with tamponade may pass away completely with anti-tuberculous drugs alone (Schrire 1967). However, if constriction persists, as in Case No. 3, pericardiectomy is indicated.

SUMMARY

Five cases of tuberculous pericardial disease as seen in T.T.S.H. are described. The various clinical syndromes encountered in T.B. pericardial disease, their pathogenesis, prognosis and management are discussed.

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Ketamine (CI-581): The new parenteral general anaesthetic—The answer for one anaesthetic problem

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Introduction

KETAMINE HYDROCHLORIDE (trade name "Ketalar", Research Drug No. CI-581) is a non-barbiturate, short-acting, parenterally administered phencyclidine derivative. Its chemical structure is 2-(0-chlorophenyl)-2(methylamino)-Cyclohexanone-Hydrochloride (See fig. 1).

Ketamine is the latest parenteral general anaesthetic. It is a cataleptic and anaesthetic agent with low toxicity and powerful analgesic activity of rapid onset and relatively short duration. When given intravenously or intramuscularly, it rapidly produces unconsciousness, a quiet patient and a degree of analgesia which permits surgical intervention.

The anaesthetic state as observed clinically is characterised by profound analgesia combined with a peculiar state of unconsciousness. The entrance into

this state of disconnection from the surrounding (dissociation anaesthesia) is heralded by marked horizontal and vertical nystagmus which occurs while the patient's eyes abruptly open. Shortly thereafter the eyes become centred and appear in a fixed gaze. The pupils are moderately dilated and promptly react to light. Tearing is common, as is salivation, if not counteracted by antisialogogue drugs.

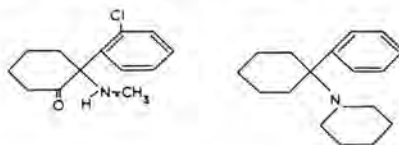


Fig. 1. The Chemical Structure of Ketamine compared to that of its parent drug (Phencyclidine).

The cardiovascular system is stimulated, resulting in a moderate to marked rise in heart rate and an increase in both systolic and diastolic blood pressure for several minutes. The pulse rate and blood pressure then gradually return to preinjection levels. Ketamine is said to have an anti-arrhythmic property (Corssen, Miyasaka, Domino, 1968).

Respiratory function is usually unimpaired; following rapid intravenous injection, it may be depressed briefly with return to normal respiratory exchange within 15–30 secs. One of the most striking and useful features of Ketamine induced anaesthesia appears to be the maintenance of an adequate airway regardless of the extremes of position. Since intra-oral musculature, especially the tongue, fails to relax, mechanical obstruction is virtually absent and there is no need for an oropharyngeal or endotracheal tube for artificially support-

ing the airway. The increase in muscle tone allows the patient to hold up his own jaw throughout the anaesthesia. In addition, the preservation of the protective laryngeal and pharyngeal reflexes throughout anaesthesia makes it unlikely for aspiration to occur. Evidence for this is found from the fact that of the eight cases out of a series of 116 cases in which vomiting did occur, during the procedure or post-anaesthetic recovery, the patients had no difficulty in clearing the airway (Corssen, Groves, Gomez and Allen, 1969).

Arterial blood gas studies by various groups of workers (Domino, Chodoff, Corssen, 1965; Virtue, Alanis, Mashiro, Lafargue, Vogel and Metcalf 1967; King and Stephen, 1967; Vayden, Hunt, Willis and Stephen 1968) before, during, and after ketamine-induced anaesthesia have revealed no significant deviation from accepted physiological values.

Fig. 2. Data on Emergency Anaesthesia for Incision and Drainage of 4 cases of Submandibular Abscesses with Floor of Mouth Swelling ++ and Trismus

Case	Age (Yrs) & Sex	Wt. (Kgm)	Premed.	Duration (mins) – injection to dressings	Systolic B.P. (mm.Hg)	Recovery (min) Identity and place,	Dreams
1.	6, Male	22.5	I/V Atropine 0.6 mgm.	14 mins	↑ (44 mm. maxm. – back to normal in 10 mins. after injection).	40 mins	?
2.	9, Male	28.0	I/V Atropine 0.6 mgm.	17 mins	↑ (40 mm. maxm. – back to normal in 12 mins. after injection).	50 mins	+ (Pleasant)
3.	17, Male	36.0	I/V Atropine 0.6 mgm.	8 mins	↑ (60 mm. maxm. – back to normal in 8 mins. after injection)	40 mins	–
4.	30, Female	40.0	I/V Atropine 0.6 mgm.	11 mins	↑ (70 mm. maxm. – back to normal in 8 mins. after injection)	40 mins	+ (Pleasant)

I/V Ketamine (CI-581) Used for General Anaesthesia.
 Dosage: 1.5 mgm/kgm (to next higher 10 mgm) initial dose.
 Booster doses: (cases 1 and 2) ½ initial dose.



Fig. 2a. This is a case of submandibular abscess with Trismus and swelling of the floor of the mouth.

CI-581 appears to be metabolised very rapidly in the body (Chen, Glazko and Kaump, 1965; work done on laboratory animals) with the appearance of several metabolic products in the urine. Very little unchanged drug was excreted, even in animals receiving massive doses of the drug by intravenous infusion over a period of hours. Two metabolic products have been isolated from monkey urine and identified chemically as the free amine produced by demethylation (metabolite I) and the cyclohexene derivative produced by oxidation of the amine (metabolite II).

The most commonly cited undesirable side-effects are elevation of blood pressure, vivid dreams during emergence from anaesthesia, purposeless muscular movements and possibly respiratory depression with usage of too high a dose.

Material, Methods and Results

Taking into account the advantageous features of ketamine, four cases of submandibular abscesses with marked floor of mouth swelling and trismus were given intravenous ketamine as general anaesthesia for emergency incision and drainage in the University Hospital, Petaling Jaya.

Material

There was no selection of patients. All four cases presented as emergencies when the author was on duty during the period July – December, 1969. Their ages, sex and weights are given in Fig. 2.

Method

All four cases were treated as emergencies, irrespective of the interval between the last drink or meal and the induction of anaesthesia; the intervals were

2½ hours, 3 hours, 5 hours and 4 hours respectively for cases 1 to 4. Premedication was the same in all cases – 0.6 mgm I/V Atropine just before induction, leaving the needle in-dwelling in the vein. No respiratory depressive narcotic-analgesics were used in premedication. The patients were anaesthetised on the operating table with the surgeon scrubbed up and in all readiness so as not to waste anaesthetic time. Intravenous 1% ketamine was administered for all cases as the sole anaesthetic with the patient breathing air in a dosage of 1.5 mgm/kgm body weight (to the nearest next highest 10 mgm). Booster doses (½ the initial dose) were given if indicated. The indication being facial grimacing or movement in response to surgical stimulus, anticipating the procedure to carry on for approximately a further 10 minutes.

The duration of the procedure was timed from injection of ketamine to the final dressings applied to the site of surgery.

The systolic blood pressure was noted at two minute intervals following injection of ketamine using a sphygmomanometer cuff using the palpation method.

Recovery time was measured from time of last injection of ketamine to time of orientation of the patient (in the recovery room) as to identity and place. The incidence of dreams (description and whether pleasant or frightening) was assessed by direct questioning, after the patient was assessed to be orientated.

Results

The results from the four cases are summarized in Fig. 2. Cases 1 and 2 required a second (booster) injection. The indication was movement and facial grimacing in response to surgical stimulus. This indication came on within one to two minutes following the return of the systolic blood pressure to pre-injection levels. Thus the return to pre-injection systolic blood pressure level can serve as a warning that the indication for a booster dose will follow within one to two minutes. In all four cases, the systolic blood pressure showed a rise within two minutes of the I/V injection. The maximum rise in systolic blood pressure was 44, 40, 60 and 70 mm.Hg. in cases 1 to 4, respectively (see Fig. 2). There was no incidence of vomiting, nausea or abnormal muscular movement in the four cases.

Discussion

(See Fig. 2A) Abscesses of the floor of the mouth with the possibility of associated oedema glottidis

pose a problem regarding anaesthesia for the required surgical incision and drainage. Maintenance of the airway during the procedure in such cases is the major problem.

In the presence of oropharyngeal oedema, a general anaesthetic is contraindicated under any circumstances unless the airway can be guaranteed. Prior to the advent of ketamine, the airway could never be guaranteed unless either preliminary laryngotomy or tracheostomy had been performed or an endotracheal tube had been passed under topical analgesia. Naturally the latter method was previously preferable and in most instances, it was performed with little or no discomfort to the patient. Once the tube was in situ, any form of anaesthesia could be used without danger of oedema of the glottis causing obstruction and death. (V. Goldman, 1965).

Trismus is often an added problem in anaesthesia for cases of abscesses around the floor of the mouth and the application of the topical analgesic can thus meet with difficulty. As previously advocated, intubation was a must for ensuring the airway maintenance during general anaesthesia. The problems associated with intubation in such cases are, first, mechanical difficulties because of trismus, floor of mouth swelling and oedema glottidis; on extubation, the oedema might be made worse with consequent airway problems.

When general anaesthesia is required, an inhalational method with spontaneous respiration was advocated as the safest choice but Thiopentone was not recommended as an induction agent. Thiopentone alone is never justified since it increases reflex activity in the glottis area (Wylie and Churchill-Davidson, 1966). If a laryngeal spasm should thus occur, one can imagine the problems that can arise. The problem with inhalational anaesthesia (cyclopropane and oxygen is a good choice) in the presence of floor of mouth swelling is the technical difficulty of holding up the jaw with a mask over the mouth and nose, to ensure an unobstructed upper respiratory passage.

A simple abscess or Ludwig-type angina of the neck can be safely incised under inhalational anaesthesia without a tube provided there is no pre-operative upper respiratory obstruction present, the surgeon is speedy and unconsciousness is fleeting (Wylie and Churchill-Davidson, 1966). This is obviously not without risk.

CI-581 or Ketamine, the new intravenous general anaesthetic, seems to be one way out of the problems associated with anaesthetic techniques previously advocated for floor of the mouth abscesses requiring

incision and drainage. It is indeed an addition to the anaesthetists repertoire and armamentarium. This new intravenously or intramuscularly administered anaesthetic has distinct advantages, e.g. adequate, unobstructed airway can be maintained during ketamine-induced anaesthesia without the need of an oropharyngeal or endotracheal tube or manual jaw-support; also the protective reflexes, such as cough, gag and swallowing, are maintained throughout anaesthesia. It has been found to be useful in eye surgery (Falls, Hay, Corssen, 1966) oral surgery (Corssen, Hayward, Gunter, Groves, 1969), severely burnt patients (Bjarnesen, Corssen, 1967), neuro-radiological diagnostic procedures in children (Corssen, Groves, Gomez, Allen, 1969). The advantages, disadvantages and contraindication of ketamine have been set out in Fig. 3.

As with most intravenous anaesthetics, there is always one added danger. Those not trained in the care or resuscitation of an anaesthetised or unconscious patient might be tempted to administer the drug, thinking that the ability to perform a venepuncture is the only requisite. As with the administration of all general anaesthetics, cardio-respiratory equipment and drugs must be at hand and the administrator of the anaesthetic drug must be trained in the use of such equipment for cardio-respiratory resuscitation. It should thus be clear that only the anaesthetist should use this drug.

Summary

A description of the pharmacology and clinical effects of the new parenteral, non-barbiturate, general anaesthetic, ketamine (CI-581) is outlined. Its clinical use in the anaesthetic management of four cases of submandibular abscesses with trismus and floor of mouth swelling is described. Discussion of such cases as an anaesthetic problem follows. Ketamine is advocated as the answer to this problem. The advantages, disadvantages and contraindications of ketamine are tabulated.

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Figure 3.

Advantages, Disadvantages and Contraindications
of Ketamine (Vayden, Hunt, Willis, Stephen, 1968)

Advantages	Disadvantages	Contraindications
<ol style="list-style-type: none"> 1. Profound analgesia without significant impairment of respiratory function. 2. Stimulation of cardiovascular system thereby avoiding hypotension, instead, producing a rise in blood pressure. 3. Preservation of protective reflexes. 4. Maintenance of unobstructed airway regardless of extremes of position. 5. Absence of organ toxicity despite multiple administration. 6. Excellent tissue compatibility. 7. Virtual absence of post-anaesthetic nausea and vomiting. 8. Wide margin of safety (ratio of toxic to anaesthetic dose 16 : 1) 9. Ease of administration: I/V or I/M. 10. Anti-arrhythmic property. 11. Amnesia. 	<ol style="list-style-type: none"> 1. Vasopressor activity resulting in rise in blood pressure. 2. Salivation in absence of antisialogogues. 3. Occasional extra-pyramidal activity. 4. Dreams (usually pleasant sometimes frightening). 	<ol style="list-style-type: none"> 1. Hypertension (> 160 mm.Hg) 2. History of cerebro-vascular accident. 3. Marked cardiac decompensation. 4. Abdominal surgery and other procedures involving visceral pain. 5. Patients with a known history of psychiatric problems.

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ABO grouping studies of human seminal stains on fabrics

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SEMINAL STAIN is a useful physical evidence in a sexual crime. It is therefore important to identify its presence on garments worn by the victim and the accused at the time of the offence and also, if possible, at the place where the offence was committed. These stains would be even more valuable as physical evidence if they could be further characterised so as to establish their origin by grouping the ABO blood group substances in them.

The identification of seminal stains on garments and other articles is well documented. (2,4, 7, 8)

Nickolls has stated in a book (8) that all persons can be divided into two categories, namely those that secrete their group specific ABO agglutinogens in their body exudates and those that do not secrete these substances. He further states that the concentration of agglutinogens in the seminal fluid of secretors is approximately four times as strong as the concentration in their blood and as such, they could be readily grouped using the absorption-inhibition technique which he described earlier in the same volume for blood grouping. However, he makes no mention about seminal stains from non-secretors.

Nickolls and Pereira (9) have stated that they found their modified absorption-elution technique of grouping blood group substances works satisfactorily for saliva and semen.

Outteridge (10) has, in a recent article, mentioned that secretions of some 75 – 80% of individuals contain water soluble blood group substances and these blood group substances could be identified by a simple qualitative absorption test.

Surinder Singh and Aw Yong Heng Khuan (12), too, have used the absorption inhibition technique successfully in grouping seminal stains from secretors. They reported that they were unable to get results in the case of non-secretors by using the same technique.

Friedenreich and Hartman (11) studied the problem of secretors and non-secretors deeply and came to the conclusion that there were two distinct forms of the antigens:

- (i) A water soluble form not present in the red cells or serum but present in most of the body fluids and organs of a secretor. The presence of this water soluble antigen is

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determined by the secretor gene;

- (ii) An alcohol soluble form of the antigen, present in all tissues (except the brain) and in the red cells, but not present in the secretions. The alcohol soluble form is not influenced by the secretor gene. In the light of this knowledge, it can therefore be inferred that seminal plasma from secretors would contain water soluble ABO blood group substances and their sperms would contain both water soluble and alcohol soluble ABO blood group substances, whereas seminal plasma from non-secretors would contain no ABO blood group substances but their sperms would contain only alcohol soluble ABO blood group substances.

Experimental

The experimental work was divided into three parts, namely:-

Part I: The formulation of a suitable routine technique for grouping the ABO blood substances in seminal stains from both secretors and non-secretors.

Part II: To investigate if any modifications were required in grouping the ABO blood group substances in seminal stains on a few variety of fabrics.

Part III: To investigate grouping of the ABO blood group substances in seminal stains from oligospermic and azospermic individuals.

Part I: Samples of semen for this investigation were donated by members of the staff. In all, 30 samples from 30 individuals (6 group A secretors, 6 group B secretors, 6 group O secretors, 2 group AB secretors, 3 group A non-secretors, 3 group B non-secretors, 3 group O non-secretors and 1 group AB non-secretor) were examined (all these individuals had more than 200,000,000 sperms in a single ejaculate). The semen were absorbed on cotton fabrics and allowed to dry at room temperature (70°–80° F).

The secretor or non-secretor status of the individuals were determined from their saliva using the technique described by Race and Sanger (11).

Commercially purchased "Ortho" anti-A and anti-B anti sera were used and they were found to have a titre of 256. The anti-H was obtained from *Ulex europaeus* seeds according to the method described by Boorman and Dodd (1) and it was found to have a titre of 128. Isotonic saline was used for dilutions of all the above anti sera.

Several variations of the absorption-inhibition (3) and absorption-elution (5) techniques were tried with the following considerations:-

(i) reliability for interpreting results

(ii) adaptability as a routine technique in a busy laboratory.

Part II: Samples of semen for this investigation, too, were donated by members of the staff. The semen were absorbed on nylon, terylene and wool fabrics respectively and allowed to dry at room temperature (70°–80° F). The successful grouping techniques of Part I were used to determine the ABO blood group substances of seminal stains on the above three fabrics with the view to determine if any further modifications were necessary, dependent on the fabric.

Part III: Samples of semen for this investigation were donated by the Pathology Department of the University Hospital, University of Malaya. In all, 25 samples, made up of 10 azospermic and 15 oligospermic semen, were examined. The samples of semen were absorbed on cotton fabrics and allowed to dry at room temperature (60° F). The successful grouping techniques of Part I were used to determine the ABO blood group substances of the above seminal stains.

Results

Part I: It was found that seminal stains from secretors could be unequivocally grouped by a simple absorption – inhibition method. However, seminal stains from non-secretors could not be grouped by this same technique. The absorption-inhibition method found reliable and suitable for routine purposes was as follows:-

- (i) a piece of stained fabric about 1 sq. cm. was cut into two equal halves and placed in two small dryer's tubes, marked S1 and S2 respectively. Likewise, a piece of similar unstained fabric of 1 sq. cm. was cut into two equal halves and placed in two dryer's tubes, marked B1 and B2 respectively.
- (ii) using pasteur pipettes, three drops of an equal mixture diluted anti-A and anti-B (1:16) were added to tubes S1 and B1 respectively and two drops of diluted anti-H (1:8) were added to tubes marked S2 and B2 respectively.
- (iii) the absorption was allowed to proceed overnight (approximately 16 hours) at room temperature (60° F)
- (iv) as much extract as possible were removed from the above four tubes (by means of suction, using pasteur pipettes with rubber teats) and trans-

Table I

Blood group of donor	Secretor or non-secretor	Agglutination of the serial 2-fold dilutions					
		Slide SA	Slide SB	Slide SO	Slide BA	Slide BB	Slide BO
A	secretor	----	++++	----	++++	++++	++++
B	secretor	++++	----	----	++++	++++	++++
O	secretor	++++	++++	----	++++	++++	++++
AB	secretor	----	----	----	++++	++++	++++
A	non-secretor	++++	++++	++++	++++	++++	++++
B	non-secretor	++++	++++	++++	++++	++++	++++
O	non-secretor	++++	++++	++++	++++	++++	++++
AB	non-secretor	++++	++++	++++	++++	++++	++++

Key:- + represents agglutination
- represents no agglutination

"Slide SA" shows agglutination results of serial 2-fold dilutions to 4 places of the equal mixture of anti-A and anti-B sera after absorption by the semen stained fabric with group A2 red cells.

"Slide SB" shows agglutination results of serial 2-fold dilutions to 4 places of the equal mixture of anti-A and anti-B sera after absorption by the semen stained fabric with group B red cells.

"Slide SO" shows agglutination results of serial 2-fold dilutions to 4 places of the anti-H serum after absorption by the semen stained fabric with group O red cells.

Slides BA, BB and BO correspond to Slides SA, SB and SO respectively but they show the corresponding results on an unstained fabric.

ferred to fresh dryer's tubes and centrifuged.

- (v) the supernatant of the extract from tube S1 was divided into two equal aliquots and each aliquot was serially 2-fold diluted to 4 places on to 4 cavity slides, marked SA and SB respectively. The supernatant of the extract from tube S2 was serially 2-fold diluted on to another 4 cavity slide marked SO.

The extracts from tubes B1 and B2 were correspondingly similarly treated to extracts from tubes S1 and S2 and serially diluted on to 4 cavity slides marked BA, BB and BO respectively.

- (vi) using platinum loop, fresh group A2 indicator red cells were added to the dilutions in the 4 cavities of slides SA and BA respectively. Likewise, fresh

group B indicator red cells were added to the dilutions on slides SB and BB respectively and fresh group O indicator red cells were added to the dilutions on slides SO and BO respectively.

- (vii) all the above slides were placed in a moist chamber and after about half an hour standing, the slides were examined for agglutination under a microscope (x 40 magnification).

Typical agglutination results obtained from secretors and non-secretors of the four different groups are shown in table I.

It was further found that seminal stains from non-secretors could be unequivocally grouped by a simple absorption-elution method similar to that described by Nickolls and Pereira (9). However, similar success was not obtained for grouping of seminal stains from secretors by this same technique.

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The absorption-elution method found reliable and suitable for grouping seminal stains from non-secretors was as follows:-

- (i) about 2 or 3 threads of approximately 1 cm. long were cut from the stained area of the fabric and placed into each of the 3 cavities of a slide marked S1. Likewise, threads from an unstained area of the same fabric were cut and placed into each of the 3 cavities of a slide marked B1.
- (ii) one drop of the 'Ortho' anti-A serum was added to each of the first cavities of slides S1 and B1 respectively and one drop of 'Ortho' anti-B serum was added to each of the second cavities of the above two slides respectively and one drop of anti-H serum was added to each of the third cavities of the above two slides respectively. The threads in the various cavities must be completely immersed in their respective anti-sera.
- (iii) absorption was allowed to proceed for at least 4 hours at room temperature (60°F).
- (iv) the excess anti sera were removed as completely as possible by mild suction with a water pump furnished with a pasteur pipette at its end.
- (v) ice cold saline was added into each of the cavities containing the threads and the saline removed as in step (iv). This process was repeated 6 – 10 times. The exact number of washings can only be decided by experience and it would vary from one worker to another. It would be prudent to subject the threads on slide B1 to at least one washing less than the threads on slide S1. In this way, agglutination results read subsequently could definitely be interpreted as that not due to under-washing.
- (vi) the threads from slide S1 were removed and placed in 3 corresponding cavities on a fresh slide marked S2. Similarly the threads from slide B1 were removed and placed in 3 corresponding cavities of another fresh slide marked B2.
- (vii) one drop of 0.2% suspension of fresh group A2 red cells (in saline) was added to each of the first cavities of slides S2 and B2 respectively, and one drop of 0.2% suspension of fresh group B red cells (in saline) was added to each of the second cavities of slides S2 and B2 respectively, and one drop of 0.2% suspension of fresh group O red cells (in saline) was added to each of the third cavities on slides S2 and B2 respectively.
- (viii) the slides S2 and B2 were placed in a dry chamber and incubated in an oven at 55°C for 15 minutes.
- (ix) after incubation, the slides S2 and B2 were transferred into a moist chamber and rotated on a rota-test.
- (x) after about half an hour, the slides were examined for agglutination under a microscope (x 40 magnification).

Typical agglutination results obtained from secretors and non-secretors of the four different groups are shown in table II.

Part II: It was found that the same two techniques described under Results of Part I could be successfully used for grouping seminal stains from secretors and non-secretors respectively on nylon, terylene and wool fabrics. It was, however, found that it was desirable to reduce the number of washings in step (v) of the absorption-elution method for seminal stains from non-secretors on nylon and terylene fabrics. No further modifications were found to be necessary.

Part III: Agglutination results obtained for the abnormal seminal stains using the absorption – inhibition method described under Results Part I are shown in table III.

Discussion

It was found that no single grouping technique could be used to successfully group seminal stains from both secretors and non-secretors. Seminal stains from non-secretors could not be grouped by the absorption-inhibition technique, probably because of the comparative poor sensitivity (10) of the technique. Only the sperms portion of the semen of a non-secretor would contain the blood group substances, and these represent less than 10% of the semen in human beings (6). However, seminal plasma and sperms from secretors contain blood group substances and as such, there are sufficient blood

Table II

Blood group of donor	Secretor or non-secretor	AGGLUTINATION					
		Slide S2			Slide B2		
		1st cavity	2nd cavity	3rd cavity	1st cavity	2nd cavity	3rd cavity
A	secretor	-	-	-	-	-	-
B	secretor	-	-	-	-	-	-
O	secretor	-	-	-	-	-	-
AB	secretor	-	-	-	-	-	-
A	non-secretor	+	-	-	-	-	-
B	non-secretor	-	+	-	-	-	-
O	non-secretor	-	-	+	-	-	-
AB	non-secretor	+	+	-	-	-	-

Key:- + represents agglutination
 - represents no agglutination

"Slide S2 - 1st cavity" shows absorption-elution agglutination results by semen stained fibres of anti-A serum with group A2 red cells.

"Slides S2 - 2nd cavity" shows absorption-elution agglutination results by semen stained fibres of anti-B serum with group B red cells.

"Slide S2 - 3rd cavity" shows absorption-elution agglutination results by semen stained fibres of anti-H serum with group O red cells.

The 3 cavities on slide B2 correspond to the 3 cavities on slide S2 but they show the corresponding results on unstained fibres.

group substances in seminal stains from secretors to be detected by the absorption-inhibition method.

Seminal stains from secretors could not be very successfully grouped by the absorption-elution technique, probably because most of the blood group substances in such semen are in a water soluble form and as such are washed away during the washing process employed in the technique. However, this method worked very satisfactorily for seminal stains from non-secretors because (i) it is very sensitive (10) And (ii) the blood group substances in the semen of a non-secretor is not in a water soluble form.

Our experimental work, using the absorption-inhibition technique of grouping on 20 seminal stains from secretors and 10 seminal stains from non-secretors, has consistently shown that semen from secretors showed absorption-inhibition of anti-H activity whilst semen from non-secretors showed no absorption-inhibition of anti-H activity. Perhaps this

phenomenon stain is from a secretor or non-secretor and thence use the appropriate grouping method described earlier in this article.

Grouping results of semen absorbed on three other fabrics showed that the same grouping techniques could be used without any significant modifications.

The grouping studies of seminal stains from azoospermic and oligospermic individuals showed that such stains from secretors could be readily grouped by the absorption-inhibition method but could not be satisfactorily grouped by the absorption-elution method. These findings are consistent with the theory. However, though the two azoospermic seminal stains from non-secretors did not show grouping results for the absorption-inhibition method, nevertheless they showed grouping results for the absorption-elution technique. These results are probably due to cellular debris in the semen as explained by Outteridge (10).

ABO GROUPING STUDIES OF HUMAN SEMINAL STAINS

Table III

Stain No.	Azoospermic/ oligospermic	Agglutination of the serial 2-fold dilutions						Remarks
		Slide SA	Slide SB	Slide SO	Slide BA	Slide BB	Slide BO	
1	azoospermic	++++	++++	----	++++	++++	++++	Group O secretor
2	azoospermic	++++	----	----	++++	++++	++++	Group B secretor
3	azoospermic	++++	++++	++++	++++	++++	++++	non-secretor
4	azoospermic	++++	++++	++++	++++	++++	++++	non-secretor
5	azoospermic	++++	----	----	++++	++++	++++	Group B secretor
6	azoospermic	++++	++++	----	++++	++++	++++	Group O secretor
7	azoospermic	++++	++++	----	++++	++++	++++	Group O secretor
8	azoospermic	----	++++	----	++++	++++	++++	Group A secretor
9	azoospermic	----	++++	----	++++	++++	++++	Group A secretor
10	azoospermic	----	----	----	++++	++++	++++	Group AB secretor
11	oligospermic	++++	----	----	++++	++++	++++	Group B secretor
12	oligospermic	----	++++	----	++++	++++	++++	Group A secretor
13	oligospermic	++++	----	----	++++	++++	++++	Group B secretor
14	oligospermic	----	++++	----	++++	++++	++++	Group A secretor
15	oligospermic	++++	++++	----	++++	++++	++++	Group O secretor
16	oligospermic	----	++++	----	++++	++++	++++	Group A secretor
17	oligospermic	++++	++++	----	++++	++++	++++	Group O secretor
18	oligospermic	++++	----	----	++++	++++	++++	Group B secretor
19	oligospermic	----	----	----	++++	++++	++++	Group AB secretor
20	oligospermic	++++	++++	----	++++	++++	++++	Group O secretor
21	oligospermic	++++	++++	----	++++	++++	++++	Group O secretor
22	oligospermic	----	++++	----	++++	++++	++++	Group A secretor
23	oligospermic	++++	++++	----	++++	++++	++++	Group O secretor
24	oligospermic	++++	----	----	++++	++++	++++	Group B secretor
25	oligospermic	++++	++++	----	++++	++++	++++	Group O secretor

Key:- + represents agglutination
- represents no agglutination.

"Slide SB" shows agglutination results of serial 2-fold dilutions to 4 places of the equal mixture of anti-A and anti-B sera after absorption by the semen stained fabric with group B red cells.

"Slide SO" shows agglutination results of serial 2-fold dilutions to 4 places of the anti-H serum after absorption by the semen stained fabric with group O red cells.

Slides BA, BB and BO correspond to slides, SA, SB and SO respectively but they show the corresponding results on an unstained fabric.

Conclusion

The method of choice for grouping seminal stains from secretors is the absorption-inhibition method and for seminal stains from non-secretors is the absorption-elution method.

Acknowledgement

The authors of this article wish to record their thanks to all the colleagues who donated specimens and also to the staff of the Pathology Department, University Hospital, University of Malaya, who collected and supplied the abnormal specimens. Special thanks also to the Director of Chemistry, Malaysia, for his advice and encouragement.

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ABO GROUPING STUDIES OF HUMAN SEMINAL STAINS

Table IV

Stain No.	Azoospermic/ oligospermic	AGGLUTINATION						Remarks
		Slide S2			Slide B2			
		1st cavity	2nd cavity	3rd cavity	1st cavity	2nd cavity	3rd cavity	
1	Azoospermic	-	-	-	-	-	-	no results
2	Azoospermic	-	-	-	-	-	-	no results
3	Azoospermic	+	-	-	-	-	-	Group A
4	Azoospermic	+	-	-	-	-	-	Group A
5	Azoospermic	-	-	-	-	-	-	no results
6	Azoospermic	-	-	-	-	-	-	no results
7	Azoospermic	-	-	-	-	-	-	no results
8	Azoospermic	-	-	-	-	-	-	no results
9	Azoospermic	-	-	-	-	-	-	no results
10	Azoospermic	-	-	-	-	-	-	no results
11	oligospermic	-	+	-	-	-	-	Group B
12	oligospermic	-	-	-	-	-	-	no results
13	oligospermic	-	-	-	-	-	-	no results
14	oligospermic	+	-	+	-	-	-	Group A
15	oligospermic	-	-	-	-	-	-	no results
16	oligospermic	-	-	-	-	-	-	no results
17	oligospermic	-	-	-	-	-	-	no results
18	oligospermic	-	+	-	-	-	-	Group B
19	oligospermic	-	-	-	-	-	-	no results
20	oligospermic	-	-	-	-	-	-	no results
21	oligospermic	-	-	-	-	-	-	no results
22	oligospermic	+	-	-	-	-	-	Group A
23	oligospermic	-	-	-	-	-	-	no results
24	oligospermic	-	-	-	-	-	-	no results
25	oligospermic	-	-	-	-	-	-	no results

Key:- + represents agglutination
- represents no agglutination.

"Slide S2 - 1st cavity" shows absorption-elution agglutination results by semen stained fibres of anti-A serum with group A2 red cells.

"Slide S2 - 2nd cavity" shows absorption-elution agglutination results by semen stained fibres of anti-B serum with group B red cells.

"Slide S2 - 3rd cavity" shows absorption-elution agglutination results by semen stained fibres of anti-H serum with group O red cells.

The 3 cavities on slide B2 correspond to the 3 cavities on slide S2 but they show the corresponding results on unstained fibres.

Agglutination results obtained for the abnormal seminal stains using the absorption-elution method described under Results Part I are shown in table IV.

Potency of therapeutic adrenaline in injections

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INTRODUCTION

LITTLE INFORMATION is available on the stability and hence the potency of adrenaline in injections packed locally or imported. This is important particularly in the tropics since fluctuations in temperature tend to accelerate the rate of decomposition of adrenaline in injections with a marked loss of pharmacological activity (Munch, Sloane and Latven, 1950; Backe-Hensen, Aares, Vennerod and Jensen, 1963). In view of this and the therapeutic importance of adrenaline as cardiac stimulant and bronchodilator, the present study was carried out to assess the potency of some proprietary adrenaline in injections.

SUMMARY

The potency of four samples of proprietary adrenaline in injections was compared with a reliable standard adrenaline. The potency of adrenaline was assessed by its pressor activity on the pithed rat. Of the four samples of adrenaline bioassayed, samples A and B possessed pressor activity which was significantly higher than the standard, while sample C was approximately equipotent. Sample D was the least potent compared with the standard.

Paper chromatography of samples A and D were carried out with reference to the same standard adrenaline. It was found that sample A separated out

into two spots on the chromatogram; one did not correspond to the Rf value of the standard adrenaline or to the standard noradrenaline (an additional standard used in the chromatography). The extra spot, however, had a colour reaction characteristic of the standard noradrenaline. No spot could be detected on the chromatogram of sample D.

METHODS

Rats of the Sprague-Dawley strain weighing between 200 and 300 g were used. The rat was pithed by the technique described by Shipley and Tilden (1947). The blood pressure was monitored from the left common carotid artery via a Statham pressure transducer (P23AC) coupled to a Grass Polygraph (Model 5). In pithed rat preparation, adrenaline is approximately equipotent as noradrenaline (Muscholl, 1959) and the preparation could therefore be used to bioassay adrenaline.

The potency of four samples of proprietary adrenaline in injections, A, B, C and D was studied. There were four ampoules in each sample and their activity was compared with freshly prepared standard 1-adrenaline bitartrate (Sigma, USA). Adrenaline was diluted in normal saline solution immediately before use. The drug was injected via the cannulated right femoral vein. The total volume injected was 0.3 ml

(0.1 ml adrenaline + 0.2 ml saline).

One dimensional paper chromatography of samples A and D were carried out using Whatman No. 1 paper. The solvent system used was n-butanol saturated with 1 M HCl (Euler and Hamberg, 1949). The solvent was run in the descending direction at 25°C for 14–16 hours (overnight).

The standard solutions consisted of 1-adrenaline bitartrate (Sigma, USA) and 1-noradrenaline bitartrate (Sterling-Winthrop, USA) dissolved 1 M HCl to a concentration of 5 mg/ml.

Following chromatography, the colour reaction of catecholamines was developed with ninhydrin and potassium ferricyanide (James, 1948).

RESULTS

Bioassay of adrenaline:

The net change in systolic pressure (mmHg) of pithed rat produced by 4 samples of adrenaline in injections A, B, C and D is shown in Fig. 1. With the exception of sample D, the responses produced by the others were equal or much greater than the standard adrenaline. At a dose level of 5 ug, it was seen that (Table I) the blood pressure change due to samples A and B was significantly higher than the standard (t-test, $P < 0.001$). The activity of sample C was approximately the same as the standard, while the activity of sample D was very much lower than the standard (t-test, $P < 0.001$).

The relative potency of 4 samples of adrenaline is summarised in Table 2. Sample A was about twice the

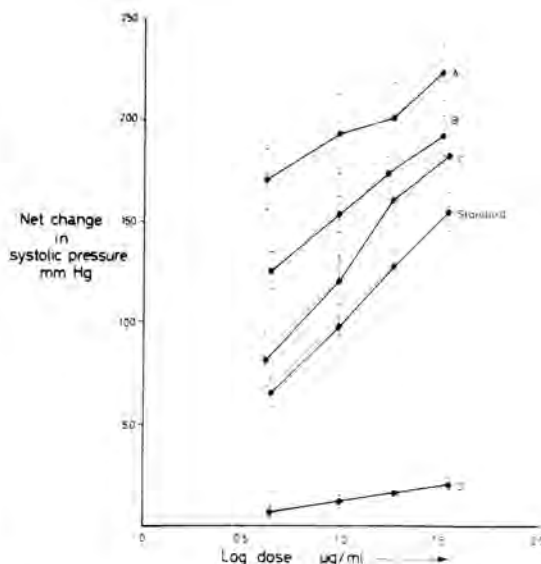


Figure 1: Net change in blood pressure of pithed rat produced by various adrenaline in injections (Samples A, B, C and D) and by standard adrenaline. Each point is the mean of 4 observations and the vertical strokes indicate the standard errors of these means.

potency of the standard on its action on the blood pressure of pithed rat. Sample B was one-and-a-half times stronger than the standard, while sample C was

TABLE I
CHANGE IN BLOOD PRESSURE OF PITHED RAT PRODUCED BY 5 ug OF VARIOUS ADRENALINE IN INJECTIONS

Sample	Change in blood pressure mmHg	No. of observations	P value (t-test)
Standard	97.5 ± 5.0	24	—
A	192.5 ± 20.0	4	< 0.001
B	160.0 ± 14.0	4	< 0.001
C	120.0 ± 12.5	4	—
D	12.5 ± 3.0	4	< 0.001

Figures refer to Mean ± standard error

TABLE II
RELATIVE POTENCY OF ADRENALINE IN INJECTIONS

Adrenaline in Injections	Potency Ratio = $\frac{\text{Adrenaline in Injection}}{\text{Standard Adrenaline}}$
Samples	3.1 ± 1.2
A	2.2 ± 0.5
B	2.2 ± 0.5
C	1.4 ± 0.5
D	0.10 ± 0.07

Figures refer to mean ± standard error of 4 (2+2) bioassay experiments.

POTENCY OF THERAPEUTIC ADRENALINE IN INJECTIONS

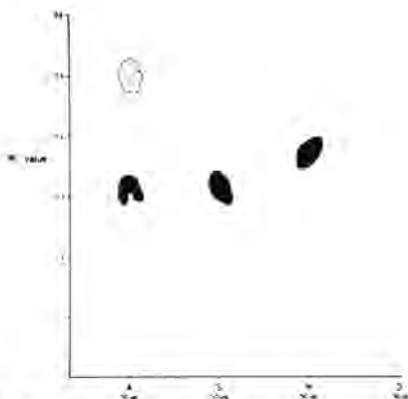


Figure 2: Paper chromatogram of adrenaline taken from Samples A and D. The standard adrenaline and noradrenaline are represented by S and N respectively.

approximately equal. With sample D, the potency was only about a tenth of the standard.

Chromatography of Samples A and D

Since the activity of adrenaline from samples A and D was very much different from the standard, it was thought of interest to investigate their purity, using one dimensional paper chromatography. The chromatogram in Fig. 2 showed that sample A separated out into 2 spots, one having a Rf value of the standard adrenaline, and the other having a Rf value which was not related to either the standard adrenaline or to the standard noradrenaline. However, the additional spot showed a colour reaction similar to that of noradrenaline.

No apparent spot corresponding to standard catecholamine was detected with sample D (fig. 2). This probably accounts for its weak effect on the blood pressure of pithed rat.

DISCUSSION

The results of the present study indicate that the potency of various adrenaline in injections varies considerably from one sample to another when compared with a reliable standard. Of the four samples of adrenaline investigated, only one of them was close to the potency of the standard, while the potency of the others was significantly different from the standard. The potency of sample A adrenaline is of particular interest, since it produced the largest change in the blood pressure of pithed rat, suggesting perhaps that the sample may be contaminated with some pressor agent. This view is supported in part by the results obtained with chromatography of the

sample. Alternatively, it may be that the sample contains more than the usual amount of adrenaline of 1 mg per ml specified by British Pharmacopoeia.

On the other hand, the pressor activity of sample D was only about one-tenth of the standard. The bioassay results are consistent with those obtained with chromatography of the sample. No apparent spot could be detected on the chromatogram. Incomplete oxidation of adrenaline may contribute to the marked loss of activity. Oxidative degradation of adrenaline results in the formation of a colour complex in the solution (West, 1947) but this was visually absent in all the ampoules of the sample. According to Girard and Kirny (1950), a loss of pharmacological activity can occur with an apparently clear solution of adrenaline. Loss of activity may also arise from a chemical reaction between adrenaline and sodium metabisulphite (a recognised stabilising agent) resulting in the formation of adrenaline sulphonate. This substance is pharmacologically inactive and is invariably found to be present in adrenaline in injections (Backe-Hansen et al, 1963). Whether this substance is actually present in sample D is not known and its study requires chemical analysis which is now in progress.

ACKNOWLEDGEMENTS

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Scintillation scanning in the diagnosis of neurological disease

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INTRODUCTION

THE CHIEF TYPES of scintillation scanning procedures available in CNS investigation includes

- 1) Brain scanning
- 2) Myeloscintigraphy and
- 3) Radioisotope ventriculography and cisternography.

The brain scan attempts to detect the presence of a brain lesion (SOL), characterise its size, shape and position and finally identification of its nature. It depends on the administration of a radioactive agent which is localised in the lesion, to a higher concentration than the surrounding normal brain, so that it is shown up on scanning or on scintiphotography using a gamma camera. Mode of action of the scan agent has been put down to the following:

1. increased vascularity associated with the lesion
2. uptake in neoplastic cells
3. breakdown in blood brain barrier involving increased capillary permeability and uptake in the increased interstitial space associated with the lesion.

RADIOPHARMACEUTICALS USED

There have been a large variety of radioactive substances used for brain scanning and the desirable properties of such agents includes:

1. ability to be measured when present in small amounts
2. gamma emitter with energy range of 0.1 to 0.5 MEV to allow detection of deep seated lesions and still not offer too many problems due to collimation.
3. Beta emission absent or weak
4. concentration in the tumour compared to normal brain tissue should be as high as possible and maintained during the entire period of scanning.
5. tumour to muscle ratio should also be high to detect lesions in the posterior fossa.
6. Physical and effective half lives should be short to reduce dosage and there should be no areas of prolonged retention with resultant high dosage to this organ.

The chief scan agents in use are:

1. ¹³¹I Albumin

SCINTILLATION SCANNING OF NEUROLOGICAL DISEASE



Fig. 1: 57-year-old female patient with signs of left frontal lobe SOL. Scan shows area of increased uptake in the posterior frontal area.

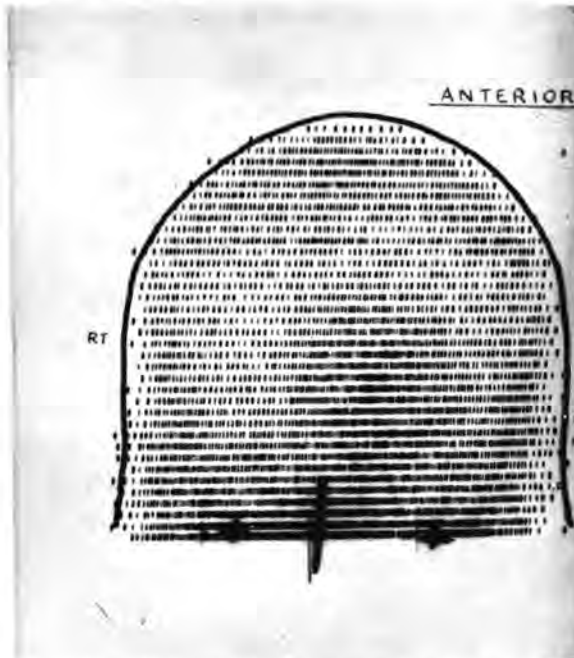


Fig. 2: Anterior view of same patient. Note lesion is strictly to the left and does not cross midline. Final diagnosis at surgery meningioma.

2. 203 or 197 Hg Neohydrin
3. 99mTc Per technetate
4. 113m Indium DTPA

Most centres, including the Department of Radiotherapy and Nuclear Medicine here, use 99 mTc as the scan agent because it is easily available and very effective. A dosage of 10 to 15 millicuries is used and the whole body radiation dose is 0.18 rads with 1-3 rads to the large bowel. Technetium is milked from a 99Mo generator. The agent could be given orally or parenterally although the latter method is preferable as absorption might be irregular orally and higher dosages may be needed. The majority of SOL are demonstrated, using any one of the several available tracers; however, certain lesions are demonstrated only, or more clearly, by a particular tracer. Chiro (March 68) has pointed out that specific tropism exists towards certain lesions, the classical case being radioiodine for thyroid metastases.

131 HSA for metastases

197 and 203 Hg Chlormerodrin for Gliomas

131 I Antifibrinogen for sarcomatous lesion
labelled albumin tracers AV malformation

Multiple tracer study is justified where strong clinical or neuroradiological evidence exists of a SOL. For routine scans 99mTc is the best. Where a scan is equivocal, it must be repeated with a different agent.

INSTRUMENTATION

There are numerous types of instruments available for scintillation scanning. A single crystal (5 inch) Na I thallium activated detector scanner was used here. Multiple detector scanners make it possible for more than one view to be done at the same time. Position emitters 18F and 68 Ga have been used with special position cameras and dual crystal moving detector scanners — the advantage here being ability to localise the lesion more precisely. The gamma camera has a useful speed advantage over the typical scanner for equivalent quality results. Also the camera for dynamic studies is unrivalled.

ORDER OF INVESTIGATION

The majority of patients referred for brain scans have suspected neoplasms, abscess or cerebrovascular accidents. Routine neurological work is needed in all such cases, and skull X-ray, EEG and LP are needed. However, arteriography and PEG and ventriculography are best done after the scan, one reason for this being they are formidable investigations and may not be needed once the scan is done. Recently, there have been several reports of false positive isotopic

brain scans following arteriography. However, Heinz and his colleagues (Nov. 66) showed that carefully performed angiograms do not produce abnormalities in the brain scan. Scans and angiography define two quite different parameters of brain. The angiogram defines with high spatial resolution and rapidity of flow of opacified blood. The scan is a low resolution map of the blood brain barrier.

METHODS AND MATERIALS

Over the past year, a number of brain scans were done, using a Scintimat scanner with a 5" crystal and a coarse 55-hole collimator. Initially, a fine 163-hole collimator was used; however later, the coarse collimator was found to be more effective. The reduced resolution was more than compensated by the increased count rate obtained. With Technetium - 99m, the patient had 200 mgm of Potassium Perchlorate about 1/2 hour before the scan to reduce Choroid plexus activity. Where RISA was used, the scans were done shortly after injection to outline the vascular anomalies and repeated in 24-48 hours to show localisation. Iodides were administered 7 days before and after RISA to reduce thyroidal uptake of free 131I. The patient was made comfortable in a recumbent posture on a special scan trolley. Reference was made to the nasion, inion and external auditory meatus. The brain scans were started about 15 minutes after injection, in the case of 99mTc. Usually both laterals and anterior view were obtained. The posterior view was done only in special cases. Special views such as the vertex view (Overton 1965) and the 'angled posterior' view (Witcofski and Roper 1965) were reserved for difficult cases.

A count rate of 10,000 to 30,000 counts/minute were obtained, and the scanning speed varied between 42 to 90 cm/minute. The colour calibration was adjusted so that the range of activity from the superior saggital sinus to the normal brain covered its full range. A line spacing of 2 mm was routine. All the scans were interpreted after the patient's clinical presentation was studied to appraise the problem at hand. They were classed as positive, negative or equivocal. Increased activity should be in 3 consecutive lines for a scan to be classed positive (McAfee and Taxdal 1961).

Results And Discussion

Total number done	44
Positive	14
Negative	28
Equivocal	2



Fig. 3: Area of crescentic uptake in the frontal area. Metastatic deposit from a carcinoma of uterus.



Fig 4: Anterior view of same scan lesion on the right side and solitary.

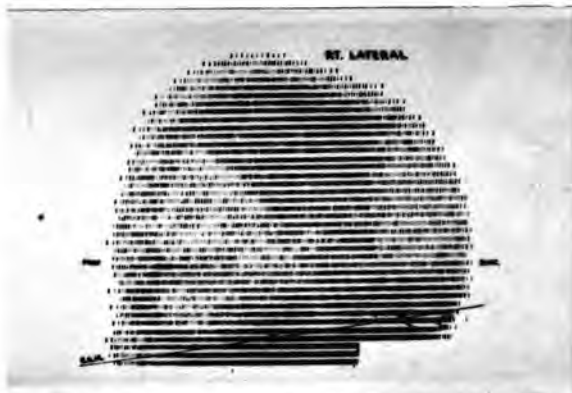


Fig. 5: Positive scan in A/V malformation. Lateral view angiogram confirmed diagnosis.

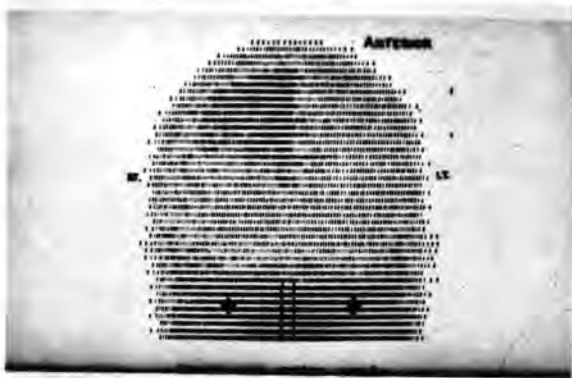


Fig. 6: Anterior view of AV malformation.

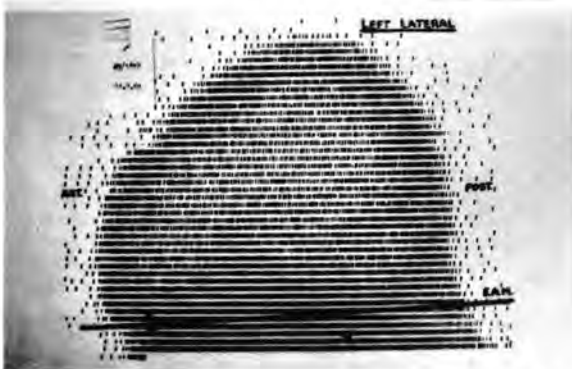


Fig. 7: Scan in craniopharyngioma area of uptake seen in the sellar region. Air studies showed obliteration of the third ventricle.

Equivocal scans are those with assymetry between the right and left sides in the anterior, posterior and lateral views. Assymetry was most common in the posterior fossa and around the superior saggital sinus.

Diagnosis in positive scans

Meningioma	2
Metastases	3
Glioblasoma	1
TB Meningitis	1
A/V malformation	2
Pinealoma	1
Craniopharyngioma	1
Ependymoma	1
Cystic astrocytoma	1
Pituitary tumour	1

Lesions not detected by the scan

Midline cerebral tumour	1
Pontine Glioma	2
Pituitary tumour	1
Cerebellar sarcoma	1
Intraventricular tumour	1
Diagnosis not known	4

Initially, when scanning was attempted, they were often negative, even in the presence of known lesions. A number of factors are responsible for these false negative scans.

1. **Low count rate:-** Low dose or poor absorption when given orally are important factors. There has been a lot of stress to optimisation of technetium brain scan. Immediately after 99mTc injection, the count rates rise to a maxi in 16 secs., after which they fall to a plateau which lasts for about 8 minutes before declining to reach half its value in 2½ hours time. Too early scanning would miss some lesions (Levy L.M.et al 1966). Early scanning is needed in some cases to detect AV malformations. Delay of ½ hour is optimum as at this stage the tumour/brain ratio is higher and the blood/brain ratio has fallen sufficiently. On delaying the scan too long after injection, the count rates may fall too low to make a good scan – this was common with our earlier cases.
2. **A benign lesion -** Where blood supply and metabolism are of the same degree as normal brain
3. **A small lesion -** This was the case in tumours which are situated in critical locations – for example, a patient with a pinealoma had a scan which was equivocal. However, the air study was conclusive. Lesions less than 2 cms may be missed.

4. **An unfavourable site** - Where such a lesion is distant from the scanner, as in deep lesions near the midline or close to areas of high activity such as venous sinuses or the base of the skull. Posterior scans are difficult to interpret for the same reason because of high activity in the nuchal muscles and venous sinuses.

5. **Symmetry** - Bilateral lesions near the surface which are symmetrical may be missed with moderate increases in activity.

The pathology of the lesion cannot be got from the scan unless serial scans are done with long lived isotopes (Planiol 1963). There are, however, clues as to the nature of the lesion from scan appearances.

(a) The relationship to the falx, tentorium, corpus callosum, and the convexity of the dura was stressed by Bull et al (1965). The glioma usually crosses the midline in the region of the corpus callosum while a falx meningioma crossed anterior, posterior or superior to it.

(b) There were three cases which gave a crescentic pattern of activity. One was a glioblastoma multiforme, and the remaining two were metastases. Such patterns are also seen in several other conditions (Heiser, Quinn, and Mollihan, 1966), and includes granular pachymeningitis, Paget's disease of the skull, extracranial haematoma, meningioma en plaque, and subdural haematoma. Metastases in the dura show a localised area of high activity in the lateral scan but subdural haematomas seldom show much increase except in the region of the sylvian fissure.

(c) There were two patients whose history and findings suggested a cerebrovascular accident. One patient had a complete occlusion of the middle cerebral artery as in the angiogram. However, the brain scan was negative in both. Where positive, the scan would show uptake with the shape of a horn rising in the temporal region and curving upwards and backwards, where the middle cerebral or the ant cerebral is occluded. The scan is positive in about 83% of patients in a CVA involving the hemisphere (Williams, 1966). It becomes faintly positive after 3 to 6 days, reaches a peak in 10-14 days and returns to normal after 40-80 days. The intensity of uptake was proportional to the degree of severity of the CVA as assessed clinically. The primary diagnostic use of brain scanning in cerebral infarction is to distinguish it from a neoplasm. A clear positive scan in the first few days after an episode (stroke) makes neoplasm the likely diagnosis. One of our cases had such a positive brain scan after an episode of hemiplegia of sudden onset. Here the diagnosis was cerebral metas-



Fig. 8: Positive scan in pituitary tumour. Interpretation can be difficult because of cavernous sinus activity.

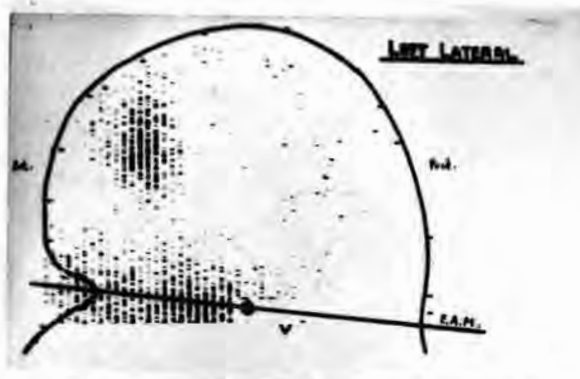


Fig. 9: Risa scan in case of cerebral metastases from a bronchogenic carcinoma. Risa is suitable in showing up metastases.

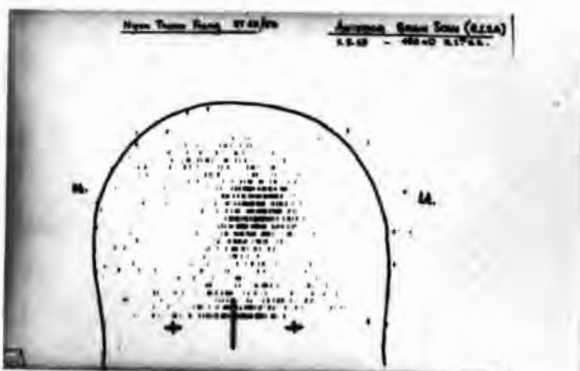


Fig. 10: Anterior view same patient. Lesion on the left but some increased uptake on the right side as well.

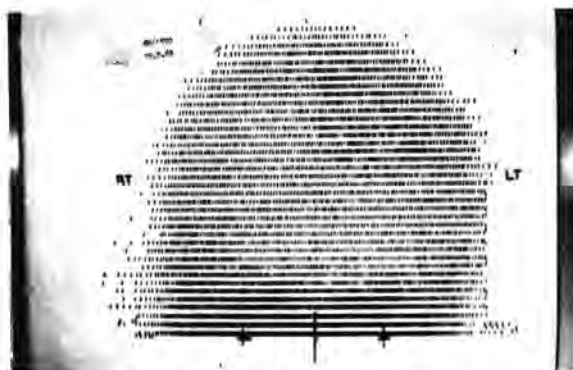


Fig. 11: 36-year-old female Malay with history of fever for 2 weeks, headache and a right hemiplegia. Scan showed uptake in the left posterior frontal area. Angiograms and air studies negative. CSF showed AFB. Cerebritis and ependymitis could give positive uptake in the absence of a SOL.

tases from a carcinoma of the breast.

(d) In the patients with positive scans who had meningioma at operation, the scan showed high activity over the lesion. The degree of uptake correlates well with the vascularity or activity of the lesions. Where the count rates over the lesion is equal to or higher than that over the Superior Saggital Sinus, the lesion was almost always a malignant tumour, a meningioma or an abscess (Forster 1969).

(e) The brain scan image correlates well with the pathology as shown by Bierwaltes (Jan. 66). Apart from the degree of uptake, which was highest for glioblastomas and meningiomas, followed by metastatic carcinoma, meningiomas show sharply demarcated, round concentrations on scanning with characteristic location parasagittal, parasylvian, sphenoid ridge and olfactory groove regions. Astrocytomas usually are small and round with locations in the posterior fossa, in many cases. Glioblastomas were large and irregular with high uptake ratios, whereas metastatic carcinomas were characteristically small and round, often situated in the occipital, posterior parietal, and posterior temporal region, being the commonest cause of more than one positive image in the scan.

Many of the patients have had operations often burr holes for ventriculograms or shunts for relief of hydrocephalous. In all cases, there was increased localisation of isotope in the craniotomy site, for at least 4 weeks. The intensity of localised activity decreased as the postoperative period increased. The localised activity in the operations site is due to the replaced bone rather than the soft tissue, after 4 weeks. In spite of this, scanning is useful after

craniotomy 2 to 3 months later to localise a recurrent tumour, a second primary tumour, or possible second metastatic tumour.

Wilkins (August 1967) showed that superficial retention is common in postoperative scans but deep retention was not seen unless there was tumour recurrence. Many patients have had radiotherapy in this series. The scan is not positive after radiotherapy unless there is persistent tumour. The brain scan helps not only in localising the tumour but also following the status after radiotherapy. Where the tumour is located over a less critical area (for example in the frontal lobe) higher doses of radiotherapy could be given; the localisation obtained permits more exact portal placement and intensive treatment could be given without compromising essential cerebral function. In posterior fossa lesions, pituitary and brain stem lesions, and tumours at the base of the brain, the scan is unsatisfactory for this purpose. However, it is of value in localisation and follow-up of glioblastomas and cerebral astrocytomas, (which form 75% of cases of cerebral tumours requiring radiotherapy).

Comparison with other diagnostic procedures.

It is difficult to give any definite figure for merits of scintillation scanning in comparison with other neurological investigations. The LP, Skull X-ray and the EEG are a must in all cases subjected to a scan. The EEG may detect up to 70% of meningiomas and 85% of glioblastomas whereas scintillation scanning detects about 96% of meningiomas and glioblastomas. Obviously in diffuse brain disorders, the EEG is superior. As a screening test, it is best to combine all three and scintillation scanning. The angiogram, and air studies, however, are procedures with a definite mortality and morbidity and could be reserved much later, to provide more information. Besides its role as a screening procedure, the scan may reveal a lesion too small to provide the vascular distortion needed to produce a positive angiogram (Sweet et al).

One of our cases, a 36-year-old female, had a positive brain scan. She had a history of fever and headaches and weakness of the right limbs for about 2 weeks prior to this. The scan showed uptake in the left posterior frontal region. The CSF changes were suspicious of tuberculosis. The angiograms and air studies were, however, negative for a localised space-occupying lesion. It is possible here that there may be a localised process in this area such as a tuberculoma which only the brain scan revealed. However, the diagnosis is unconfirmed.

This second role of scintillation scanning as a more

definitive neurological investigation is bound to increase in importance with further improvements in scan agents, instrumentation and better understanding of the pathophysiology and underlying basis for uptake of radioactive agents by tumours.

SUMMARY

1. The procedure involved in radioisotope scanning is explained, with relative merits of different types

- of scan agents and instrumentation available.
2. An analysis of experiences with brain scanning at the General Hospital, Kuala Lumpur, is recounted.
3. Pitfalls of scan interpretation, and possibilities for more exact scan diagnosis is explained.
4. Role of scintillation scanning in postoperative evaluation and radiotherapy is discussed.
5. Lastly, the role of scanning as a screening procedure and in relation to other neuro-diagnostic procedures is evaluated.

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Clomiphene citrate in Asian women

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CLOMIPHENE CITRATE, sold under the trade name of "Clomid," has not been freely available in this part of the world for use in Asian women and this is a preliminary report on 11 cases out of which 7 pregnancies resulted up till the time of writing.

Due to its scarcity, it has only been given to the most deserving cases for the sole purpose of inducing ovulation for fertilisation. Careful evaluation of patients includes preliminary dilatation and curettage, tubal insufflation, hysterosalpingogram and seminal analysis to ensure that at least physically there is no bar to conception – except for failure to ovulate.

Failure to ovulate was considered conclusive if the endometrium showed no secretory phase in the second half of the menstrual cycle, no biphasic basal body temperature curve and an oestrogenic smear in the second half of the cycle. Presumptive evidences considered are irregular menstrual cycles and failure to conceive after the patient was given advice about coitus during the imaginary fertile period of approximately 14 days before the onset of the next expected period.

Unfortunately, it is at present not possible to arrange estimation of urinary excretion of pregnanediol, oestrone, oestradiol or oestriol. Such procedures would be prohibitively expensive for the

management of private patients of which this series is made up. Therefore to provide a measure of control, the help of a cytologist was enlisted.

In the series of cases, where possible, vaginal smears were taken in the second half of the menstrual cycle prior to therapy. This forms a good baseline for comparison with subsequent smears taken at various intervals following "Clomid" therapy. Of the cases studied, anovulatory smear patterns were seen in cases with non-secretory endometrium. This was also consistent with the presence of a monophasic temperature chart. Subsequently, smears were taken in the first half of cycle prior to "Clomid" therapy and in the third week following therapy. Smears were labelled "positive" for evidence of ovulation or "negative" when the smear pattern showed no change in pattern from a proliferative type smear in the first half of the cycle to a secretory type smear as seen in the post-ovulatory period in the second half of the cycle.

The accepted criteria for evidence of ovulation are the changes produced by the influence of progesterone on vaginal epithelium. Progesterone stimulates the proliferation and maturation of squamous epithelial cells as far as the intermediate cell stage. The characteristic "progesterone effect", seen in squamous cells obtained during the secretory phase,

consists of the curling of the cytoplasm of the cells resulting in the typical "rolled edge" appearance. The thinner cytoplasm of the more superficial squamous cells are folded back to give the "envelope effect". The cytoplasm attains a translucent granular appearance with a progressive increase in the number of cyanophilic cells which tend to aggregate in clumps. There is also progressive increase in neutrophils and histiocytes until just before menstruation, and with the proliferation of bacteria and fragmentation of cells, a late secretory phase smear gives a "dirty" appearance to the smear.

The initial dose is one 50 mg tablet, taken daily for 5 days, beginning on the fifth day of the cycle. Should ovulation occur, this dosage is maintained; otherwise, the dosage will be pushed up to 100 mg. daily and in a few cases 150 mg. daily were tried. To ensure a good seminal volume and count, the couples are advised to refrain from coitus until the 13th day of the cycles. It is believed that Clomiphene Citrate acts through the pituitary, causing an increased output of gonadotrophin, which stimulates the ovaries to develop and mature its follicles. Overstimulation is minimised by careful adjustments of dosage as outlined above and pelvic examinations done before treatment and at the time of taking the second smear in the third week. Any ovarian enlargement has been treated with care and the patients were asked to report any acute lower abdominal pain which may indicate the rupture of multiple matured follicles.

Up to date, no serious untoward symptoms like nausea, hot flushes, blurring of visions and a host of others reported by European users, have been noted and this may be due to the small doses and short courses used in this series.

The following are summaries of the successful cases:-

(1) Mrs. V., Indian national, age 28. She is extremely obese, weighing 170 lbs. and is married 7 years with one abortion at 2½ months, occurring 5 months after marriage. She has, thereafter, consulted various gynaecologists in India and Singapore. Investigations completed by 24.6.68. The endometrium was non-secretory and showed cystic hyperplasia. Clomid was started on 14.10.68. She then consistently had Mittelschmerz (smear positive) and following L.M.P. on 2.6.69, complained of nausea on 12.7.69. Pregnancy test was positive but on 14.7.69, she began to stain and despite hospitalisation and hydroxyprogesterone caproate injections the pregnancy test became negative on 9.8.69 and products of conception was

evacuated at D & C.

However, she reported amenorrhoea again following the next period on 17.8.69 and as a prophylaxis, weekly hydroxyprogesterone caproate was given. She is now 24 weeks pregnant. Foetal movement is felt and foetal heart heard.

(2) Mrs. V. P., Indian girl, age 26 and married 4 years. Normal girl who was first seen before marriage on account of oligomenorrhoea. One-and-a-half years following marriage, she was investigated for infertility and by 25.4.67, it was established she was anovulatory but nothing could be done. Her cycles continued to vary from 3 weeks to 4 months. Clomid was first started on 25.6.69 — that is, 27 months later, and by the fourth course, using 3 tablets daily, she ovulated and registered her L.M.P. on 18.10.69. Pregnancy tests done here and by an independent laboratory are positive and the uterus is now 14 weeks in size.

(3) Mrs. W. C. Y. Chinese, age 30. Normal girl, married 4 years. Usual treatment and most investigations completed by other gynaecologists except for hysterosalpinogram which was done on 6.1.69. Clomid started on 14.1.69 and she responded to the 2 tablets regime. Reported L.M.P. on 28.4.69 and except for morning sickness, pregnancy was progressing normally until 16.12.69 when the breech was found presenting. Attempt at external cephalic version resulted in mild vaginal staining which settled after 5 days of hospital rest. She was delivered of a healthy 5 lb. 9 oz. boy by L.S.C.S. on account of disproportion.

(4) Mrs. P. T. French girl (an exception) married to a Chinese. Age 23 and married 3 years. She has a good growth of hair along the linea alba and is a thin, tall girl. Routine investigations completed by 8.11.68 were all normal except for non-secretory endometrium and a flat temperature chart throughout menstrual cycle. Patient refused Clomid therapy till 19.6.69. She responded to the first course and got pregnant after the second at the same dosage. Her L.M.P. was on 19.7.69 (smear positive). She had a short admission for severe hyperemesis gravidarum but is doing well now with the uterus at 28 weeks size. Foetal movement felt and foetal heart heard.

(5) Mrs. S. N. Chinese. Age 24 and married 2½ years with no issue. Investigations completed by 12.6.68 with non-secretory endometrium and a flat basal temperature chart. She responded well on the first course and in October 1968 became pregnant after the second (smear positive). She went on to have an uncomplicated pregnancy and was delivered by mid forceps of a normal 6 lb. 11 oz. baby girl.

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(6) Mrs. L. K. L. Chinese. Age 22 and married 2½ years. Her problem was anovulation again – the investigation was completed on 22.7.68. She was started on Clomid on 16.10.68 and responded to the first course and was pregnant on the third (smear positive). Her pregnancy progressed smoothly and she delivered a normal 6 lb. 10 oz. baby girl on 12.9.69.

(7) Mrs. N. C. H. 28-year-old Chinese girl, married 6 years. She had one delivery 5 years ago. Despite no family planning, she was unable to conceive again. Investigations were completed by 25.4.69. After three months, there was no result and therefore on 22.7.69, she started on Clomid. She responded immediately and reported L.M.P. on 20.11.69. She is now 10 weeks pregnant and having mild morning sickness. Pregnancy test is positive and uterine enlargement present;

Of the remaining 4 cases, one case is of secondary infertility of 13 years' duration and she has had 4 courses with no evidence of ovulation having taken place. Two are married for 4 years and they, too, have taken 4 and 3 courses respectively. No result up to date. The last patient is married for one year and

there has been no response after 2 courses.

Conclusion

This drug has been in use only recently and has shown very encouraging results in cases where it can be proved that failure to ovulate is the factor responsible for infertility. Perhaps the surprising fact is the one of secondary infertility who has failed to respond as she is the sort of patient deemed very suitable for treatment by Human Chorionic Gonadotrophin.

Three single pregnancies and none to suggest multiple ones show that simple clinical methods and cytology prove more than adequate in controlling patients put on this drug. It is indeed gratifying for both patients and doctors that so many patients have responded favourably and the fear of multiple pregnancies has not materialised. The cytologist report has not only added confidence when increasing dosage of the drug but it also saved wastage notwithstanding the fact that the drug at present is hard to come by and cost private patients a good deal of money.

A thermoprecipitin test for rapid diagnosis of cholera

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THERMOPRECIPITIN TESTS, in which antigen extracted by boiling a sample of infected tissue is layered on antibacterial serum to obtain a ring of precipitate, are well established in veterinary diagnosis, e.g., in anthrax and plague. They are simple, rapid, and usable even when the pathogen has become nonviable or overgrown with contaminants. Such tests have not been used in man, except that ring tests can be made with unheated cerebrospinal fluid for instant diagnosis of meningococcal and haemophilus infections.

Since cholera stool is almost watery and contains a high concentration of dissolved antigen (Finkelstein et al., 1963) the ring test appeared suitable for rapid diagnosis. In the absence of cholera cases animal experiments were made, the stool of infected baby rabbits being virtually identical with that of cholera patients (Burrows, 1968).

Materials and Methods

A strain of *Vibrio cholerae* Inaba and another El Tor vibrio of Ogawa serotype, both isolated from

patients, were used to infect baby rabbits by inoculation into the duodenum (Ghosh, 1969a). As soon as diarrhoea developed, the watery fluid in the colon containing flakes of mucin and other debris was collected. About 2 ml fluid was boiled over a spirit lamp for about a minute, and then centrifuged for 2-3 minutes at c. 1000 x g. The coagulated debris settled or floated, leaving a faintly opalescent middle layer. Antigen controls were broth cultures of 2 strains each of *Escherichia coli*, *Alcaligenes faecalis*, *Shigella flexneri*, *Salmonella enteritidis* and NAV of Heiberg's Group I incubated for 7 days at 37° C.

The antiserum was made by injecting intravenously 2 adult rabbits with agar culture of the cholera vibrio strain suspended in saline to contain c. 10⁹ cells per ml, and steamed for 2 hours. An initial dose of 0.5 ml was followed by 3 weekly 1 ml doses. The serum, collected 7 days later and pooled, had an agglutinin titre of 1:3200. This was diluted with 3 volumes of normal serum.

The test was performed at c. 26° C by layering 2-3 drops of heated stool or broth culture on a drop of

THERMOPRECIPITIN TEST FOR CHOLERA

antiserum or normal serum in a narrow tube made by cutting a pasteur pipette at the neck and sticking the shaft in plasticene.

Results

In view of the consistent results and the exploratory nature of the experiments, each vibrio strain was used to infect only 6 baby rabbits: 2 at a time. All stools gave a distinct precipitation within 5 minutes, usually even when diluted with 2 volumes of saline (figure). With the noncholera broth cultures or with normal serum, nonspecific precipitation sometimes appeared after c. 15 minutes.

Discussion

With increasing incidence of cholera and the popularity of fast modes of travel, there is considerable interest in rapid laboratory confirmation of suspected cholera. The quickest method is based on immobilisation of vibrios by antiserum (Pfeiffer and Vagedes, 1896). Using dark-ground microscopy to observe motility, about 75% of culture-positive cases can be diagnosed rapidly (Benenson et al., 1964). Some culture-negative cases also give positive results. This test has not been popular presumably owing to operational problems. The same appears true of fluorescent-antibody staining of stool smears (Finkelstein and Gomes, 1963).

The ring test described here can be performed with portable apparatus. The ratio of antigen to antibody is not critical in ring tests, and they would detect traces of antigen. It is likely that boiling the stool for clarification also increases the concentration of dissolved antigens (Ghosh, 1969b).

It is hoped that the test will be evaluated clinically by workers in endemic areas, using stool from severe non-cholera diarrhoea as controls. It would be an advantage to use a serum with high precipitin titre instead of depending on the agglutination test.

Summary

On gentle boiling and centrifuging the stool of



From left to right: (i) Saline on antiserum, (ii) Cholera vibrio stool on antiserum, (iii) El Tor stool on antiserum, (iv) El Tor stool diluted threefold, and (v) Cholera stool on normal serum.

baby rabbits infected with cholera vibrio, one obtains a clear fluid that gives a specific ring of precipitate when layered on high-titre serum. A plea is made for evaluation of this simple and rapid diagnostic procedure in natural cholera.

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A case of pulmonary hydatid disease

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Introduction

HYDATID DISEASE characterised by hydatid cysts in various organs like the liver, lung, spleen, bone and other rare sites, is known to be endemic in many countries — America, Iraq, India, Australia and Europe. The condition was not reported in Malaya till Khaira in 1955 reported its occurrence in an Indian who had spent 4 years of his early childhood in India from where he could possibly have contracted the infection. However, the second case report by Duguid et al (1968) of hydatid disease in a 6-year-old Chinese boy, resident in Malaya throughout, established the possibility of local occurrence. In view of its rarity, the following case is deemed worthy of report.

Case Report

A 6-year-old male Indian child was admitted to the Lady Templer Hospital on 24.7.1969 for abnormalities discovered in chest X-rays. His complaints of "asthma-like" symptoms, treated unsuccessfully by various doctors developed a year after a three-month visit to India where he stayed on a cattle farm.

On clinical examination, the only positive finding was that of diminished breath sounds in the lower



Fig. 1: X-ray — A.P. view shows two opacities.

PULMONARY HYDATID DISEASE

chest, both laterally and posteriorly, on both sides. Chest X-rays showed large rounded opacities in both lungs. While in the A.P. view, there appeared to be two opacities in the right middle lobe and one in the left lower lobe; in the lateral views, the exact number of opacities in the right lung was found to be three.

A clinical diagnosis of metastases from a renal or adrenal tumour was made, but investigations along these lines, including I.V.P., proved negative. Consequently, a left postero-lateral thoracotomy was done on 5.8.69 and a cyst 3" in diameter was removed intact, followed by an uneventful recovery. A right thoracotomy was scheduled for four weeks later but in the meanwhile the patient developed right basal pneumonia. At the time of the right thoracotomy, three cysts, one in the middle lobe, one in the posterior basal segment and one in the lateral basal segment with evidence of the lower lobe pneumonia, were found.

The third cyst proved difficult to remove because of dense adhesions following the recent infection and when it ruptured, 10% formalin was instilled into it. The diagnosis of hydatid cyst was then obvious and part of the cyst was sent for histopathological examination which confirmed the diagnosis made at the second operation. Unfortunately, overwhelming bilateral pulmonary infection in the immediate post-operative period, unresponsive to treatment, occurred and the child died of respiratory failure on the fourth day.

Discussion

Of the four species of the genus *ECHINOCOCCUS RUDOLPHI*, the larval forms of *E. GRANULOSUS* is the commonest and the larvae, adapted to develop in comparatively long-lived intermediate hosts, grow relatively slowly. Under natural conditions at higher altitudes, the final host is the wolf and various wild ruminants serve as intermediate hosts. With the domestication of animals however, the dog has become a common definitive host and cattle, sheep, pigs, goats and man are the intermediate hosts.

A greater number of cysts in the sheep have been found to contain viable scolices than in those found in cattle, supporting the concept that sheep are the oldest intermediate hosts of *E. GRANULOSUS*, because of a more perfect host-parasite relationship (IMARI 1962), the hooked embryos usually being too large to pass the portal capillary filter. Lung involvement occurs in about 25% (IMARI 1962) and though generally pulmonary cysts are associated with cysts elsewhere, isolated lung cysts are frequently



Fig. 2: X-ray — Lateral view shows three opacities.



Fig. 3: The cyst as seen on thoracotomy.

encountered. The lung tissue, because of its poor resistance, is a good medium for the growth of the echinococcal larvae, the cysts being commoner in the right lung because of its greater circulation.

The case under report is in accordance with this observation and with the general observation that the



Fig. 4: Solitary cyst from left side is seen.

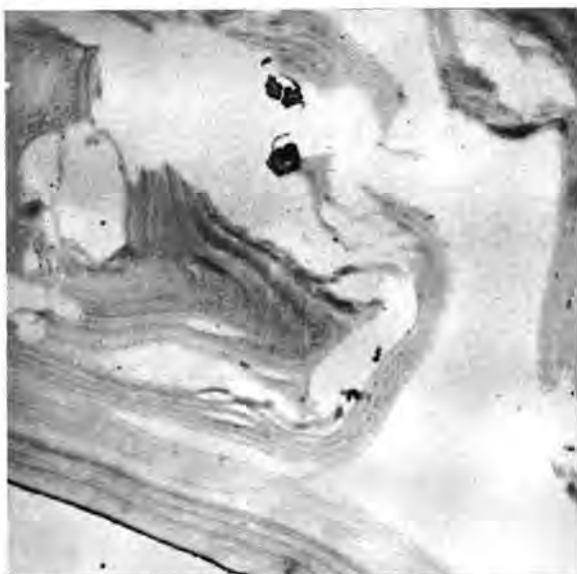


Fig. 7: Histology shows the characteristic laminated hyaline membrane with evidence of brood capsule.



Fig. 5: Close-up view of hydatid cysts from right side.

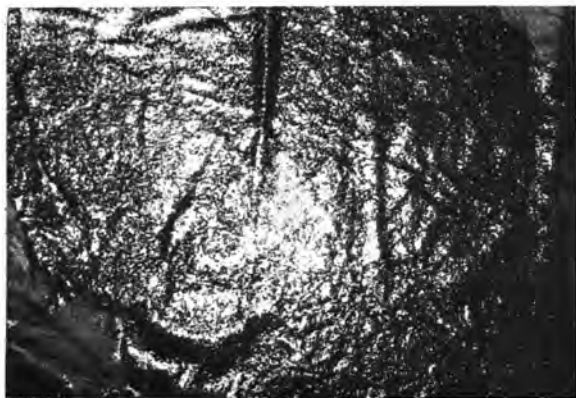


Fig. 6: Scolices viewed on a black background.

cysts are more common in the basal rather than in the upper lobes. The finding of isolated pulmonary cysts suggests inhalation as a route of entry (Reddy et al 1968;) though this has not been proved experimentally. Napier (1946) estimated that about 25% of people with hydatid disease are asymptomatic and symp-

toms, if present, are referable to any number of respiratory complaints—cough productive or non-productive, haemoptysis, chest pain or asthma-like attacks as in the case presented.

Unusually large cysts, causing mechanical obstruction and collapse, rupture of cysts causing hydropneumothorax, or anaphylactic shock are some of the rare causes of an acute presentation in pulmonary hydatid disease. The typical rounded opacities on radiological examination are often diagnostic in countries where the disease is common, though sometimes they pose difficulties to the clinician. In unusual locations, as for example in the mediastinum, the cysts may simulate dermoid cysts or aortic aneurysms. Irregularly outlined posterior shadows may be difficult to differentiate from the neurofibromas.

In countries where the condition is rare, as in Malaya, in the differential diagnoses, primary or metastatic tumours, tuberculomas, gummas, non-specific abscesses and amoebic abscesses are generally entertained. It is relevant, at this point in the discussion, to stress the importance of lateral chest films to determine the exact number of cysts which is unreliable from A.P. views alone. Various laboratory aids to confirm the radiologic impression are available. A high eosinophilic count, up to 25% has been observed (Anderson 1966), resulting as an allergic response to small leakages of hydatid fluid. The reliability of this is obviously limited, particularly in

PULMONARY HYDATID DISEASE

countries where other parasitic infections are common.

Casoni's skin test is the most wellknown diagnostic procedure and reliability, varying from 75% (Reddy et al 1968) to 95% (Kagan 1968), has been reported. Despite the high false positives observed by some (Chordi 1962; Sorice et al 1966), which according to Kagan (1966) can be considerably reduced by decreasing the concentration of the antigen used, the test is of value in diagnostic and epidemiologic studies.

In view of the fact that hydatid disease is now a recognised entity in this country, Casoni's antigen would be of tremendous advantage if made available to the clinician in the face of a diagnostic problem, as in the case under report, so that the patient need not be subjected to unnecessary and cumbersome procedures, like I.V.P., etc.

Among the various serological tests, which include complement fixation, Bentonite-flocculation and haemagglutination, haemagglutination is considered to be the most sensitive, though in pulmonary hydatid cysts a lower sensitivity has been observed (Garabedian et al 1959; Jonathan 1960; Arabatzis and Papaganagiotou 1963). They have immense post-operative assessment value, but the complement fixation test reverts to negative more quickly than the others following removal of cysts and a persistent complement fixation titre 6–12 months after cystectomy may indicate presence of a second cyst (Kagan 1968). Fluorescent-antibody test, using protoscolices of fertile cysts as antigen, has shown to produce excellent results (Pozzuoli et al 1965; Sorice et al 1966) but needs further evaluation.

The final diagnosis, however, rests on the histopathologic examination of the cyst. When the parasitic larvae reach a susceptible organ, they develop into cysts of varying sizes. The tissue response consists of hyperemia, proliferation of connective tissue, epithelioid cells, eosinophils and foreign body giant cells, which results in the formation of the adventitious layer of the cyst. The parasite's contribution to the formation of the cyst wall consists of an outer laminated layer and an inner germinal layer from which brook capsules containing scolices develop over a period of months.

The cysts may undergo a variety of changes, including suppuration, collapse, fibrosis and calcification. Though the presence of typical scolices in the cyst fluid or cyst wall clinches the diagnosis, the eosinophilic laminated cyst wall is characteristic enough to make a definite histologic diagnosis, when one is dealing with acephalo cysts.

Conclusion

A case of pulmonary hydatid disease in a 6-year-old male Indian child who succumbed to a fulminating lung infection following surgical removal of the cysts is described, with a brief discussion on the common clinical and pathologic findings. Though there is a history to suggest that he may have contracted the infection while in India, from the large size of the cysts and the general observation of the short interval between exposure to infection and development of the cysts, we feel that it is highly possible that he may have acquired the infection locally.

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Unusual presentation of chorion epithelioma malignum

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THIS CASE is reported by us as it is of interest in more than one way. In the first place, the site of the secondary lesion in the nose and nasopharynx, which is a very uncommon one; secondly, there was no evidence in the uterus of a primary lesion; and thirdly, the patient, on her first admission, gave a history that she was unmarried.

SITE OF THE SECONDARY

In the literature, no mention is found of the nose or the nasopharynx as a site of a secondary of chorion epithelioma malignum. Willis, in his book of Pathology of Tumours, gives a list of the organs in which secondaries have been found — commonly, in the lungs, spleen, brain, kidney and liver, and uncommonly, in the adrenals, pancreas, thyroid, etc. It is conceivable, anyhow, that once secondaries establish in the lungs, any part of the body may be the site of further secondaries, spreading through the general circulation.

ABSENCE OF A PRIMARY LESION IN THE UTERUS WITH HISTORY OF NOT MARRIED

The patient sought medical aid, not for any uterine condition, but for cough and blood-stained sputum. Though she said she was unmarried at first admission on 9.9.69, it was later, on further questioning, found that she was married four years back, but divorced three months after marriage. As the patient was not very co-operative, it was found difficult to get any history of pregnancy followed by abortions

or miscarriage. In fact, she absconded on 13.10.69 when she was referred to the gynaecological department, to investigate more completely, to establish whether she was married, any history of pregnancies or signs of a primary lesion, as the gravindex test on her urine was positive and the biopsy report was chorion epithelioma malignum (secondary). Anyhow, further investigations were possible as she got worse and was readmitted to the hospital on 7.11.69 with a history of pain in the right chest, dyspnoea and any primary lesion in the uterus. Gravindex test was repeated on 10.11.69 and was reported positive. The first gravindex test was done on 11.10.69 and was also reported positive.

LESION IN THE LUNG AND NOSE

The patient, when first seen at the outpatient department of the hospital on 23.8.69, gave a history of cough with blood-stained sputum. She was thus X-rayed and also her sputum was examined for acid-fast bacillus.

The Mantoux test was negative. The sputum was negative to acid-fast bacillus. X-ray report of 23.8.69 — "oval shadow 3½" x 2¼" on the mid-zone, posteriorly on the right chest (lung) rest of lung clear. Probably tumour or encysted fluid. Suggest, repeat after chemotherapy."

Patient admitted to the hospital on 9.9.69, as she did not improve with chemotherapy. The complaints were cough with blood-stained sputum, pain in right chest and blocked nose with purulent discharge, at times blood-stained. She was seen by the surgeon, and

CHORION EPITHELIOMA MALIGNUM

the obstruction of the nose was found to be due to ulcerating growth protruding behind the soft palate. Tonsils were not enlarged, also the glands in the neck. Provisionally diagnosed as nasopharyngeal carcinoma. Punch biopsy of the growth of 21.9.69 was reported – "small bits of vascular tissue with areas of lymphocytic infiltration, please repeat." Excision biopsy of 27.9.69 was reported, "most areas show necrotic tissue and blood clots, with islets of cancer cells, very anaplastic, almost resembling chorionic carcinoma. Not a nasopharyngeal carcinoma (lympho-epithelioma). Suggest urine for pregnancy test."

X-ray report of 9.9.69 – "The shadow is much bigger – 4" x 2¾" Left nose occluded by a mass. Marked mucosal thickening of right maxillary antrum."

X-ray report of 20.9.69 – The shadow getting bigger – 4½" x 3¾"

X-ray report of 10.11.69 – Opacity of the whole of right side.

SHORT SUMMARY OF THE DETAILS OF THE CASE

Malay, female, age 21 years, from Alor Setar district.

First seen at the outpatient department on 23.8.69 with a history of cough with blood-stained sputum.

She was admitted to the hospital on 9.9.69 as she was not improving with treatment.

When the gravindex test was positive and supported the biopsy report of 27.9.69 as chorion epithelioma malignum, the case was transferred to the Gynaecology Department for further investigations but the patient absconded on 13.10.69.

She was readmitted to the hospital on 7.11.69 as she was getting worse, complaining of dyspnoea and pain on right side. X-ray report of 10.11.69 showed shadow on the whole of right side of chest. She died

on 12.11.69. It was not possible to get permission for an autopsy.

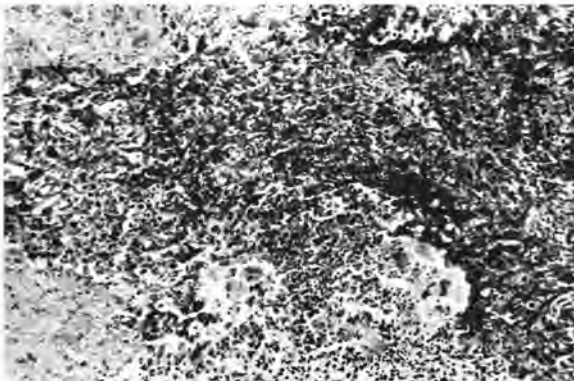
COMMENTS

As already mentioned, this case is reported because of the unusual site of the primary, negative primary lesion in the uterus and misleading history by the patient that she was not married. In the literature, cases have been reported without a primary lesion in the uterus and we, too, have come across similar cases. Since this is a tumour of the trophoblasts of the foetus, the absence of the primary lesion in the uterus, in some cases, is quite explainable and understandable. In this case, the patient was not very intelligent and her social conditions were such that it was not possible to get her full co-operation to get more definite details of the primary lesion in the uterus. Obviously, there must have been conception and the tumour in the lung is a secondary and the nasal lesion is from the secondary in the lung. Probably there may be secondaries elsewhere in the organs, etc. but, as already mentioned, no autopsy was possible, and thus it is not possible to give full detailed findings of the case as regards secondaries.

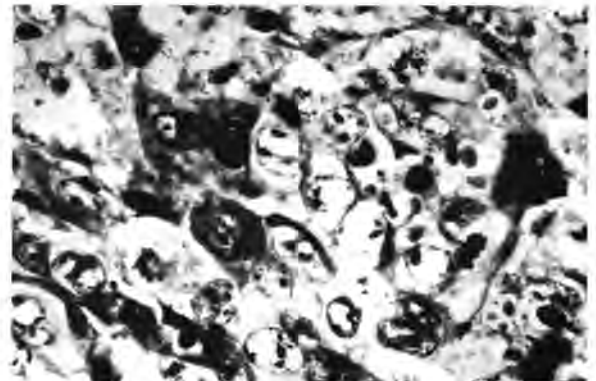
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We have to thank the Director of Medical Services for giving us permission to publish this case. We are also much obliged to Dr. Liew Meng Leong, the gynaecologist, and his staff in supplying us with the notes of the case. For the photomicrographs, we are very thankful to Professor Shanmuga Ratnam of the University of Singapore (Medical Faculty).



Magnification x 75 showing islets of cancer cells in the necrotic mass and blood clots.



Magnification x 500 showing cancer cells – Langhans type.

Hyperosmolar nonketotic diabetic coma

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HYPEROSMOLAR NONKETOTIC diabetic coma is an unusual and uncommon complication of diabetes mellitus. It was first described by Dreschfeld in 1881; he reported two patients whose diabetic coma was not associated with dyspnoea and in whom acetone was not detected in the urine. Between 1915 and 1924, 7 similar cases were reported but with incomplete data (Sheldon and Pyke, 1968).

The condition gained recognition as a distinct clinical entity following the publication of Sament and Schwartz in 1957. Since then Sheldon and Pyke (1968) have collected 53 cases from the literature and reported two cases of their own. As it is a rare complication of diabetes and early recognition is essential for its successful therapy, we report our experience with 2 cases of the syndrome.

CLINICAL RECORD

Case One

P.S.J. a 55-year-old unemployed Southern Indian,

presented with drowsiness, slurred speech and weakness of 48 hours' duration. Two weeks before the onset of his illness, he had polyuria and polydipsia.

Physical examination showed that his temperature was 99.8°F and his blood pressure was 130/80. The respiratory and cardiovascular systems were normal. He was drowsy and confused; the tendon reflexes were present and the plantar response was normal. The fundi were normal. At this stage, the diagnosis of a cerebrovascular accident was made.

His diabetic state was not recognised until 32 hours later. At this stage, he was comatose (responding only to noxious stimuli), dehydrated, sweaty and his breathing was stertorous. His temperature was 100°F and his blood pressure was 80/60. The tendon reflexes were sluggish and the plantar response was normal.

Repeated tests of the urine only showed massive glycosuria (brick red with Benedict's test) but no acetonuria (Rothera's test). The blood sugar was 980

HYPEROSMOLAR NONKETOTIC DIABETIC COMA

mg% and the blood urea was 166 mg%. The serum sodium, chloride and potassium were 145, 108 and 4.5 mEq./L. respectively. The calculated effectively plasma osmolality* was 334 mOsm./L. (normal: 285 to 295 mOsm./L.) His alkaline reserve was 51 vol.% (normal: 50-70 vol.%).

Patient died 14 hours after his hyperglycaemic hyperosmolar nonketotic diabetic coma was recognised. During this period, he was given soluble insulin 300 units intravenously and 525 units subcutaneously; the blood sugar remained high (610 to 1000 mg%). He also received intravenous infusion of 1880 ml. of hypotonic (half normal) saline, 540 ml. of normal saline and 540 ml. of Darrow's solution; his calculated plasma osmolality remained elevated (328 to 344 mOsm./L.). Terminally, he became acidotic (alkaline reserve 38 vol.%; arterial blood pH 7.120) and was given 370 ml. of 8.4% sodium bicarbonate intravenously. Antibiotics and vasopressors were administered. His coma and hypotension deteriorated and he perished. A postmortem examination was not done.

Case Two

L.C.M., a 50-year-old fruit seller, presented with fever, anorexia and weight loss of two weeks' duration. He had no symptoms of diabetes before the onset of his illness.

Physical examination showed that his height was 63 inches and his weight was 122 lbs. He was moribund and was in shock (blood pressure 70/0 mm. of Hg.) He was dehydrated and was areflexic.

Investigations showed presence of sugar in the urine (red with Benedict's test) but no acetone (Rothera's test) on repeated examinations. The blood sugar was 960 mg.% and the blood urea was 127 mg.%. The alkali reserve was 49 vol.%. The serum sodium, chloride and potassium were 159, 118 and 3.0 mEq./L. respectively. The calculated plasma osmolality was 361 mOsm./L.

After being given 258 units of soluble insulin intravenously and subcutaneously during a 24-hour period, his blood sugar fell to 228 mg%. He also received 12 pints of hypotonic (half-normal) saline and 1 pint of Darrow's solution intravenously during this period; as a result of which, his plasma osmolality fell to 305 mOsm./L. He received antibiotics cover with penicillin and streptomycin injections. For his hypertension, noradrenaline infusion was administered.

After 24 hours of infusion therapy, his hyperglycaemia, hyperosmolality and dehydration were

corrected but his coma and hypotension persisted. Over the next 3 days, he was maintained on intravenous infusion of noradrenaline, aramine, hydrocortisone and soluble insulin (average 72 units per day by subcutaneous injections). On the fifth day, his general condition improved and mentally he was more alert. His blood pressure returned to normal. Intravenous fluid therapy was discontinued and oral feeding started. He continued to receive subcutaneous injections of soluble insulin. On the 13th day, his soluble insulin was replaced by 48 units of lente insulin daily. On 48 units of lente insulin, his 2-hour post-prandial blood sugar was 161 mg%. He was discharged on the 15th day.

His diabetes was well controlled on 48 units of lente insulin daily. An oral glucose tolerance test (50 grams of glucose load) was performed 3 months later: the fasting, ½ hour, 1 hour, 1½ hours and 2 hours blood sugar were 324, 380, 448, 474, 445 mg%. respectively. He continued to receive daily injection of 48 units of lente insulin. He has been followed up for 5 months and has remained well.

DISCUSSION

The syndrome of hyperosmolar nonketotic diabetic coma consists of (1) absence of ketosis; (2) extreme hyperglycaemia; (3) extreme dehydration; and (4) depression of sensorium (Johnson et al., 1969).

The absence of ketoacidosis indicates that endogenous insulin exists, though relatively small in amount for the level of blood glucose. Thus in patient No. 2 reported by Johnson et al. (1969) the plasma immunoreactive insulin level was 29 μ U./ml. at a blood sugar level of 720 mg%. and in Case 2 described by Sheldon and Pyke (1968) the insulin was 40 uU./ml. (blood sugar was 2500 mg%).

This syndrome occurs mainly in the adult onset diabetics in whom endogenous insulin is present. The ages of our two patients are 55 and 50 years; the mean age of the 55 cases collected by Sheldon and Pyke (1968) was 62 years and the age range was 10 to 84 years. A striking exception regarding age of onset was reported by Enrich and Bain (1967) who described the condition in a 1½-year-old child. The paradox of this syndrome is that once they recover from the coma, they are easily controlled with diet alone though some may require insulin as is seen in our second patient. Absence of ketosis in the hyperosmolar syndrome allows for a degree of protraction of the illness not seen in diabetics with ketoacidosis.

* Plasma Osmolality (mOsm./L.) = 2 x Serum Na (mEq./L.) + Blood Glucose in mg%

This protraction accounts for the more profound osmotic diuresis and dehydration (Johnson et al., 1969).

Hyperglycaemia is extreme in hyperosmolar nonketotic diabetic coma due to a slow, prolonged and progressive deterioration of islet cell function but with persistence of sufficient insulin production to prevent ketosis and to allow time for the syndrome to develop (Johnson et al. 1969). The initial blood sugar in our two patients were 980 and 960 mg%; in the 55 cases collected by Sheldon and Pyke (1968) the mean initial blood sugar was 1120 mg% and the range was 360 to 2760 mg%.

The extreme dehydration and hyperglycaemia account for the hyperosmolarity of the plasma. The calculated plasma osmolarity in our patients were 344 and 361 mOsm./L.; in the series of Sheldon and Pyke (1968), the mean was 371 mOsm./L. and the range was 295 to 462 mOsm./L.

Central nervous system manifestations are seen in most cases; these include coma and fits. Coma was present in our patients. Johnson et al (1969) believe that the degree and duration of hyperosmolarity are important factors in the causation of coma.

Both our patients were not known diabetics before the onset of their illnesses; this is a common feature in hyperosmolar nonketotic diabetic coma.

The mortality of the condition is about 50% (Schwartz and Apfelbaum, 1965 - 1966); one of our two patients perished.

Hyperosmolar nonketotic diabetic coma has been reported as a complication of haemodialysis (Potter, 1966), acute pancreatitis (Halmos, 1966), extensive

body burns (Sevitt, 1955), steroid and immunosuppressive therapy (Spenny, Eure and Kreisberg, 1969) and Dilantin (diphenylhydantoin) administration (Goldberg and Sanbar, 1969).

The therapy of hypersomolar nonketotic state of the diabetic embodies the following principles (Johnson et al., 1969):

- (1) Early recognition and prompt treatment;
- (2) frequent and adequate amount of soluble insulin;
- (3) rapid infusion of hypotonic saline solutions initially, followed later by 5% dextrose, and
- (4) potassium supplement.

SUMMARY

The syndrome of hyperosmolar nonketotic state in the diabetic consists of

- (1) depression of sensorium,
- (2) absence of ketosis,
- (3) extreme hyperglycaemia, and
- (4) profound dehydration.

Two cases of the syndrome in a 55-year-old Indian and a 50-year-old Chinese are described. Both are not known diabetics before the onset of their illnesses. The disease was fatal in one.

The principles of therapy are described.

ACKNOWLEDGEMENTS

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The bite of a bird-eating spider *Lampropelma violaceopedes*

by *B.L. Lim and C.E. Davie*

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ENVENOMATION through bites of poisonous Arachnida, particularly spiders, has rarely been reported in Malaysia. Speculations have been made that several of the large tarantula-like spiders in Malaysia possess highly potent venom (Keegan et al 1964 and Tweedie, 1951), but no human cases have been reported previously.

One of these large Malaysian spiders is the common "bird-eating spider", *Lampropelma violaceopedes* (Mygalomophae). This spider is widely distributed throughout the country. It nests in holes on banks of forest pathways, in tree holes about 5 - 10 feet above ground level and in crevices in rocks. It feeds on arthropods, such as scorpions, crickets, etc. and birds which it drags into its nest to eat in the wild. According to the aborigines (Orang Asli), this spider is very dangerous and they believe that its bite is likely to cause death.

Lim (1964) performed some feeding experiments with this particular species of spider. The spider which was studied lived for five years in captivity. During this period the spider was fed principally on white mice. White mice, five grams in weight, were killed in less than four minutes after a bite. Those that weighed 10-12 grams were killed within 7-10 minutes, and a wild tree mouse, *Chiropodmys gliroides*, which weighed 20 grams, was killed within 10 minutes. Common house sparrows, *Passer montanus malaccensis* with average weight of 25 grams, were killed immediately after they had been attacked.

Lim (1964) concluded that birds were less resistant to this spider's bite than were small mammals. It appears that the response to the toxicity of the spider's bite is related to the size of the victim as well as its sensitivity to the venom.

One of our field assistants, Mr. Chai Koh Shin, was

bitten by this spider. An account of the accident, the symptoms and reaction of the victim, is given below. This constitutes the first recorded case report of man being bitten by a "bird-eating spider" in Malaysia.

Case Report

At 7.30 p.m. on 12 November 1968, while collecting specimens of mammals at Kampong Tamok near Bekok, Johore, a 22-year-old Chinese laboratory assistant, was bitten on the left 3rd finger by a large "hairy" spider (Plate 1). He had accepted the spider from an Orang Asli (Aborigine) who was paid to collect specimens of mammals for the Bio-Medical Museum at the IMR.

While arranging specimens in the vehicle prior to his departure from the village, he inadvertently picked up the polyethylene bag containing the spider in order to make room for cages. He suddenly felt a severe "biting" pain of the distal portion of the left third finger (Plate 2).



Plate 1 — Bird-eating Spider (*Lampropelma violaceopedes*): It measures five inches across the span of its legs.

His initial impression was that a rat had escaped from a cage and bitten him. He expressed blood from the wound by compressing the finger proximal to the bite. Within 30 seconds, he noted a constricting sensation within the chest which seemed to vary in intensity with a crescendo-descrescendo pattern. A tourniquet was placed around the finger and an Orang Asli sucked blood from the bite. The patient experienced no headache, no paresthesia and no alterations of consciousness. The finger and hand were diffusely swollen within 10-15 minutes.

He was taken to Segamat Hospital about 1½ hours after the bite. Physical examination at the time of admission revealed only edema and erythema of the left third finger. Blood pressure, pulse and respiration were normal on admission to the hospital and at hourly intervals throughout the night. Treatment consisted of an injection of local anesthesia at the site of the bite and an injection of penicillin in the right arm. He was discharged from the hospital the following morning without further treatment. After discharge, he experienced mild, migratory nyalgia and headache for 36-48 hours but was entirely asymptomatic by 15 November 1968, 72 hours after the bite.

Physical examination 36 hours after the incident revealed no abnormalities except for slight, residual swelling of the affected hand and finger. Two small lacerations, 1-2mm apart, of the distal aspect of the left third finger were healing without apparent superficial infection.

Laboratory studies at the time of the physical examination revealed the following:

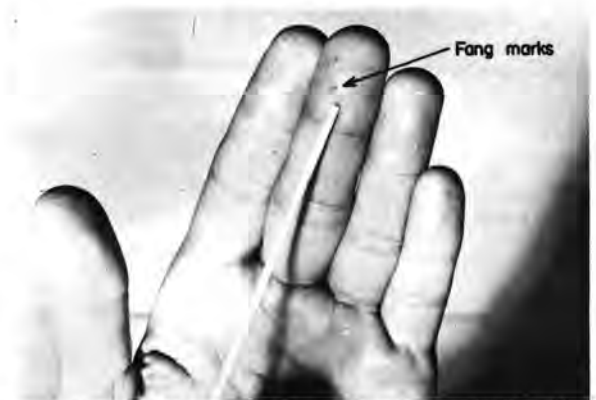


Plate 2 — Left third finger showing the fang marks of the spider's bite.

THE BITE OF A BIRD-EATING SPIDER

1. Hemogram	
Hematocrit	: 46%
WBC	: 10,600
PMN	: 54%
Bands	: 4%
Lymphocytes	: 31%
Eosinophiles	: 8%
Basophiles	: 3%
2. Sedimentation Rate	: 24mm/hour
3. Urinalysis	
pH	: 5.0
Sp. gravity	: 1018
Albumin	: Negative
Sugar	: Negative
Acetone	: Negative
Bilirubin	: Negative
Occult Blood	: Negative
Microscopic	: Not remarkable

Serum bilirubin, serum transaminases and serum lactic dehydrogenase were within normal limits.

Physical examination and laboratory tests failed to reveal evidence of hemolysis or muscular damage secondary to this spider bite. The systemic symptoms (constriction of the chest, headache, and myalgia) are difficult to evaluate because they could have been manifestations of anxiety. The local manifestations of erythema and edema, which did not progress to obvious tissue necrosis, are the only objective findings that can be attributed to the bite of this spider.

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A case of Stein-Leventhal Syndrome complicated by large multiple fibromyomas

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Introduction

ALTHOUGH STEIN-LEVENTHAL syndrome¹⁵ has been extensively documented since 1935, it often remains a diagnostic problem. That such confusion exists is made clear by a study of the literature on the subject.^{6, 9}

In recent years, there have been reports of cases of Stein-Leventhal syndrome complicated by such pelvic lesions as ovarian neoplasms,^{2, 7} endometrial carcinoma^{1, 3, 8} and endometrial hyperplasia.^{11, 14} So far, the author has been unable to find in the literature any report of large fibromyomas complicating Stein-Leventhal syndrome. The purpose of this case report is to draw attention to just such a case erroneously diagnosed as ovarian tumour.

Case Report

A 26-year-old nulliparous, unmarried Chinese woman was first seen on 26.7.69 because of secondary amenorrhoea of two years' duration. She also complained of swelling of the lower abdomen for three months, and swelling of both legs for six days.

Menarche had occurred at 14 years of age but menstruation was always irregular, occurring at two to six-month intervals, with a three-day moderate

flow. From the age of 22 years, she began consulting several doctors about this, and many attempts had been made to regulate her periods with oral progestogens with no success. There was no history of obesity or voice changes. She was the seventh child in a family of nine siblings. Her two sisters had normal menstrual histories.

Physical examination revealed a healthy looking young woman with no acne or hirsutism. The breasts were well developed. Abdominal examination showed a smooth, tense firm swelling arising out of the pelvis to the level of the umbilicus. No shifting dullness was detected. On rectal examination, the lower pole of the tumour could be felt in the Pouch of Douglas. The uterus could not be identified. No other masses were felt. The external genitalia were normal.

Gravindex test was negative. Nuclear sexing showed a female chromatin pattern. Straight X-ray of the abdomen showed a large soft tissue pelvic mass rising to the level of the 4th lumbar vertebra. A provisional diagnosis of ovarian tumour was made.

On 30.7.69, a laparotomy was carried out. The uterus was found to be enlarged by a fundal fibromyoma 6 cm in diameter, a posterior intramural

STEIN-LEVENTHAL SYNDROME

fibromyoma 12 cm in diameter and 4 anterior subserous fibromyomas. Both ovaries were cystically enlarged, each to 6 cm in diameter and covered by thick glistening opaque yellow capsules. The Fallopian tubes and the pelvic peritoneum were normal. Bilateral wedge resection of the polycystic ovaries and myomectomy were performed.

The postoperative period was complicated by the development of persistent pyrexia which resisted antibiotic therapy and which only subsided following the drainage of an unexpected pyometra on 21.8.69.

Twenty-eight days after she left hospital, menstruation occurred spontaneously; this lasted five days. Since that time, she has had two more normal periods, at monthly intervals.

Pathology Report

- (1) **Posterior fibromyoma.** Gross: Specimen consisted of an encapsulated circular mass of tissue 12 cm in diameter. It weighed 350 grams. Cut section showed circular whorls.



Fig. 1: Photomicrograph of a section of polycystic ovary showing numerous cysts.



Fig. 2: Photomicrograph of fibromyoma showing hypercellularity.

Microscopic: Sections showed a tumour composed of dense aggregates of cells of varying shapes, from spindle to round. Some areas of hypercellularity were noted.

- (2) **Ovaries.** Gross: Each section showed several cysts up to 1 cm in diameter.

Microscopic: Moderately thickened and fibrotic tunica albuginea; below this were several small cysts lined either by granulosa or theca cells. No corpora lutea seen.

Comment

The crucial point causing diagnostic difficulty in the young woman is the history of amenorrhoea. The occurrence of amenorrhoea in Stein-Leventhal Syndrome is to be expected. But a woman with fibromyomas seldom has amenorrhoea, even of short duration, unless she is pregnant or past the menopause. Retrospectively, in this case amenorrhoea may be explained by the abnormal hormonal influences arising from a disturbed hypothalamic-pituitary-ovarian relationship postulated for Stein-Leventhal syndrome.^{5, 9, 13} Whether the adrenal cortex is overactive in this syndrome remains a mystery.¹²

It is not known how often Stein-Leventhal syndrome and fibromyomas co-exist. This may be due to the following factors:-

- (i) The difficulty in diagnosing Stein-Leventhal syndrome per se. Although this condition is characterised by menstrual irregularities (amenorrhoea and oligomenorrhoea), infertility, obesity, hirsutism and polycystic ovaries, most investigators agree that none of them is present consistently. There are many cases in which obesity and/or hirsutism may be totally absent.^{5, 9} In the single woman, even infertility is only potential. Indeed, some authors would dispute the existence of Stein-Leventhal syndrome as a clinical entity.^{9, 11} It has been stated that the sine qua non in the diagnosis of Stein-Leventhal syndrome is the presence of palpably enlarged polycystic ovaries.¹⁰ Adopting such an arbitrary standard has occasionally resulted in the lax acceptance of cases with mere enlarged ovaries as Stein-Leventhal syndrome, unsupported by any consistent ovarian histopathologic picture or biochemical findings.⁴
- (ii) A survey of the literature found little description of the state of the uterus in Stein-Leventhal syndrome. The few who did so, remarked that three-quarters of such uteri were hypoplastic; the rest were normal in size.^{10, 15}

None reported a case of Stein-Leventhal syndrome complicated by large fibromyomas. Considering the relative frequency of fibromyomas, this discrepancy is all the more surprising. Perhaps it may partly be explained by the fact that the majority of small fibromyomas, and some large ones, are symptomless. Obesity may interfere with an accurate estimation of uterine size. It is also suggested that the silent presence of fibromyomas in patients with Stein-Leventhal syndrome could conceivably be overlooked, even by operators performing wedge resection on the polycystic ovaries.

Summary

1. A patient with the Stein-Leventhal syndrome who was found to have large multiple fibromyomas has

been described. The fibromyomas were discovered at laparotomy.

2. Fibromyomas complicating Stein-Leventhal syndrome should be included in one's differential diagnosis, whenever a young woman with an unaccountably long history of secondary amenorrhoea, is found to have a large pelvic tumour.
3. It is recommended that more attention be paid to the state of uteri in cases of Stein-Leventhal syndrome.

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Reviews

"INTRODUCTION TO THE ANATOMY AND PHYSIOLOGY OF THE NERVOUS SYSTEM" by David Bowsher, 1st Edition (1967) Blackwell Scientific Publications, Oxford and Edinburgh. pp. 180; Illustrations, 55; 15s net.

DUE TO OUR relative lack of information and to the highly developed and complicated human central nervous system, the study of the structure and function of this system (CNS) is not always easy to comprehend. The lengthy nomenclature, furthermore, adds to its confusion. The aim of this book is to provide a concise but a compact guide to the subject.

This book covers the basic elements of the neuron, the properties of excitable tissues, the receptors and effectors and the different regions of the central nervous system. The block diagrams and other illustrations are well-designed to simplify the approach. However, there are a few short-comings; namely, the treatment of some topics such as the action potential and the synaptic transmission, is too superficial; the selected bibliography is inadequate and the last chapter on the blood supply to the central nervous system seems to be out of place. Nevertheless, Dr. Bowsher has successfully combined simplification with the presentation of sufficient information to enable the reader, especially the preclinical student, to understand the subject at an introductory level.

T.T. Loh

A POCKET GYNAECOLOGY

by S.G. Clayton, 6th edition 1967
J. & A. Churchill Ltd. London. pp. 125. 16s.

THIS HANDY book contains a wide yet basic information on all aspects of Gynaecology. Facts are well tabulated and is easy reading. It is a very useful book for students preparing for examination and a reference book for general practitioners.

S.L.

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S.L.

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THIS BOOK is a very comprehensive one giving in detail all aspects of obstetrics necessary for training of physiotherapists in this field. Physical and mental preparation of the mother and follow-up during labour and puerperium is given in great detail as well as analgesia during labour. The most suitable exercises are very well illustrated. Although these forms of exercises are not popular among local women, general practitioners could help them greatly improve their performance by advocating these simple exercises to ensure an easier and more comfortable childbirth.

S.L.

THE SOUTHEAST ASIAN JOURNAL OF TROPICAL MEDICINE AND PUBLIC HEALTH

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As pointed out in a Foreword by Professor Brian Maegraith of the Liverpool School of Tropical Medicine, there is a real need for a Journal, with a wider scope than the national publications, in which regional and international as well as national aspects of the endemic problems could be discussed.

In the past, medical men of Southeast Asia have been working in isolation in spite of the similarity in the incidence and prevalence of diseases in the region. Now they are in a better position to benefit by each other's experiences in the diagnosis, treatment, prevention and control of the endemic diseases which have been stifling the natural development of the people.

The first issue is a very impressive one and contains original articles, reviews, research papers and case reports as well as notes on Laboratory Demonstrations and abstracts of articles which have a reference to this region.

It will be a welcome addition to the book-shelves of all clinicians and health workers in Southeast Asia.

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