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EDITORIAL

A chronic and so far insoluble problem in Malaya has been the reluctance of doctors to enter Government Service or to stay in it. Recently it has been seriously suggested that doctors should be forced to serve Government for two years or so in addition to their years housemanship. There would be no objection if the doctor had previously freely entered into a contract to do this, say as a student, in return for some personal advantage. There is objection to it if it is to be a rule that every newly qualified doctor must continue to serve Government for two years after his housemanship.

It has been argued that since nearly all doctors in Malaya have been educated largely at the taxpayer's expense it is fair for them to be forced to repay this debt by service. But all education in Malaya is heavily subsidised. This argument therefore applies to nearly every educated person in Malaya and could be used to justify a chain gang of engineers, miners, rubber tappers or any other group of Malaysians besides doctors. A medical service staffed in this way could hardly be a good one.

To attract doctors into the service a few changes are suggested. Obviously money is the main reason why a man works and keeps on working for a lifetime. Doctors are not saints or sinners but ordinary men with a standard of living to maintain for themselves and their families. If a doctor believes that he will double his salary by resigning he may do so. But what is his salary? He thinks it is the number of dollars he receives each month and will naively tell you so. In fact he receives about double this amount. To find out what his real earnings are he would have to consult an accountant and an actuary. He has pension rights, sick leave and ordinary leave with pay, housing at far below cost and security of employment. Many doctors do not put any value on these things until they have resigned and have to provide them for themselves. Moving out from under the Government umbrella into the cold rain of earning his living in private practice washes away many of a doctor's illusions. Perhaps it would be too drastic to pay doctors in future exactly what they really earn in hard cash and leave them as responsible adults to find their own houses and insure themselves against sickness and old age. It would be worth while to make clear to doctors what the real value of their salaries is.

A second suggestion is that the Ministry should encourage lost doctors to return to it. At the moment resignation is an abrupt and complete severance. The Ministry could, instead, allow a doctor who has resigned to return at any time within a year, and retain his seniority and any other rights his previous service has earned him. Some doctors could be brought back into the service in this way.

A major reason why doctors stay in Government service is that the opportunities for good work are better than outside it. Facilities for the investigation and treatment of illness are there and almost nowhere else in Malaya. When doctors find these facilities lacking, serving Government becomes a foolish waste of their lives. A bland civil service type of explanation for shortages simply proves to be the last straw. Given the present salary scales, good hospitals with good equipment would in themselves keep the service well staffed. A doctor nearly always joins the service expecting to find these things, their absence soon puts the thought of resignation into his head. We cannot stress too strongly the importance of this point.

A fundamental change in organisation is also suggested. We feel that the medical service is too centralised. Only a part of medicine, mainly that concerned with public health, needs to be administered centrally. The present centralisation means that doctors can be moved about the country and they don't like it. Decentralisation so that states or specially created medical regions had full control of medical matters would improve our service. Posts that fell vacant would be advertised independently by the local authority concerned and applied for by anyone in Government service. Such a system would mean that doctors moved because of their own choice and stayed put if their post suited them. Some regions offering less comfortable living would have to offer larger salaries than others. This would be a local decision determined by the laws of supply and demand. Hospitals would and should develop local interest, local loyalties and be under local control. We visualise regional or state boards responsible for finance, staff, supply and equipment of all hospitals. Doctors would be able to develop local loyalties and to get to know the regional medical authorities as persons and be known by them. Many of the irritations and frustrations of a doctor's life arise because the Ministry of

Health seems to him remote, arbitrary, political and unprofessional.

We hope that thinking along lines such as these will replace ideas of using force. A

doctor can do much or little for sick people according to his mood. He will not work well under duress. Such duress may prove in practice an administrative blunder.

RESULTS OF FILARIASIS CONTROL PROGRAMME IN THE FEDERATION OF MALAYA

By Professor A. A. SANDOSHAM,*
Senior Malaria and Filariasis Research Officer,
Institute for Medical Research,
Federation of Malaya.

Filariasis in man in the Federation of Malaya is due to two species — *Wuchereria bancrofti* (Cobbold, 1877) and *Brugia malayi* (Brug, 1927).

Wuchereria Bancrofti

Infection by *W.bancrofti* has long been regarded as rare in Malaya. Small endemic foci of low grade infection have been recorded from Penang and Singapore. More recent work (Polunin 1951, 1953; Wharton, 1960; Laing and Wharton, 1960; Wharton *et al.*, 1963; Warren *et al.*, 1963) has shown that this infection is more widely distributed than was originally suspected, especially in the rural areas affecting the Malays and the aborigines (Fig. 1). The chief vector of *W.bancrofti* in urban Malaya is *Culex pipiens fatigans*; in the rural areas of Pahang Wharton (1960) has shown that it is transmitted by *A.whartoni* while Warren *et al.*, (personal communication) found *A.maculatus* the vector in Pulau Aur, an island some 50 miles off the East Coast of Johore. Wharton found experimentally that *C.p.fatigans* was twenty times more efficient as a vector of the urban than of the rural strains of *W.bancrofti*.

Brugia Malayi

B.malayi is mainly associated with the swamp forests bordering the big rivers as they run into the sea, and the rice fields to the North-west of the Peninsula. It is also widely distributed in scattered areas in the country, including hilly districts, among the Malays and aborigines, though the people here are not infected so heavily. The vectors in the hilly country are not definitely known but it is felt that *Mansonia dives*, *Anopheles donaldi* and *Aedes chrysolineatus* may be involved in

some of the areas. *B.malayi* occurs in two forms, one referred to as the periodic, because the microfilariae exhibit nocturnal periodicity, and the other semi or sub-periodic, in which the microfilariae are found by day as well. This was first noticed by Turner and Edeson (1957). These two forms are transmitted by different vectors.

B.MALAYI; PERIODIC FORM — The periodic form is characteristic of the coastal settled rice fields (Fig. 2) and open swamp country of South Kedah, Province Wellesley, Penang and N. Perak. The houses (Fig. 3) are found on either side of roads running through this area. Filariasis here is transmitted by *Anopheles campestris* Reid, 1962 (formerly known as the dark-winged *A.barbistrotris*) and to a lesser extent by *Mansonia uniformis*, *M.indiana* and *M.annulifera*. This type of terrain has no reservoir of animal infection which could prove a zoonosis.

B.MALAYI; SEMI-PERIODIC FORM — The semi- or sub-periodic form which is characteristic of swamp forest areas (Fig. 4) such as occurs in East Pahang has animal reservoirs of infection particularly the dusky leaf-monkey *Presbytis obscurus* (Fig. 5) which has a natural infection rate of 70 per cent. This type of *B.malayi* is transmitted by various species of *Mansonia* particularly *M.bonneæ*, *M.dives*, *M.annulata* and *M.uniformis*. The *Mansonia* larvae and pupae obtain their oxygen supply from the submerged portions of water plants (Fig. 6).

Clinical Features in Malaya

W.bancrofti infection in Malaya is not heavy and clinical features attributable to this species are relatively rare. Occasional cases of lymphangitis, hydrocœle and chyluria have been noted in association with microfilariaemia.

Turner (1959) gave an account of filariasis in Malaya and showed there was no signifi-

* A paper read by invitation at the Seventh International Congresses in Tropical Medicine and Malaria at Rio de Janeiro, Brazil, in Sept. 1963.

Fig. 1. Map of Malaya showing distribution of filariasis.

DISTRIBUTION OF FILARIASIS IN MALAYA.



Fig. 2. Rice fields of the coastal plains in N.W. Malaya (a breeding place of *Anopheles campestris*) where the periodic type of *B.malayi* occurs.

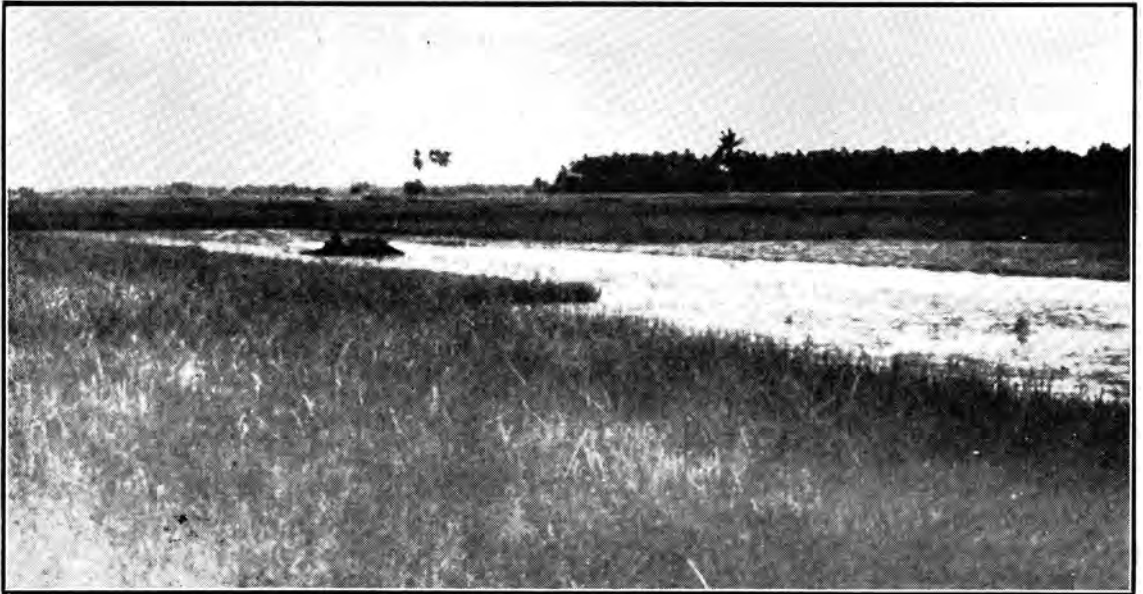


Fig. 3. A typical Malay house raised on stilts, with wooden floors and walls, and attap roof.



Fig. 4. The edge of a typical swamp forest in East Pahang (a breeding place of *Mansonia* spp.) where the semi-periodic type of *B.malayi* occurs.



cant difference in clinical manifestations between the two forms of *B.malayi* infection. Experimentally infected human volunteers developed enlargement of lymph glands, a retrograde lymphangitis and transient swelling of the affected limb with a slight eosinophilia (Edeson *et al.*, 1960), or a marked leucocytosis and eosinophilia associated with preliminary changes (Buckley, 1958). These early stages probably pass unnoticed by the rural population. Attacks of adeno-lymphangitis lasting 3 to 5 days often with associated fever occur at irregular intervals. The affected limbs, nearly always the legs below the knee in *B.malayi* infection, may show transient swelling during these attacks ultimately leading to elephantiasis (Fig. 7 and Fig. 8). Sometimes abscesses are associated with these attacks. Recent work by Beaver *et al.*, (personal communication) suggests that eosinophilic lung or

tropical eosinophilia in Malaya may have a filarial etiology.

Prevalence of Filariasis in Malaya

It was estimated in 1960 that about 5 per cent of the total population of Malaya had filariasis, mainly due to *B.malayi*, about half of them living in the more heavily infected areas on the banks of the large rivers as they run into the sea. In such areas 45 per cent of the people may have microfilariaemia and 5 to 6 per cent elephantiasis of the legs.

Filariasis Control in Malaya

As the result of researches carried out by the staff of the Institute for Medical Research a programme of control was drawn up for the whole country. The aim of the campaign was not to set out to eradicate the infection but to bring it down and keep it at a level at which no clinical symptoms would occur. Wilson (1961) has reviewed the preliminary work and the field work in Kedah and Pahang which led to the final adoption of the regime for mass control in Malaya which was to give 5 mg. diethylcarbamazine citrate per kg. body weight once a week for six doses.

Outline of Method for Control

The method of control was outlined in an Institute for Medical Research Report No. 61 drawn up by Reid and Laing (1960). A team of four was to be trained at the Institute for Medical Research in the techniques of census taking, making blood surveys (Fig. 9), calculating and administering the drug (Fig. 10), following up cases and keeping accurate records. The team which is to work under the supervision of a Health Officer was to consist of (1) a Health Inspector or Hospital Assistant, (2) a Laboratory Assistant, (3) an Attendant and (4) a Driver (or Boatman). It was estimated that a team should be able to treat between 3,000 and 4,000 people a year at an all-in cost of M.\$25,000 (about U.S.\$8,300) per annum, i.e., about M.\$6.50 (U.S.\$2.15) per person treated. The control programme was to be divided into two phases. In the first one all persons (about 155,000) in the more heavily infected areas were to be treated; in the second phase the work was to be extended



Fig. 5. Dusky leaf monkeys (*Presbytis obscurus*) which live in swamp forests and which are found naturally infected with the semi-periodic type of *B.malayi*.

Fig. 6. The water hyacinth (*Eichornia crassipes*) is one of the many aquatic plants to the roots of which the larvæ and pupæ of *Mansonia* spp. are commonly found attached.



Fig. 7. A case of elephantiasis of both legs resulting from long-standing *B.malayi* infection.



to the less heavily infected areas at the same time carrying out resurveys in the areas covered by the first phase and retreating where necessary. It was expected that phase one should be completed by 1965 involving the use of 12 teams at an estimated cost for the five years (1961-1965) of M.S1,350,000 (U.S. \$450,000).

CENSUS — Houses are visited first and given numbers which are painted on the front so that each house can be identified. A map (scale, 8 chains to the inch) is prepared and the distribution of the houses is indicated. During the house to house visits information is obtained with the aid of the penghulu or headman which is entered in a loose-leaf sheet to be filed in the binder kept in the base headquarters. House number, name, age, sex and details of clinical filariasis are entered straight-away. Subsequently this register is used to record blood survey results and details of treatment, including reactions to treatment. Although a person may have a negative blood film, a febrile or lymphatic reaction to treatment may denote infection. Details of births, deaths, new arrivals, etc., are entered as the information becomes available by a system of monthly returns provided by the headman.

BLOOD SURVEYS — These have to be carried out at night because of nocturnal periodicity of microfilariaemia. Before a blood survey is planned the penghulus have to be consulted as to the date and place where the people are to assemble — schools, shops and headmen's houses have been found the most convenient central spots. Thick blood films are taken from at least a third of the population to include both sexes of all age groups. The finger (or toe in the case of an infant) is pricked and a measured 20c.mm. of blood is drawn up a Sinton's pipette to make a thick film. About 200-300 films can be taken in an evening by one team. These films are stained by Giemsa stain subsequently in the base laboratory and examined. The microfilariae are identified and all of them counted. The findings are recorded as (1) the microfilaria rate (the number of positive films expressed as a percentage of the total examined) and (2) the microfilarial density or load expressed as the mean number of microfilaria per 20c.mm. blood (i.e., the total num-

Fig. 8. Another case of elephantiasis due to *B.malayi* affecting both legs.



ber of microfilaria in all films upon the total number of films, both positive and negative).

MASS TREATMENT — This is done by day at a centre selected in consultation with the penghulu. Male adults who go out to work the field may not be available till the afternoon or evening. The drug is the citrate salt of diethylcarbamazine (a piperazine derivative) given orally in a standard dosage of 5 mg. per kg. body weight in weekly doses to 6 weeks. The dosage is in terms of the citrate salt put out by druggist firms such as Hetrazan (Lederle), Banocide (Burroughs-Wellcome) and Carbilazine (Union-chemique Belges) and represents approximately 50 per cent base. The people are weighed and the amount of drug is determined by reference to a table prepared in advance. There are several proprietary compounds of this drug usually made up in

50 mg. tablets and it may be prepared in syrup form for children. School children are generally treated in schools and they are provided with sweets after they have taken their drug. Pregnant women, the sick and infirm, and infants under 4 months of age are not treated.

The first dose causes a febrile reaction with headache and aches and pains which may be severe and last for periods up to five days in the case of heavy infections. Febrile reactions are unusual after the second or subsequent doses, but side effects, nausea, vomiting, abdominal pain, occur in a few persons and may be associated with *Ascaris* infection. The people are appreciative of the anthelmintic effect of the drug and generally speaking are very co-operative. Some propaganda is carried out in advance, warning the people

Fig. 9. A team engaged in taking blood films at night in a rural district.



Fig. 10. A team giving mass treatment to people living in a rural area where filariasis is prevalent.



of the possible side effects from taking the drug. As far as possible all the members of the house-hold are not treated the same day in order to prevent everyone being prostrated at the same time. House visits are made for 2 or 3 days after treatment to provide palliatives in the form of advice, aspirin, fomentation, etc. During these house visits absentees may be found and treated. Lymphatic reactions due to the effect of the drug on the adult worms occur in up to four per cent of the people treated, commonly after the second or third dose. These take the form of a circumscribed patch of lymphangitis usually in the thigh or calf, or acute adenitis in the inguino-femoral or popliteal regions with retrograde lymphangitis and œdema of the limb, and sometimes becoming suppurative with abscess formation.

The number of people who can be included in a mass treatment campaign at any one time will depend upon the density of the population and ease of access to the area. Under ordinary circumstances 300 to 400 people can be dealt with by the team in one day. The weekly programme of the team is to treat during 2 days, spend the next two days alleviating reactions due to treatment, and two days in the laboratory staining and examining blood-films, checking records, entering up the register, etc. In this way the team should be able to treat about 3,000 people in one year.

It has been arranged that all areas which had been treated should be re-examined at the end of two years and all positives re-treated. It is considered that if the microfilaria rates rise to ten per cent or more and there is evidence of clinical filariasis, retreatment of the whole population would probably be necessary.

Control Programme

Work was started in Penang, Province Wellesley, Kedah, Lower Perak, Kuala Selangor, Muar and East Pahang. Whereas the work in East Pahang and Kedah had progressed according to plan, the other areas have had set backs mainly from the difficulty of retaining trained men in the service of the filariasis campaign. The Health Inspectors and Hospital Assistants are in such short

supply that they were withdrawn for more urgent work in the Government service or they left for more lucrative posts outside. The inaccessibility and difficult nature of the terrain in which they have to work and the inability to provide suitable housing for the staff and their families have made the campaign unpopular with some of the medical staff. In some areas there have been frequent changes with loss of efficiency and in others the campaign had to be temporarily suspended. Continuous work as scheduled has continued in Kedah and East Pahang and the results in these two areas are presented here.

The Bukit Meriam District of Central Kedah

This area is part of the Kota Area which is separated from Province Wellesley on the South by the Muda River and bounded on the North by the Merbok River. It is a low-lying swampy area of about 20 square miles with much wet rice cultivation towards the sea side of a road which runs from South to North. On both sides of the road are the villages with scattered wooden houses usually on stilts and with attap (palm thatch) roofs. The people are Malays and number about 4,000.

Mohamed Yusof (1959) had described the conditions obtaining in this area before and in the early years following the introduction of mass treatment with diethylcarbamazine in 1956. Before commencement of treatment 3,227 were examined and the microfilaria rate was 26 per cent, the mean number of microfilariae per 20 c.m. of blood was 2.6 and 1.2 per cent had elephantiasis. Ninety-one per cent of the people were given treatment and were re-examined 7 to 12 months later. It was found that the microfilaria rate had dropped from 26 per cent to 1.5 per cent and the mean number of microfilaria in 20 c.mm. blood from 2.6 to 0.18. Treatment had no effect on elephantiasis, the rate having altered only as a result of death or emigration. In part of this area involving about 1,000 people there was a resurvey at the end of 2 years after treatment and it was found that the microfilaria rate had dropped from 23 to 0.5 per cent and the mean number of microfilaria in 20 c.mm. blood fell from 3.36 to 0.02.

In 1962 a blood survey was carried out by the Institute for Medical Research staff

in collaboration with Mohamed Yusof covering the whole of the Bukit Meriam District. A total of 2,972 people were examined and excluding the untreated new arrivals it was found that the microfilaria rate was 0.58 per cent and the mean number of microfilaria in 20 c.mm. blood was 0.058. Of the 555 new arrivals 324 had been born in the District since 1957; none of these had contracted the infection. No fresh cases of elephantiasis were encountered in the area. The immigrants were largely from the neighbouring areas from across the rivers where control measures had not been started and accounted for 13 introduced cases of filariasis.

The Pahang Tua Area of East Pahang

This had been chosen as the experimental area by the Institute for Medical Research as early as 1953. The preliminary survey which represented 90 per cent of the total population of the area showed a microfilaria rate of 41 per cent and an elephantiasis rate of 6 per cent. This was used as a base-line for judging the effects of various experimental control measures tried out in the field. It was noted that neither in the Kampong sprayed with dieldrin nor in the drug-treated areas had there been any reduction in the proportion of mosquitoes carrying the infective stages of *B. malayi* type of larvæ. Subsequent work showed that there was a reservoir of animal infection in the swamp forest, particularly the dusky leaf monkey *Presbytis obscurus*. Whereas in the drug-treated areas the microfilaria rate and mean microfilaria count had dropped considerably, there was no change in the area sprayed with the residual insecticide. This suggested that little reliance could be placed on insecticides where the mosquitoes bred in large numbers in the swamp forests and fed readily and indiscriminately on man and monkeys but that by reducing and maintaining a low level of microfilariaemia in man by periodical exhibition of drug we could prevent clinical filariasis from developing. The effect of mass treatment was the same whether it was administered in 6 weekly or 6 monthly doses and in practice the former was found more satisfactory under Malayan conditions.

Following the experience gained of mass treatment in small areas, a large scale control

campaign was started in May 1957, in the Pahang Tua Irrigation Area with a population of 2,000 in four kampongs, Lamir, Pahang Tua, Langgar and Benta. Pre-treatment surveys earlier in the year revealed an overall microfilaria infection rate of 31 per cent, a mean microfilaria count in 20c.mm. of 7.1 among 1,647 persons examined. There was retreatment of positives in 1959 which showed a microfilaria rate of 3 per cent and a mean microfilaria count in 20c.mm. of 0.3. The following two years showed a slight increase in the microfilaria rate and the survey by the Institute for Medical Research staff in collaboration with Khoo in 1962 showed the fairly marked rise in the indigenous population of the microfilaria rate to 12.4 and the mean microfilaria count in 20c.mm. to 0.6.

This represents about a 300 per cent increase in 3 years in the number of positive cases, strongly suggesting continuation of transmission; and since the microfilaria rate and load were fairly low (3% and 0.3 respectively) following retreatment of positives in 1959 it would be logical to assume that the increase was due to the presence of an animal reservoir and with a high infection rate in the neighbouring swamp forests. This is supported by the findings in Bukit Meriam area of Kedah where there is no reservoir of infection among the animals. From enquiries made during the survey in the Pahang Tua Irrigation Area there was some evidence of increased clinical manifestations although it was not so evident as in the early years of the campaign. It would seem that retreatment of all positives every two years would not be sufficient in such areas but mass treatment should be resorted to every six years or so in areas where there was a reservoir of infection in animals and where control of vectors is not a practicable proposition.

Discussion

It has been found that the co-operation of the rural Malays has been very good, the control teams often being able to get 90 per cent or more of the people submitting themselves for the blood survey or mass treatment. The value of good public relations has been emphasised and public meetings are organised with the aid of the District Officer and head-

Effect of mass treatment in Kedah and Pahang compared
Kedah (Bukit Meriam)

	No. exam.	Mf. rate %	Mean No.Mf.20c.mm.
1956/7. Before treatment	3,227	26	2.59
1958. 7-12 months later	3,135	1.5	0.18
1960. Survey of 4 villages 10 months after treatment of Mf. positives	815	0.5	0.02
1962. Survey of whole area	2,972	0.9	0.1
Excluding immigrant adults from untreated areas	2,741	0.51	—

E. Pahang (Pahang Tua Irrigation Area)

	No. exam.	Mf. rate %	Mean No.Mf.20c.mm.
1953. Before treatment	1,519	36	17.5
1957. Commencement of mass treatment ...	1,632	31	7.1
1958.	1,712	5	0.5
1959. Retreatment of Mf. positives	1,009	3	0.3
1960.	851	4	0.3
1961.	804	5	0.3
1962.	729	12.4	0.6

man, sometimes with a film show to enlist support for the campaign. The inclusion in the team of a hospital assistant who can provide some medical aid in the case of reaction to treatment and also for minor ailments like coughs and colds has helped to maintain morale and the appreciation of the filariasis campaign by the people.

In the planning of the campaign in Kedah it would have been preferable to carry out mass treatment with the people of both sides of the river banks at the same time because often river boats provide the only means of communication and there is considerable movement of people from one side of the river to the other. If this had been done the introduction of infected people from across the Muda River or Merbok River could have been avoided and the prevention of transmission more easily achieved.

The good results obtained in Kedah have not been solely due to mass treatment; they

are partly due also to anti-mosquito measures adopted in the district by the Health Department. However, the main vector appears to be *A.campestris* which breeds on the sides of the rice fields and little can be done to control the breeding of this species without interfering with the rice crops. The spraying of houses with residual insecticides has been haphazard and occasional. The *Mansonia* spp. appear to play a relatively smaller part in the transmission of the periodic *B.malayi* and the occasional clearing of water hyacinths (*Eichornia crassipes*), water lettuce (*Pistia stratotes*) and water convolvulus (*Ipomoea reptans*) from the swamps, borrow pits and deep roadside drains is unlikely to have played a big part in lowering transmission. The resurvey this year of the neighbouring Merbok area to which the team has just moved over shows that in spite of similar health measures there the incidence of filariasis is much the same as before. Among the points that favoured the greater success of the campaign

in Kedah as compared with East Pahang are (1) the absence of an animal reservoir of infection, (2) the relatively lower microfilaria rate and microfilaria load to start with, (3) the relative fewness of vectors (which do not breed much when the rice fields are in fallow) and (4) the generally higher living standards obtaining here.

Mass treatment of an area may be necessary when the microfilaria rate in a community goes up above ten per cent and there is reappearance of clinical filariasis. It is proposed to do that in Pahang Tua Irrigation Area.

ACKNOWLEDGEMENTS

The staff of the Institute for Medical Research at Kuala Lumpur has carried out considerable pioneering research in filariasis in Malaya. They have shown the existence of the strains of *B.malayi*, the occurrence of animal sources of infection of human filariasis, the distribution of filariasis and the vectors in different areas. They have unravelled an extremely complex epidemiological situation. They have carried out much experimental work on animals particularly on longevity, periodicity of human and animal filarial worms and the susceptibility of mosquitoes. They have carried out pilot control projects and compared the relative merits of residual insecticides and drugs and laid down firm foundations for the extension of control to all parts of Malaya where the infection occurs. It now remains for the Health Department to pursue a vigorous policy of bringing relief to the unfortunate rural population affected with this crippling and unsightly disease. It is difficult to give credit to any one person for any particular advance made in the course of these studies; it has been largely a co-operative endeavour among my predecessors in the Malaria and Filariasis Division and the Entomology Division. I would like to pay special tribute to Drs. T. Wilson, J.F.B. Edeson, J.A. Reid, R.H. Wharton, L.H. Turner, L.S. Sodhy, J.D. Poynton, E.P. Hodgkin, I. Polunin, J.C.C. Buckley, A.B.G. Laing, D. Colless, J.H. Strahan, V.N. Norris, Mohamed Yusof b. Hassan, C.L. Khoo and many others for our present knowledge of the disease in Malaya.

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ADOPTION IN SINGAPORE

By Rosemary Mills, Formerly in the Department of
Social Medicine and Public Health,
University of Singapore.

Some aspects of the problems relating to adoption may concern medical practitioners, nurses and almoners. In Singapore, mothers giving birth in Kandang Kerbau Maternity Hospital (Vickers 1953) or at home, sometimes wish to give away their babies; and in the Paediatric Department, Civil General Hospital, and in the Infant Welfare Clinics, babies who have been adopted frequently present special problems. The purpose of this study was to find out what happens in Singapore where children are adopted, whether by legal adoption under the Adoption of Children Ordinance (1939), or by registration as transferred children by the Social Welfare Department under the Children and Young Persons Ordinance (1949), or by private arrangement.

METHOD.

In June, 1960, three field investigators, while doing a survey on Sickness in (a) Bukit Panjang, (b) around Amoy Street and (c) Kampong Amber, Singapore, on 3,597 males and 3,333 females (Lloyd Davies and Mills 1961) asked those over 21 years of age (and under 21 years of age if not living with parents or guardians) the following questions: -

Were you given away or adopted? (recorded as adults adopted).

Have you adopted or received any child who is not your own child into your family? (recorded as children adopted).

Have any of your children been given away or adopted? (recorded as children given away).

Those who said yes to any of the questions were interviewed by me with the help of an interpreter during May and June, 1961.

Standard forms were used for ascertainable facts, and free conversation provided further information. Where the adoptive parents of an adopted adult and the adopted adult were living in the survey area, both the adoptive parents and the adopted adult were interviewed, and the interviews recorded separately. Likewise, where the adoptive parents and the natural parents who gave away the child lived in the survey area, both the adoptive and the natural parents, but not the child, were interviewed. Those who had

moved out of the area since June, 1960 were not interviewed; but a few others, including some who had adopted or who had given away babies born after June, 1960, who had not been included in the 1960 survey on Sickness in Singapore, were interviewed, if living in the survey area.

RESULTS.

Two hundred and ten persons (adults adopted 39, children adopted 98, children given away 73) were included. About a quarter of the subjects were Muslims and three-quarters followed the Chinese Traditional Religions. There were 8 Christians who were Protestants. There were no Hindus. There were three times as many females as males. Half of the males and a quarter of the females were adopted by relatives. Adoption by relatives was more common with Muslims than with followers of the Chinese Traditional Religions (Table 1). The present ages of the subjects are given in Table II and their ages at adoption in Table III. About 80% were adopted under the age of one year. Over half of the children adopted knew about their adoption and 133 of the 210 subjects saw their natural parents after they were adopted, although 12 of these had stopped seeing their natural parents by the time they were 5 years old.

Forty-three mothers had given away children. Six gave away 3 or more children. This included one who gave away 7 children. All mothers who had given away 3 or more had given birth to at least 8 children. Seven mothers or fathers who gave away children had been given away themselves. Children who had been given away ranged from the eldest in the family to the fourteenth, but the average position was the fifth.

Too many children was the reason most commonly given for giving away Chinese girls and poverty or sickness for Chinese boys. Malays usually gave away sons because relatives begged for them (Table IV). No children or lack of children of one sex was the usual reason for wanting to adopt children. Ten adoptive mothers adopted children because they were sorry for the child. Three Chinese adoptive mothers wanted a future daughter-in-law (Table V). Adoption for the purpose

TABLE I.
Persons by Whom Adopted

Ethnic Group & Religion	Relatives		Friends		Strangers		Did not know		Total
	M	F	M	F	M	F			
<i>Muslim</i>									
Malay	10	8	2	8	1	6	M	F	36
Boyanese	2	4	1	—	—	—	—	1	7
Javanese	2	2	—	—	—	—	—	—	4
Arab	—	1	—	—	—	—	—	—	1
Indian	—	2	—	—	—	—	—	—	2
Pakistani	—	—	—	—	1	—	—	—	1
TOTAL	14	17	3	8	2	6	0	1	51
<i>Chinese Traditional Religions</i>									
Hokkien	11	16	7	45	8	20	—	10	117
Teochew	2	2	1	—	—	—	—	2	7
Cantonese	—	—	—	—	—	—	—	1	1
Khek	3	4	2	12	1	4	—	—	26
TOTAL	16	22	10	57	9	24	0	13	151
<i>Christian</i>									
Hokkien	1	3	—	—	2	2	—	—	8
GRAND TOTAL	31	42	13	65	13	32	0	14(a)	210

(a) All adults adopted.

of acquiring a future daughter-in-law was more common in the past and altogether 17 girls were adopted to be daughters-in-law. Two girls married their adoptive fathers. Eight adopted children had the same surname as their adoptive families and 9 natural mothers gave away their children to families with the same surname. Fifteen adoptive mothers were unmarried or widows.

One hundred and thirty-four of the 159 Chinese knew their animal year, but only 6 of these were born in the year of the Tiger. The horoscopes of 10 adopted children had been taken, either by the natural or the adoptive parents. No natural mother said she gave away a sick baby, but 5 Malay and 8 Chinese adoptive mothers said the baby had been sick at the time of the adoption. One adopted boy was mentally defective and one adopted girl had a deformed foot. Two

adoptive mothers regretted the adoption and one of these and one other adoptive mother complained of the adopted child's behaviour. Eight adoptive mothers resented neighbours' comments about the adoption. The mothers of 10 children were sorry they had given the child away and in 5 families a sibling, aged between 2 and 4 years, was distressed when the child was given away.

No adoptive mother adopted more than 4 children: the majority adopted one child. More than half of the adopted children and all but 7 of the adults adopted were adopted into homes where the adoptive mother had one or more natural children. Seventy-five per cent of the children were adopted or given away without a written contract. Ten were adopted or given away legally under the Adoption of Children Ordinance (1939), and 18 were registered as transferred children

TABLE II.
Present Age

Age in Years	Adults Adopted						Children Adopted						Children given away							
	Muslim		Chinese Traditional Religions		Christian		Muslim		Chinese Traditional Religions		Christian		Muslim		Chinese Traditional Religions		Christian			
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Total	
Under 5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	34
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	50
10—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	42
20—29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	38
30—39	2	1	1	9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	24
40—49	—	1	1	8	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	11
50 and over	1	2	1	6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	11
TOTAL	3	4	3	29	0	0	0	9	21	24	37	3	4	7	7	8	50	0	1	210

TABLE III.
Age at Adoption

Age	Adults Adopted						Children Adopted						Children given away							
	Muslim		Chinese Traditional Religions		Christian		Muslim		Chinese Traditional Religions		Christian		Muslim		Chinese Traditional Religions		Christian			
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Total	
Under one month	1	2	1	8	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	94
1—11 months	—	2	—	10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	71
1—4 years	1	—	1	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	30
5—9 years	1	—	1	5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	11
10 years and over	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
TOTAL	3	4	3	29	0	0	0	9	21	24	37	3	4	7	7	8	50	0	1	210

TABLE IV.
Reasons for Giving Children Away

Reason	Muslim		Chinese Traditional Religions		Christian		Total
	M	F	M	F	M	F	
Too many children	—	2	1	20	—	—	23
Too many girls	—	—	—	2	—	1	3
Mother sick	—	1	1	4	—	—	6
Mother-in-law sick	—	—	—	1	—	—	1
Father sick	—	—	2	1	—	—	3
Father out of work	2	—	1	7	—	—	10
Poverty	1	1	2	6	—	—	10
Business bad	—	—	—	2	—	—	2
Mother a widow	—	—	—	2	—	—	2
No time to care for child	—	1	—	1	—	—	2
Relative wanted child	4	2	—	2	—	—	8
To save child's life	—	—	1	—	—	—	1
Attached to foster mother	—	—	—	2	—	—	2
TOTAL	7	7	8	50	0	1	73

TABLE V.
Reasons for Adopting Children

Reason	Muslim		Chinese Traditional Religions		Christian		Total
	M	F	M	F	M	F	
No children	7	8	8	16	2	3	44
Wanted a boy	—	—	12	—	1	—	13
Wanted a girl	—	3	—	7	—	—	10
Too few children	1	2	—	—	—	1	4
Likes children	—	3	—	1	—	—	4
Lonely	1	2	1	2	—	—	6
Own child died	—	1	—	2	—	—	3
Pity	—	2	3	5	—	—	10
To be a daughter-in-law	—	—	—	3	—	—	3
To be a servant	—	—	—	1	—	—	1
TOTAL	9	21	24	37	3	4	98

under the Children and Young Persons Ordinance (1949), (Table VI). Only 7 natural and 13 adoptive parents thought that an adoption

society would be helpful. About half the followers of Chinese Traditional Religions and three-quarters of the Muslims had consulted

TABLE VI.
Method of Adoption

	Legal		Transferred Child		Given with Contract		Given without Contract		Total
	M	F	M	F	M	F	M	F	
<i>Children Adopted</i>									
Muslim	3	2	—	3	—	—	6	16	30
Chinese Traditional Religions	1	—	1	6	5	3	17	28	61
Christian	1	—	—	—	—	—	2	4	7
<i>Children Given Away</i>									
Muslim	1	—	2	2	—	—	4	5	14
Chinese Traditional Religions	—	2	1	3	2	4	5	41	58
Christian	—	—	—	—	—	—	—	1	1
TOTAL	6	4	4	14	7	7	34	95	171

TABLE VII.
Use of "Go-Between" in Adoption

	None		Relatives		Friends		Others		Total
	M	F	M	F	M	F	M	F	
<i>Children Adopted</i>									
Muslim	9	14	—	3	—	4	—	—	30
Chinese Traditional Religions	15	20	4	7	5	9	—	1	61
Christian	1	2	2	—	—	2	—	—	7
<i>Children Given Away</i>									
Muslim	5	6	2	1	—	—	—	—	14
Chinese Traditional Religions	4	31	2	5	1	14	1	—	58
Christian	—	1	—	—	—	—	—	—	1
TOTAL	34	74	10	16	6	29	1	1	171

at least one grandparent before the child was adopted or given away, and in 5 cases a grandmother adopted the child. Nearly two-thirds of the adoptions were arranged directly between the natural and the adoptive parents. Relations or friends arranged the adoption for the other third (Table VII). Half of the natural mothers received M\$10/- (£1. 3s. 4d.) or more at the time of the adoption. Chinese

adopters paid considerably more money for boys than for girls and as much as M\$1,000 was given for one boy. Where the Malays adopted Chinese girls they frequently followed the Chinese custom of giving money, otherwise among the Muslims the difference in value between a boy and a girl was small (Table VIII).

TABLE VIII.
Money Given or Received

Malayan Dollars	Children Adopted						Children given away						Total
	Muslim		Chinese Traditional Religions		Christian		Muslim		Chinese Traditional Religions		Christian		
	M	F	M	F	M	F	M	F	M	F	M	F	
None	6 ⁽¹⁾	14 ⁽³⁾	7	18	1	3	5	4	3	15	—	1	77
Under 10	—	1 ⁽¹⁾	—	2	—	1	—	—	—	7	—	—	11
10 — 19	—	—	—	5	—	—	—	1	—	7	—	—	13
20 — 49	2	1	2	5	—	—	—	—	—	7	—	—	17
50 — 99	1	2 ⁽¹⁾	1	2	—	—	2	1	2	9	—	—	20
100 — 199	—	—	5	2	—	—	—	—	1	2	—	—	10
200 — 399	—	1 ⁽¹⁾	5	1	2	—	—	—	1	—	—	—	10
400 and over	—	—	3 ^(a)	—	—	—	—	—	—	—	—	—	3
Amount not known ^(b)	—	2 ⁽²⁾	1	2	—	—	—	—	1	1	—	—	7
Other gifts	—	—	—	—	—	—	—	1	—	2	—	—	3
TOTAL	9 ⁽¹⁾	21 ⁽³⁾	24	37	3	4	7	7	8	50	0	1	171

Raised figures represent Chinese Children adopted by Muslims (included in total).

(a) M\$400, M\$700 and M\$1,000.

(b) Includes money paid in China, during the Japanese occupation of Singapore, and money paid by a relative.

DISCUSSION.

Adopted Adults.

It is likely that there were more adopted adults in the Survey areas than those who recorded their adoption. The proportion of Chinese men to Chinese women who said that they were adopted was considerably smaller than the proportion of adoptive parents who said that they had adopted sons to those who said that they had adopted daughters. This would suggest that in the past either Chinese sons compared with daughters were more wanted and less available for adoption, or that sons more than daughters, who had been adopted, had not been told about it. It is also likely that some adults who knew about or suspected their adoption did not wish to admit to this. How far those who say they are adopted differ from those who do not cannot be assessed. Adoption is a subject with a strong subjective and emotional element which would, to some degree, influence the responses.

Most of the adopted adults seemed to have been happy with their adoptive parents. The giving away of sons to brothers is common among the Chinese, and where a brother is childless it may be considered a duty (Cheng 1953). Three Chinese men adopted in China by uncles said that they were happy in their adoptive homes, but the impression was that one of the men whose parents were living at the time of the adoption rather resented the fact that the parents had given him away, while the other two men, who were adopted because their parents had died, had accepted the adoption as the best that could be done under the circumstances.

A cheerful 57-year old Hokkien sampan man said that he had been adopted by his father's eldest brother, a farmer in China, when he was 2 years old, as both his parents were dead. He had 2 older cousins. He said that he had been very happy with his uncle and aunt, whom he regarded as his own parents. When he was 18 years old he came to work in Singapore, but continued to keep in touch with them.

The Chinese women who said they were adopted by relatives also seemed happy in their adoptive parents' homes. Occasionally the relative also died and the woman was re-adopted by a neighbour. Where this had happened the woman seemed grateful to the neighbour for the kindness.

A Hokkien woman aged 51 years said she had been looked after by her grandmother from the time when, at 3 years old, her parents died, until she was 9 years old, when the grandmother died. A washer-woman then cared for her until she married at 19 years old. She thought this had been a good arrangement, and added that recently she had heard about the washer-woman's death and regretted that she had not seen more of her after marriage.

Although adoption is accepted by many Chinese as a sensible method of getting rid of an unwanted child or of acquiring a child, the adopted women varied from those who accepted their adoption as natural and those who resented the fact that their parents had given them away. Some adopted women said they wondered what their natural mothers were like, others said they never thought about them.

A Hokkien woman, aged 26 years, was given away by her mother in China, after her father's death, when she was 9 years old, to a family going to Singapore, as her mother, who was very poor, had heard that Singapore was better than China. The mother worked on a small farm and remained in China. The woman said that she missed her mother, but she was glad she had been adopted as she had been well treated and not made to do housework, as the adoptive mother servants.

A Hokkien woman aged 48 years said that she was given away when she was about 6 years old for money, as her father was sick and could not pay for the treatment. She thought she might have been the one to have been given away because she was born in the year of the "Tiger", and that was not a good year. Soon after her adoption the adoptive parents separated and the woman went with her adoptive mother to Singapore. When she was 12 years old her adoptive mother died so she was taken over by neighbours until she married at 17 years. The woman said that she often used to think about her natural mother but would try to dismiss the thought of her from her mind. She had been well treated by her adoptive mother.

A Hokkien woman aged 24 years had been adopted when she was a few days old. She said that she was happy in her

adoptive mother's home and did not wish to see her natural parents because had they loved her they would not have given her away.

Some of the adopted adults had always known about their adoption, others learnt about it from neighbours or were told about it by their adoptive parents. The latter frequently occurred at marriage. The responses to the information varied considerably. Some refused to believe their adoption, others accepted it without being unduly surprised, while another group were uneasy at discussing the matter with their adoptive parents. Several of the adopted adults learnt little about their natural families, while others kept in touch with them. Where the adopted adults had been happy in their adoptive homes, knowing the natural family did not seem to lessen their affection towards their adoptive families.

A Hokkien woman, aged 43 years, who had a deformed foot, said she had learnt about her adoption when she was 12 or 13 years old, through neighbours. Although she used to wonder what her natural family was like, she did not like the idea of discussing the matter with her adoptive mother.

A Teochew woman aged 43 years was told by neighbours about her adoption into a well-to-do family when she was very small. At first she refused to believe it. Later she believed, but the idea did not worry her nor did she seem interested in her natural family.

A Hokkien woman aged 50 years learnt about her adoption through the woman who had arranged a marriage between her natural brother and the chief tenant's daughter. Her adoptive mother then told her that she had adopted her and the son. Neither of them had admitted surprise at the news, nor did the woman resent the fact that her mother had given her away. She said she was glad to know about her natural family and, at the time of the Survey, saw her natural mother about three times a year.

Sometimes a Chinese woman adopts a girl with the intention of bringing her up to marry a son. By this means she has a daughter-in-law trained by her in housewifery. The women in this survey who were adopted for the purpose of becoming a daughter-in-law were divided over whether they thought it was a good idea or not. The advantage to the

woman was that if the adoptive mother was kind and some of the adopted women had been the favourite, she was happy to remain within the family. The disadvantage appeared where the adopted woman had not wanted to marry her adoptive brother.

A Hokkien woman aged 51 years was adopted when she was about 4 months old, as her natural mother died. She said that she had frequently gone to her father's house and had always known she had been adopted to be a future daughter-in-law. She added that she did not have to marry her adoptive brother, but she had wanted to do so, as she was happy with her mother-in-law. She was considering adopting a girl to be her daughter-in-law, as she had no daughter and would like to have one.

A Hokkien woman aged 44 years was given away at birth to be a future daughter-in-law. The adoptive mother had no natural daughter and the woman was her favourite and tended to get what she wanted. When she was 19 years old she was told about her adoption, and that she should marry her adoptive brother. She was very pleased about this as she had the love of her mother-in-law and thought the system was a good one.

A Khek 43-year old woman was given away when she was 10 years old to be a future daughter-in-law, as her mother could not afford to keep her. She said that she had been well treated and was happily married to her adoptive brother, but thought that it would have been better to have remained with her natural mother and chosen her own husband as then she might have married a richer man.

Occasionally Chinese adopted women married their adoptive fathers.

A high-grade mentally defective Teochew woman, aged 60 years, was adopted for M\$400-500 when she was 15 years old, in order to do housework. A year later she became the second wife of her adoptive father. The adopted woman, who bore no children, appeared to be very much dominated by the first wife, who treated her as an unpaid servant.

One adopted woman had natural parents who were Chinese, but adopted into a Malay family. The adoption appeared happy.

A Chinese woman aged 58 was adopted

into a family where the adoptive mother was Malay and the adoptive father French. The woman was educated in a Convent and cared for by her adoptive grandmother. The woman said that looking Chinese did not create difficulties, but the grandmother became very angry if anyone remarked that she was Chinese, and would never admit the adoption. The adoptive mother adopted the girl because she had no children of her own, and the natural mother, a close friend, asked her to adopt her baby, just before she died. Later the adoptive mother was re-married to a Malay. The adopted woman also married a Malay and changed her religion from Roman Catholicism to Muslim.

The other Muslim adopted adults had been adopted by relatives or by a close friend because the natural mother had died, and were happy in their adoptive homes. The only exception to this was a Pakistani man.

A Pakistani man, aged 38 years, was given to his aunt in Bombay, who had three daughters but no sons. He lived with her until he was 5 years old, when he met one of his brothers and complained that he was ill-treated, so his mother took him back. When he was 7 years old his father died and the boy came to Singapore with his elder brother. He looked after his brother's employer's youngest child. The brother did not tell the employer that they were brothers, and when the employer paid for the brother to return to Bombay for a holiday he remained with the employer. The brother was expected to return to Singapore, but did not do so. When he was 10 years old the boy left his employer and worked with a company of painters for 2 years. Then he joined a travelling acting company for 3 to 4 months. After that he worked in the "New World" selling things. The man said that everyone had been kind to him but he felt lonely and longed for his mother. He sent two letters but had no reply. He thought he had addressed the letters wrongly.

Children Adopted.

The purpose of this section was to find out the opinions of the adoptive parents about the adoption. As only two adoptive parents said they regretted the adoption, and most said that they were pleased about it, it would seem in general, from the adopter's

point of view, the adoptions were successful. One adoptive mother who regretted the adoption complained that her husband had deserted her and married the adopted daughter, for whom she paid M\$200 when she was 10 years old, to do the domestic work. The other adoptive mother who complained was the second adoptive mother of an adopted girl.

An unmarried Hokkien adoptive mother, who was a temple-keeper, adopted a 7 year old girl who had previously been adopted when she was one year old by a married woman who frequented the temple. This woman was an opium-smoker, and as she neglected the girl and the girl was fond of the temple-keeper, friends suggested to the temple-keeper that she should adopt the girl and bring her up properly. When the girl was 12 years old the second adoptive mother went to Sarawak for a year, leaving the girl with a friend. After this the girl's behaviour became difficult. The second adoptive mother complained that the girl often visited the first adoptive mother without telling her, and neighbours told the girl she need not obey as she was only adopted.

In most cases the children were handed over to the adoptive parents without even a written statement about this, and yet no adoptive parent said that the natural parent had tried to get the child back afterwards. Sometimes the adoptive parents were afraid that the adopted child might wish to find out about his natural parents and want to return to them, and for this reason some wished to hide the fact of the adoption from the child. Where the adoptive parents and the adopted child had different surnames the birth certificate could be a source of concern, as this had to be produced first when a child was registered for school and later when he obtained an identity card. One adoptive mother, who was anxious that the adopted girl should not know about her adoption, said that she told the girl that her birth certificate had been burnt so she had borrowed someone else's; another adoptive mother said that the adopted boy's birth certificate was so faded that no-one could read it, therefore it would not present a problem.

It was mainly to safeguard their rights as adoptive parents that a few adoptive parents, including 3 Malays who had adopted Chinese children, would have liked to have

used an adoption society. The majority, however, were not worried that the adopted children would wish to return to their natural parents and often allowed the natural mother to visit the child after adoption. Some adoptive mothers only allowed this while the adopted child was too young to remember; with others the visiting continued, and one adopted child even lived in the same house as the natural family and frequently fed with them. In the case of adoption arranged between Muslims the child is supposed to know about the adoption and the natural father attend the ceremony when the child is married.

Adoptive mothers who did not mind their adopted children knowing about their adoption were divided between those who left it for the child to find out either through neighbours or through the birth certificate, and those who would say things like "It is some time since your mother visited" or would point out members of the adopted child's natural family to him. Some of the latter adoptive mothers said that the adopted child refused to believe that he had been adopted. The general feeling expressed was that as the child was fond of her why should he wish to leave? A few adoptive mothers said that the adopted child resented the fact that the natural parents had not wanted him and others that they did not wish to tell the child about the adoption because they did not wish to hurt his feelings.

A Hokkien couple adopted a boy at birth as they had no sons and the natural parents had many children. The adoptive and natural parents worked as labourers at the same place. The adoptive mother said that although the fathers met at work she was not afraid that the boy, 13 years old at the time of the Survey, would leave her when he finds out about his adoption, but added that later she will talk in such a way that he will know about it. She said that the boy was happy in their home and that he was a good boy. She was quite contented with the way in which the adoption had been arranged.

A Hokkien adoptive mother adopted twin girls when they were a few days old, as the natural mother had several children. She said she had registered the girls at the Social Welfare Department as she thought that would make it easier for them to attend school. She would have liked the girls' names to have been

changed to hers, but she was not afraid that they would want to return to their natural parents, who were neighbours, as they were happy with her. She had also adopted another girl, as her parents had returned to China.

The Chinese custom of adopting a girl to bring her up to be a daughter-in-law is declining in Singapore. Some adoptive mothers thought that if the girl wished to marry her son she would be pleased, but rarely was there any evidence to show that pressure would be brought to bear on the girl to do so.

A Hokkien adoptive mother said she adopted a girl when she was 4 years old, as the natural mother had died and she herself had no daughters. The natural father, who continued to visit, had owed the adoptive family M\$60/- and on adoption the debt was cancelled. The adoptive mother said that she had hoped that her natural son would marry the girl, but if he had not wanted to she would not have minded. Her husband, though, was very anxious for him to marry the adopted girl and would have tried to persuade him to do so had he been unwilling.

The adopted girl, who married the younger son, said that she had been quite happy about the idea of marrying her adoptive brother, as their adoptive mother had been kind to her, but even if she had not wanted to marry him she would still have done so.

A Hokkien adoptive mother said that she adopted the daughter of a great friend when she was 12 days old to become the wife of her adopted son. She had always called the girl daughter-in-law, so that she would know about her adoption. Neither the adopted son nor the adopted daughter wished to marry the other, but she was glad about this as she will have both a daughter-in-law and a son-in-law.

Some adoptive mothers had the adopted child's horoscope taken to confirm the desirability of adoption. Occasionally the horoscope originally suggested an adoption.

A Hokkien adoptive mother said that when her sister's daughter was a baby she was sick, so her horoscope was taken. This said that her niece should be adopted, so she adopted her.

Although grandmothers were frequently consulted at the time of the adoption, unless

the grandmother took an active part in family activities the consultation was often only formal, and had she objected the adoption would still have taken place. Cases where the grandmother's objection had been effective would not have been discovered in this Survey, as the child would not have been adopted. Therefore no conclusions can be drawn from this Survey about the extent of the influence of grandmothers on adoption. The higher proportion of Muslims than of Chinese who consulted grandmothers was partly because fewer Chinese grandmothers were available for consultation. Where the grandmother herself was adopted, the grandchild could reduce her loneliness after her children had grown up and left the home.

Most adoptors adopted children to meet their own needs, and it was quite common for unmarried women or widows to adopt children. In one case a man whose wife was in China adopted a boy for company. The boy accompanied him when he went to work. Children adopted by single persons usually received much affection. Most Asian women, on marriage, do not expect to love or be loved by their husbands, but to serve them and bear their children. The woman is usually content if her husband supports her adequately. For this reason the child may not normally share his mother's love with his father, although he would share her attention with him, and in respect of having to share affection the presence or absence of a father might be relatively unimportant. A good father does, however, support his family, and in this respect the effect of the absence of the father in the home would largely depend upon the alternative forms of support available for the woman. Also, in many cases, he may play a part in the upbringing of his children. To what degree the absence of a father in the home affected the child, or to what extent there were father substitutes was not enquired into, but there was no overt evidence to suggest that these adoptions were unsuccessful from the child's point of view.

A Hokkien actress said that her husband died a year after her marriage. She adopted two girls, one now 15 years old, when she was 4 years old, and the other, now 9 years old, when she was one month old. The girls were first cared for by a servant who was really their mother substitute. Later the adoptive aunt helped to bring them up. The woman said she adopted the girls because she liked children.

Children Given Away.

Although only 10 out of 73 natural parents said they were sorry they had given away their children, this is likely to be an under-estimate. People often repress unpleasant feelings, and this may have happened in some cases. One mother who regretted giving away her daughter said business had been bad at the time. Another mother said she regretted she had given a son away, as she had been poor at the time, but as she has had several other children since, she no longer minded. One father had forgotten he had given away a daughter.

During the Japanese occupation a Khek father and mother gave away their eldest daughter, now 23 years old to a friend of the natural grandmother, as the father was out of work and they were afraid that there would be no food for the baby. The natural mother had not seen the child since she was 3 to 4 years old, but the grandmother who lived near the girl told them how she was getting on. The father was the one at home when we called to interview the parents. He had quite forgotten that he had given a child away. This may have been because the child having been given away had either left so little impression on him that he had forgotten, or that it had been such an unpleasant experience that the memory had been repressed.

Another mother was sorry she had given away her daughter and was anxious to know whether we could arrange for her to see her.

A Khek father and mother said that they agreed to give away their baby if it was a girl when the mother was pregnant, as business was bad at the time and they could not afford a servant for the mother. They only saw the girl once after she was given away, but had heard from a friend that the girl was attractive and intelligent. They said they had promised the adoptive mother not to see the daughter, but they would like to do so without her knowing. She said she would not have liked to have used an adoption society, as they wished to investigate themselves that the home was a good one. The natural father, a dispenser of Chinese traditional medicines, said business had improved, they had a servant and they had not given away any other children. They regretted having given away that one.

Although most of the children were given away without a written contract none of the natural mothers considered claiming back the child. Only 7 mothers thought an adoption society would help, either because it would mean that the adoptive mother would feel more secure or because the adoption society would ensure that the adoptive mothers treated the adopted children kindly. For their own peace of mind many natural mothers liked to see their children after adoption to find out how they had settled in their adoptive homes, and would only agree to adoption under those conditions. Sometimes the visiting continued, at other times it stopped as the child became old enough to remember. Had fewer mothers been able to see their children after giving them away probably more would have regretted it and more also might have favoured an adoption society.

Most mothers preferred to give their children to close relatives or friends. If a stranger adopted the child the go-between would be either a relative or a friend.

Some of the inter-family adoptions were in order to carry on ancestor worship, and where the relative had no-one to do this it was considered a duty (Cheng 1953); at other times it was a matter of convenience.

A Hokkien man had no son to worship his ancestors. He would not let his only daughter adopt a boy as the surname would be different, but adopted his brother's son as his grandson. The natural mother was glad to give the boy away as 5 out of her 8 other children had died, and she was afraid that this one might die if he was not given away.

Where there was some misfortune in the family the natural mother would sometimes say that she was too poor or too busy to keep the child and that she was glad she had given him or her away, as the adoptive mother loves the child. A few mothers held their duty to their family to be stronger than to their child. One child was given away to pay for his father's medicine. Sometimes the child would be given away at a mother-in-law's request.

A Hokkien mother gave away a child at her mother-in-law's request to a childless domestic servant whose husband had deserted her. The adoptive mother paid for the child's keep and the natural mother looked after her.

In a Hokkien family 7 out of all children were given away for M\$50 to M\$60 each because the father was out of work. The other 4 children were kept because the parents were getting old and they wanted children to look after them. The children were adopted by childless friends who would let the mother see the children for a few months and would then disappear. No contracts were signed.

In every case where siblings were reported to be distressed when the child was given away the siblings were between 2 to 5 years old. This could be because at that age children are old enough to realise what is happening but are very dependent upon their parents for support. It is likely that more siblings had been upset but that their parents had forgotten the fact.

The Malay children were given away because a relation or close friend begged for the child and the natural mother had several children. These mothers said that they would not have given away their children otherwise, and that they did not regret it because the adoptive parents loved the child. Two families who said they gave away children because of poverty were the only exception to this.

A Malay father had been adopted by an aunt who had 4 daughters. He had been spoilt when a boy, and only went to school when he wanted to go, and was not required to contribute his earnings to the home. He gave away 4 out of his 8 children during periods when he was unemployed. One child went to a grandmother, one to another relative and two to friends. He said that he did not regret giving them away but added one of his sons was very upset when his brother was given away.

CONCLUSION.

From the evidence available from this Survey, it would seem that the system of adoption in Singapore had worked reasonably well. This is probably largely due to the fact that it is a generally accepted practice and considered a sensible way of dealing with the problem of unwanted children on the one hand, and lack of children on the other. Most natural mothers were anxious to ensure that their children would be happy in their adoptive homes and took trouble to investigate before giving the child away. If the children were

not given away to friends or relatives, friends or relatives would be used as go-betweens. The adoptive mothers were anxious to have the children, and tended to treat them well. Although there was no evidence to show that there was any ill-treatment of adopted children in the areas of the Survey, had there been cases of this the fact of adoption might not have been disclosed.

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THE IMPORTANCE OF LEPTOSPIROSIS IN MALAYA

By Dora S. K. Tan, M.B., B.S.

Virus Research Officer, Institute for Medical Research,
Kuala Lumpur, Malaysia.

INTRODUCTION

Although the significance of leptospirosis as a major cause of febrile diseases in civilians and military personnel in Malaya has been established for the past 10 years (Broom, 1953; Robinson and Kennedy, 1956; McCrumb *et al.*, 1957) it would appear that this fact is far from being adequately recognised by general practitioners and government medical officers in this country. Danaraj (1950), Trimble (1954) and Turner *et al.* (1959) pointed out that many cases of leptospirosis escaped recognition either because the actual clinical features of leptospirosis did not always conform with the generally accepted picture of it (i.e. Weil's disease) or because clinicians failed to consider it in the differential diagnosis of febrile illnesses. All three papers were published in local journals, but apparently escaped the attention they deserve.

The main purpose of this paper is to emphasise the following points: (a) leptospirosis is much more common in Malaya than is generally realised (b) leptospirosis can be mild and may even be subclinical and deceptive (c) leptospirosis can be diagnosed easily by a relatively new serological test called the Sensi-

tized Erythrocyte Lysis (SEL) test (see below) or by culture methods.

LEPTOSPIROSIS IS COMMON IN MALAYA

Studies of Malayan leptospirosis have revealed a high prevalence of leptospiral antibodies in human beings, domestic and wild animals — especially in wild rodents (Wiseman *et al.*, 1955; Smith *et al.*, 1961; Annual Reports of the IMR, 1955 —). Moreover, the presence of a multiplicity of leptospiral serotypes, about 30 in number, in Malaya was determined by serologic and cultural studies by Alexander and his colleagues (1955 and 1957).

Out of a recent study of 584* cases of pyrexia of unknown origin (PUO) over a period of 4½ years (June 1958 to December 1962) 173 (29.6%) were found to be positive, the diagnosis being based on blood cultures, significant serological (SEL) titres, or both (table I). Increases in SEL titres of 16-fold or more in paired sera were observed by Chang *et al.* (1957) in his study of 40 proved cases of leptospirosis. A similar increase was found in 74.0% of the cases considered as

TABLE I.
Results of the test for leptospirosis in 173 positive patients

Titres	No.	%	Remarks
16-fold or more increases	128	74.0	Diagnostic
Positive cultures	14	8.0	
* Less than 16-fold increases in paired convalescent sera	11	6.3	
Stationary Titres			Presumptive positive
320 or 640	3	1.7	
1280	5	2.9	
† 5120 or more	12	6.9	

* The intervals between the dates on which the sera were taken were less than 4 days. The SEL titres range from 320 to 5120 or more.

† Maximum dilution employed in test.

positive in our study. Not all paired sera were obtained at optimal times during the course of the illness and sera with high titres (320 to 5120 or more) but increases of less than 16-fold (often 4-fold or more) were encountered in 11 patients from whom the blood specimens were taken during convalescence and at less than 4 days' interval apart. Twenty cases showed no rise in titre but the titres were high (320 to 5120 or more) and were therefore presumably indicative of recent infection (Cox, 1957). We have therefore regarded this last group as one of "presumptive positive" cases.

Leptospire were isolated from blood specimens of 14 patients in this study. Out of 12 of these sent to Dr. L. H. Turner of the Wellcome Laboratories of Tropical Medicine in London for identification, 11 have been identified to-date. The remaining 2 were not available from the laboratory which isolated them. The serotypes of the 14 isolates and the localities from which they were obtained are outlined below:

Kuala Lumpur: *caniloca* (2), *pomona* (1)
 Tampin: *cunicola* (1)
 Bentong: *pyrogenes* (1), *autumnalis* (1)
 Klang: *pyrogenes* (1)
 Mentakab: *autumnalis* (1)
 Malacca: *pyrogenes* (3), unidentified (2)
 Penang: unidentified (1).

Table II shows the localities from which paired specimens of the PUO patients were received. The results would seem to indicate that an overall proportion of nearly 1 in 3 PUO cases in the Federation can be considered as being due to leptospirosis. The proportion, however varies from locality to locality. While in Kuala Lumpur and some other areas the proportion is approximately 1 in 5, in certain areas it is considerably higher — e.g. it is 1 in 2 in Melaka and 3 in 5 in Penang. The figures for places other than those commented on are too small for any valid conclusions to be drawn. It is regretted that an urban/rural analysis is not yet available owing to lack of data.

Observation was made also of the occupations of patients diagnosed as having leptospirosis (table III). It is noteworthy that rubber estate workers are apparently very highly infected. So also is a group classified

as labourers in which are included those dealing with sewage, drainage, town-cleansing, forestry and anti-malarial work. It is unfortunate that full details are not available for the purpose of sub-grouping the large number of labourers listed as "Miscellaneous." Farm workers and the army being constantly exposed to leptospirosis have understandably high seropositivity rates of infection. The relatively high rates obtained for police personnel, however, probably apply only to the field force and not to the police force in general. The results shown against the category "business" would appear to be surprisingly high in view of the fact that business executives would not normally be exposed to infection to the same extent as outdoor workers. However a possible explanation for this relatively high percentage of positive cases is the inclusion of rural hawkers and keepers of shops selling sundry goods in this category. These 2 groups of "business" people have a relatively high rate of exposure to infection, the former understandably so, while the latter are constantly being exposed to infection from the usually high rodent population in their shops. The relatively common occurrence in housewives may be attributed to the outdoor chores like farming, padi planting, wood-chopping which many rural housewives in Malaya have to perform while their husbands are engaged in some other occupation elsewhere. As only a few padi planters were investigated this group is included under the Unemployed/Miscellaneous category.

The incidence of leptospirosis with respect to sex, racial and age groups is summarised in table IV. The occurrence in males, though higher than in females, is not markedly so. The same remarks regarding incidence in housewives may be repeated here. In addition to this is the fact that women and girls form a very considerable proportion of the labour force in rubber estates and tin mines. The differences noted in the results for different racial groups have no statistical significance, and the incidence may be regarded as having no racial bias. The rates occurring among the age-groups ranging from 11 to 60 have also been determined to be essentially the same. However, the number of patients examined in the age groups 0-10 and over 60 are too small for any valid conclusions to be drawn from them. Moreover samples of blood taken from these groups tend to be selective, since only patients considered well enough are subjected to additional investigations of this nature.

* Some of the cases are included in the results of the preliminary report by Turner *et al.*, (1959), Med. J. Malaya, 14, 83-98.

TABLE II
Incidence of Leptospirosis in PUO Cases in different parts of Malaya

Place	June '58—Dec. '59		1960		1961		1962		June '58—Dec. '62		% pos.
	Pos.	No. Exam.	Pos.	No. Exam.	Pos.	No. Exam.	Pos.	No. Exam.	Pos.	Total No. Exam.	
Alor Star	—	—	1	1	—	—	4	5	5	6	—
Batu Gajah	—	—	0	3	1	3	—	—	1	6	—
Batu Pahat	—	—	—	—	1	1	1	2	2	3	—
Bentong	2	8	—	—	—	—	—	—	8	8	—
British Mil. Hosp.	8	15	0	3	0	2	—	—	2	20	40.0
Butterworth	—	—	1	2	1	1	—	—	2	3	—
Grik	—	—	—	—	0	2	—	—	0	2	—
Ipoh	—	—	—	—	2	4	4	6	6	10	60.0
Jelebu	—	—	0	4	—	—	—	—	0	4	—
Johore Bahru	—	—	2	3	0	1	—	—	2	4	—
Kampar	—	—	2	14	1	6	—	—	3	20	15.0
Klang	1	3	—	—	1	1	0	1	2	5	—
Kluang	0	7	0	7	0	2	—	—	0	16	0
Kota Bahru	—	—	2	2	2	3	—	—	4	5	—
Kuala Kangsar	—	—	1	3	—	—	1	4	2	7	—
Kuala Krai	0	1	0	4	—	—	—	—	0	5	—
Kuala Kubu Bahru	—	—	0	0	3	10	—	—	3	13	23.1
Kuala Lipis	1	4	0	3	3	6	2	16	4	30	13.3
Kuala Lumpur	4	37	7	20	6	25	9	50	26	132	19.7
Kuala Pilah	—	—	—	—	—	—	1	4	1	4	—
Kuantan	0	1	0	1	0	1	—	—	0	3	—
Kulim	—	—	—	—	3	11	—	—	3	11	27.3
Lumut	—	—	0	3	1	4	1	1	2	8	—
Melaka	5	15	12	17	19	41	11	21	47	94	50.0
Mentakab	2	8	2	7	—	—	0	2	4	17	23.5
Pekan	—	—	0	1	0	1	—	—	0	2	—
Penang	0	2	4	7	11	15	7	11	22	35	62.8
Port Dickson	0	5	1	1	—	—	—	—	1	6	—
Raub	1	14	0	8	—	—	—	—	1	22	4.5
Seremban	1	6	—	—	1	2	4	7	6	10	20.0
Sungei Lembang	—	—	1	1	4	17	5	25	10	43	23.2
Sungei Patani	—	—	—	—	1	2	—	—	1	2	—
Taiping	0	1	—	—	2	2	—	—	6	10	60.0
Tampin	1	4	—	—	—	—	—	—	1	4	—
Tapah	—	—	0	1	0	5	—	—	0	6	—
Telok Anson	0	1	0	1	0	1	0	5	0	8	—
	26	132	36	121	61	169	50	162	173	584	29.6

TABLE III.
Incidence of Leptospirosis in PUO cases by occupation

Group	No. Positive	No. Examined	% positive
Rubber Estate workers	28	56	50.0
Labourers (miscellaneous)	43	97	44.3
Tin Miners	3	7	42.8
Farm Workers	5	14	35.7
Police	5	14	35.7
Army	21	70	30.0
Business	6	22	27.3
Housewives	7	27	25.9
Unemployed/Miscellaneous	44	180	24.4
School children	8	50	16.0
Office workers	3	39	7.7
Hospital staff	0	8	0
Total	173	584	29.6

TABLE IV.
Incidence of leptospirosis in PUO cases by sex
racial and age groups

Group	No. positive	No. examined	% positive
Males	149	476	31.4
Females	24	108	22.6
Indians	47	132	35.6
Chinese	56	182	30.8
Malays	55	224	24.5
Other Races	15	46	32.6.
0 — 10 years of age	1	25	4.0
11 — 20	30	117	25.6
21 — 30	65	200	32.5
31 — 40	42	126	33.3
41 — 50	18	62	29.0
51 — 60	13	40	32.5
Over 60	4	14	28.5

LEPTOSPIROSIS CAN BE MILD AND DECEPTIVE

Although a fair proportion of the patients investigated had the signs and symptoms indicative of leptospirosis, especially in the military group, the majority of the cases investigated for leptospirosis might well have been diagnosed as influenza, acute respiratory disease, gastritis, dengue, malaria, typhoid or infective

hepatitis. Out of the 584 cases examined, 243 had fever alone with no other clinical manifestations. Of these 35 were found positive. The clinical features of the 173 positive cases were analysed and the results are summarised in table V. Seven of these cases were manifested as meningitis, 2 as encephalitis and 3 as broncho-pneumonia.

Fever. Fever was present in every case

TABLE V.
Clinical features in 173 cases of leptospirosis
(in descending order of frequency)

Feature	No. positive	% of total positive
Fever	173	100.0
Muscle pain	83	48.0
Conjunctival Injection	74	42.8
Jaundice	70	40.0
Muscle tenderness	68	39.3
*Gastric symptoms	46	26.6
Chills/Rigors	39	22.5
Headaches	35	20.2
Palpable Liver	27	15.6
Tender Liver	19	11.0
Palpable spleen	9	5.2
Haemorrhagic signs	5	2.9
Cough	5	2.9
Diarrhoea	5	2.9
Sore Throat	4	2.3
* Anorexia/Nausea/Vomiting		
Renal function		
Abnormal urine analysis (Proteinuria & casts)	38	22.0
Raised blood urea (48-222 mg. %)	20	11.6
Other manifestations of leptospiral infection		
Meningitis	7	4.0
Bronchopneumonia	3	1.7
Encephalitis	2	1.1

and it varied from 99.2° to 104°F. The majority of cases had mild temperatures of 99.2° to 100°F.

Conjunctival injection and headache. It is surprising to note that in a large proportion of cases these two clinical features were recorded as being absent. One explanation is that most of these cases belong to the 3rd and lowest degree of severity usually called "benign leptospirosis" (Alston and Broom, 1958) in which the "onset may be sudden with

fever, muscular pains, sore throat, slight or no jaundice and slight or no nephritis." Neither headache nor conjunctival injection is mentioned as typical symptoms here although both these are characteristic features of the first and second degrees. Another possible explanation is that these signs and symptoms were not specifically noted or recorded. This mild degree of leptospirosis could easily be mistaken for influenza. The serotypes causing this mild degree of illness are usually *canicola*, *grippotyphosa*, *hebdomadis*, *hyos*, *pomona*,

sejroe and ballum, all except the last of which have been isolated in Malaya, (Trimble, 1954; Alexander *et al.*, 1955 and 1957).

Clinical jaundice. This sign was seen in less than 50% of cases which confirms the findings of previous investigators (Danaraj, 1950; Turner *et al.*, 1959). The jaundice was usually mild in severity and some doubt was even expressed in a number of cases owing to the fact that the sclera of many anicteric Indian patients tend to assume a yellowish tinge.

Gastric symptoms. These appear higher on the list than generally expected and may often lead to mis-diagnosis. The usual symptoms are anorexia, nausea and vomiting.

Chills/Rigors. These two terms are usually used to mean the same feature and are therefore considered together. They were noted in only 22.5% of the cases. Presumably, most of the fevers were mild.

Haemorrhagic signs. Two of these 5 patients had blood-streaked sputum. In the remaining 3 cases mild petechial rash was observed. No case of epistaxis was recorded although it is suspected that this sign would have been quite common if sought for.

Hepatomegaly and splenomegaly. Both enlargements were mild and were usually 1-2 finger breadths below the costal margin. The spleen was never tender but the liver was tender in 11.0% of the cases.

Abnormal urine analysis. Albuminuria, white cells and casts were noted in 22.0%. It is suspected that the occurrence of this feature is actually much higher than that recorded here as complete laboratory data were frequently not submitted with each specimen. The haematological data were omitted in most reports and therefore cannot be included here.

Raised blood urea. Seventeen cases (11.6%) were reported to have raised blood urea levels of 48-222 mgm.%. Here again owing to lack of complete laboratory data it is possible that the actual number might be

higher than that recorded. Several positive cases, however, had normal blood urea values of 35-47 mg.%. This was also noted by other investigators (McCrum *et al.*, 1957).

DIAGNOSIS OF LEPTOSPIROSIS

(a) Serological.

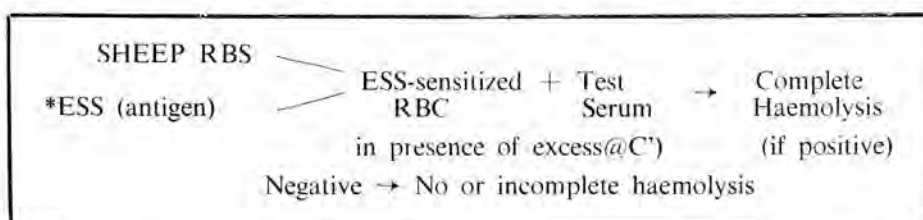
The agglutination test has been the standard method of diagnosis for several years. The patient's sera are tested for antibodies which will agglutinate suspensions of living or formalized leptospire of known serotypes. Unfortunately cross-reactions are common and the sera often agglutinate a variable number of serotypes in addition to the causative one. Moreover, because there are so many serotypes in Malaya the possibility of false negative results occurring can only be avoided if the sera are tested against a battery of serotypes representing the known sero-groups: this procedure is tedious and time-consuming. It is therefore not a practical test for routine diagnostic purposes.

Numerous complement-fixation (CF) tests have been employed using antigens prepared by various methods. However, although the range of serotypes required in the test is much reduced, the sensitivity and specificity of different preparations of antigens tend to vary.

Recently an antigen capable of sensitizing human erythrocytes so that they agglutinate in the presence of leptospiral antibodies, was extracted from leptospire (Chang and McComb, 1954). Subsequently Cox (1955) described a haemolytic modification of this technique which was more sensitive in the detection of leptospiral antibody. This test is named the *Hæmolytic* (HL) test or the Sensitized *Erythrocyte Lysis* (SEL) test. The latter description, being more explicit, is favoured by the IMR.

The principle of the SEL test is as follows: (see diagram).

The antigen, prepared by chemical extrac-



* Erythrocyte Sensitizing Substance @ Complement

tion of leptospire is mixed with a suspension of normal sheep red cells. The antigen is absorbed to the cell surface thereby sensitizing the cells so that they lyse when exposed, in the presence of excess complement, to serum containing leptospiral antibody. The antigen is aptly described as *Erythrocyte Sensitizing Substance* (ESS).

As the SEL test detects genus-specific antibody, any leptospiral infection can be diagnosed regardless of the serotype of the causal agent. As in most serological tests, however, detection of a significant rise in titre is necessary for conclusive diagnosis, and it cannot be stressed too often that both acute (taken as early in the illness as possible) and convalescent sera (taken 10-14 days later) are (minimum) required specimens for the tests.

The SEL test has been evaluated extensively with good results in America (Cox *et al.*, 1957), in Australia (Chang *et al.*, 1957) and also in this laboratory (unpublished). As far as is known, the use of antibiotics in the treatment of leptospirosis does not alter the development of SEL antibodies in the patient but this problem requires further investigation.

A faster method of diagnosis, the Fluorescent Antibody (FA) technique is being tested and evaluated but it will be some time before it can be used for routine diagnosis.

(b) Cultural.

In the past it was usual to inoculate body fluids into laboratory animals which were then observed for febrile response and development of jaundice as well as for death with characteristic autopsy findings. The most severe limitation of this method is the extreme range in virulence for laboratory animals encountered in different serotypes of leptospire and even in strains of the same serotype. The usefulness of animal inoculation is nowadays limited to the isolation of leptospire from contaminated material, such as urine. Even this has been supplanted by a recent method (Menges *et al.*, 1958 and 1960) for isolation of leptospire by direct culture not only of urine obtained aseptically by bladder tapping, e.g. in animals, but also of voided urine which is usually contaminated. In this method contamination was successfully controlled by a simple dilution technique in which serial (10-fold) dilutions of the urine were inoculated into the media. The specific medium and the relatively low incubation temperature (28°-30° C as opposed to 37° C) may not favour the growth of bacteria, especially

in the higher dilution where the numbers may be small.

Usually, however, the patient's blood taken early in the illness (1st-5th day of disease preferably) and not the urine is employed; it is cultured directly into Fletcher's (Fletcher, 1928) and/or Korthof's medium, (Korthof, 1932). Only 1-2 drops of bloods are inoculated into each of 3 tubes containing about 5 cc of the medium. Leptospire are rarely detectable before the 7th day and usually around the 14th day of incubation. Cultures must be incubated for at least 28 days before they may be safely discarded as negative.

Most of the blood specimens sent from various parts of the Federation reach the laboratory after 12 hours or so and are not cultured until then. It is suspected that many of the specimens found negative might have given positive results, especially those from patients with a positive SEL test, if they had been cultured immediately after they were obtained, i.e. AT THE BEDSIDE.

SUMMARY

Although established some 10 years ago as a major cause of febrile disease in the Federation of Malaya, leptospirosis has not received recognition as such by most local medical practitioners.

The following 3 points are emphasised:

(a) Leptospirosis is common in Malaya. A recent study of 584 PUO cases over 4½ years revealed 173 positive cases (29.6%). The incidence in the different localities, occupations, races, sex and age groups was also studied.

(b) Leptospirosis can be mild and deceptive. The clinical features of the 173 positive cases are analysed. Some of the cases were manifested as meningitis (7) or encephalitis (2) and some as bronchopneumonia (3). Thirty-five had fever alone with no other clinical manifestations.

(c) Leptospirosis can be diagnosed easily by the SEL test and by direct culture into Korthof's or Fletcher's medium. The SEL test is described and its advantages over other serological tests explained. The importance of submitting paired specimens for the serological test is stressed. Methods for culture of blood and urine directly into media, replacing the technique of animal inoculation are briefly described. The value of culturing patient's blood at the bedside is pointed out.

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DRUG-RESISTANCE IN FALCIPARUM MALARIA IN SOUTH-EAST ASIA

by

Prof. A. A. SANDOSHAM*

Senior Malaria and Filariasis Research Officer,
Institute for Medical Research, Federation of Malaya.

Dr. DON E. EYLES,

Scientist Director, U.S. Public Health Research Unit,
Institute for Medical Research, Federation of Malaya.

and

Col. R. MONTGOMERY,

Medical Specialist, British Military Hospital,
Kinrara, Kuala Lumpur.

Pampana (1963) defines resistance to an antimalarial as the capacity of a particular strain to survive when the drug has been administered to the vertebrate host at a dose that would normally destroy the parasites in the same stage of life cycle. Strains of *Plasmodium falciparum* in different parts of the world may differ in their degree of susceptibility to various drugs while the indigenous population of an area may be susceptible to infection to a varying extent. In order to determine if drug resistance in falciparum malaria existed in South-East Asia it would be desirable to establish what constituted the "dose that would normally destroy the parasites" among the indigenous population.

The most comprehensive work on the action of drugs on falciparum malaria in this part of the world has been carried out by the staff of the Institute for Medical Research, Federation of Malaya and published as a series chiefly in the Medical Journal of Malaya under the heading of "Studies on the chemotherapy of malaria, I to VII" during 1952-1959. Their work, however, does not include the recurrence rate of parasitaemia after the initial clearance following treatment in the absence of reinfection. This would have been difficult and expensive in an area where active transmission was going on. The information obtained in Malaya is outlined briefly and will provide some base line data for comparison with strains suspected of showing

drug-resistance. It should be realized that information obtained in Malaya may not be equally applicable to other parts of S.-E. Asia.

In attempting to determine if a resistant strain existed in the country one could compare the results of treatment of the suspected strains with those obtained with the normal susceptible strains preferably in the same area and among the same ethnic group. One could compare (1) the rate of disappearance of parasitaemia in the blood, (2) the rapidity of disappearance of clinical malaria especially of fever, (3) the reappearance or otherwise of parasitological and clinical malaria in the absence of reinfection, and (4) the presence of parasitaemia in relation to the concentration of the drug in the blood plasma. If possible the suspected strain should be inoculated into a susceptible volunteer and tested for its reaction to the drug in question.

4 - AMINOQUINOLINES

Chloroquine

Wilson and Edeson (1954) using Resochin (a Bayer product of chloroquine diphosphate) gave 300 mg. chloroquine base to 7 cases of indigenous people in Tampin with falciparum infection (av. count 13,800 per c.mm.) and found that parasitaemia cleared in 2 days and fever in 0.6 days. Using Nivaquine (a May & Baker product of chloroquine phosphate) they gave 300 mg. chloroquine base to 40 cases of falciparum malaria (av. count 19,300 per c.mm.) and found that parasitaemia cleared in 2.3 days and fever in 1.1 days (Figs. I & II).

* A paper read by invitation at the Seventh International Congresses in Tropical Medicine and Malaria held at Rio de Janeiro, Brazil in September, 1963.

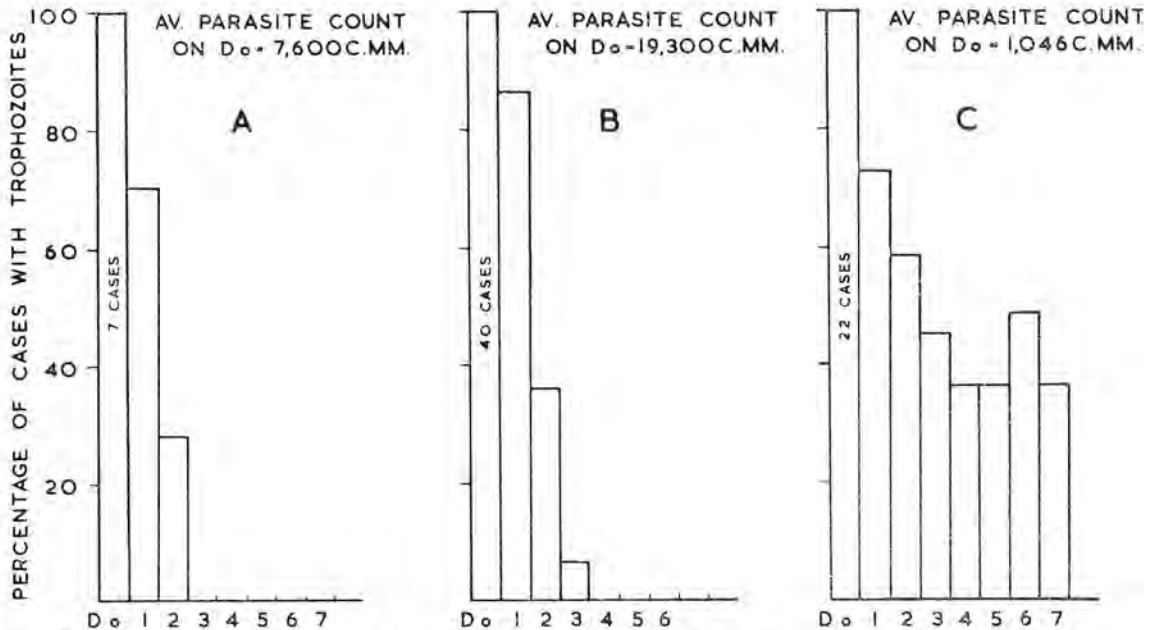


FIG. 1. 300 MG. GROUP ORAL CHLOROQUINE TREATMENT

- A. 7 CASES FROM TAMPIN WITH RESOCHIN (WILSON & EDESON, 1954)
- B. 40 CASES FROM TAMPIN USING NIVAQUINE (WILSON & EDESON, 1954)
- C. 22 CASES FROM PERLIS WITH "SPECIA" CHLOROQUINE DIPHOSPHATE (SANDOSHAM *et al.*, 1963)

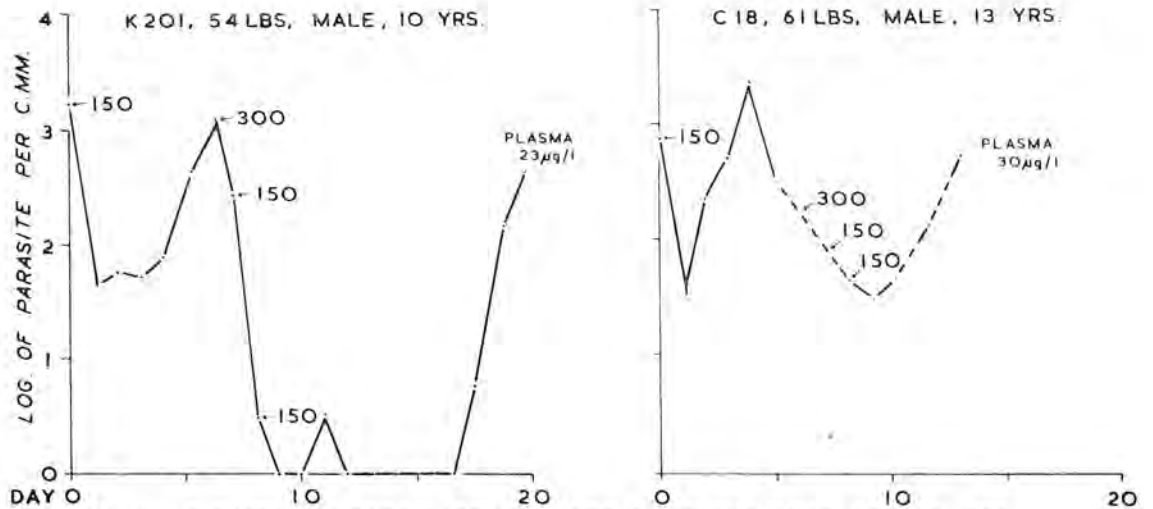


FIG. II. 2 CASES BELONGING TO THE 300MG GROUP (HALF DOSAGE FOR CHILDREN) FROM PERLIS WHICH BROKE THROUGH AFTER FULL TREATMENT (1200MG). INTERRUPTED LINE MEANS NO BLOOD FILMS WERE EXAMINED DURING THAT PERIOD.

They gave single dose treatment of 600 mg. chloroquine base to 114 cases of falciparum malaria (av. count 28,250 per c.mm.) and found that parasitemia cleared in 2.5 days

and fever in 0.9 days. Several of their cases had trophozoite counts of over 100,000 per c.mm. and they concluded that 600 mg. was an effective single-dose treatment for the aver-

age Asian adult with acute falciparum malaria in Malaya. Laing (1955) working at Kuala Kangsar gave 600 mg. chloroquine base (Nivaquine) to 97 cases of falciparum malaria (av. count 8,356 per c.mm.). All but one (99 percent) had no parasitaemia within 48 hours and there was a 100 percent clearance within 72 hours after treatment (Figs. III & IV). However, for full treatment they used 1,500 mg. and this dosage should, according to Covell *et al.*, (1955) produce radical cure. This is substantiated by the work of Jeffery *et al.*, (1956) who found that only one of 46 cases relapsed after this dosage.

RESISTANCE TO CHLOROQUINE IN MALAYA — About 600 Australian soldiers belonging to the British Commonwealth Units stationed in Malaya were engaged in jungle operations near the Thai border in North Perlis during a period of about two months from August to October 1962. They were a non-immune population and were taking a daily prophylactic dose of 200 mg. of proquanil (Paludrine). About 10 percent of these men were admitted to medical units with malaria, *Plasmodium falciparum* predominating. The men were aware of the danger of contracting malaria and military discipline was such that there is no reason to believe that the prophylactic routine was not followed. A number of these cases were brought away from Perlis to their base camps near Malacca or Taiping. Although they had returned to places where there was little or no likelihood of reinfection, cases were said to have relapsed after full chloroquine therapy.

It was decided to find out if the Australian troops could have contracted their infection from the people of North Malaya near the Thai border. A brief survey in December 1962 (Sandosham *et al.*, 1963) showed that in the adjoining area to where the troops were camped about half the indigenous people had malaria of which *P. falciparum* accounted for nearly 60 percent. *Anopheles balabacensis balabacensis* caught near the tents occupied by the troops were found with oocysts and sporozoites.

A further study of this area was undertaken during March and April, 1963 by the Institute for Medical Research in collaboration with U.S.P.H. Service Research Unit and

the World Health Organization to determine the effect of chloroquine on falciparum malaria among the semi-immune indigenous population there. The study (Sandosham *et al.*, in press) showed that when they were given 300 mg. chloroquine base 24 out of 81 failed to clear within 5 days after treatment and a further 29 recurred before the 19th day giving a total break-through of 65 percent. When those whose blood became positive were given 1,200 mg. chloroquine base 24 percent recurred within 4 weeks of treatment. Some of these had parasitaemia in spite of blood levels for chloroquine varying from 10 to 57 $\mu\text{g/litre}$. Seven out of 12 given 600 mg. chloroquine base either failed to clear or became positive between the 5th and 18th day and their blood levels for chloroquine soon after the break-through varied from 15 to 81 $\mu\text{g/litre}$. It was concluded that there was little doubt of the existence of chloroquine-resistant strains of *P. falciparum* occurring amongst the indigenous population of Perlis, N. Malaya and that the Commonwealth troops had contracted the infection while at manoeuvres there.

Montgomery and Eyles (1963a) studied 27 Australian patients who returned from N. Malaya and were treated at the base British Military Hospital at Kinrara on the outskirts of Kuala Lumpur. Of these, ten cases were considered to show evidence of resistance to chloroquine, and two were described in detail. In none of these ten cases did chloroquine produce radical cure although 9 out of the 10 cases had received more than the generally recommended 1,500 mg. of the base. When the relapse attacks were treated again with chloroquine more than half of them were not cured as was evident from the persistence of low parasitaemia. Some of these cases relapsed a third time. The authors noted that the clearance of parasites and the disappearance of symptoms were slow. Though not cured by chloroquine, ordinary doses had an effect on the parasites and controlled the infection. The resistance, however, was not overcome even by increasing the amount of chloroquine to three times the recommended dosage. In two of these cases plasma levels of chloroquine were as high as 111 $\mu\text{g/litre}$ and 66 $\mu\text{g/litre}$ at the time when relapse occurred. One of the strains of *P. falciparum* from this group has been passed to prison

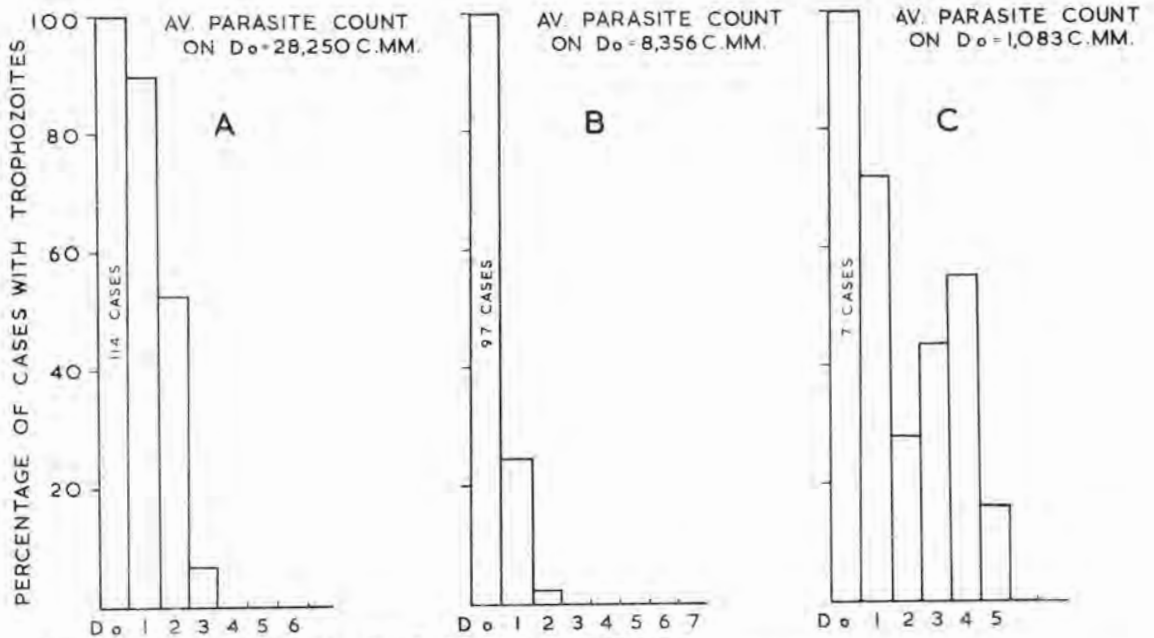


FIG. III. 600 MG ORAL CHLOROQUINE TREATMENT
 A 114 CASES FROM TAMPIN WITH NIVAQUINE (WILSON & EDESON, 1954)
 B 97 CASES FROM KUALA KANGSAR WITH NIVAQUINE (LAING, 1955)
 C 7 CASES FROM PERLIS WITH "SPECIA" CHLOROQUINE DIPHOSPHATE (SANDOSHAM *et al.*, 1963)

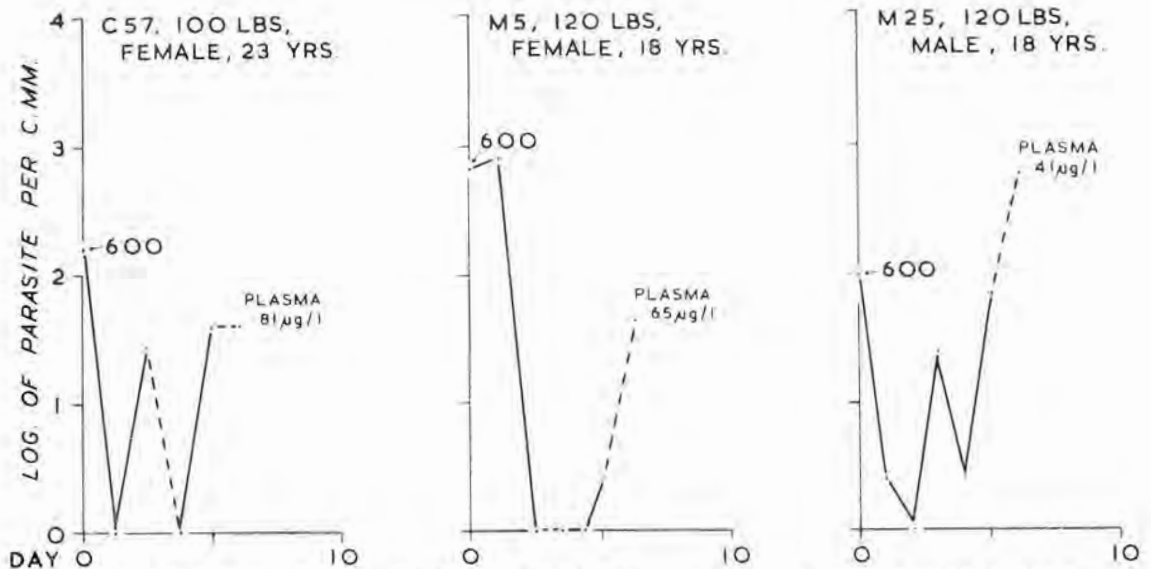


FIG. IV. 3 CASES GIVEN 600 MG CHLOROQUINE WHICH HAD PARASITAEMIA ON THE 5th DAY OR LATER AFTER INITIAL TREATMENT GIVING PLASMA LEVELS OF CHLOROQUINE

volunteers in the United States and Contacos *et al.*, (1963) have confirmed that it is resistant to chloroquine.

Montgomery and Eyles (1963b) had the opportunity to follow up the malaria histories of a similar group of Commonwealth troops (New Zealanders) who replaced the former group for a similar period. There were 137 cases of malaria notified of which 53 were diagnosed clinically. Of the 84 microscopically confirmed malaria cases 51 (61 per cent) had *P. falciparum* infection. Since this unit had the benefit of experience of the previous group the prophylactic measures were more stringent. The troops took 200 mg. proguanil daily while in the area and in addition were given 300 mg. chloroquine base before going on leave during the operation. This leave was spent in places in Penang or Malacca where little or no transmission of malaria was taking place. One of the Companies was given 150-300 mg. of chloroquine base at approximately weekly intervals for 2 or 3 doses while it was operating in what was considered to be a highly infectious area.

In general, the first attacks of *P. falciparum* infection were treated with 2,400 to 2,700 mg. chloroquine base over a five to six day period. Of about 51 such cases 31 relapsed and laboratory confirmation of resistance was obtained in 28 of them. The chloroquine level in plasma was determined at relapse and before commencement of the treatment in 23 cases and the mean level was 27 $\mu\text{g}/\text{litre}$. In 14 cases the level was over 20 $\mu\text{g}/\text{litre}$. Six out of 12 cases under continuous hospital observation relapsed. Parasites recurred on the average of 14.2 days after the end of treatment and the mean chloroquine level was 43 $\mu\text{g}/\text{litre}$. Burliner *et al.*, (1948) consider 20 $\mu\text{g}/\text{litre}$ as the minimum therapeutic level but it must be remembered that in many of the cases studied in Malaya blood was drawn some time after the appearance of the parasites during which there would have been some decay in the chloroquine level. Two strains from this group have been passed to prison volunteers in the United States and resistance to chloroquine has been confirmed (Contacos *et al.*, 1963).

Alving *et al.*, (1963) studied in prison volunteers a strain of *P. falciparum* contract-

ed in Malaya which also originated from the Commonwealth troops and found it resistant to chloroquine.

Chloroquine-resistant strains appear to be confined to the North of Malaya bordering Thailand. Physicians in Malaya who have been alerted to the existence of this condition (Sandosham, 1963) have so far produced no evidence of its existence in the rest of Malaya. A brief survey carried out in Pulau Aur an Island about 50 miles to the East of Johore State by Warren *et al.*, (personal communication) showed no resistant strains there.

RESISTANCE TO CHLOROQUINE IN CAMBODIA — Seven members of the staff of the Institute for Medical Research, Federation of Malaya, Kuala Lumpur went on a field study to the Pailin District of the State of Battambang in Cambodia. The specific locality of exposure to infection was in and near the village of Pangrolim which lies within the World Health Organization medicated salt experimental project area. Chloroquine was used in the salt at the time of study although pyrimethamine had been used earlier. In spite of chloroquine prophylaxis three members came down with *P. falciparum* malaria on return to Kuala Lumpur (Eyles *et al.*, 1963). One of them (a Malay) relapsed twice after standard 1.5 gm. treatment and the chloroquine level in the plasma at time of relapse was 50 $\mu\text{g}/\text{litre}$ and 80 $\mu\text{g}/\text{litre}$. Infection was ultimately eliminated with quinine. Blood was inoculated into prison volunteers in U.S.A. and the strain proved to be chloroquine-resistant. Another (a Malayan Chinese) also relapsed twice after chloroquine and pyrimethamine therapy. The third (an American) who had an attack of falciparum malaria responded to chloroquine treatment and did not relapse. Blood taken from him at the time of the first attack was inoculated into a prison volunteer in U.S.A. and the strain proved sensitive to chloroquine at the standard dose, but resistant at a 600 mg. dose (Contacos *et al.*, 1963).

CHLOROQUINE - RESISTANCE IN THAILAND — Dr. (Mrs.) Harinasuta of the University of Medical Sciences, Bangkok at the Unesco Symposium on Scientific Knowledge of Tropical Parasites in Nov. 1962 gave clinical case histories of several cases from

various parts of Thailand which had not responded normally to chloroquine. There were one or two relapses after 1,500 mg. chloroquine base and in one case given 3,300 mg. it took 7 days for the parasitemia to disappear.

Young *et al.*, (1963) studied a case of *P. falciparum* contracted by an American in Thailand which had shown poor response to chloroquine and confirmed that the strain was resistant to chloroquine by inoculating it into prison volunteers in the U.S.A. Alving *et al.*, (1963) confirmed the above findings by inoculating the same strain to volunteers. Montgomery and Eyles (personal Communication) found Cpl. L. a member of a Commonwealth Unit who had exposed himself to infection in Ubon, Thailand in mid year 1963 returned to Malaya with a chloroquine-resistant strain of falciparum malaria. He was given 2,800 mg. of chloroquine including 400 mg. given intramuscularly over a five day period. This is nearly double the standard dose. The parasite count the day after the start of the treatment period was 19,255 p.c.mm. The treatment did not clear the infection. The number of trophozoites dropped to 132 p.c.mm. and then immediately rose into the thousands. The patient was fever-free only for four days. Quinine was finally used to terminate the infection.

CHLOROQUINE - RESISTANCE IN VIETNAM — Powell *et al.*, (1963) have studied a strain of falciparum malaria contracted by an American in S. Vietnam near Nha Trang. He relapsed after each treatment with chloroquine and inoculation into prison volunteers in U.S.A. confirmed that the strain was resistant to chloroquine.

Amodiaquine

Edeson *et al.*, (1955) had established that amodiaquine (Camoquin) was effective in curing all 187 patients with falciparum malaria in the Tampin area with a single dose of 300 to 600 mg. They obtained good results with a similar dose against vivax malaria also.

RESISTANCE TO AMODIAQUINE IN MALAYA — Cross resistance to amodiaquine is to be expected of strains of malaria parasites resistant to the closely related chloroquine. Montgomery and Eyles (1963b) selected four

cases of New Zealand troops who had contracted the chloroquine-resistant strains of *P. falciparum* in Perlis and kept them under observation in the British Military Hospital at Kinrara. All four patients had previously relapsed after treatment with chloroquine and were having their first relapse except one whose relapse was the second. Two of these relapse cases had been treated with pyrimethamine without success and another of these had received 1,500 mg. proguanil without marked effect. Three of the four cases received 2,000 mg. of amodiaquine over a four-day period and one received 3,200 mg. One failed to clear, two relapsed in 10 to 15 days and the other one that had received the higher dose of amodiaquine and the proguanil treatment did not relapse.

Alving *et al.*, (1963) showed that the Malayan chloroquine-resistant strain transmitted to a prison volunteer in U.S.A. showed only a partial temporary response to amodiaquine (Camoquin) in 1,400 mg. dose.

BIGUANIDES

Proguanil (Paludrine)

RESISTANCE TO PROGUANIL IN MALAYA — Edeson and Field (1950) showed that whereas naturally acquired falciparum malaria in the Tampin area was effectively treated with a single proguanil dose of 100 mg. in 1947 and early 1948, it began to show resistance towards the end of 1948 and in the early months of 1949. In April, 1949 came the first failure after a standard proguanil course of 300 mg. daily for 7 to 10 days and there has been a steady increase in the number of cases that resisted proguanil. Wilson, Munro and Richard (1952) working in the same area reported fresh infections of falciparum malaria late in the year 1950 and in 1951 among British troops on an official suppressive dosage of 100 mg. of proguanil daily.

Walker and Reid (1953) showed that gametocytes of a proguanil-resistant strain of *P. falciparum* readily infected mosquitoes while daily doses of 100 mg. proguanil were still being taken; and also that daily doses of 100 mg. started 3 days before infective bites and continued for 10 days thereafter did not prevent the onset of falciparum malaria in the

recipient on the 11th-12th day. Laing (1956) produced evidence that naturally acquired proguanil-resistant infections of *P. falciparum* in the Tampin area of Malaya could readily infect mosquitoes and complete the sporogonic cycle while gametocytes were exposed to therapeutic doses of proguanil. He maintained that continued use of proguanil as a suppressive drug in preference to other antimalaria drugs in Malaya would appear to have an element of uncertainty. The British troops in Malaya have continued to rely on proguanil as the prophylactic drug.

Field *et al.*, (1954) pointed out that the Tampin District was not the only area with proguanil-resistant strains because when they started proguanil treatment in Kuala Lumpur in 1951 resistant falciparum infections were soon found there also and that the condition has since been found wherever it has been looked for in Malaya.

Presumably, proguanil was ineffective as a suppressant of both the chloroquine-resistant and susceptible strains of *P. falciparum* in Commonwealth troops exposed in North Perlis. In view of the fact that the troops were on proguanil prophylaxis at 200 mg. daily at the time of exposure it is justifiable to assume that there were strains of malaria parasites in N. Perlis which were resistant to proguanil. Montgomery and Eyles (1963b) gave one of the patients with chloroquine-resistant falciparum malaria 1,500 mg. (300 mg. per day for 5 days) proguanil. There was only a lowering of parasite count at the end of eight days after commencement of treatment. *Anopheles maculatus* fed on a patient after proguanil treatment developed sporozoites normally whereas Maekerras and Ercole (1947) had shown that in proguanil sensitive strains the maturation of sporozoites was prevented. Contacos *et al.*, (1963) found all three chloroquine-resistant Malayan strains transferred to prison volunteers in U.S.A. were also resistant to proguanil.

RESISTANCE TO PROGUANIL IN CAMBODIA — Contacos *et al.*, (1963) tested one of the chloroquine-resistant falciparum strains from Cambodia transmitted to prison volunteers in U.S.A. and found it resistant to proguanil as well.

RESISTANCE TO PROGUANIL IN THAILAND — Young *et al.*, (1963) found the

chloroquine-resistant falciparum malaria transmitted to prison volunteers in U.S.A. also resistant to proguanil. Alving *et al.*, (1963) using the same strain as above and another from Thailand in volunteers in U.S.A. were able to obtain only temporary therapeutic effect with 2,610 mg. proguanil base.

RESISTANCE TO PROGUANIL IN VIETNAM — Powell *et al.*, (1963) found the chloroquine-resistant falciparum malaria transmitted to three volunteers in U.S.A. also resistant to proguanil in dosage of 2,610 mg. base.

RESISTANCE TO PROGUANIL IN OTHER PARTS OF S.E. ASIA — According to the W.H.O. report (1961) of a technical meeting on chemotherapy of malaria, resistance to proguanil in falciparum malaria has been reported in local strains in Indonesia, Assam, New Guinea and Vietnam.

MEPACRINE

Field (1938) reported that in 560 cases of uncomplicated acute malaria treated in Kuala Lumpur either by oral atebrin or oral quinine atebrin had a slower action than quinine in falciparum malaria but had a more rapid action than quinine in vivax malaria. Wilson and Edeson (1958) found oral mepacrine to be less effective than oral chloroquine or amodiaquine. It was less rapid in its effect on heavy falciparum infections, and less reliable as a single dose treatment. No authenticated case of resistance to mepacrine has been reported in Malaya.

RESISTANCE TO MEPACRINE IN MALAYA — In a series of seven cases of chloroquine-resistant falciparum malaria treated with mepacrine Montgomery and Eyles (1963b) found that all relapsed after regimens ranging from 3,100 to 4,200 mg. over a period of 6 to 8 days. The mean time for clearance of parasites was 5.1 days after treatment and the mean time for recurrence was 12.9 days. The mean plasma level for 5 cases at time of relapse was 76 $\mu\text{g/litre}$ ranging from 31 to 180 $\mu\text{g/litre}$. Contacos *et al.*, (1963) found that of the two strains (both from New Zealand) of chloroquine-resistant falciparum malaria transmitted to prison volunteers in U.S.A. one was susceptible and the other resistant to mepacrine.

RESISTANCE TO MEPACRINE IN CAMBODIA — Contacos *et al.*, (1963) tested one of the chloroquine-resistant falciparum strains from Cambodia transmitted to a prison volunteer in U.S.A. and found it resistant to mepacrine as well.

RESISTANCE TO MEPACRINE IN THAILAND — Young *et al.*, (1963) found that the chloroquine-resistant strains of falciparum malaria from Thailand transmitted to prison volunteers in U.S.A. relapsed after 2,800 mg. of mepacrine. Alving *et al.*, (1963) using the same strain as above and another from Thailand in volunteers in U.S.A. were able to obtain only temporary therapeutic effects after 2,198 mg. of atebirin.

RESISTANCE TO MEPACRINE IN VIETNAM — Powell *et al.*, (1963) found that the chloroquine-resistant strains of falciparum malaria from S. Vietnam transmitted to prison volunteers in U.S.A. showed only temporary therapeutic effect after a dosage of 2,198 mg.

Pyrimethamine

Wilson and Edeson (1953) treated 126 Asian patients from Tampin and Kuala Lumpur areas suffering from acute malaria with pyrimethamine and concluded that it was unsuitable for use against Malayan strains. This drug has therefore not been used much in Malaya. It was found that the response to pyrimethamine was not affected by *P. falciparum* strains having become resistant to proguanil.

RESISTANCE TO PYRIMETHAMINE IN MALAYA — Montgomery and Eyles (1963b) treated four cases of chloroquine-resistant falciparum malaria with 1,500 mg. of pyrimethamine over 3 days. In two cases the parasite count was not materially altered. In one case the count increased while the patient was under treatment and in the fourth only a slight lowering of the parasite count was produced. Confirmation of resistance to pyrimethamine was obtained by experiments which showed the development of mature sporozoites in *Anopheles maculatus* since Shute and Maryon (1954) had shown that such development did not occur with susceptible strains. Contacos *et al.*, (1963) found that of the three strains of chloroquine-resistant falciparum

malaria transmitted to prison volunteers one was susceptible to pyrimethamine while the other two were resistant.

RESISTANCE TO PYRIMETHAMINE IN CAMBODIA — Contacos *et al.*, (1963) found that the chloroquine-resistant falciparum malaria strains from Cambodia tested in prison volunteers in U.S.A. was resistant to pyrimethamine as well.

RESISTANCE TO PYRIMETHAMINE IN THAILAND — Young *et al.*, (1963) found that the chloroquine-resistant falciparum malaria strain from Thailand in the American patient who had contracted it there and in the prison volunteers in U.S.A. was resistant to pyrimethamine as well in dosage of 100 mg. The parasites failed to clear at all or actually increased in numbers within 48 hours of administration of the drug. It failed to exert a sporonticidal effect and both the sexual and asexual parasites were resistant to pyrimethamine. Alving *et al.*, (1963) using the same strain as above and another from Thailand in volunteers in U.S.A. had no effects in one case and only temporary effects in 4 cases after 150 mg. daraprim.

RESISTANCE TO PYRIMETHAMINE IN VIETNAM — Powell *et al.*, (1963) found that the chloroquine-resistant falciparum malaria strain from S. Vietnam transferred to prison volunteers in U.S.A. was susceptible to pyrimethamine, all 8 cases treated with 150 mg. being radically cured.

RESISTANCE TO PYRIMETHAMINE IN NEW GUINEA — Meuwissen, J.H.E.T., (1961) showed that three months after the initiation of a test project wherein pyrimethaminised salt was distributed among the population of West Irian (New Guinea). *P. falciparum* appeared to have developed resistance to pyrimethamine. This strain was also cross resistant to proguanil.

Quinine

Quinine has been used extensively before World War I and Fletcher (1928) investigated a number of so-called quinine-resistant cases of malaria and showed that the resistance was apparent and not real. In most cases the quinine was not swallowed or was vomited.

RESPONSE TO QUININE IN MALAYA — Montgomery and Eyles (1963b) found quinine entirely satisfactory in 20 cases of chloroquine-resistant falciparum malaria, mostly given 20 gm. over 10 days. Contacos *et al.*, (1963) found all 3 chloroquine-resistant falciparum strains transferred to prison volunteers in U.S.A. sensitive to quinine. Alving *et al.*, (1963) found that the chloroquine-resistant falciparum malaria strain from Malaya transferred to a prison volunteer in U.S.A. was sensitive to quinine, a radical cure being obtained after 1620 mg. quinine base daily for 7 days.

RESPONSE TO QUININE IN CAMBODIA — Contacos *et al.*, (1963) found all three strains of chloroquine-resistant falciparum malaria transferred to prison volunteers in U.S.A. were sensitive to quinine.

RESPONSE TO QUININE IN THAILAND — Young *et al.*, (1963) found that the chloroquine-resistant falciparum malaria strain from Thailand transferred to prison volunteers in U.S.A. proved susceptible to quinine. All the infections treated with 8 or more gm. of quinine, given at the rate of 2 gm. daily, and 1 or 2 infections treated with 6 gm. total, appeared to be eradicated. Smaller doses of quinine exerted a rapid temporary effect. Alving *et al.*, (1963) using the same strain as above and another from Thailand had similar results with quinine.

RESISTANCE TO QUININE IN VIETNAM — Powell *et al.*, (1963) found that only in two out of four volunteers inoculated with the chloroquine-resistant falciparum malaria from Vietnam could radical cure be achieved after giving 1620 gm. quinine base daily for seven days.

Discussion

The existence of chloroquine-resistant falciparum malaria has been firmly established over an extensive area of South-East Asia including the countries of Vietnam, Cambodia, Thailand and Malaya. In the latter country, the resistant strains are known only from the area of the Thailand border. The exact extent of the distribution of the strains is not known in the other countries, except that in Thailand Harinasuta has studied patients whose infections failed to respond to chloro-

quine from areas East, North and Southwest from Bangkok.

Further work will be necessary to determine the actual extent of the problem, and this points to the necessity of stating clearly criteria adequate for the recognition of the resistance. Obviously, the chloroquine resistance, which has been shown to exist so clearly could not have been recognised had not the various investigators really had criteria in mind. On the other hand, most of these investigators had wide experience with malaria and were either engaged in research or had access to advice from laboratories conducting research. Criteria must be established that will enable the malariologist or physician who is not so fortunately located to recognise the resistance. They must be rigid, so that undue alarm will not be caused by incorrect evaluation. On the other hand, they must be sufficiently practical to allow recognition as the resistance does present a dangerous problem which must be detected where it exists so that remedial measures may be taken.

The detection of chloroquine resistance, and the establishing of criteria has been the subject of another paper on this programme and need not be discussed further at this time. It should be pointed out, however, that at the time the resistance of falciparum malaria to chloroquine was noted there were no laboratories in the S.E. Asian region performing the tests for the estimation of plasma chloroquine levels. It is to be hoped that facilities for doing the tests will be developed and made available for workers throughout the region. It should also be noted that Malaya was particularly fortunate in that clearance studies of chloroquine-sensitive strains had been made and were available for comparison. It would be desirable for more studies of this type to be done in S.E. Asia for possible future reference.

In light of the existence of chloroquine resistance, the failure of the strains to respond to amodiaquine is not surprising. A similar mode of action would be expected for the drugs as they are closely related. Likewise, it is probable that a similarity of mode of action is involved in the mepacrine resistance.

The resistance to proguanil is undoubtedly

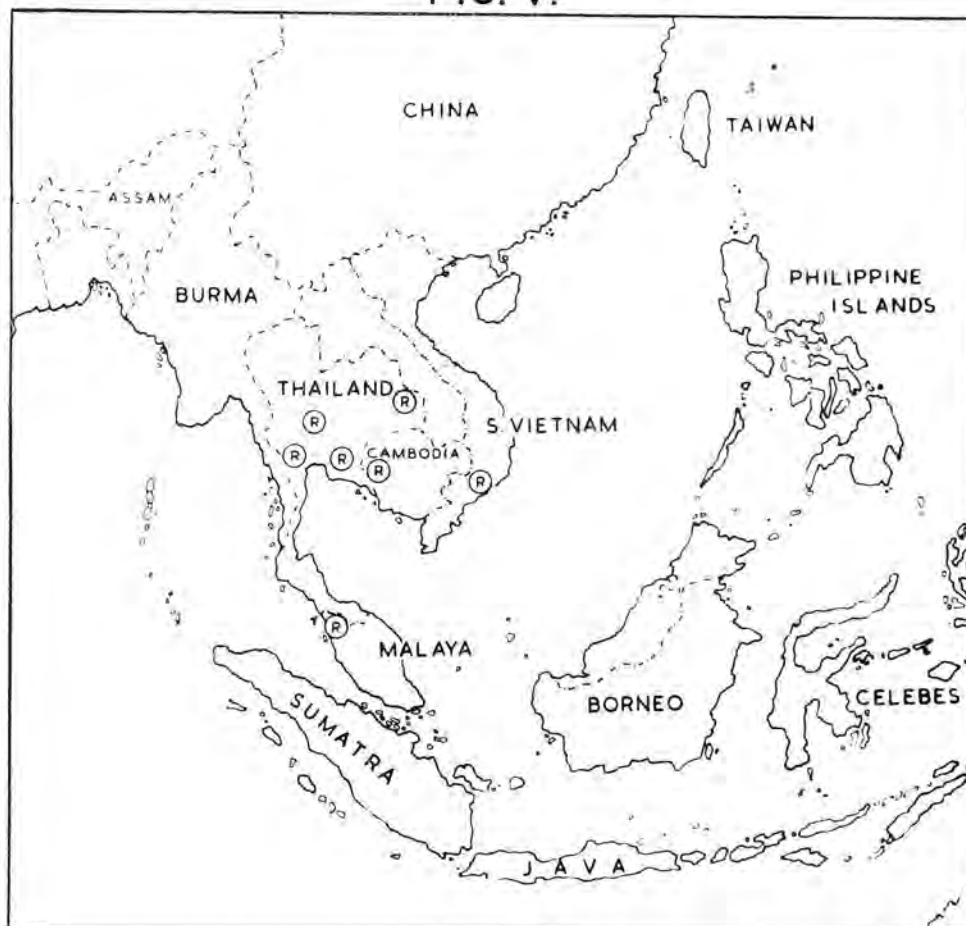
unrelated and is presumably due to the widespread use of this drug in S.E. Asia. Possibly the pyrimethamine resistance represents a cross-resistance to proguanil, or in some areas perhaps to the use of pyrimethamine. This problem has been recognised for many years, so further discussion is unnecessary.

The implications of the widespread existence of drug-resistant falciparum malaria are great. In the first place, the cases of highest resistance pose a danger to life as in the case of Cpl. L. of a Commonwealth Unit, exposed to infection in Thailand, described earlier by Montgomery and Eyles. This patient was under close medical supervision. It is easy to visualise tragic results had not supervision been close. This is a clear instance of a dose near-

ly double the standard failing to clear parasites and alleviating symptoms only temporarily.

The resistance to chloroquine also poses a problem in the use of drugs in malaria eradication programmes in areas where the resistance exists. The cross resistance to related drugs and the coincident resistance to others makes the problem more serious and points toward the necessity of continuing the research for new and better antimalarial drugs. Certainly the mass treatment with 600 mg. of chloroquine frequently advocated would have little more than a temporary effect as the studies in a semi-immune population in Perlis showed that the majority of persons given this dosage soon had recurrence of parasitæmia if the parasites were cleared at all.

FIG. V.



(R) INDICATES AREAS IN S E ASIA WHERE CHLOROQUINE-RESISTANT STRAINS OF P FALCIPARUM HAVE BEEN SHOWN TO EXIST

The fact that chloroquine resistance was first seen in non-immune persons was probably not due to their immune status but to the fact that these persons returned to non-malarious areas where the recurrences and the failures to clear stood out in sharp relief, since reinfection was not possible.

The cause of the chloroquine resistance is not known. The use of chloroquine is so widespread that exposure to the drug might be the explanation, but in Malaya its emergence would not have been expected in rural Perlis where medical care is not nearly so readily available as near some of the larger centers.

A fascinating coincidence is that the principal mosquito vector in most if not all of the localities in S.E. Asia from which chloroquine resistance is known is *Anopheles balabacensis balabacensis*. Whether or not this is of significance is not known, and it must be acknowledged that a hypothesis to explain a connection is difficult to conceive.

Summary

The development of resistance of falciparum malaria to proguanil was recognised in Malaya about fifteen years ago. It has been reported to occur in several other parts of S.E. Asia.

Pyrimethamine-resistant strains of *P. falciparum* have been reported from many parts of the world and the drug has not been used much in S.E. Asia. The use of the drug in a medicated salt project in New Guinea and possibly also in Cambodia induced resistance to it; this New Guinea pyrimethamine-resistant strain showed cross resistance to proguanil.

Strains of falciparum malaria resistant to chloroquine (see Fig. V) have been shown to exist in N. Malaya, Cambodia, Thailand and S. Vietnam. If the existence of chloroquine-resistant falciparum malaria is not recognised the patient's life may be endangered. Chloroquine-resistance is associated with cross resistance to some of the other antimalarials and malaria eradication programmes may be adversely affected.

Chloroquine-resistant falciparum malaria could be expected to show cross resistance to the chemically allied amodiaquine. This was

shown to be so in the Malayan strains. Chloroquine-resistant strains of falciparum malaria from Malaya, Cambodia, Thailand and S. Vietnam also proved to be resistant to proguanil, mepacrine and pyrimethamine. Generally, the chloroquine-resistant falciparum malaria strains have proved sensitive to quinine; the S. Vietnam strain however was refractory to quinine in two out of the four cases tested.

ACKNOWLEDGEMENTS

This paper reviews the efforts of a large number of people who studied the problem of drug resistance in S.E. Asia and who made their information freely available. The work involved the willing co-operation of a number of organizations including the World Health Organization, the Institute for Medical Research and the Division of Medical Services of the Federation of Malaya, the Royal Army Medical Corps Units in Malaya, the Laboratory of Parasite Chemotherapy of the U.S. Public Health Service (installations in Malaya and the United States) and others. The aid of the various persons serving these organizations is hereby recognised and acknowledged.

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NOTES ON THE BIONOMICS OF *ANOPHELES CAMPESTRIS*, REID, AND ON ITS DISAPPEARANCE FOLLOWING HOUSE- SPRAYING WITH RESIDUAL INSECTICIDES

By Douglas E. Moorhouse, World Health Organisation,
P. O. Box 13, Kuala Lumpur and
C. K. Chooi, Malaria Eradication Pilot Project,
Kuala Lumpur.

Summary.

Entomological surveys made in the malaria eradication pilot project area in Selangor prior to the start of house spraying revealed the presence of *Anopheles campestris* Reid, an important vector of malaria and filariasis in Malaya. It was mainly confined to a narrow coastal belt which extended beyond both the northern and southern boundaries of the experimental area. *A. campestris* is anthropophilic, it is also both endophagic and endophilic.

Following house spraying with DDT, this species disappeared from the project area, but it could still be demonstrated beyond the boundaries of the sprayed area. There is convincing evidence that *A. campestris* also disappeared from another area which has been regularly sprayed with dieldrin for malaria control purposes.

It is considered that house spraying with residual insecticides would be the most effective and most convenient method of malaria control in any area where *A. campestris* is the sole, or the more important vector of malaria. So far as any future malaria eradication programme is concerned, the response of this mosquito is extremely encouraging.

Introduction.

In February 1960 a malaria eradication pilot project was started by the Government of the Federation of Malaya, with the assistance of the World Health Organisation, in a part of the State of Selangor. The purpose of this pilot project was to investigate the possibility of malaria eradication in Malaya by means of the simultaneous spraying of houses with a residual insecticide (DDT) and the distribution of anti-malarial drugs. An area of approximately 500 square miles considered typical of the rural parts of western Malaya was chosen for the project. It stretches from the west coast, inland across the coastal plain, to the central spinal hill range.

Prior to the introduction of malaria eradication techniques into the area, a thorough entomological survey was made by a variety of methods so as to ascertain the distribution of the known malaria vectors and other anopheline mosquitos. Surveys were also made in localities contiguous with the project area.

During these preliminary surveys, *Anopheles campestris* Reid, (1962), which was previously known as the dark-winged form of *A. barbirostris* (Reid 1942) was commonly found along a coastal belt, which continued beyond both the northern and southern boundaries of the experimental area and also extended inland for a short distance along the Selangor River. Information available shows that this species is an important vector of human malaria in Malaya, (Hodgkin, 1956; Reid, 1962), although at times in the past its status as a vector has been in doubt because of confusion with other members of the *A. barbirostris* group, and also because it is usually found in association with other vectors such as *A. letifer* and *A. sundaicus*. *A. campestris* is also a vector of filariasis due to the periodic form of *Brugia malayi*. (Reid 1953).

The Study Area

The area chosen for the project has a coastline about twenty four miles in length, fringed by mangrove swamp. The coastline is broken by the estuary of the Selangor River. Generally the limits of the mangrove are the bunds built to protect cultivated areas from periodical inundation by the sea. Inland of the mangrove is the flat coastal plain which leads to the foothills of the central spinal hill range of Malaya. Apart from the fishing villages and small towns on the coast, there is a well-settled and highly cultivated coastal strip devoted to small-holdings (Malay kampongs) running the whole length of the study area; this also extends beyond both its northern and southern boundaries. This strip is centred about the coastal road which follows the main bund, it averages perhaps four miles in depth. One of the principal crops grown

within this coastal strip is the coconut palm. Except for this, the rest of the coastal plain is mostly devoted to rubber and oil-palm estates, but there are also some kampongs identical with those of the coast, except that as one proceeds inland the cultivation of coconuts becomes less frequent. Part of the northern boundary of the study area, inland of the coastal kampongs, is formed by the rice fields of Tanjong Karang. The cultivation of rice is not typical of this part of Malaya, and these fields are a relatively recent development.

Previous to the start of the project the only anti-malarial measures carried out within the study area were drug prophylaxis in some schools where there was evidence of much malaria and drainage and oiling of possible breeding places close to the larger villages. There is no evidence that residual insecticides had ever been used in the area for health purposes, although small amounts have been used for agriculture.

Survey Methods.

Coincident with the start of the entomological surveys in the study area a complete house survey was made. All houses were numbered and maps drawn to the scale 11 inches per mile (these were based on the existing land utilization maps). Each individual map covered an area of $2\frac{1}{2}$ miles (north to south) \times $3\frac{1}{2}$ miles. Because of this it was possible to locate breeding and resting sites of mosquitos accurately, later these same maps were used to assess the efficiency of the spraying operations.

Throughout these investigations all larval surveys were made by teams of four to six men working under a supervisor, each survey usually occupying one entire working day. The supervisor was responsible for allocating work in the area under survey, and for producing sketch maps of the various places from which larvæ were collected. So far as was possible all '*harbistrostris*' larvæ collected were hatched out in the laboratory, so as to make certain of the identification.

House searches were made by teams of two men, who together searched each house for ten minutes. Collections from cattle shelters were usually made with more than four men, who worked from dusk until at least 2230 hours. Night catches on human baits were made from either dusk to midnight or from dusk to dawn on a number of occasions. These catches were made by teams of

three men, one team catching inside a house, another team catching outside in the open.

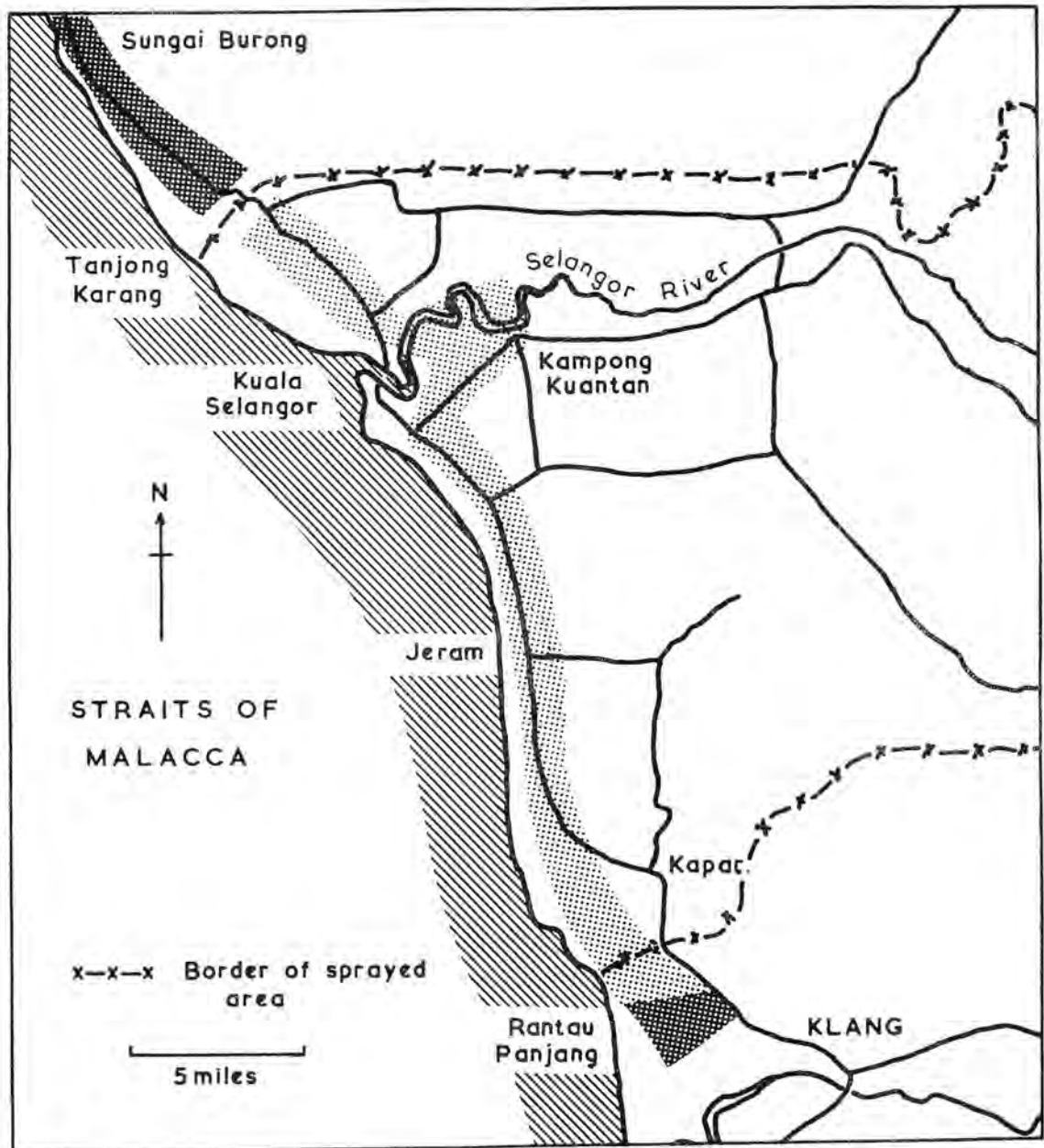
Pyrethrum knock-down catches were introduced in 1962 after it was found during work outside the sprayed area that this method of survey was more sensitive than simple house searches for resting mosquitos (Moorhouse and Wharton, to be published)

Findings before the start of spraying operations.

Breeding of *A. campestris* in the study area was found to be limited to those parts of the coastal plain where the soil is composed of stiff clays (recent marine alluviums) as previously described by Reid (1962). The larvæ were commonly in wells; ditches with standing water; and "borrow pits" between the coconut palms. Always the water was deep, with some vegetation, and with moderate shade such as is given by the coconut palm. The larvæ do not tolerate pollution of the water; because of this it was not usual to find breeding in the immediate vicinities of the villages, but breeding was widespread between the more scattered houses of the kampongs. Hodgkin (1940) recorded *A. campestris* from breeding places with salinities up to 15 per cent of sea water, but in these present investigations the larvæ have never been found in saline waters. Apart from places where pollution of the possible breeding sites occurred, or where the waters were demonstrably salty, breeding was found along the length of the whole coastal kampong strip. Breeding was not found in the rice fields at Tanjong Karang as was expected after Reid's (1962) observations in the Krian (State of Perak) rice fields. This absence is probably explained by the lack of sufficient shade trees at the edges of the fields.

Wharton (personal communication) found that the average number of eggs laid by the gravid female under laboratory conditions was high, as many as four hundred. Despite this, the density of fourth stage larvæ in individual pools in the study area was always very low, it seems that mortality during development must be extremely high. This is possibly due in part of the predacious habits of certain culicine larvæ which are found in the same habitats.

Studies on the behaviour of *A. campestris* show that it is probably the most endophagic and anthropophilic of all the Malayan anophelines. Man-biting catches conducted inside and outside houses demonstrate that unlike



Legend to map.

Map showing the distribution of *A. campestris* (stippled areas) in the malaria eradication pilot project area, and in its environs in the State of Selangor, Malaya, in 1960. The fine stippling shows those areas from which it has since disappeared following house spraying; the heavy stippling shows where it can still be found outside the sprayed area.

other Malayan anophelines, *campestris* bites more readily inside the house than outside. During investigations into the biting cycle of this mosquito, simultaneous indoor and outdoor man-biting catches were made from 1800 hours until 0600 hours the following morning, on six occasions at Sungei Burong. A total of 74 specimens were caught biting indoors and 17 outdoors, a ratio of 4.3:1 in favour of indoor biting. (Moorhouse and Wharton, to be published). These same studies on the biting activity of *campestris* show that it is active throughout the whole night, but that there is a moderate peak of biting between 2300 and 0300 hours.

Reid (1961) first demonstrated the anthropophilism of *campestris* when he exposed man and calf simultaneously in net-traps placed about fifty yards apart. The total numbers of mosquitos caught produced a ratio of 3.4:1 in favour of biting man as opposed to calf. During the man-biting catches mentioned above at Sungei Burong, various animal shelters were also searched at night but *A. campestris* was not found, although small numbers were found resting in nearly all the nearby houses visited at the same time. However, on other occasions during these present investigations a few specimens have been found in animal shelters during night catches. By means of serological tests, Reid and Weitz (1961) identified the origins of blood meals in 27 *campestris* caught resting outdoors during the daytime at Rantau Panjang. Of these 17 had fed on man and eight on monkey, (it was not possible to determine the origins of the other two feeds with accuracy). These find-

ings differ from those of Wharton and Eyles (personal communication) who exposed man and monkeys (*Macaca irus*) in separate net-traps on the ground, and monkeys in the forest canopy for thirty nights. They obtained a ratio of slightly more than 11:1 in favour of *A. campestris* biting man rather than monkey. Monkeys exposed in net-traps on the tree platform did not attract any *campestris*.

A. campestris is also endophilic or house-haunting. During the preliminary surveys daytime house searches for resting anophelines, and pyrethrum knock-down catches revealed that unlike the other Malayan anophelines, *campestris* frequently rests in the houses throughout the day. Generally they are found on mosquito nets or on clothes hanging on the walls in the more quiet parts of the house. Bonne-Webster and Swellengrebel (1953) are almost certainly referring to this particular species when they remark on *A. barbirostris* as often being found in houses in Malaya, resting on the walls and on mosquito nets. However, their mention in the same paragraph of large numbers also being found in cattle shelters, and to a low avidity for human blood must relate to other members of the *barbirostris* complex, possibly to *A. barbirostris sensu stricto*. All stages of ovarian development are to be found amongst those resting in the houses during the day, which suggests that some at least, may spend the greater part of the time between the blood-meal and egg-laying within the house.

An example of the frequency of house-resting during the daytime is given in table 1.

TABLE 1.

Showing the results of day-time house searches for *A. campestris* at Sungai Terap in the six weeks previous to the start of house spraying. Each house searched by two men for ten minutes.

Date	Number houses		Number of <i>campestris</i> found	
	searched	with resting <i>campestris</i>	Total	N'ber blood-fed
27.3.61	3	2	5	4
29.3.61	10	3	4	3
7.4.61	21	8	20	15
24.4.61	21	10	41	— *
8.5.61	24	8	14	6

* Information not available.

This gives the results of house searches made at Sungai Terap, a kampong on the coast road between Tanjong Karang and Kuala Selangor, in the six weeks prior to the start of spraying operations. It was probable that *campestris* was the only vector of malaria in the kampong. A further example is provided by a survey made in houses along the coast road between Tanjong Karang and Sungei Burong outside the experimental area in May 1962. In this locality *A. campestris* is the principal if not the sole vector of malaria. Twenty eight houses were searched, each by two men for approximately ten minutes between 1600 hours and 1800 hours. A total of 19 *A. campestris* were found in eight of the twenty eight houses visited; 15 of these had partially digested blood-meals. During these same surveys the only other anophelines caught were two specimens of *A. lesteri*, both found in the same house. *A. lesteri* is the most common anopheline of this coastal area.

Susceptibility to DDT.

Throughout these investigations it has not been possible to catch a sufficiently large number of adult *campestris* at any one time to undertake insecticide susceptibility tests. However, Wharton (1958) reared *campestris* in the laboratory from eggs laid by wild-caught females. He determined that the LC 50 of DDT for blood-fed adults reared in the laboratory was 1.3 per cent.

Relation to Malaria.

The relation of *campestris* to malaria has recently been discussed by Reid (1962), who shows that on the west coast of Malaya it must be considered an important vector. Within the project area it has usually been found along with either *A. sudaicus* or *A. letifer*, because of which it is not easy to assign any particular role to the species in this area. In 1960, parasite rates varying from 0% — 46% were found amongst children (aged 6-9 years) living in the coastal strip within the project area where *campestris* was a vector. It may be significant that the lower parasite rates were found in the more densely populated parts of the kampongs and the small villages, where generally this particular species is absent. But because distances are so small it is very difficult to draw conclusions. At Sungai Burong where *campestris* is considered to be the sole vector, epidemiological surveys made in 1962 show that there was a parasite rate of 16% amongst the Malay children and a spleen rate of 14.6%. Similar

spleen rates are to be found in neighbouring kampongs along the road.

Reid (1962) summarised the dissection data from this species and records that an average sporozoite rate of 0.33% was obtained from almost 15,000 specimens dissected from localities on the western side of Malaya. In these present investigations 321 *campestris* have been dissected, one was found with oocysts.

House Spraying and its results.

The insecticide used in this project was DDT, supplied as a 25 percent emulsifiable concentrate. The spraymen used compression sprayers; they were trained to work with an insecticide concentration, spray pressure, width of swath and speed, such as to give a deposit on the wall of two grammes of technical DDT per square metre. All the internal walls of the houses, the outside porches, and the eaves were treated; also the undersides and the back of all pieces of furniture. Where the houses were raised on stilts, the underfloor area was sprayed along with the various supporting pillars. Spraying of animal shelters and ancillary buildings was carried out only when they were attached to; or were less than ten feet from the house.

The first cycle of spraying started in March 1961, since when spraying has been repeated at intervals of six months. To the present four cycles are complete (August 1963). Few house-holders object to spraying, in fact, most welcome it. In each cycle more than 98 per cent, of the houses have been sprayed.

Following house-spraying *A. campestris* rapidly disappeared from the project area. At Sungei Terap which has previously been mentioned, spraying started on 17th May 1961 and was completed one week later. A daytime search for house-resting mosquitos was made on 10th June but no *campestris* were found. Because of this the whole locality was surveyed intensively during the next weeks, but without any success. Larval surveys were also made for *campestris*, but none were found. In an adjacent kampong (Ujong Permatang) a single adult was found resting in an unsprayed house three weeks after the start of spraying in the area, and at the same time larvæ were found nearby. Larvæ were also found near to Jeram three weeks after the completion of the spraying in the area. Surveys for both the larvæ and the adults were then made along the whole length of the coastal belt where this species

had formerly been present, but none were found.

Since this time frequent surveys have been made especially for this species throughout the project area. Methods used have been house-searches and pyrethrum knock-down collections during the day, larval surveys (with hatching out), night catches from both human and animal baits, and house searches at night; but the presence of *A. campestris* has not been demonstrated. A summary of the surveys made is to be found in Table 2. Outside the sprayed area, to both the north and the south, *campestris* can still be found, as it has been at all times of year since these investigations began.

During these various surveys along the coastal strip the larvæ of *A. sinensis*, *A. lesteri*, *A. barbirostris*, *A. vagus*, *A. sundaicus*, *A. separatus*, and *A. letifer* have been found, as have the adults of *A. lesteri*, *A. sinensis*, *A. vagus*, *A. sundaicus*, *A. subpictus*, *A. separatus*, *A. letifer*, *A. tessellatus* and *A. kochi*.

A completely independent check for the presence or absence of *A. campestris* in the project and the contiguous areas, was made by staff of the Institute for Medical Research, Kuala Lumpur in June 1962. This was after two complete cycles of spraying. The persons who made the surveys were fully conversant with the habits of this mosquito. Anopheline larvæ were collected from 109 likely sites along the coastal belt in which the species had previously been found, these collecting sites being centred on each milestone along the coast road. All '*barbirostris*' larvæ were bred out. The results agreed with the previous findings that although *campestris* can be demonstrated to both the north and south of the sprayed area, it is absent where spraying has been carried out.

Irritant effects of DDT.

The rapid disappearance of *A. campestris* after house spraying precluded the possibility of making observations on the irritant effects of DDT. However, the work of Reid and Wharton (1956) on trials of residual insecticides in window-trap huts is of considerable interest. These workers showed that DDT has the effect of driving an increased percentage of *campestris* out of the trap-huts into the window-traps before feeding, but that the effect is small. Previous to spraying the trap-huts with DDT 74.3% (90/121) of *campestris* found in the window traps were blood-fed. In the first four weeks after spraying the hut, the

percentage blood-fed in the trap dropped to 60.7% (31/51), in the second four weeks after spraying 72.2% (13/18) of those in the traps were blood-fed. If the lowered percentage of blood-fed mosquitoes in the window trap can be accepted as a measure of the irritability of the species to the insecticide then it would appear that *campestris* is mildly irritated by DDT. However the present findings that the species disappeared after widespread spraying suggests that this irritation is of no significance.

Spraying with dieldrin at Rantau Panjang (Klang).

In March 1957 house spraying was started by the health authorities in Rantau Panjang, a coastal kampong adjacent to the northern boundary of Klang, because of the high endemicity of malaria. The insecticide used was dieldrin (Dieldrex 15), applied with a "Four Oaks Sprayer" so as to give a deposit of 40 mgs dieldrin per square foot. A second cycle of spraying started at the beginning of May 1958, since then spraying has been repeated at approximately six monthly intervals up to the present time. During the first three years of the spraying only the internal walls of the houses were treated. But in November 1960 it was also decided to spray under the eaves, the outside porches, and where the house was raised on stilts, the under floor area; as was to be done in the malaria eradication pilot project a few miles to the north. This has been carried out in the subsequent cycles.

Although entomological records are not complete for this kampong, there can be no doubt that *A. campestris* was an important vector of malaria in Rantau Panjang prior to the start of spraying operations, but *A. sundaicus* was also present. Human-baited net traps were operated in the kampong in both 1951 and 1952. In 1951, these net-traps were operated in 166 nights. The anophelines caught included 1,222 *campestris* and 12 *A. sundaicus*, 750 of the *A. campestris* were dissected and one had a heavy sporozoite infection. (Reid, 1952). In the following year 1952, 1,525 *campestris* and 27 *A. sundaicus* were caught in the net-traps. Of the *campestris* 1,362 were dissected and 14 had sporozoite infections (Reid 1954). There are no records of the malaria parasite rate in the area at this time.

In March 1957, a parasite survey was made amongst the school children of the kampong; of 117 examined, 25 were found to be infected, a parasite rate of 12.3%. At the

TABLE 2.
Summary of Principal surveys for *Anopheles campestris* in the study area.

	Larval surveys		House-resting surveys by day and night				Cattle shelter catches				
	Number surveys made	Number surveys <i>campestris</i> found	Number houses searched	Houses with <i>campestris</i> resting	Total Number <i>campestris</i> found	Knock-down catches	Searched	With <i>campestris</i>	Total number caught		
	Day	Night	Day	Night	Day	Night	Day	Night			
Before spraying 1960-61	15	12	248	16	52	3	79	4	5	4	12
After spraying 1961	18	1* 1**	412	2	1*	0	1*	0	6	0	0
1962	49	0	201	2	0	0	0	0	13	0	0
1963 until August	28	0	105	33	0	0	0	0	3	0	0

* three weeks after spraying at Ujong Permatang

** three weeks after spraying at Jeram

same time a pyrethrum knock-down catch for anophelines was made in twenty houses during the day and a single specimen of *A. campestris* was taken. After this the kampong was sprayed with dieldrin. The parasite survey and the knock-down catch were repeated in May 1958, at this time a parasite rate of 22.3% was found amongst the children, and once again a single specimen of *campestris* was caught in one of twenty houses searched. These surveys were again followed by house-spraying with dieldrin; the spraying has since been repeated every six months. Since the start of the regular spraying the parasite rate of the school children has shown a decline; 8.4% in 1959 (7 of 83 children examined), 6.5% in 1960, (7 of 107 examined) 0% in 1961, (0 of 125 examined) and 2.8% in 1962 (3 of 104 examined). Fluctuations can be expected in the parasite rate of these children because of some of them live in unsprayed areas and also because both *A. campestris* and *A. sundaicus* are present in unsprayed areas immediately to the north of the kampong where malaria is endemic.

Wharton (personal communication) operated human-baited net-traps on many occasions in 1961 and 1962 in the same general localities at Rantau Panjang as Reid used in 1951 and 1952. In 1961 he recorded two specimens as belonging to the *A. barbirostris* group, the exact species is not known. In 1962 *A. campestris* was not caught in the net-traps. Larval surveys and pyrethrum knock-down catches were made in the kampong especially for *A. campestris* in November 1962, but none were found.

Conclusions.

Reid and Wharton (1956) remark that the factors involved in determining the degree of control of a vector mosquito which can be achieved by a residual insecticide may be summarised under three headings. These are, the susceptibility of the species to the insecticide; the frequency of contact with the insecticide, which as they remark depends upon the frequency of entry into the sprayed premises, which in turn depends on the mosquitoes' habits; and finally, upon the duration of contact with the insecticide on each occasion of entry.

Although the Lc50 of DDT to this species is high (1.3%) Reid and Wharton, (1956) working with sprayed trap-huts demonstrated that during the first month after spraying with DDT at the rate of two grammes per square metre, an average mortality of 72 per cent.

was obtained with *campestris*. In these experiments the trap-huts were emptied of all mosquitoes by 0700 hours in the morning. All living specimens were placed in cages so as to observe the mortality during the following twenty four hours. The period of contact with the insecticide is thus likely to have been shorter than under natural conditions. In the second month after spraying the trap-huts, the mortality over 24 hours dropped to an average of 32 per cent., and in the third and subsequent months the deposit failed to kill this species. Because of this Reid and Wharton came to the "disturbing conclusion" that so far as this particular species was concerned it was not very susceptible to DDT at the concentration used, (which is the same as is now being used in the malaria eradication pilot project), and that,

"the kills (of many species) were too low, or lasted too short a time, for practical purposes. With species likely to make frequent contact with the insecticides these low kills might be sufficient but not with species having only occasional contact, i.e., all these investigated excepted *C. p. fatigans*."

These present findings, however, suggest that *A. campestris* has far more contact with residual insecticides than was previously realised. It is considered that it fulfils all the requirements for enabling highly successful control to be achieved by the use of residual insecticides, and that in any anti-malaria programme unless there are special reasons for avoiding the use of insecticides, then house-spraying is the method of choice as far as this species is concerned. So far as any future malaria eradication program is concerned, the response of this mosquito is extremely encouraging.

ACKNOWLEDGEMENTS.

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FILARIASIS AMONG ABORIGINES AND MALAYS LIVING CLOSE TO KUALA LUMPUR

By C. P. RAMACHANDRAN, C. C. HOO,
ABU HASSAN bin OMAR,
Institute for Medical Research,
Federation of Malaya.

Introduction

Surveys to determine the incidence of filariasis among aborigines in Malaya are not many. Polunin (1951, 1953) while studying their medical problems reported the existence of malaria and filariasis (**Brugia** only) among aborigines inhabiting the hill forests of Pahang, Perak and Selangor. Wharton, Laing and Cheong (1963) made a number of preliminary investigations for malaria and filariasis among groups of aborigines in Selangor, Pahang and Perak states and their findings show a surprisingly high incidence of filariasis among aborigines living in comparatively close proximity to Kuala Lumpur, many of them being infected with **Wuchereria bancrofti**. It used to be thought that **W. bancrofti** infection occurred only among immigrants from India and China, until the findings of Wharton (1960) showed that the infection was present among rural Malays in Pahang living in complete isolation from urban populations. Laing and Wharton (1960) also found another focus of **W. bancrofti** among aborigines in the same locality and since then various small endemic foci have been recorded from several parts of Malaya, but these have not yet been fully investigated.

Laing and Wharton (1960) reported a 16% microfilariae rate among aborigines living in Bukit Lanjan, a small village 10 to 12 miles from the city of Kuala Lumpur. 9 out of 43 people examined were positive for microfilariae, and of these, 6 were a mixed infection of **W. bancrofti** and **B. malayi**, 2 of **B. malayi** and 1 of **W. bancrofti**. In most parts of Asia, **W. bancrofti** is transmitted by mosquitoes belonging mainly to the **Culex pipiens** group. In Malaya **C. pipiens fatigans** is a common house breeding mosquito and is found in abundance all over Kuala Lumpur. Thus with a focus of infection so close to the city of Kuala Lumpur, and with mosquitoes which

may be potential transmitters, an investigation to assess the risks, if any, of the infection spreading to the urban areas of Kuala Lumpur was decided upon.

The investigations based on (a) a house to house population census, (b) blood parasite survey of man and domestic animals and (c) preliminary entomological investigations are reported here.

Topography, population and occupation

Bukit Lanjan is a small village situated in an inland hill area between the 10th and 11th milestones of Sungei Penchala Road in the Mukim of Batu and Sungei Buloh. It is about 3 miles from the town of Kepong, 5 to 6 miles from the new town of Petaling Jaya and 10 to 12 miles from the city of Kuala Lumpur. The village adjoins the border of Sungei Buloh forest reserve and has a population of 230 Temiar aborigines living in 3 groups and 148 Malays in 2 groups, all in close proximity to each other (see Fig. 1).

The houses are mostly on stilts with wooden walls and attap palm roofs. Most of the Malay population work in the towns of Kepong and Petaling Jaya. The aborigines, with the exception of a few who work in a nearby granite quarry, obtain their living from various pursuits in the jungle. They are under the protection of the Department of Aborigines. The aborigines and Malays have been living in the area for well over 60 years.

Parasitological Investigations

POPULATION SURVEY:

A house to house census of each group of aborigines and Malays was made. Each house was given a number which was exhibited clearly on the front. The following particulars of each family were recorded:— number in family, age, sex, length of residence,

TABLE I

Total Population	Total Examined	Percentage Examined	F I L A R I A S I S					CLINICAL HISTORY	
			Number Positive	Microfilariae Rate	B. malayi	W. bancrofti	Mixed Infection	Filarial Fever	Elephantiasis
148 MALAYS	110	74	2	1.8	2	0	0	2	0
230 ABORS.	167	73	29	17.3	15	10	4	11	0

clinical history of filariasis infection, and number and type of domestic animals kept. A sketch map of the locality showing the distribution of houses was also made.

BLOOD SURVEY:

Blood films of all those who could be persuaded to co-operate were taken after 7.00 p.m. 20c.mm. of blood was taken from the finger with a measured pipette and a thick smear made. Films were stained in Geimsa and examined for microfilariae.

Random samples of blood were also taken from domestic animals available at each house during the day. Samples taken were from dogs, cats and monkeys.

Results

Table I summarises the results of blood surveys on the Malay and aborigine populations. There was no infection of *W. bancrofti* among the Malays and no cases of elephantiasis were seen in either group. Although a history of "kelinja" meaning filarial swelling or fever was recorded from a few persons, their accuracy cannot be taken without reservation. Of the 14 cases of *W. bancrofti* infections 8 were males between 20 to 40 years old and only 3 were adult females. The youngest person infected with *W. bancrofti* was a girl aged 4 and the oldest was a woman aged 60.

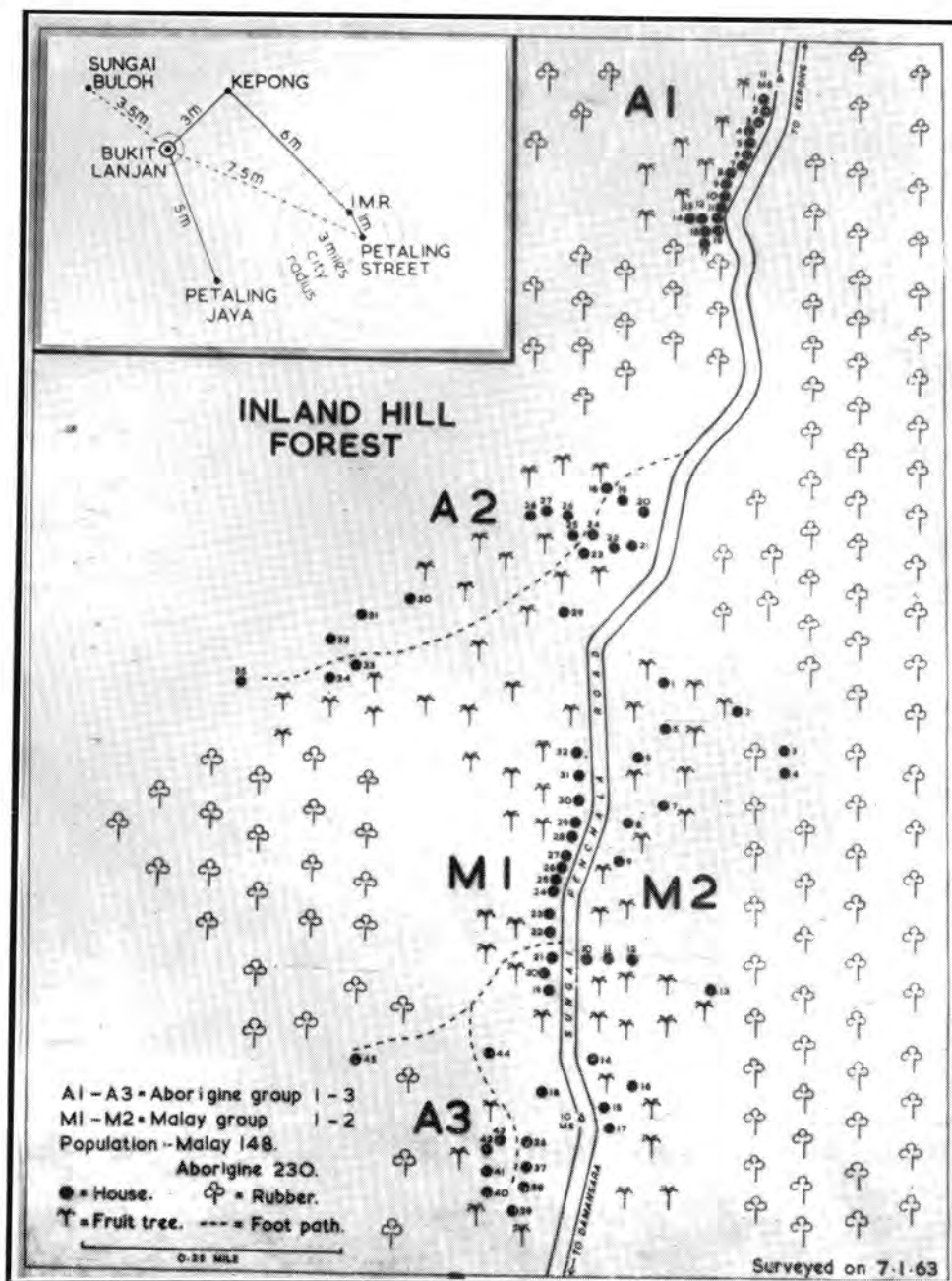
The results of the blood examination for filarial parasites in various domestic animals examined at Bukit Lanjan village is given in Table II. None of the animals showed infection with *B. malayi* although *B. pahangi* was found in 4 of the dogs examined.

Periodicity studies were made on 6 abori-

TABLE II

Animal	Number Examined	FILARIAL INFECTION		
		B. Malayi	B. Pahangi	D. Immitis
Cats	15	0	0	0
Dogs	10	0	4	4
Macaca Monkey	3	0	0	0

FIG. 1. Showing map of Bukit Lanjan vottage.



gines. 2 of them having *W. bancrofti* infection, 2 *B. malayi* and 2 having both the infections. 2 hourly microfilariae counts on 20c.mm. of blood taken by finger prick was made starting at 10.00 a.m. and ending at 10.00 a.m. the following day. All the infections exhibited characteristic nocturnal

periodicity, thereby showing infections were of periodic *W. bancrofti* and periodic *B. malayi*. The periodic *B. malayi* blood films when stained with Geimsa showed characteristic empty sheaths as well. Table III gives the microfilariae counts obtained from the aborigines at 2 hourly intervals.

TABLE III

S P E C I E S	Name of Carrier	10.00 a.m.	Noon	2.00 p.m.	4.00 p.m.	6.00 p.m.	8.00 p.m.	10.00 p.m.	Mid-night	2.00 a.m.	4.00 a.m.	6.00 a.m.	8.00 a.m.	10.00 a.m.
W. bancrofti	J	0	0	1	0	3	7	13	11	10	11	10	6	0
	D	10	4	1	2	11	206	279	219	213	305	209	109	15
B. malayi	MO	3	0	1	1	1	5	28	35	35	43	23	25	8
	MA	2	0	0	0	2	39	78	126	92	149	126	32	4
Mixed Infection	8	8	0	0	0	6	22	94	131	157	125	111	23	20
	L	12	1	0	0	0	1	18	45	98	55	53	31	40
	W. bancrofti	0	0	1	0	2	13	9	15	33	32	8	4	0
	B. malayi	0	0	0	0	0	1	2	0	0	0	0	0	0

Entomological Investigations

A total of 70 nights of mosquito trapping with human bait traps starting at sunset and ending at sunrise were instituted at Bukit Lanjan aborigine settlement between the months of January and June 1963. A summary of the numbers and species of mosquitoes caught and results of their dissections for filariae are given in Table IV.

No infections of *Brugia* or *Wuchereria* were found in any of the mosquitoes examined, but on 2 occasions *Dirofilaria immitis* infection was found in *Mansonia dives* and *Culex annulus*.

Anopheles

A. maculatus was the dominant anopheles caught while *A. letifer* was occasionally found. *A. maculatus*, although experimentally it can support the development of *W. bancrofti*, is most unlikely to be of any importance as a natural vector. *A. letifer* on the other hand has been incriminated as a vector of *W. bancrofti* in East Pahang (Wharton, 1960) and could transmit the infection if conditions are favourable, but no natural infection in this species has been found in the present investigations.

Culicines

Among the wide variety of culicines caught, *Aedes*, *Culex* and *Mansonia* species were most common. *C. fatigans* which may be a vector of *W. bancrofti* at Bukit Lanjan (and has been shown to support development in subsequent experimental infections) were caught in the traps on a few occasions, but not in the large numbers as would be thought to maintain an active transmission. The paucity of *C. fatigans* trapped may be due however to their tendency to rest inside houses, and their preference for indoor baits.

Large numbers of *Aedes albopictus* and *Armigeres* species were caught but they are of no importance as vectors of *W. bancrofti* or *B. malayi*.

M. dives was the commonest of the *Mansonia* mosquitoes caught but Wharton (1962) has shown that they are poor hosts for periodic *B. Malayi*. *M. uniformis* were caught on a

TABLE IV
Showing the numbers of mosquitoes from Bukit Lanjan examined for *Filaria* Infection during the period from January — June, 1963.

Species of Mosquito	No. caught in Human Bait Trap (70 nights)	No. examined for <i>Filaria</i>
<i>Mansonia</i>		
<i>Mansonioides</i>		
<i>bonneæ</i>	1	1
<i>dives</i>	259	256*
<i>uniformis</i>	20	19
<i>Coquillettidia</i>		
<i>annulifera</i>	2	2
<i>crassipes</i>	2	2
<i>ochracea</i>	1	1
<i>Anopheles</i>		
<i>aitkeni</i>	1	1
<i>letifer</i>	7	5
<i>maculatus</i>	70	69
<i>karwari</i>	1	1
<i>kochi</i>	1	1
<i>Culex</i>		
<i>annulus</i>	213	213*
<i>bitæniorhynchus</i>	2	2
<i>cinctellus</i>	11	10
<i>fatigans</i>	39	38
<i>gelidus</i>	94	89
<i>mimulus</i>	9	9
<i>nigropunctatus</i>	12	12
<i>pseudovishnui</i>	69	66
<i>sinensis</i>	1	1
<i>sparthifurca</i>	5	4
<i>tritæniorhynchus</i>	25	25
Undetermined species	7	7
<i>Aedes</i>		
<i>albopictus</i>	243	241
<i>Armigeres</i>		
<i>confusus</i>	6	6
<i>durhani</i>	4	4
<i>malayi</i>	40	38
<i>moultoni</i>	5	5
<i>subalbatus</i>	57	57
<i>Uranotænia</i>		
<i>campesteris</i>	5	4
Undetermined species	2	—
<i>Tripterioidea</i>		
<i>aranoidea</i>	1	—
<i>cæruleocephala</i>	2	1
<i>Malaya</i>		
<i>genurostris</i>	1	—
<i>Aedomyia</i>		
<i>catastica</i>	1	—

*On two occasions *Dirofilaria immitis* infection was found.

few occasions and is the most probable vector for periodic *B. malayi* in the area, although no filarial larvæ were found in any of them on dissection.

During the first 3 months of trapping there was an unusually prolonged dry period resulting in relatively poor catches. These results although rather limited, have however provided some useful information on the mosquito fauna at Bukit Lanjan.

Experimental infections

C. fatigans being a common house breeding mosquito in and around the city of Kuala Lumpur would be the most likely vector to establish *W. bancrofti* infections in the urban areas. It is essential therefore to know the potentiality of the different strains of this mosquito species to support development of the microfilariae of *W. bancrofti* to the infective stage.

5 different strains were tested. Each strain was fed on a *W. bancrofti* carrier from Bukit Lanjan and were then dissected 14.5 to 16.5 days later.

Adult mosquitoes of the various strains used in the experimental infections were obtained from the following places:—

(see Fig. 1, top left hand corner)

1. Bukit Lanjan strain — house catches at Bukit Lanjan aborigine settlement.
2. Petaling Jaya strain — house catches at Petaling Jaya.
3. Kepong strain — house catches at Kepong.
4. "Petaling Street" strain — house catches in Petaling Street situated in the heart of Kuala Lumpur.
5. I.M.R. laboratory colony — originally obtained from the island of Penang, and which has been maintained in the Institute for Medical Research insectarium for more than 90 generations.

The results of feeding the various strains of *C. fatigans* on a *W. bancrofti* carrier on different occasions are given in Table Va.

All the strains exhibited different rates of infectivity, the Bukit Lanjan and Petaling

Street strains both giving an over 45% infectivity rate. It was thought that these differences may be due to variations in the microfilariae density in the carrier's peripheral blood at the time of mosquito feeding.

Experiments were then carried out in which all the strains of *C. fatigans* were fed on the same carrier at the same time. The results of 2 such simultaneous feedings of the 5 strains are shown in Table Vb and Vc.

It appears from the results that variations in infectivity rate still occurred, though to a lesser extent, when the strains were fed under almost similar conditions. The occurrence of different gene frequencies in the different mosquito populations may partly explain these differences. However, if there is only one major gene controlling susceptibility in *C. fatigans* (similar to that of *Aedes aegypti* to *B. malayi* — Macdonald 1962), one wonders why the gene should vary so much in frequency. It is beyond the scope of this paper to discuss the genetical aspects of susceptibility to *W. bancrofti* infections in *C. fatigans*, but it is hoped further work on these lines will be pursued.

Discussion

That there is no active transmission of *W. bancrofti* maintained in Bukit Lanjan village itself is shown by the low microfilariae load which was found to be only 0.4; the absence of *Wuchereria* larvæ in any of the mosquitoes dissected and the absence of detectable infection in the Malays who had been living so close to the aborigines for such a long time.

It is an interesting finding that 11 out of the 14 *W. bancrofti* infections were in adult aborigines. As most, if not all of the working aborigine population enter the jungle to make their living, it is conceivable that they acquired their infection while at their place of work. If this is so, the vector which remains unknown, may turn out to be *A. letifer*, similar to the findings of Wharton (1960) in his Pahang survey on rural Malays.

The risk of the infection spreading to the urban areas of Kuala Lumpur is remote in spite of the existence of a focus of infection

TABLE Va. — FED. ON THE SAME DONOR AT DIFFERENT OCCASIONS

EX P. No.	Strain of Culex fatigans	Generation	Age of mosquito in days at the time of feeding	No. of microfilariae per c.mm. at the time of feeding	No. of mosquito dissected	% infective
110	Bukit Lanjan	F2	6—7	0.8	146	53.0
108	Petaling Jaya	F2	6—7	4.4	148	13.0
116	Kepong	F1	5—6	3.0	149	26.0
106	Petaling Street	F2	6	2.7	214	45.0
100	I.M.R. Lab. colony	F92	2—7	4.0	198	12.0

TABLE Vb. — FED. ON THE SAME DONOR AT THE SAME OCCASION

117	Bukit Lanjan	F3	5—6	1.8	100	30.0
	Petaling Jaya	F3	5—6	1.8	100	14.0
	Kepong	F1	5—6	1.8	100	12.0
	Petaling Street	F3	5—6	1.8	100	14.0
	I.M.R. Lab. colony	F93	5—6	3.0	56	11.0

TABLE Vc. — FED. ON THE SAME DONOR AT THE SAME OCCASION

125	Bukit Lanjan	F4	6—7	4.3	100	25.0
	Petaling Jaya	F4	6—7	4.3	100	21.0
	Kepong	F2	6—7	4.3	100	25.0
	Petaling Street	F4	6—7	4.3	100	9.0
	I.M.R. Lab. colony	F94	6—7	4.3	100	4.0

nearby, and the presence of a potential vector in *C. fatigans*. In order to transmit the infection effectively, the aborigine carrier would need to have a sufficiently high microfilariae density in his peripheral blood at the time of his visiting any of the nearby towns, and also remain long enough for *C. fatigans* to feed. The tendency of the aborigine to remain in his home rather than visit the towns, especially in the evenings and nighttime, decreases such transmission risks.

The findings of the present investigation indicate that this focus of infection can best be controlled, if not eliminated entirely by the proper administration of the di-ethylcarbamazine drugs.

Summary

1. 167 aborigines and 110 Malays were investigated for filaria infections. 31 were positive, 10 being *W. bancrofti*, 17 *B. malayi* and 4 mixed infections. No *W. bancrofti* infections were detected in the Malays.

2. 70 nights of mosquito trapping with human bait traps were instituted at Bukit Lanjan village. The dominant mosquitoes caught were *A. maculatus*, *M. dives*, *C. annulus* and *Aedes albopictus*. No infective larvae of *W. bancrofti* and *B. malayi* were found in any of the mosquitoes dissected.

3. Experimental feedings of various strains of *C. fatigans* on a *W. bancrofti* carrier showed that all the strains were capable of supporting

development of the microfilariae to the infective stage. All the strains exhibited different infectivity rates.

4. It is concluded that any risk of the infection being transmitted to the urban areas of Kuala Lumpur can be eliminated by proper drug treatment of the aborigine population.

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THE ISOLATION OF HISTOPLASMA CAPSULATUM FROM A PATIENT IN A CHEST HOSPITAL

By J. T. Ponnampalam, Department of Bacteriology,
Institute for Medical Research, Kuala Lumpur.

The isolation of *Histoplasma capsulatum* from the soil of a cave infested with bats in Malaya is the first report of the presence of the fungus in Malayan soil (Ponnampalam, American Journal of Tropical Medicine & Hygiene, in publication).

Marsden (1953) in the Annual Report of the Institute for Medical Research, Kuala Lumpur, mentioned a case of histoplasmosis on histopathological examination. Kunaratnam *et. al.* (1960) described a case of histoplasmosis in Singapore.

Histoplasmin skin testing and serological examination of patients admitted to the Lady Templer Hospital, Kuala Lumpur, have indicated that a certain percentage show evidence of infection (Ponnampalam, unpublished data).

In one of these cases *Histoplasma capsulatum* was isolated from the sputum.

The case history and laboratory examination are herewith described.

Case Report.

J. A., a Malay girl aged 13 was first admitted to the Lady Templer Hospital on the 23rd July, 1962 with a history of cough productive of yellow sputum and fever off and on for a year, with recurrent episodes of haemoptysis during this period. Previously she was admitted to a General Hospital in May the same year for two weeks where X-ray examination showed fibrous markings and cystic disease of the right lung adjacent to the mediastinum (Fig. 1). At the end of this period she was referred to a chest clinic where a bronchogram (Fig. 2) revealed the extent of the cystic disease affecting the right lower lobe. She was referred to Lady Templer Hospital with a view to surgery as the lung lesion was not responding to medical treatment.

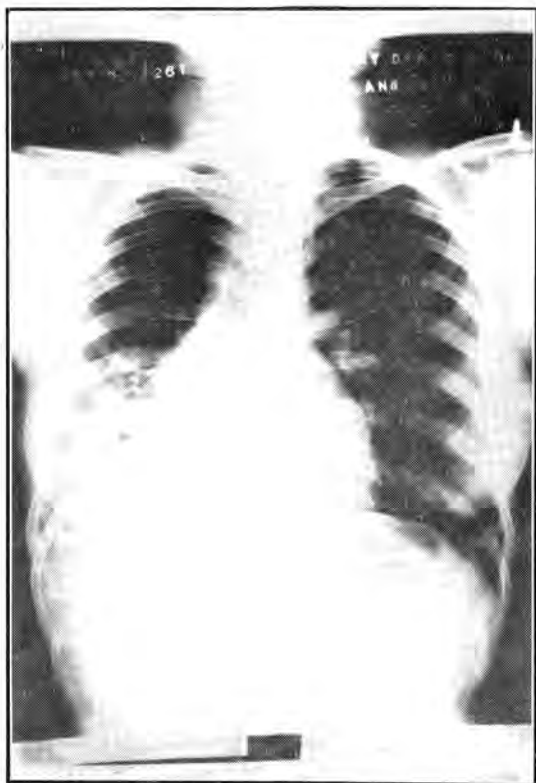


Figure 1.
Radiological Examination on 16.5.1962, showing fibrous markings and cystic spaces in the right lower lobe.



Figure 2. (Right).
Bronchogram on 17.6.62 showing the extent of the cystic disease.



Figure 3.

Radiological examination of chest on 20.7.62.

At the time of admission on 27.7.62 she had a chronic discharge from the left ear. Temperature was 98.4° F. The result of the radiological examination (Fig. 3) was similar to that of 16.5.62. The left lung was normal. ESR = 13 mm; Haemoglobin = 80%; white cell count = 8000, with polymorphonuclears = 52, lymphocytes = 44, and eosinophils = 4, the eosinophil count rising to 12 four months later and remaining at this level on discharge on 10.1.63. Pus from the left ear grew *Pseudomonas pyocynaeus*. Direct examination and culture of the sputum at intervals of a month during hospitalisation failed to demonstrate *Mycobacterium tuberculosis*. The tuberculin reaction on 23.7.62 was 12 mm. induration.

She received no anti-tuberculosis therapy in view of the negative sputum cultures. During her stay of 6 months in hospital the temperature remained fairly constant at 98.4° F, except on a few occasions when it was 99.4° F. A right pneumonectomy was done on 4.9.62, and histopathology revealed a non-tuberculous granuloma of the lung. Culture of the lung

removed at operation, and sputum cultures for histoplasmosis were not carried out as the patient was not being investigated with histoplasmosis in view. It was only a month later that she was included in the survey of patients for histoplasmosis at the Lady Templer Hospital, and it was incidentally found that she had a positive complement fixation test for histoplasmosis.

The Mantoux test, histoplasmin skin test, and the complement fixation test for histoplasmosis carried out between October, 1962 and January, 1963 prior to her discharge home were:—

24.10.62. Mantoux test — 24 mm. induration. Histoplasmin skin test — negative. Complement fixation test with histoplasmin and other antigens — Histoplasmin 1:16; Yeast 1:16; Blastomycin 1:8.

The complement fixation test for histoplasmosis was repeated on 10.12.62 and was as follows:—

Histoplasmin — negative; Yeast — 1:8; Blastomycin — negative.

In view of an elevated complement fixation test for histoplasmosis following operation, six specimens of sputum collected on alternate days over a period of two weeks were examined, commencing 7.1.63. Each specimen was injected into 5 Swiss white mice, the animals not receiving any antibiotic cover. Each specimen of sputum was diluted with an equal amount of sterile physiological saline prior to inoculation. At the end of 8 weeks 8 mice were found alive out of a total of 30, the rest having succumbed to bacterial infection due to a Gram negative organism. When the surviving mice were sacrificed peritoneal adhesions, exudation, enlargement of liver and spleen were noted. These organs were removed, pooled and ground in a mortar with sterile sand and inoculated on to Sabouraud dextrose agar and blood brain heart infusion agar. A month later *Histoplasma capsulatum* (with its characteristic tuberculate chlamydospores on microscopical examination) was isolated from the pooled livers and spleens. The yeast phase was demonstrated in mice.

Direct examination of the Giemsa stained smears of the sputum prior to mouse inoculation did not reveal the presence of *Histoplasma capsulatum*. The patient was discharged home on 22.1.63.

While at home after discharge she had

pyrexia for 3 weeks associated with an exacerbation of her cough with increased amounts of purulent sputum. She was re-admitted for review on 18.7.63 still complaining of cough with a fair amount of sputum. Serological and skin tests carried out a day after readmission were as follows: -

- 19.7.63. Mantoux test — 19 mm. induration.
 Histoplasmin skin test — Negative.
 Complement fixation test — Histoplasmin — negative Yeast — 1:8.

Six specimens of sputum were collected and examined as described above, following readmission, and found to be negative for *Histoplasma capsulatum*.

DISCUSSION.

Histoplasmosis may occur as an acute self-limiting catarrhal condition which is a primary infection or may progress to the chronic cavitary state. The signs, symptoms, and prognosis vary greatly with the clinical type of infection. Mortality in disseminated cases of the disease is 83 per cent while in the chronic pulmonary type it is 32% (U.S. Public Health Service Co-operative Mycoses Study 1961). Infection occurs via the respiratory tract with primary lesions in the lungs as a result of inhalation of spores of *Histoplasma capsulatum* from the soil. As this patient lived at a distance of many miles from Kuala Lumpur, examination of soil from the neighbourhood of her home was not carried out. Serological examination of patients at Lady Templer Hospital pointed to a high incidence (19.8%) of histoplasmosis in these patients (Ponnampalam, unpublished data). Sputum studies in patients with a positive serology have confirmed the findings of Furcolow (personal communication) that the fungus is recovered infrequently and with great difficulty from their sputum. The histoplasmin skin test is of limited value, being negative on two occasions in this patient. The serological test is a useful screening test to select those patients on whom sputum studies are to be carried out. If emphasis were placed only on the skin test this patient would have been missed. From a survey of over 250 patients at Lady Templer Hospital it was found that only 10.5% had a positive histoplasmin skin test, while 19.8% had a positive serology. It appears that the histoplasmin skin test is depressed in illness, and that patients suffering from histoplasmosis would be missed if only skin testing were done without serological examination

Complement-fixing antibodies appear after a few weeks of infection. The titres may be as low as 1:2 to 1:8 with histoplasmin antigen, while they may vary from 1:40 to 1:160 with the yeast phase antigen. A small percentage of normal individuals have antibodies in low dilution. A single specimen of serum would be of little value in interpreting antibody response in either proven or unproven infections. Serial tests should be done throughout the infection. Such tests in proven histoplasmosis have shown a rise in antibody titre with a peak during the second and third week of the disease and a gradual falling off at 4 to 8 months until a baseline is reached.

Cross-reactions with *Blastomyces* antigens sometimes occur in the complement-fixation test from patients with histoplasmosis. In almost all instances, however, the titre is greatest with the homologous antigen.

Hypersensitivity. Intradermal injection of 1:000 dilution of standardised histoplasmin shows a positive reaction a few weeks following infection. The test is read after 48 hours, and the reaction must show at least 0.5 cm. of induration to be considered positive. The skin test is sometimes depressed in illness. A positive histoplasmin skin test means past or present infection.

Patients sensitive to histoplasmin also may have cross reactions to blastomycin and coccidioidin. Histoplasmin injected into a site where a previous Mantoux test was carried out may cause a bigger induration than that caused at a site where no previous Mantoux test was carried out.

A single injection of histoplasmin in known negative and positive reactors does not affect humoral antibody formation. Multiple injections, however, may cause a rise in antibodies in positive reactors but not in negative reactors.

As *Histoplasma capsulatum* was isolated from the Sputum of this patient after pneumonectomy, and as the complement fixation tests have been repeatedly positive, and in view of the previous findings of a sputum repeatedly negative for *Mycobacterium tuberculosis*, it may be concluded that this was a case of chronic cavitary histoplasmosis. Radiological findings provide supporting evidence for this diagnosis, although per se radiological examination is not diagnostic. She will be reviewed periodically with a view to treatment with amphotericin B should the disease become progressive.

SUMMARY.

The first case of histoplasmosis in Malaya diagnosed on a positive culture and serology is described. The isolation of *Histoplasma capsulatum* from Malayan soil and the presence of positive reactors to the histoplasmin skin test suggests the possibility of histoplasmosis being present in the country to a significant extent. It presents an important differential diagnosis in the treatment of chronic chest conditions.

ACKNOWLEDGEMENT.

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FOETAL SALVAGE IN CORD PROLAPSE*

By T. A. SINNATHURAY, M.B., B.S. (Malaya),
F.R.C.S. (Ed.), F.R.C.S. (Glasg.), M.R.C.O.G.,
Kandang Kerbau Hospital, Singapore-8.

Introduction

Presentation and prolapse of the umbilical cord are frequent obstetrical emergencies associated invariably with a high foetal mortality. Rhodes (1956) has estimated that in England and Wales, prolapse of the cord is responsible for about 1,500 perinatal deaths annually, and 1 in every 16 still births. A high proportion of the foetuses are viable and devoid of lethal congenital abnormalities, and should theoretically at least be saved.

Regime of Investigation

This publication is a preliminary report, and it is based upon study of all cases of cord prolapse (including cord presentation) delivered in the Aberdeen Maternity Hospital during the two-year period of 1959 to 1960. During this period there were 7593 deliveries (Table I) and of these 85 per cent (Table IV) were hospital booked cases, i.e., patients who have had their ante natal care by members of the hospital staff. The remaining 15 per cent

(Table IV) were emergency admissions into hospital from the North-Eastern Regional area of Scotland. As there is relatively little migration of this population (allowing for the natural increase of population) and the incidence of prolapse of the cord in each of the two years is very similar, the findings presented in this study could be regarded as representative for this hospital.

Results

The incidence of cord prolapse in the hospital 2-year series is 1 in 115 cases (Table I) and cord prolapse is responsible for 5.6 per cent of all the hospital perinatal deaths. However, after omitting 2 stillbirths and 2 first-week neonatal deaths (Table XI) where cord prolapse was only incidental, this percentage falls to 4.3 per cent.

Table II shows that cord prolapse is associated with many obstetrical complications. Foetal malpresentations, especially complete breech presentation, was found to be a con-

TABLE I
Incidence and Results

	Total Cases	No. of Prolapsed Cords	Incidence	Perinatal Death Rate
Deliveries	7593	66	0.87%	Gross Perinatal Death Rate. = 5.6 per cent.
Gross S.B.	207	11	5.3%	
Gross 1st week NND.	117	7	6.0%	
Corrected S.B. due to Cord Prolapse	9		4.4%	Corrected Perinatal Death Rate = 4.3 per cent.
Corrected 1st week NND. due to Cord Prolapse	5		4.3%	

S.B. = Still births

NND. = Neonatal Deaths.

* Study undertaken during tenure of office as Honorary Research Worker/Senior Registrar at Aberdeen Maternity Hospital, Aberdeen University, Scotland, United Kingdom. This

publication is a preliminary report of an M. D. Thesis Project, now being undertaken at the University of Singapore.

TABLE II
Predisposing Causes of Cord Prolapse

Predisposing Causes	No. of Cases	Percentage
Malpresentations	29	43.9
Prematurity	19	28.8
Twins	15	22.7
Artificial Rupture of Membranes	15	22.7
Hydramnios	5	7.6
Disproportion	4	6.1
Minor Degree of Placenta Prævia	3	4.5
Fœtal Abnormality	1	1.5
Unusually Long Cord (No record)	—	—
Other Causes (Minor)	12	16.2

TABLE III
Fœtal Salvage Rate

Total No. of Cord Prolapse Cases	66
Total No. of Perinatal Deaths	18
Uncorrected Perinatal Mortality	27.3%
Perinatal Deaths not due to Cord Prolapse (Table XI)	4
Corrected Perinatal Mortality	21.2%

TABLE IV
Fœtal Mortality Studies in Hospital Booked and
Emergency Admissions

Percentage of Hospital Booked Deliveries at Aberdeen Maternity Hospital during the 2-year period	85%
Percentage of Emergency Admission Deliveries at the Aberdeen Maternity Hospital during the 2-year period	15%
Percentage of Cord Prolapses occurring in the Hospital Booked Deliveries	85%
Percentage of Cord Prolapses occurring in the Emergency Deliveries	15%
Percentage of Salvageable Fœtal Deaths from Cord Prolapse in the Hospital Booked Cases	50%
Percentage of Salvageable Fœtal Deaths from Cord Prolapse in the Emergency Deliveries	27.8%
Ratio of Fœtal Mortality in the Hospital Booked Deliveries with Cord Prolapse is	$\frac{50 \text{ per cent}}{85 \text{ per cent}} = 0.6\%$
Ratio of Fœtal Mortality in the Emergency Deliveries with Cord prolapse is	$\frac{27.8 \text{ per cent}}{15 \text{ per cent}} = 1.9\%$

tributary factor in more than 40 per cent of the cases. Prematurity, twins and artificial rupture of the membranes were each found to be responsible in about 25 per cent of cases. Hydramnios has not been a major factor (7.6 per cent), probably because of the low incidence (1 in 300 deliveries) of this condition. No record of foetal cord length has been kept, and hence its importance cannot be evaluated. "Other Minor Causes" are varied, and their significance difficult to evaluate.

The uncorrected perinatal mortality is 27.3 per cent and when those deaths not due to prolapse of the cord are omitted, the rate falls to 21.2 per cent.

Clinical data as presented in Table IV has not been made available from other series reviewed. Yet it presents a very illuminating feature. Despite the fact that the ratio of hospital booked deliveries/emergency admission deliveries, and the ratio of cord prolapses occurring in these two groups of deliveries are constant (85 per cent: 15 per cent) it is found that the foetal mortality is thrice as high (1.9: 0.6) in the emergency admissions with cord prolapse. Further reference to this point will be made in the discussion.

TABLE V
Foetal Mortality and Maternal Age

Maternal Age	Under 25 years	25 to 29 years	30 years and over
No. of Prolapsed Cords	18	21	27
No. of Perinatal Deaths	2	7	9
Mortality Rate	11%	33%	33%

Table V shows a rise of the perinatal mortality in cord prolapse with maternal age.

TABLE VI
Foetal Mortality and Parity

Parity	1st	2nd	3rd & over
No. of Prolapsed Cords	17	19	30
No. of Perinatal Deaths	2	5	11
Mortality Rate	12%	26%	37%

Although the bulk of the deliveries and the cord prolapse cases (over 60 per cent) occurred in patients under third parity, it is evident from Table VI that the perinatal mortality is lowest in Parity 1 and 2, and rises steeply thereafter.

TABLE VII
Foetal Mortality and Presentation

Foetal Presentation	Cephalic	Breech	Shoulder
No. of Prolapsed Cords	43	16	7
No. of Perinatal Deaths	6	7	4
Mortality Rate	14%	44%	57%

Table VII shows that the foetal mortality with vertex presentation is the lowest (14 per cent). In the breech cases prematurity is a very important contributory factor to the high mortality, and delayed hospital admission is an important factor in the shoulder presentations.

TABLE VIII
Foetal Mortality and Weight

Foetal Weight	Under 5½ lb.	5½-6½ lb.	Over 6½ lb.
No. of Prolapsed Cords	19	15	32
No. of Perinatal Deaths	10	3	5
Mortality Rate	53%	20%	16%

Besides being an important predisposing factor to cord prolapse (Table II) it is apparent from Table VIII and XI that the co-existence of prematurity with cord prolapse carried a fetal mortality of over 50 per cent.

TABLE IX

Fœtal Mortality and Time-Lag between Detection of Cord Prolapse and Delivery

Detection—Delivery Time Lag	Under 1 hour	Between 1–2 hours	Over 2 hours
No. of Prolapsed Cords	49	7	10
No. of Perinatal Deaths	8	2	8
Mortality Rate	16%	29%	80%

On studying the case records, the exact time of prolapse of the cord was difficult to

ascertain in most instances, and estimation of the Detection-Delivery time interval is the most likely to serve as a measure of the Prolapse-Delivery time interval. Table IX shows that the fetal mortality is lowest (16 per cent) if delivery is effected within 1 hour of detection, and fetal prognosis is very poor after the 2-hour time lag.

Table X shows that delivery by Cæsarean Section gives the lowest perinatal mortality (7 per cent). But if the dictum of "Immediate Delivery on Diagnosis" is to be implemented then certainly delivery by forceps, breech extraction, or internal version and breech extraction can be effected more rapidly than Cæsarean Section when the diagnosis is made in the second stage of labour. Two of the breech extraction deaths were abnormal fetuses and further two were dead in utero on admission, hence the corrected fetal mortality in the breech extraction series is 21 per cent, and similarly the corrected mortality for the internal version series is 33 per cent.

TABLE X

Fœtal Mortality and Treatment

Method of Treatment	Caesarean Section	Forceps Delivery	Breech Ex- traction	Internal Version & Breech Ex- traction	Spontaneous Deli- very	Cranio- tomy	Decapita- tion
No. of Prolapsed Cords	28	13	14	4	5	1	1
No. of Perinatal Deaths	2	2	7	2	3	1	1
Mortality Rate	7%	15%	50%	50%	60%	100%	100%

TABLE XI

Causes of the 18 Fœtal Deaths based upon Autopsy Findings

Fœtal Deaths due primarily to Intra Uterine Asphyxia following Prolapse of the Cord	8
Fœtal Deaths due partly to Asphyxia following Prolapse of the Cord and partly to Prematurity	6
Total	14
Fœtal Deaths where Prolapse of the Cord was incidental	4

Causes of Death were as follows:—

- Case 1: Anencephalic Fœtus (Stillbirth).
- Case 2: Macerated Premature Stillbirth.
- Case 3: Oesophageal Atresia. Died 2nd day post-operatively.
- Case 4: Oesophageal Atresia. Died 2nd day post-operatively.

Autopsy on all perinatal deaths in Aberdeen Maternity Hospital is a routine procedure, and Table XI summarises the autopsy findings of the 18 perinatal deaths in this study. "Prolapse of the Cord" is contributory or responsible for only 14 of the 18 deaths, giving a corrected perinatal mortality of 21.2 per cent.

Discussion

The incidence of prolapse of the cord in hospital deliveries has been stated to vary very widely from 1 in 74 deliveries to 1 in 1018 deliveries (Slate and Randall, 1956), but most hospital series display an incidence of about 1 in 200 deliveries (Myles, 1959). The high incidence of 1 in 115 deliveries for Aberdeen Maternity Hospital is probably due to the heavy concentration of abnormal, and relatively large number of emergency obstetrical cases from a large surrounding area, in the hospital.

Table XII summarises the Fœtal Mortality Rate for Cord Prolapse cases, as reported in various publications on this subject. They all refer to "Hospital Deliveries" rather than to the total population. Further, in only four of the thirteen series quoted, has correction been made for foetal deaths where cord prolapse is incidental and not the cause of the

death. In the present series and in those of Rhodes (1956) and Cox (1951) the number of cord prolapse cases reviewed is less than 100, but the others are much larger. The uncorrected foetal mortality varies widely from 11.4 per cent to 52 per cent. The Aberdeen Maternity Hospital rate of 27.3 per cent and corrected rate of 21.2 per cent is the second lowest. The very low foetal mortality rate of 11.4 per cent attained by Cox (1951) at the Liverpool Maternity Hospital seems to have been due to a planned attack at "Fœtal Salvage in Cord Prolapse," conducted by an organised obstetrical team led by Cox personally. As a result of this experience he advocated a policy of "Immediate Delivery on Diagnosis, including the wider use of Cæsarean Section in those cases where immediate vaginal delivery was not possible. The Cæsarean Section rate was 37.1 per cent (Table XIII) in his small series.

Since then several others, namely Rhodes (1956), Myles (1959) and Seligman (1960) have fully concurred with Cox's view, that to attain maximal foetal salvage the principle of "Immediate Delivery on Diagnosis" has to be implemented, provided that at the time of diagnosis the foetus appears to be free from congenital abnormalities, and is of viable maturity. Thus obstetrical procedures, such as manual replacement of the cord, Dührssen's incision

TABLE XII
Review of Fœtal Mortality Rates

Source	Uncorrected Fœtal Mortality Rate	Corrected Fœtal Mortality Rate
Rodes (1956)	52 %	—
Bourgeois (1941)	49.7%	40.6%
Cope (1951)	47.5%	—
Mengert and Longwell (1940)	46.6%	—
Kurzrock (1932)	43.9%	—
Slate and Randall (1956)	42.8%	—
Morgan (1948)	40.0%	—
Fenton and D'Esopo (1951)	37.5%	—
Myles (1959)	36.4%	—
Brandeberry and Kistner (1951)	35.3%	29.3%
Seligman (1960)	28.0%	—
Personal Study (Table III)	27.3%	21.2%
Cox (1951)	11.4%	11.4%

TABLE XIII
 Review of Relationship of Cæsarean Section to Fœtal
 Mortality

Source	Uncorrected Fœtal Mortality Rate	Cæsarean Section Rate
Rhodes (1956)	52 %	6 %
Cope (1951)	47.5%	12 %
Fenton & D'Esopo (1951)	37.5%	3.5%
Myles (1959)	36.4%	19.4%
Seligman (1960)	28 %	28 %
Personal Study (Tables III & X)	27.3	42.4%
Cox (1951)	11.4%	37.1%

of the cervix, Braxton Hick's version and hydrostatic bags, have been largely abandoned in most hospitals. All such procedures are associated with very high fœtal mortality due to asphyxia, resulting either from the delay of delivery, from cord spasm, or excessive manipulation (Fenton *et al.*, 1951; Tables VI and VII). Table IX clearly shows that the fœtal mortality is lowest if delivery is effected within one hour of diagnosing cord prolapse (16 per cent) whereas the mortality is extremely high after a 2-hour lapse (80 per cent). Similar conclusions were reached by Fenton *et al.*, (1951) who showed a fœtal mortality rate of over 70 per cent after a 3-hour lapse.

In implementing the policy of "Immediate Delivery on Diagnosis," vaginal delivery, either by forceps or breech extraction, or internal version and breech extraction immediately the diagnosis is made, is now the usual practice both in this hospital and in most other centres, provided the usual prerequisites for a safe vaginal delivery are fulfilled. Under these circumstances, I am of the opinion that "Pudendal Block Anæsthesia (Regional)," is superior to a general anæsthetic for the following reasons:—

- (1) It greatly lessens the attendant risk of a general anæsthetic to the mother, especially since the operation has to be done on the unprepared patient.
- (2) It can be done quickly by the obstetrician himself. This is of immense importance, in cord prolapse, because it

shortens the Detection-Delivery time lag by at least 30 minutes.

Seligman (1960) has stated that "although immediate delivery is indicated in these cases, even more skill and care than usual must be taken, since the fœtus is already in a precarious state and degrees of trauma, which do not affect the healthy fœtus, may be sufficient to jeopardise its existence." In his study he found that traumatic vaginal delivery was responsible for more than 20 per cent (6 out of 28 deaths) of the perinatal deaths. In the present limited series, none of the perinatal deaths were due to traumatic delivery (Table XI).

Where the fœtus is alive, normal and viable at the time of diagnosis, but where an immediate vaginal delivery is not advisable, then immediate Cæsarean Section gives the best results from the point of view of the child at least. Myles (1959) had a fœtal mortality of 6.2 per cent, and Seligman (1960) a mortality of 7.1 per cent with Cæsarean Section, and Cox (1951) had no perinatal deaths in 13 cases treated by Cæsarean Section. In this study, 2 out of 28 babies born by Cæsarean Section died (Table X).

Table XIII shows that there is some correlation between the incidence of Cæsarean Section and perinatal mortality since the very high death rates are associated with a low Cæsarean Section rate and vice versa. The exceptional perinatal death rate of 11.4 per cent reported by Cox was achieved with a Cæsarean Section rate of 37.1 per cent.

Conclusion

It is apparent from this review that prolapse of the cord is still a very dangerous complication for the baby and contributes substantially to perinatal mortality. High standards of obstetrical technique can prevent many of the deaths. The first essential is early detection of the condition and the immediate delivery of the baby either by the vagina or by Caesarean Section.

The best results will be attained only in those highly efficient hospitals where there is good team work. A skilled obstetrician and anaesthetist must be available at very short notice, and the paediatrician has an important role to play in the resuscitation of the severely asphyxiated neonate and in the subsequent care of the baby especially when it is premature (Table VIII). It is clear, therefore, that in this respect at least home confinement is much more dangerous than hospital.

There seems to be general agreement that if the cord prolapses before full dilatation of the cervix, the best chance for the fetus is provided by immediate Caesarean Section. The main drawback to the wider use of Caesarean Section for prolapse of the cord is the danger to the mother. Under modern conditions this risk is slight, but even so it must always be weighed against the possibility that the baby may not survive, no matter what method of delivery is employed.

ACKNOWLEDGEMENT

I am very much indebted to Professor Sir Dugald Baird, Regius Professor of Midwifery, Aberdeen University for his invaluable advice and encouragement in the preparation of this paper, and for having granted me free access to the Aberdeen Maternity Hospital case records. My grateful acknowledgement to the University of Singapore for granting me permission to publish the above preliminary review of my proposed M.D. Thesis project.

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THE MANAGEMENT OF THE THIRD STAGE OF LABOUR

By Derek Llewellyn-Jones, M.D., M.A.O., F.R.C.O.G.
Obstetrician and Gynaecologist,
Maternity Hospital, Kuala Lumpur.

The problem of postpartum haemorrhage is considerable amongst a population whose average haemoglobin level is 10 g. per 100 ml. and amongst whom about 5 percent of the pregnant women have a haemoglobin level of less than 6.5 g. per 100 ml.

In Western countries the traditional "hands off" conservative attitude to the third stage of labour has changed in the past 20 years. Following the papers of Davis and Boynton (1942), Lister (1950) and Martin and Dumoulin (1953) increasing numbers of obstetricians have used an injection of intravenous ergometrine, given as the anterior shoulder of the baby was born, to stimulate a uterine contraction and placental separation. Embrey and Garrett (1958) have shown that such an injection causes a firm contraction of the uterus in 41 seconds, a tonic spasm lasting about 45 minutes and an oxytocic effect lasting up to 3 hours.

Unfortunately, intravenous therapy is not always easy to administer and Kimbell (1954) suggested that intramuscular ergometrine, with hyaluronidase to enhance its more rapid absorption, was effective and could be used routinely, especially by midwives. Using this method Kimbell reduced the incidence of postpartum haemorrhage considerably. He admitted, however, that the injection took longer to act than intravenous ergometrine. This was subsequently confirmed by Embrey (1961) using an external tocograph.

Intramuscular oxytocin (pitocin) had its advocates, but had fallen into disfavour be-

cause although it acted quickly, the duration of its effect was short (averaging 20 minutes, Embrey, 1959) and delayed bleeding could occur from a relaxed uterus when the patient had returned to the lying-in ward.

In an effort to combine the rapid action of oxytocin with the prolonged action of ergometrine and to avoid the more complicated intravenous approach, "Syntometrine", a combination of 5 units of syntocinon and 0.5 mg. of ergometrine, was introduced. Several workers in the United Kingdom (Embrey *et al.*, 1963, Kemp, 1963, Chukudebelu *et al.*, 1963, and Stearn, 1963) have commented favourably upon its action and have compared it with intravenous, and intramuscular, ergometrine in clinical trials. The consensus of opinion is that intramuscular Syntometrine is more efficient than intramuscular ergometrine, with or without hyalase, and almost as efficient as intravenous ergometrine. Embrey (1961) has shown that Syntometrine acts on the uterus, on an average, in 157 seconds and the duration of the effect is long, owing to its ergometrine content.

Expulsion of the Placenta.

In the papers referred to discussion persisted over the proper management of the third stage of labour after injecting Syntometrine intramuscularly. Embrey, *et al.* (1963) and Stearn (1963) attempted to expel the placenta from the uterus with the first contraction, Stearn using the Brandt-Andrews technique. Kemp (1963) used intermittent cord traction from the moment of delivery of the baby in

TABLE 1.

To show the blood loss related to the management of the third stage of labour, after the use of Syntometrine intramuscularly.

Author	No. of patients	Blood loss %		Manual removal placenta (%)
		20 oz.	10 - 20 oz.	
McGrath and Browne	80	5.0	—	5.0
Chukudebelu <i>et al.</i>	500	4.6	22.8	3.4
Embrey <i>et al.</i>	590	2.9	12.3	1.6
Stearn (from)	448	2.9	9.6	2.0
Llewellyn-Jones	100	2.0	6.0	2.0

addition. McGrath and Browne (1962), and Chukudebelu, *et al* (1963) watched for signs of placental descent and then expelled the placenta either by fundal pressure or by cord traction. The differences in the results of these two methods can be seen in Table 1. These findings indicate that an active third stage after injection of intramuscular syntometrine will reduce the blood loss, and the incidence of retained placenta.

This is perhaps because an active third stage, by removing the placenta from the upper uterine segment, prevents its incarceration above a constriction ring. Oxytocin has been found to produce such a muscular contraction and this was one of the reasons for it falling into disfavour as a third stage oxytocic.

Method.

In the present study 100 healthy patients were studied (primigravidae 30; gravida 2 - 5, 60; gravida 6+, 5). All had attended the antenatal clinics regularly and were attended in labour by the author. All came from the higher socioeconomic groups and although 32 were delivered by forceps and 63 required an episiotomy, labour was otherwise normal.

An ampoule of Syntometrine was injected intramuscularly as the head of the baby was being born. The remainder of the delivery was controlled and took one minute to complete. The uterus was then palpated gently to await the first contraction, when the placenta was delivered by suprapubic pressure, lifting the uterus upwards and backwards, with the left hand, cord traction being practised with the right hand. The total blood lost from the time of delivery to the completion of the repair of the episiotomy (including that blood lost from the perineal wound) was collected and measured.

Results.

In Table 2 the *time* taken from the injection of Syntometrine to the expulsion of the placenta is noted. The mean was 157.84 seconds, which compares closely with Embrey's (1961) tocographic studies. In only two patients did the time exceed 10 minutes and in both of these women the placenta was removed manually, one after 60 minutes and the other after 40 minutes. Neither of these women lost more than 10 ozs. (285 ml.) of blood.

In Table 3 the *blood loss* can be seen. The mean loss was 134 ml. (4.8 ozs.) and in 74 percent of patients less than 150 ml. (5 ozs.)

TABLE 2.

To show the time interval between the injection of Syntometrine and the delivery of the placenta

Time in minutes	Gravida			Total
	1	2-5	6+	
Less than 3	23	43	3	69
3 - 5.59	8	12	2	22
6 - 8.59	4	3	—	7
9 or more	0	2	—	2
	35	60	5	100
Mean 157.84 seconds.				

TABLE 3.

To show the blood loss after the injection of Syntometrine

Blood loss in ml.	Gravida			Total
	1	2-5	6+	
0 - 149	26	44	4	74
150 - 299	6a	13	1	20
300 - 449	2a	2b	—	4
450 - 570	—	—	—	—
+ 570	1	1ab	—	2
	35	60	5	100
Mean Loss 134 ml.				

a — In one patient of each group, intravenous ergometrine given because of further bleeding (3 patients).

b — Traumatic bleeding in addition (2 patients).

blood was lost. In two patients traumatic bleeding was considered to have added significantly to the blood lost, (one patient losing a total of 420 ml., the other 700 ml.). Two patients had a postpartum haemorrhage and intravenous ergometrine 0.5 mg. was given to these two patients and to one other (blood loss 370 ml.).

Discussion.

The results in this clinical trial confirm those of the British workers that Syntometrine is a useful oxytocic drug in the third stage of labour and that its action is rapid (mean 2 minutes 38 seconds). The controlled method

of delivery together with an active third stage was associated with a postpartum haemorrhage rate of 2 per cent (2 patients) and in only 6 per cent of patients was the blood loss more than 10 ozs. (270 ml.). Manual removal of the placenta was required in 2 patients.

These results can be compared with those of Embrey, *et al* (1963). In a series of 590 patients (208 primigravidae) blood loss exceeded 20 ozs. in 2.9 percent, and 10 ozs. in 9.5 percent; manual removal of the placenta was required in 2.4 percent of patients.

It must be confirmed that in the third stage of labour Syntometrine is the best available intramuscular oxytocic and is almost as effective in its action as intravenous ergometrine. Its use should be accompanied by a slow controlled delivery of the baby (30 to 60 seconds being taken) and by using the Brandt-Andrews technique with cord traction for delivery of the placenta with the first contraction, which occurs about $2\frac{1}{2}$ minutes after the injection.

In several series using this method of management of the third stage of labour the postpartum haemorrhage rate was less than 3 percent, and the incidence of manual removal of the placenta did not exceed 2 percent.

Since blood loss can be disastrous in anaemic women, the routine use of intramuscular Syntometrine with an active third stage is recommended in all Maternity Units.

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ADDENDUM

Since submitting this paper a further 100 patients have been treated with intramuscular syntometrine. The results of the 200 patients are as follows:

- Blood loss more than 20 ozs.—1.5 percent.
- Blood loss 10-20 ozs.—9.5 percent.
- Manual removal of the placenta—1.5 percent.
- Mean time interval between injection and delivery of placenta—164.4 seconds.
- Mean blood loss—127 ml.

The results of treatment of the second 100 patients confirmed the value of intramuscular syntometrine combined with an active third stage in the prevention of postpartum haemorrhage.

NOTICES

SIX MEDICAL FELLOWSHIPS TO BE AWARDED TO OVERSEAS DOCTORS BY SMITH AND NEPHEW NEXT YEAR

Six more medical Fellowships, open to overseas doctors only and each worth £1,200, are to be awarded in 1965 by Smith & Nephew Associated Companies Limited, a British group of companies internationally known for its medical and surgical products.

The Fellowships provide one year's post-graduate study in the United Kingdom in a selected branch of medicine, and are available to doctors in British Commonwealth and developing countries who are studying for the higher qualifications. Applications will close on May 31 this year.

The scheme was inaugurated in 1961 by Smith & Nephew to enable outstanding overseas doctors to complete their studies in Britain for the benefit of their own countries; it is a condition of the award that Fellows

should return home within 12 months of completing their Fellowship work.

Fellowships, awarded alternately for surgery and medicine, have already gone to doctors from Canada, Australia, India, Pakistan, Ceylon, Ghana, Hong Kong, Singapore, the Sudan, Nigeria, Jordan and Ethiopia.

Smith & Nephew, whose most well-known products are probably Elastoplast, Tensoplast and Gypsona and tubercular drugs, have a long record of charitable help to the medical world, particularly in under-developed countries in field trials into the treatment of T.B.

Application forms can be obtained from: The Fellowships' Administrator, Smith & Nephew Associated Companies, 2, Temple Place, Victoria Embankment, London, W.C.2.



GALLOWAY MEMORIAL LECTURESHIP 1964

Application is now open for the above lecture to be delivered towards the end of 1964 in Singapore. The subject must be one pertaining to the Medical Sciences and consist of original work. An honorarium of \$100/- will be awarded to the lecturer. Application with personal curriculum vitae and an outline of the subject matter embodied in the lecture may

be sent to:—

Mr. J. E. Choo,
Scribe, Academy of Medicine,
General Hospital,
Singapore, 3.

The closing date for applications is 30th April, 1964.

NUTRITION SOCIETY FORTHCOMING MEETINGS

Committee of Enquiry into Experiments on Animals

The attention of members of The Nutrition Society is drawn to the evidence which has been sent by the Research Defence Society to the Departmental Committee of Enquiry into Experiments on Animals. The Nutrition Society was represented on the Committee which drew up this memorandum, copies of which can be obtained from the Secretary of the Research Defence Society (Mrs. K. Williams, 11 Chandos Street, London, W.1, price 1/-). Please state that you are a member of the Nutrition Society when sending for your copy.

Individual members of the Nutrition Society may like to submit evidence personally to the Committee of Enquiry, in which case they should write to P. Beedle, Esq., E.4 Division, Home Office, Whitehall, S.W.1.

It is understood that the Biological Council, on which the Nutrition Society is represented, is also proposing to submit evidence to the Committee.

Sixth International Congress of Nutrition Exhibition on "Food and Survival"

In the section of "Foods of the World" there were separate displays of available food supplies in five regions of the world viz. Western Europe, South Asia, West and Central Africa, Central America and Oceania. The displays showed the actual amounts of the various foods available, calculated from the figures published by F.A.O. for food supply at retail level per head per week.

Black and white prints (10 x 5 in.; 5/- each) and colour transparencies (4/- each) are available for each of these five displays. Colour transparencies (4/- each) showing caloric and animal protein distribution throughout the world are also available. Copies can be obtained from Miss K. Rose, Shalimar, Longniddry, East Lothian, Scotland, to whom requests with appropriate remittance should be sent.

DATIN LADY THOMSON, M.R.C.S., L.R.C.P.
*Hon. Overseas Correspondent in Malaya,
Institute for Medical Research,
Kuala Lumpur.*

—oOo—

Differences of opinion between the Malayan Medical Association and the Government do not indicate fundamental antagonism. The Association's duty is to consider proposed changes in Malayan Medical affairs and agree or disagree or modify as seems wise and right for the public good. Once a decision has been taken then our Association gives its utmost support to achieve success for it. There has never been any question of the Association acting to obstruct the Government in carrying out its policies. Last November our President assured the Prime Minister that the Government can rely on our Association for support and help at all times.

—oOo—

A LETTER FROM THE PRIME MINISTER

16 November, 1963

Dear Doctor,

Thank you for your letter of 2nd November.

I appreciate the sense of loyalty and patriotism of the members of the Malayan Medical Association in pledging support to the Government. Please convey my grateful thanks to everyone concerned.

(TUNKU ABDUL RAHMAN PUTRA)