WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE EASTERN MEDITERRANEAN

الهيئة الصحية العالمية
المكتب الاقليمي لشرق البحر الابيض المتوسط

ORGANISATION MONDIALE DE LA SANTÉ
BUREAU REGIONAL DE LA MEDITERRANEE ORIENTALE

REGIONAL COMMITTEE FOR THE EASTERN MEDITERRANEAN

Sixteenth Session

Agenda item 10 (a)

EM/RC16/4
15 July 1966

ORIGINAL: ENGLISH

TECHNICAL PROBLEMS MET IN MALARIA ERADICATION PROGRAMMES OF THE REGION - METHODOLOGY OF THEIR STUDIES AND SOME SCOPE FOR THEIR SOLUTION

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I INTRODUCTION

The WHO Expert Committee on Malaria at its eighth session in July 1961 considered the causes of failures in Malaria Eradication Campaigns, classifying these causes into three main groups:

- technical
- operational, and
- administrative.

Amongst the causes of failures of a technical nature, the biology of the vector, its resistance and human habits as well as socio-economic conditions were emphasized.

While Malaria Eradication Programmes continued to progress in many parts of the world, in some countries technical difficulties manifested through resistance or avoidance of the vector to applied insecticide have hampered the further progress of the campaign.

In spite of the fact that there were increasing reports on technical difficulties encountered in some Malaria Eradication Campaigns, an evaluation of the situation has indicated that the population involved in areas having true technical problems did not overpass one per cent of the total population covered by Malaria Eradication activities. Nevertheless, the WHO Expert Committee on Malaria reviewed once again the technical problems at its meeting in 1963, and stated in its Tenth Report that "A problem area is a defined geographical area within which an adequate epidemiological evaluation shows that the transmission of malaria persists despite total, complete, regular and sufficient coverage with residual insecticide, and where careful studies have revealed that administrative or operational factors are not responsible for the persistence of transmission and where additional measures are required in order to prevent the occurrence of new cases".

As it can be seen from the above definition, "problem areas" are restricted only to those areas where the persistence of transmission is due only to technical difficulties. Following the definition of the term "problem area", the WHO Expert Committee on Malaria has considered the nature of the technical difficulties and their etiology, the practical methodology for the study of causative factors and the interpretation of results thus obtained, as well as the possible remedial measures to be applied.

Further experience gained in Malaria Eradication Programmes reported as having met technical difficulties indicates that the persistence of transmission is not solely caused by non-response of the vector to the applied insecticide. In fact, a combination of technical, operational and administrative factors are responsible for the failures to interrupt transmission, at least in the countries of the Eastern Mediterranean Region. Methodology of the studies conducted in areas with technical difficulties and results obtained will be the subject of discussion in this paper.

II TECHNICAL PROBLEMS MET IN COUNTRIES OF THE EASTERN MEDITERRANEAN REGION

The present scheme of a malaria eradication project or programme mainly relies upon residual spraying of premises aiming at interrupting the transmission of malaria followed by surveillance operations to detect the persisting parasite reservoir and to treat radically the positive cases. If the domiciliary spraying campaign is well planned, properly administered and correctly executed in terms of timing and coverage with an insecticide at a proper dosage maintaining a residual effect throughout the transmission season, the interruption of transmission should be achieved after the first or second year of spraying operation. However, in some instances in spite of the spraying operation being conducted, there is evidence of fresh transmission in the sprayed areas. This is the case in southern Iran and Iraq where it was found that the local vector species did not respond to insecticidal attack in an expected manner. Subsequent studies undertaken revealed the development of double resistance of A.stephensi to DDT and DLD in southern Iran and Iraq, while A.fluviatilis in southern Iran was reported to behave in such a way (exophily and exophagy) that it would have little or no contact with the insecticide applied.

The first indication of DDT resistance in A.stephensi was reported by Daggy (1957) from Saudi Arabia in 1953, where A.stephensi was found to rest on recently DDT-sprayed surfaces. Subsequently an increase of malaria incidence was recorded in the A.stephensi areas of Saudi Arabia. This finding was confirmed by Davidson (1958) in 1955. During the following two years, DDT resistance in A.stephensi was reported to spread to practically all areas where this vector species was found in the Eastern Mediterranean Region, with the exception of West Pakistan where the vector was found to be still susceptible to this insecticide, though some increase of tolerance to DDT had been recorded in a few localities.

The replacement of DDT by dieldrin was suggested for all areas in the Eastern Mediterranean Region where DDT-resistance in A.stephensi was detected. It met with success, as evidenced in Iran and Iraq by a significant reduction of the vector mosquito to a level almost undetectable by routine entomological vigilance undertaken by the Malaria Eradication Programmes in the DDT-sprayed areas and, consequently, a drastic drop of the incidence of malaria. However, dieldrin-resistance was first detected in the foot-hills of the Zagros mountains in south-eastern Iran in 1959 and it spread gradually in the following two years to practically all the areas of its distribution in the country. In Iraq, A.stephensi reappeared in August 1961 after discontinuation of DLD spraying for three consecutive years in 1958-1960, first among the villages on the bank of Shatt al Arab, and was later detected in practically all nahias of Basrah liwa where suitable breeding places for this species existed. Susceptibility tests conducted (Chang, 1961) in October 1961 in Basrah liwa revealed that the reappeared A.stephensi was totally resistant to dieldrin, and also to DDT although of a much lower order - with an estimated LC50 of less than 4%. It was therefore concluded (Chang, 1961) that the complete dieldrin resistance as observed would rule out the possible use of dieldrin and other related compounds. DDT-resistance, on the other hand, was of such a low degree that it would leave a margin to use this insecticide in case of renewed transmission. Owing to the extremely favourable climatic conditions prevailing in Iraq in 1962, the vector population increased rapidly and an outbreak of malaria was reported in 1962 in Basrah town and its suburbs.

On the basis of the above-mentioned conclusion, DDT spraying was applied as a means to control the outbreak and later as the main attack measure in the malaria eradication programme in southern Iraq, which has produced good results as will be seen in the discussions in the subsequent paragraphs of this paper.

The role of A.fluviatilis in transmitting malaria was not recognized in Iran prior to 1958. Up to the present time, over 3 000 specimens of this species have been dissected in various areas of Iran with an overall sporozoite rate of 2.0 per cent. However, its role as a malaria vector in Saudi Arabia, where this species is a very prevalent mosquito in the Eastern Province and is known to be resistant to DLD, still has not been established.

Due to its exophagic and exophilic habits, it is reported in Iran that interruption of transmission of the A.fluviatilis-borne malaria could not be achieved by DDT-residual spraying of premises.

In Iran, A.fluviatilis has been found to rest both indoors and outdoors. It has been collected from human habitations as well as cattle sheds. It is also found resting in outdoor harbourages, such as caves, holes, cracks, etc. Female specimens with various stages of blood digestion have been found in either natural outdoor shelters or in houses or animal sheds. As the local human population in the areas of A.fluviatilis distribution is accustomed to sleeping outdoors, the exophagic tendency of A.fluviatilis seems quite natural. Furthermore, observations made in Kazeroun and Jiroft indicate that despite the fact that both man and animal sleep outdoors during most of the year, the human blood ratio of A.fluviatilis captured from human habitation or animal sheds is about the same. However, the human blood ratio of this mosquito captured from human dwellings in Bandar Abbas is much higher in comparison with those caught from pit shelters in the same locality with a ratio of about 2:1. This would seem to indicate that transmission of malaria by this vector species could be interrupted, provided the houses are treated on the basis of total coverage both in space and time. This is, indeed, the experience with A.fluviatilis-borne malaria in other parts of the world.

Besides the technical difficulties experienced with the above two vector species, the development of physiological resistance by A.culicifacies has been found in a limited area of West Pakistan, but this resistance does not seem to be of epidemiological significance so far. Another vector species, A.pharoensis, has developed high tolerance to DDT in the United Arab Republic which would require very intensive attack measures if interruption of transmission is to be achieved in areas where this mosquito is the principal vector.

Anti-malarial drugs and in particular 4-aminoquinoline derivatives have been extensively used in Malaria Eradication programmes of the Region. However, there is no evidence of the development of resistance in plasmodia to these compounds in any of the countries of the Eastern Mediterranean Region.

III STUDIES CONDUCTED IN COUNTRIES WHERE TECHNICAL PROBLEMS WERE ENCOUNTERED

In order to cope with the technical problems manifested by the resistance of vectors to applied insecticides, a number of well-organized field trials and laboratory studies have been conducted in countries of the Region. These studies can be summarized as aiming at:

- Finding a suitable insecticide by origin other than chlorinated hydrocarbons which could safely replace DDT.
- Developing effective attack measures which can either replace the application of insecticide in areas where the movement of population makes it almost impossible to provide the required protection over the population by the standard attack measures or supplement the standard attack measures in areas where the vector resistance hampers the interruption of transmission.
- Clarifying the genetical aspect of DDT resistance in A.stephensi, in other words, the real nature of physiological resistance of A.stephensi to DDT.

Besides these field trials and research conducted in laboratories, an attempt was made in southern Iraq by combined operational, epidemiological and entomological assessment, to determine to what extent DDT can be used to interrupt transmission in areas where A.stephensi, the principal vector, has developed resistance to this insecticide.

1. Field Trials with New Insecticides

In view of the development of double resistance of A.stephensi and A.pharoensis to DDT and DLD, field trials on some promising imagocides other than chlorinated hydrocarbon compounds were carried out in Iran and the United Arab Republic during 1965 to ascertain their possible use in the respective malaria eradication programmes. Taking into consideration the preliminary results obtained through trials on a small scale, either in experimental huts or on a village basis, in respect of both the effectiveness and the operational safety, a pilot project on malathion was established in 1964-1965 in Bandar Abbas, Iran. Meanwhile in the United Arab Republic, a field trial with the simultaneous application of malathion, BHC, and DDT in comparable areas, was carried out in 1965. The results obtained through

epidemiological studies, as well as entomological observations undertaken during these field trials, are discussed briefly below:

1.1 Malathion

A malathion pilot project was established in Bandar Abbas area covering the port of Bandar Abbas, the town of Minab and 375 villages in the surrounding area with a total population exceeding 120 000. The insecticide used was malathion 50% w.d.p. at a dosage of 2 g (technical grade) per square metre, to be applied in four cycles a year. A.stephensi is the main vector in the littoral plains and A.fluviatilis in the foot-hill regions. The transmission season is estimated to be throughout the year with the exception of the two coldest months during the winter. Below is a summary of spraying data of the four rounds undertaken by the project in 1964-1965.

Round	Date of spraying	No. villages sprayed	No. house-holds sprayed	Population protected
I	7 Oct.-21 Nov. 1964	378	27 114	120 067
II	10 March-22 April 1965	442	30 391	135 547
III	10 May-25 June 1965	268	15 692	70 236
IV	23 Sept.-27 Oct. 1965	435	36 895	128 261

It is to be pointed out that spraying operations have not been carried out up to the standard. Thus during the third round of spraying with malathion, the coverage was only a little above 50%. In addition, the planned round for the period July-August 1965 has not been carried out. Nevertheless, entomological observations undertaken prior to and after the spraying operation indicate:

i. an almost complete disappearance of A.stephensi in the sprayed area;

ii. a significant drop of A.fluviatilis density as observed from pit shelters in the sprayed area - a reduction of almost 80% of this vector density as compared with that prior to spraying operation;

iii. a significant drop of gravid females (including half-gravid ones) in the composition of this species observed in pit-shelters after insecticide treatment;

iv. that the residual effect of malathion lasted only about a month, as the vector species began to appear in the indoor collection one month after treatment and increased gradually afterwards. Similar findings were also noted from the pit-shelters collections.

Other studies, such as window-trap collections, dilatations, night-biting observations, age determination of the vector mosquitoes by Detinova technique, etc., were also carried out. However, as the number of this series of observations is limited, no definite conclusion can be made.

Malariometric data collected in two selected villages, Chelow and Siahou, in October 1964 (prior to spraying operations) in comparison with those collected during the same month in 1965 (nearly one year after the commencement of the first round of the spraying campaign) indicate that there is no significant change in the general parasite rate observed prior to and one year after spraying with malathion. The parasite rate prior to the spraying campaign in Chelow and Siahou was 42.2% and 37.7% respectively, in comparison with 37.5% and 45.4% recorded nearly one year after spraying with malathion in these two villages. However, as has been pointed out earlier, the coverage with the third round of malathion spraying in the area was poor and the scheduled spraying in July-August was not carried out. Therefore, bearing in mind the fact that the residual effect of this insecticide is limited to not more than two months, a successful interruption of malaria transmission by this insecticide can only be expected if spraying rounds are carried out according to the expected residual effect of this insecticide, which is very costly.

Some evaluation of the cost of spraying with malathion was made in comparison with that of DDT. Due to the high cost of malathion and the required frequency of spraying (four rounds annually), it is estimated that the annual cost per capita protected by malathion is much higher than that of DDT - 160 rials per capita for malathion and 40 rials for DDT.

1.2 Comparative Application of Malathion, BHC and DDT

A field trial was carried out with malathion in an area in the Nile Delta of Egypt, with a population of approximately 50 000, at the dosage of 1.0 g. per square metre, applied once in the second half of May, and with BHC in an area in the neighbourhood of the malathion area,

with a population of 38 900 at the dosage of 0.5 g. per square metre, applied simultaneously with malathion in the latter part of May. In order to compare the effectiveness of these two insecticides with that of DDT, a third area with a population of 34 250 was selected for spraying with DDT at the same time, with a dosage of 2 g. per square metre. The fourth area, with a population of 37 550, was left unsprayed to serve as a control. An assessment of this field trial was made from the data collected in respect of infant parasite rate, positivity rate of the slides collected through Active Case Detection, and routine entomological observations - indoor collections window-trap collections, biting rate, bio-assay (standard WHO technique and by releasing vector mosquitoes into sprayed houses) and parous ratio of the vector population in the sprayed and control areas. No significant difference was observed in the malariometric data collected in the three field trial areas sprayed with either malathion, BHC or DDT. The positivity rates found in the malathion-sprayed area, BHC-sprayed area and DDT-sprayed area were 0.70%, 0.50% and 0.72%, respectively; only one infant was found with parasites in the malathion-sprayed area (877 infants under routine observation), three in the BHC-sprayed area (725 infants) and one in the DDT-sprayed area (550 infants). Indoor collections carried out in the three sprayed areas with three different insecticides revealed an almost absence of A.pharoensis in the DDT-sprayed houses and the highest density in the BHC-sprayed houses - almost at the same level as the unsprayed check houses, except during the first ten weeks after insecticidal treatment. The indoor density as observed in the malathion-sprayed houses indicates that the residual effect will not last more than two months. This would seem to indicate that DDT is still superior to the other two insecticides under trial.

2. Field Trial with Medicated Salt

In Iran an attempt is being made to solve much of the problem relating to nomadism by the use of medicated (chloroquinized) salt. As the tribal people have experienced difficulties and hardship in procuring salt from distant places, they readily accept medicated salt, which is supplied free of charge. In view of the encouraging results and experience gained from the small scale medicated salt trials among the tribal population which commenced in 1959, a pilot project - covering forty-two villages with a

stable population of 6 235 and a moving population of 10 982 - has been established in Kazeroun area to study the effectiveness of chloroquinized salt, and to investigate possible ways of execution including the necessary organization and operational procedures, such as daily consumption of salt, frequency and site of distribution, transportation, etc., particularly among the moving population. It was found that the overall parasite rate dropped from 18.7% recorded in 1962 (prior to the operation), to 3.4% one year after the operation and to 0.11% two years later. No positive case was detected among the population over two years of age (food eaters) eight months after the commencement of the medicated salt distribution programme. However, the distribution of chloroquinized salt is only a process of prophylactic treatment (suppressive) and is not a radical cure for the parasite carrier, particularly in the case of P.vivax - which is the predominant parasite species in the trial area - infection. There is no doubt, however, that if suppression of P.vivax lasts long enough, there is little chance for the occurrence of late relapses that may cause resumption of transmission of malaria amongst the protected population.

No drug resistance was detected among the population under protection by medicated salt. The coverage of the population with the medicated salt programme, based on a survey made by random sampling of urine analysis for the presence of chloroquine, is estimated to be above 95%.

The very encouraging results obtained in Iran with the above medicated salt project indicate a definite possibility of applying it either as a supplementary measure to standard attack operations or as a sole attack measure for moving population.

3. Study of the Real Nature of Resistance of A.stephensi to DDT

The laboratory studies carried out by Davidson (1961) on the degree, the pattern of distribution and the mode of inheritance of resistance in A.stephensi have demonstrated that:

i. resistance of A.stephensi to DDT is of a low degree and

ii. besides the mortality of heterozygotes there must occur under natural conditions some mortality of homozygous resistant individuals if DDT is applied at the usual dosage.

Consequently, DDT resistance will develop to a certain level, but will not reach 100%. This statement is supported by the fact that when susceptibility tests were carried out (Davidson 1961) with homozygous resistant females of A.stephensi (laboratory-bred, originated from Moawyia village, Basrah, and supplied by Dr. Gramiccia in 1959) by exposing them to 4% DDT for one hour followed by a 24-hour recovery period, the lowest mortality achieved through these tests was 9%. However, susceptibility tests carried out by the same investigator with laboratory-bred generations of A.stephensi obtained through back-crossing of heterozygotes with homozygous resistant or susceptible individuals, revealed mortality rates ranging from 30.5 to 81.5%, depending on the genetic background of A.stephensi population under observation (4% DDT one hour exposure).

The susceptibility tests carried out with A.stephensi in southern Iraq for the last six years indicate that there is no significant change in the susceptibility level of this mosquito to DDT in spite of the selective pressure caused by the application of this insecticide for several years. It is therefore reasonable to believe that the natural population of A.stephensi inhabiting southern Iraq is composed of three genotypes, namely, homozygous resistant individuals, homozygous susceptible ones and heterozygotes. Under these circumstances, it is also reasonable to believe that accurately carried out spraying operations with DDT will no doubt have a significant effect on the transmission of malaria in this area.

IV THE RESUMPTION OF SPRAYING WITH DDT IN RESISTANT A.STEPHENSI AREAS IN SOUTHERN IRAQ AND IRAN

The southern Region of Iraq consisting of three Liwas (Basrah, Nasiriah and Amara) has entered the consolidation phase in 1960, after successfully completing the attack phase by applying dieldrin residual spraying, A.stephensi, the only vector in the area, was reported to have disappeared in all areas under attack and the number of positive cases was brought to a negligible level (nine in 1960 and ten in 1961), thus allowing the entry of the area into consolidation phase. However, in August 1961, A.stephensi was reported as reappeared in Seeba, south of Basrah, but without epidemiological consequence. In 1962 a small flare-up took place in Basrah liwa, confined mostly to Basrah city with a total of eighty-nine positive cases. The important point was that the monthly distribution of positive cases followed the natural pattern of malaria transmission in that area.

Owing to the extremely favourable conditions prevailing in 1962 for the propagation of A.stephensi, the vector population increased rapidly.

The coincidence of two favourable factors for the propagation of malaria parasites, namely the increased vector population and the residual parasite reservoir created in the second half of 1962, was quite sufficient for the development of an epidemic in 1963. In fact, from end April to mid July, the first annual wave of the epidemic was over, leaving in the battle-field more than 2 000 victims of malaria. In order to cope with the outbreak, residual spraying with DDT was carried out in Basrah city and its suburbs from 26 June till 20 July, but it could not prevent the epidemic, since the spraying was applied too late. As a matter of fact, a detailed study of the epidemic in August 1963 revealed that DDT was still effective at least in curtailing the epidemic. Indeed the incidence of malaria disappeared or dropped significantly about two weeks after application of DDT, which lapse of time corresponds to the average incubation period for P.vivax, and it may be noted that the cases manifested during this two-week period could not be prevented by any insecticide. That this drop in incidence was not a natural course of the epidemic was shown by the fact that transmission continued in Basrah liwa where DDT was not applied, and by the fact that while in DDT sprayed area P.falciparum disappeared this was not the case in rural areas not protected by DDT spraying (Lepes, 1963).

1. Epidemiological Observations

Application of DDT residual spraying on a total coverage basis in southern Iraq was commenced in 1964 with two rounds, one in March-April and the other in July-August, at a dosage of 2 g. (T.G.) per square metre, and continued in 1965 and 1966. Basrah city and its suburban area, where the case-load was heavy and the number of domestic animals was low or nearly absent, the spraying was supplemented by larviciding operations (oiling). Surveillance operations have continued and every effort was being made to intensify these operations in order to eliminate any possible source of infection, as well as for the purpose of evaluating the effectiveness of DDT as an attack weapon for the interruption of malaria transmission.

Although the insecticide coverage in Basrah liwa, with the exception of Fao, cannot be considered as quite "satisfactory" (average coverage of households is about 80% for the last five rounds applied since the resumption of

DDT-spraying in Basrah liwa), yet the incidence of malaria has dropped significantly. The following are data on the incidence of malaria in Basrah liwa, excluding nahia Fao, prior to and after resumption of DDT-residual spraying of premises, collected through surveillance operations:

Incidence of Malaria in Basrah Liwa,
excluding Nahia Fao, Before and After Resumption
of DDT-Residual Spraying of Premises*
(Population: 637 204)

Analysis Case Detection Data		Before Resumption	After Resumption	
		June 1963-May 1964	June 1964-May 1965	June 1965-May 1966
No. of slides collected		114 982	155 204	200 622
No. positives:	P.v.	4 641	861	226
	P.f.	284	3	3
	Mixed	14	2	2
	Total	4 939	866	231
ABER, % population		18.0	24.3	31.5
API per 1 000 population		7.75	1.36	0.36
Positivity rate**		4.29	0.56	0.11

* For nahia-wise incidence of malaria, prior to and after resumption of DDT-residual spraying, refer to Annex I attached to this document.

** The positivity rate is indicated on the table in support of the significance of the API.

There is a definite decline of malaria incidence noted in Basrah liwa since the resumption of DDT-residual spraying of premises. The annual parasite incidence per 1 000 population recorded prior to, and one and two years after DDT-spraying are 7.75, 1.36 and 0.36 respectively, and the positivity rates of the total number of slides examined are 4.29%, 0.56% and 0.11%, respectively. Thus the positivity rate observed after the first year of DDT treatment is only a little over 13% of the rate recorded prior to the spraying operations, and a further reduction by approximately 80% during the second year in comparison with the rate recorded during the first

year after resumption of DDT-residual spraying. It meets ideally the criterion for the interruption of malaria transmission as laid down by the WHO Expert Committee on Malaria (Tenth Report, 1963).

There might be some reflections indicating that the malaria incidence in Basrah was reduced naturally and not owing to the effectiveness of DDT.

However, in Fao area, where the first two rounds of spraying was extremely poor with not more than a 35% coverage of households, particularly in those villages where most of the cases were detected, the epidemiological situation was different. Proper treatment with DDT in Fao was not carried out until September 1964 and afterwards. Therefore, it could hardly be considered as being protected by DDT during the main part of the transmission season in 1964. Epidemiological data recorded in Fao during this period (1964) could thus be used to serve as a comparison or check with that collected from the rest of the nahias where insecticide treatment was relatively better conducted for the year 1964. In the evaluation of the effectiveness of DDT in interrupting malaria transmission, Basrah liwa was therefore divided into two areas on the basis of insecticidal coverage, namely Fao and the rest of the Basrah liwa.

Data on the incidence of malaria prior to and after the resumption of DDT-spraying in Fao area collected through surveillance operations are tabulated below:

Incidence of Malaria in Fao, Basrah Liwa
Before and After Resumption of DDT-Spraying
(Population: 35 482)

Analysis Case / Detection Data		Before Resumption	After Resumption	
		June 1963-May 1964	June 1964-May 1965	June 1965-May 1966
No. of slides collected		7 118	12 390	27 892*
No. positives	P.v.	206	790	374
	P.f.	120	5	0
	Mixed	3	0	0
	Total	329	795	374
ABER, % population		20.1	34.9	78.6
API per 1 000 population		9.3	22.4	10.5
Positivity Rate**		4.62	6.42	1.34

* Of these about 8 000 slides were collected from mass blood examination and 10 cases of malaria were detected.

** The positivity rate is indicated on the table in support of the significance of API.

Owing to the poorly conducted DDT-spraying, as discussed in the foregoing paragraphs, an increase in the incidence of malaria was noted in 1964-65. The annual parasite incidence per 1 000 population recorded prior to the spraying operation was 9.3 and it increased to 22.4 at the end of the first year of operation. Similarly the positivity rate increased from 4.62% to 6.42%. However, after the improvement of spraying operations both in technique and in coverage, a remarkable reduction in the incidence of malaria was observed by the end of the second year of operation; the annual parasite incidence per 1 000 population dropped from 22.4 to 10.5 and the positivity rate decreased from 6.42% to 1.34%, with a reduction rate of approximately 79% which meets the criterion for the interruption of malaria transmission, as laid down by the WHO Expert Committee on Malaria (Tenth Report, 1963).

In Iran, a pilot project was established in 1963 in Fassa shahrestan (population 208 657) to ascertain whether transmission can be interrupted by using two rounds of 2 g. technical DDT per square metre when applied under strict supervision. The area represents most of the technical and operational problems observed in southern Iran, including DDT resistance to A.stephensi, exophily of A.fluviatilis and population movement of nomads. An attempt was made to issue all nomads with prophylactic drugs upon entering the area, and although this plan was carried out, it was without much success as the time of entry for the tribal population depends entirely upon grazing and therefore rainfall which makes total coverage difficult. The project is epidemiologically assessed through Active Case Detection operations at 15-day intervals. Epidemiological studies have revealed the fact that 95% of the project villages have been freed from indigenous cases. The results suggest that DDT can reduce the transmission potential to a point where additional measures, such as medicated salt for the protection of tribal population, are needed to support this insecticide in interrupting the transmission. The most formidable threat to the project is re-introduction of malaria. It would therefore have a much better chance of success if the whole area of southern Iran could come under protection.

In Khuzistan Plain, DDT was re-introduced in September 1964 and continued in 1965 with two cycles in March and September at the usual dosage of 2 g./m^2, covering a population of 527 046. It is purely an A.stephensi area.

Results obtained through Active Case Detection operations at 15-day intervals are shown below:

Period	Slides Collected	No. Positives	P.I. per 1 000
21 March-22 Sept. 1964	88 298	6 317	11.9
21 March-21 Sept. 1965	72 856	2 447	4.7

Results indicate that though transmission has not been completely interrupted by DDT-residual spraying, as evidenced by the positive infants born after September 1964, it suffices to say that transmission has been greatly reduced, though it has not met the criterion for interruption of transmission after one year of DDT application. With the experience gained in southern Iraq, that transmission has been completely stopped after the second year's application of DDT spraying, and the same can be expected in Iran.

The epidemiological data discussed above indicate very clearly that DDT residual spraying in resistant A.stephensi area may interrupt the transmission of malaria provided the spraying operation is conducted very accurately supported by intensified surveillance operations. An operational assessment of the surveillance operations in southern Iraq based upon information collected from house cards, have revealed that in 1964 and 1965 out of an index of 100 of expected house visits, 81.4% were de facto carried out, which is a high percentage taking into account local circumstances prevailing in the area. This figure indicates a high degree of reliability of epidemiological data discussed above.

An ecologically minded observer may not be satisfied with purely epidemiological data proving the effectiveness of DDT spraying in the DDT-resistant A.stephensi area. Therefore, in the subsequent paragraphs the entomological observations made in southern Iraq will be extensively discussed.

2. Entomological Observations

A number of entomological observations have been made in southern Iraq, prior to and after the resumption of DDT spraying A.stephensi area, consisting mainly of susceptibility tests, vector density studies and in respect of the

bionomics of A.stephensi. These observations will be discussed here below.

2.1 Susceptibility tests carried out with A.stephensi

Susceptibility tests were carried out at six-month intervals after resumption of DDT-spraying of premises in southern Iraq to detect the possible change in the level of resistance in the A.stephensi population. The WHO standard-technique was used for the tests on samples under observation, collected from unsprayed shelters, either human dwellings or stables, in the sprayed area or from outdoor night collections of fed mosquitoes resting on the untreated surfaces in the surroundings of the cow-baits. The critical 4.0% DDT concentration, with one hour exposure followed by a 24-hour recovery period, was used throughout this series of observations. Results of the tests are summarized as follows:

Observers	Locality	Date	DDT 4.0%			Control		
			No. Tested	No. Died	Mortality Rate	No. Tested	No. Died	Mortality Rate
Petridis & Capari*	Hartha	Mar.-Apr. 1958	80	5	6.3	84	1	1.2
Chang	Shatt-al Arab	Oct. 1961	68	44	64.7	100	1	1.0
Sacca	"	May 1962	98	76	76.5	100	0	0.0
Chang	"	Oct. 1962	56	30	53.6	35	0	0.0
Thymakis*	"	Aug. 1963	65	14	20.6	99	0	0.0
Moosami	Hartha	July 1964	177	70	40.0	57	3	5.3
Chang	Shatt-al Arab	May 1965	108	37	34.3	64	0	0.0
Chang	"	Nov. 1965	86	47	54.7	39	0	0.0
Chang	Fao	Nov. 1965	38	29	76.3	31	0	0.0
Chang & Cullen*	Shatt-al Arab	May 1966	99	65	65.7	77	0	0.0
" *	"	May 1966	112	61	54.5	88	0	0.0
" *	Fao	May 1966	24	9	37.4			

* Samples collected from sprayed shelters.

Data recorded by Gramiccia et al (1958) on the detection of resistance to DDT in A.stephensi is not listed in the present summary of the tests so far performed, as 4.0% DDT was not included in their

observations and therefore, the results cannot be readily compared with those of other tests using the critical 4.0% concentration. The highest concentration used in their tests was 2.0% DDT which gave a mortality of 27.2% of those samples collected from Moawyia, a village about 30 kilometres north of Basrah city. LC50 was estimated by them as being greater than 2.0% DDT concentration.

Mortality rates observed from the tests conducted by Chang (October 1961) and Sacca (May 1962) after DDT selective pressure had been withdrawn for about four years or more, and those recorded recently by Chang and Cullen (May 1966) after more than two years of resumed DDT residual spraying of premises in the area (five rounds have been applied), are 64.7%, 76.5% and 65.7%, respectively. Apparently, there is no significant difference in the level of DDT-resistance in the A.stephensi population under observation, i.e., before and after the resumption of DDT spraying in Basrah liwa, 1964-66. The renewed DDT selective pressure has not resulted in stepping-up the resistance level, even in the same locality, under exactly the same testing technique and conditions.

The analysis of the above-mentioned data leads to the conclusion that the natural population of A.stephensi consists of all genotypes and therefore is to be considered as a "intermediate" population as far as the susceptibility-resistance is concerned. Under these circumstances it can be expected with reasonable confidence that DDT spraying can be continued in the area if epidemiologically justified, without danger of raising the level of resistance in A.stephensi.

2.2 Observation on Vector Density

Routine collections of A.stephensi by the "space-spray capture" technique were made at monthly intervals from fixed capture stations in southern Iraq. Collections were made from sprayed houses as well as unsprayed shelters (those missed, closed or refused to be treated with DDT during the spraying campaign). Blood digestion stage of all specimens captured were noted at the time when the collections were made.

From the results obtained through these observations, it appears that a significant drop in vector density was experienced in the sprayed

bedrooms in comparison to that recorded in the unsprayed bedrooms, applying the same procedure. While the average number of A.stephensi caught per sprayed bedroom was 0.53 in 1965, the average number caught per unsprayed room was 3.09 during the same period. It has to be added that in sprayed rooms mosquitoes were found mostly on hanging objects (clothing, pictures) or underneath the bed, while in unsprayed rooms A.stephensi was found resting on the walls as well.

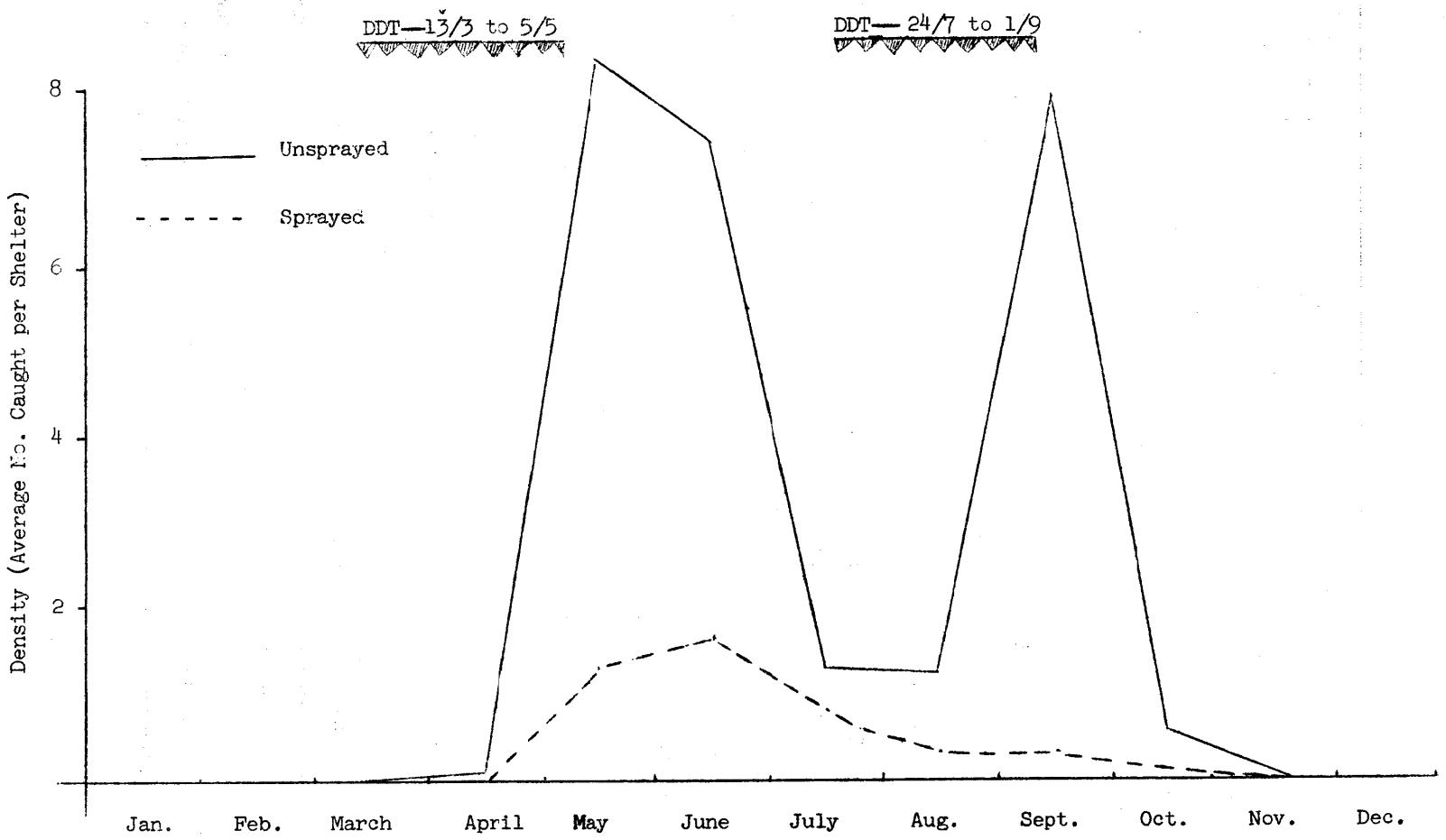
An analysis of the blood digestion stage of the specimens captured in this series of observations made during the peak of the breeding season (May-June) confirms the above finding that a noticeable mortality of A.stephensi must have occurred in the sprayed structures since a significant drop has been observed in the number of half-gravid females recorded in the DDT-treated houses in comparison to those yielded from unsprayed shelters.

The seasonal distribution of A.stephensi and its density during 1965 in sprayed and unsprayed bedrooms is presented on the graph next page.

As A.stephensi is well known as a predominantly zoophylic species, some observations were also made on its zoophylic tendency besides the observations made on susceptibility level of A.stephensi and its density in DDT sprayed area. The explosive character of the epidemic that occurred in Basrah city in 1963 was partly explained by the lack of domestic animals.

There are two observations of epidemiological importance made in southern Iraq in this respect. First: that the precipitin test carried out on 378 specimens of fed A.stephensi revealed the fact that in only 5.6% of the specimens the blood meal of mosquitoes originated from man. The second observation, which is derived from the first, indicates the epidemiological significance of the zoophylic tendency of A.stephensi. Namely, in the course of studies carried out a number of households were investigated in respect of population, insecticidal coverage, surveillance operations, etc., and among others the number of domestic animals were recorded. Shown below are indicative figures in respect of two nahias in southern Iraq, for Mamlaha (Fao) where the

Density of A.stephensi in Sprayed and Unsprayed Bedrooms in Basrah Liwa, 1965



transmission still persisted in 1965, and Shatt al Arab where the number of cases decreased as expected.

Nahia	No. of investigated households	No. of inhabitants	Cattle and horses	API		
				1963 1964	1964 1965	1965 1966
Shatt al Arab	104	896	150	5.3	1.7	0.5
Mamlaha (Fao)	104	778	35	9.3	22.4	10.5

There is no doubt that man/animal ratio as indicated above is not solely responsible for the continued transmission taking place in Mamlaha (Fao), but with other factors contributing to the development of local epidemiological situation in the A.stephensi area.

V DISCUSSION

It is well known that the basic task for the eradication of malaria is to interrupt transmission and to keep the transmission interrupted long enough to eliminate the remaining parasite reservoir amongst the already infected individuals. On the other hand, it is equally well known that the malaria endemo-epidemic potential varies considerably from one area to another.

The malaria endemo-epidemicity is dealt with in the course of a malaria eradication programme by:

i. Applying standard attack measures in order to cope with the intensity of malaria endemo-epidemicity.

ii. Ensuring total coverage of the attack operations in order to cope with the extent of malaria endemo-epidemicity.

Experience has shown that standard attack measures applied with reasonable coverage resulted in successful interruption of transmission and finally eradication of malaria in a number of countries and areas of the world that were originally considered as highly malarious. In some areas, however, particularly in those where technical difficulties occurred, the application of standard attack measures did not lead to the interruption of transmission.

It has to be pointed out that studies so far conducted in areas having met technical obstacles revealed the fact that besides the technical problems, there were always operational and administrative lacunae that have contributed to the non-interruption of transmission.

The example of the resistance of A.stephensi to DDT and the results obtained by the application of the same insecticide against the resistant A.stephensi in southern Iraq illustrates clearly that the transmission of malaria can be greatly reduced, even interrupted, provided attack measures are applied with humanly possible accuracy.

There are other examples of successful interruption of transmission and eradication of malaria in countries or areas where physiological resistance of the vector presented presumably a technical obstacle. This was the case of A.saccharovi in Greece and A.culicifacies in India and some parts of West Pakistan.

It is not the intention of this paper to deny the importance of technical problems manifested through the resistance of the vector to applied insecticide. On the contrary, this paper should further stimulate research workers in all countries of this Region to continue and even intensify their studies in the field and in the laboratories, but bearing in mind all the complexities involved including the ecological factors contributing to the transmission of malaria and the mentality of the man who is applying anti-malaria measures. For the successful execution of a malaria eradication campaign, flexibility of operations is required which means the adjustment and intensification of standard measures in accordance with the specific intensity of malaria endemo-epidemicity of the area concerned. There is no doubt that research workers and technical staff of national malaria services can greatly contribute to the achievement of this task.

VI CONCLUSIONS

Technical problems caused by the resistance of some vectors of malaria to applied insecticides have been experienced in the malaria programmes in Iran, Iraq, Pakistan, Saudi Arabia and the United Arab Republic. While the resistance of A.culicifacies to DDT in a limited area of West Pakistan has had no epidemiological consequences on the progress of the Malaria Eradication programme so far, resistance of A.stephensi in Saudi Arabia and A.pharoensis

in the United Arab Republic has to be viewed from a different angle since in these two countries the Malaria Eradication programmes are still in the planning stage.

The development of the physiological resistance in A.stephensi to dieldrin and DDT in southern Iran and southern Iraq presented a technical obstacle, particularly in southern Iran, where the application of these insecticides on a total coverage basis was withdrawn in 1961.

During an outbreak of malaria in Basrah (southern Iraq) in 1963, DDT spraying was carried out and was found useful in curtailing the epidemic according to an epidemiological study of the epidemic. On this basis, DDT spraying was recommended as the main attack measure for southern Iraq. Simultaneously with the resumed DDT residual spraying in southern Iraq, extensive field studies were undertaken aiming at a continued evaluation of the effectiveness of this insecticide against the DDT-resistant A.stephensi. These complex studies consisting of epidemiological and entomological observations lead to the following conclusions:

1. DDT spraying applied twice yearly at a dosage of 2 g./m^2, has greatly reduced and even interrupted the transmission of malaria in southern Iraq. With the exception of Fao area, the decrease of malaria incidence, in the rest of Basrah liwa, has met the criterion for the interruption of malaria transmission as laid down by the WHO Expert Committee in its Tenth Report.

2. The resumed DDT spraying in southern Iraq has not caused a further selection of resistant gene in the natural population of A.stephensi and there has been no increase in the resistance level of this mosquito in spite of continued pressure with this insecticide for over two years.

The experience gained in southern Iraq from the resumption of DDT spraying in the resistant A.stephensi area is very encouraging and allows the recommendation with reasonable confidence that this insecticide may be used as a main attack measure all over the A.stephensi area with good chances of success provided it is applied with the humanly highest possible accuracy.

However, research workers and technical staff of the national malaria services should continue with field studies on the effectiveness of this insecticide against the resistant vector(s), with a view to determining

whether this insecticide, when applied at the normal or increased frequencies, can achieve interruption of transmission or need to be supplemented with other measures, taking into full consideration the ecological conditions of the area concerned.

ANNEX I

INCIDENCE OF MALARIA IN BASRAH LIWA
BEFORE AND AFTER RESUMPTION OF DDT SPRAYING

Nahia (Population)	Analysis Case Detection Data	Before Resumption June 1963- May 1964	After Resumption 1st Year June 1964- May 1965	After Resumption 2nd Year June 1965- May 1966
Basrah city (252 994)	No. of slides collected	58 483	71 822	92 764
	No. positives: P.v.	2 888	289	64
	P.f.	208	1	1
	Mixed	12	0	2
	Total	3 108	290	67
	ABER	27.1	28.4	36.7
	API/1 000 population	12.3	1.1	0.3
	Positivity rate**	4.54	0.40	0.07
Fao (35 482)	No. of slides collected	7 118	12 390	27 892*
	No. positives: P.v.	206	790	374
	P.f.	120	5	0
	Mixed	3	0	0
	Total	329	795	374
	ABER	20.1	34.9	78.6
	API/ 1 000 population	9.3	22.4	10.5
	Positivity rate**	4.62	6.42	1.34
Seeba (22 705)	No. of slides collected	6 494	9 403	7 804
	No. positives: P.v.	220	194	44
	P.f.	8	0	0
	Mixed	0	0	0
	Total	228	194	44
	ABER	28.6	41.4	34.4
	API/1 000 population	10.0	8.5	1.9
	Positivity rate**	3.51	2.06	0.56
Abul Khassib (39 639)	No. of slides collected	8 850	8 255	11 868
	No. positives: P.v.	379	29	8
	P.f.	17	1	0
	Mixed	0	0	0
	Total	396	30	8
	ABER	22.3	20.8	29.9
	API/1 000 population	10.0	0.8	0.2
	Positivity rate**	4.47	0.36	0.07

* Mass blood examinations were conducted in September 1965 of which, nearly 8 000 slides were collected and 10 malaria cases were detected.

** Positivity rate indicated in support of API.

Nahia (Population)	Analysis Case Detection Data	Before Resumption June 1963-May 1964	After Resumption 1st Year June 1964-May 1965	After Resumption 2nd Year June 1965-May 1966
Shatt al Arab (54 426)	No. of slides collected	12 761	16 455	10 877
	No. positives: P.v.	272	93	25
	P.f.	17	1	0
	Mixed	0	0	0
	Total	289	94	25
	ABER	23.4	30.2	20.0
	API/1 000 population	5.3	1.7	0.5
	Positivity Rate*	2.26	0.57	0.23
Hartha and Zubeir (90 989)	No. of slides collected	9 917	17 140	24 267
	No. positives: P.v.	403	48	36
	P.f.	4	0	1
	Mixed	0	1	0
	Total	407	49	37
	ABER	10.9	18.8	26.7
	API/1 000 population	4.5	0.5	0.4
	Positivity rate*	4.10	0.29	0.15
Margil (60 333)	No. of slides collected	11 824	11 574	15 731
	No. positives: P.v.	219	114	32
	P.f.	15	0	1
	Mixed	1	1	0
	Total	235	115	33
	ABER	19.6	19.2	26.1
	API/1 000 population	3.9	1.9	0.6
	Positivity rate*	1.99	0.99	0.21
Swaib and Qurna (81 849)	No. of slides collected	11 748	14 171	22 026
	No. positives: P.v.	33	25	10
	P.f.	15	0	0
	Mixed	1	0	0
	Total	49	25	10
	ABER	14.4	17.3	26.9
	API/1 000 population	0.6	0.3	0.1
	Positivity rate*	0.42	0.18	0.05

* Positivity rate indicated in support of API.

Nahia (Population)	Analysis Case Detection Data	Before Resumption June 1963-May 1964	After Resumption 1st Year June 1964-May 1965	After Resumption 2nd Year June 1965-May 1966
Mudiena (34 269)	No. of slides collected	13 269	10 384	15 285
	No. positives: P.v.	227	69	7
	P.f.	-	0	0
	Mixed	-	0	0
	Total	227	69	7
	ABER	38.7	30.3	44.6
	API/1 000 population	6.6	2.0	0.2
	Positivity rate*	1.71	0.66	0.05
TOTAL (672 686)	No. of slides collected	150 454	171 594	228 514
	No. positives: P.v.	4 847	1 651	600
	P.f.	404	8	3
	Mixed	17	2	2
	Total	5 268	1 661	605
	ABER	22.4	24.9	34.0
	API/1 000 population	7.8	2.5	0.9
	Positivity rate*	3.50	0.99	0.26

* Positivity rate indicated in support of API.