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DISEASE CONTROL WITH INSECTICIDES

A Review of the Literature

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Much has been written on the control of insect disease-vectors, but far less information is available on actual disease control. This is a natural phenomenon since the vector obviously must first be reduced before disease suppression can occur. Furthermore, some vector control is apparent almost immediately after initiation of control activities, whereas several years of effective vector-control are often required before measurable results of disease suppression are possible. The expense of collecting adequate epidemiological data, together with the inherent difficulties often accompanying such a procedure, such as misdiagnosis and inadequate samples, are other complicating factors. In diseases such as malaria or endemic typhus, reported incidences may deviate considerably from actual, since mild cases may not be treated by a physician and, especially in rural areas, diagnosis is often entirely symptomatic and not confirmed by laboratory tests. It is apparent, therefore, that a reliable appraisal of disease suppression must lag considerably behind vector control.

There have been, however, what appear to be reliable data collected on actual disease control from certain intensified vector-control campaigns during the past few years.

Probably the earliest use of insecticides in disease control pre-dates any knowledge of the relation between the two. Howard [42] suggested the use of oil to kill mosquitos in 1892, before Ross had proved that mosquitos could transmit malaria. By 1914, oiling for mosquito control was a recognized part of the malaria vector-control programme in Malaya. Perhaps a better example of the unknowing control of disease by use of insecticides is the widespread control of houseflies by insecticides long before the effects of such control on the incidence of any disease had been demonstrated. As might be expected, insecticides were purely incidental in the early

attempts at disease control through vector control. Thus for many years after the discoveries that malaria, yellow fever, and filariasis were mosquito-borne, efforts at vector control emphasized such things as screening or netting to protect the individual from the vector, isolation of susceptibles from the reservoir, or reduction of the vector population through drainage or other engineering procedures. Gradually such procedures as oiling and the use of paris green were added to aid in the reduction of vector populations.

It was only after the demonstrated success of residual sprays in drastically reducing vector populations that the statement was made that an insecticide (DDT) " must be considered as the basic element in the control of malaria ".[61]

In reviewing the literature on the control of disease by the use of insecticides, it becomes apparent that there is a wide variation in criteria of disease control. A good many papers can be found in which the author merely states his opinion that a disease was controlled without presenting epidemiological evidence. In other cases, epidemiological evidence is presented but is rather obviously of meagre value from a scientific standpoint because of the lack of adequate controls or because the samples were too small. In relatively few cases has adequate scientific evidence been presented to provide irrefutable evidence of disease control. Since it is not often apparent from the published information how adequate the experimental design may have been, it would seem presumptuous in a review of this sort to attempt to evaluate such cases. All that is therefore attempted is to present the evidence in the spirit in which it is available in the published literature, or, where the original papers were not available, as nearly as can be judged from abstracts. No claim is made that this review is complete, for, with the present interest in this field, no review would remain complete for long. It is felt, however, that enough examples are included to provide a reasonable picture of the situation as it now exists.

Mosquito-borne Diseases

Malaria

Apparently the first clear-cut demonstration of the role of insecticides in disease control was by Ross.[67] He began the use of pyrethrum as an anti-adult insecticide in Natal and Zululand in 1930. The principal vectors concerned were *Anopheles gambiae* and *A. funestus.* Results as measured by mortality attributed to malaria were not dramatic until the sixth year, when 119 deaths (a little less than 0.1 per 100,000) were attributed to malaria as against over 800 deaths in the years of the experiment with the next lowest mortality figures. During this sixth year fever was said to be absent from areas that had never before been known to be free of it in any season. The author's judgment of the effectiveness of the

insecticide, apparently upon the basis of morbidity, was more striking. He claimed that

" quinine . . . failed to control the spread of fever, and . . . within three weeks or so of the commencement of the systematic use of insecticide, we have invariably had a sudden drop in the number of cases in huts and barracks and epidemic conditions have ceased to exist. Empirically, we know that a weekly spraying holds down fever . . . "

Rather striking figures are given for a native area sprayed with pyrethrum only, during the 1933-34 season. During the two seasons preceding spraying, 12 deaths and many fever cases occurred in 1931-32, and 43 deaths with 108 new infections in 1932-33. Following the introduction of the spraying programme, only one death and two new infections occurred during the 1933-34 season. Moreover, an adjoining area without insecticide (but well isolated from the test area) reported 15 deaths and a large number of new infections during 1933-34. The insecticide used was a 2% pyrethrum concentrate diluted 1 : 18 with paraffin-oil and applied at the rate of 100 ml per 1,000 cubic yards (764.5 m^3).

During the 1934-35 season, De Meillon [19] conducted a similar campaign, also in South Africa, where the chief vectors were *A. funestus* and *A. gambiae*. According to his figures, taken in November 1934 before the spraying was begun, and at the close of spraying in June 1935, the spleen-rate was reduced from 43% to 4% as a result of daily spraying. Semiweekly spraying reduced the spleen-rate from 33% to 12% and weekly spraying reduced it from 34% to 17%. The spleen-rate in the control area dropped from 38% to 30%. He reports that even more important was a marked reduction in the size of spleens examined. He states the fundamental " idea underlying malaria control by anti-adult measures—namely, that it is not intended to destroy all *A. gambiae*, but only those which are infected, which past experience has shown are largely to be found indoors ".

In 1936, Covell et al.[15] adapted the procedure to conditions in India, where *A. culicifacies* was the principal vector. They used a 2% pyrethrum concentrate diluted 1 : 19 with kerosene and applied at the rate of 2 ml per 1,000 cubic feet (28.3 m^3). Because of the popularity of the programme and the clamour for its extension, they were unable to maintain adequate checks. However, over a six-week period, during which 130 quarters were sprayed and 11 in an isolated area were held unsprayed, 1.4% of the population in the sprayed quarters had fever as against 45.5% of those in the unsprayed area. After spraying all quarters, the combined case-rate was 0.5% of the population in September and October, even though the peak of malaria in Delhi was in the last week of September of that year. The following year (1937) they reported a marked reduction in both spleen-rate and spleen size as a result of spraying twice a week.

In 1938, Russell & Knipe [68, 69, 70, 71] instituted a malaria-control programme in a rural village in southern India where *A. culicifacies* was the prin-

cipal vector. They used pyrethrum insecticide, applying it once a week, except in one area where it was applied twice a week. They conclude that spray-killing of adult mosquitos is very effective in reducing malaria transmission but that it must be continued from year to year. These conclusions were based on a comparison of malaria season parasite- and spleen-rates and spleen sizes in some seven treated villages as compared with nearly as many untreated villages.

As a contrasting experiment, Knipe & Russell [45] attempted to control malaria resulting from irrigation practices in an area of 7 square miles (18 km^2) in southern India by antilarval measures, which included the use of paris green as well as other established techniques. Their efforts were successful as is indicated by a comparison of spleen- and parasite-rates in test and untreated villages.

With the advent of DDT during the second World War, a new anti-adult measure became possible in the form of residual sprays that kill a large percentage of mosquitos that contact the treated surfaces even months after treatment. This technique has been widely exploited in malaria-control programmes. Though the major portion of such programmes has been evaluated in terms of mosquito control, some have also been evaluated in terms of reduction in disease incidence. Some typical examples from various parts of the world follow.

United States of America. A five-year eradication programme by some 13 States in co-operation with the Communicable Disease Center of the US Public Health Service was begun in 1947 following two years of preliminary experience. Malaria was at a low ebb and was gradually decreasing at the beginning of the programme. In 1934 a total of 131,980 cases was reported from 14 southern States ; this had dropped to 77,135 in 1940, to 49,966 in 1945, and to 9,356 in 1948. The effect of the programme in accelerating this trend cannot be definitely evaluated because of many factors, including improvements in reporting methods during the period. Andrews [3] has discussed the various factors that may be involved in the generally decreasing incidence of malaria in the USA. Such factors as improved economic conditions, the use of antimalarial drugs, population migration out of rural areas, increased cattle production (called anopheline deviation), and antimosquito measures, including the use of insecticides, are considered important. Variations in human or anopheline susceptibility are considered unlikely.

In the Tennessee Valley Authority's programme for malaria control around its reservoirs, DDT has been applied extensively as a larvicide for the control of *A. quadrimaculatus*, and in a limited number of areas as a residual spray to entire premises. This use of insecticides has, however, been only one factor in a broad programme in which primary emphasis is placed upon non-insecticidal practices such as reservoir preparation,

shore-line maintenance, permanent shore-line improvement, and water-level management.[40] In the annual fall malaria blood-film survey conducted around TVA impoundments in 1949, no positives were found for the first time in the history of the development. This, however, does not mean that no malaria existed around the impoundments, for there is good evidence that a limited number of cases of malaria did occur. Because of the multiple nature of the programme, it is impossible to ascertain what portion of this reduction in malaria incidence has resulted from the use of insecticides.[8]

Puerto Rico. In November 1944, a DDT residual spray programme was initiated in Puerto Rico. Three blood-film surveys showed a progressive decline in percentage of positive malaria slides from 5.8% in the rainy season, October 1944, just before the first treatment, to 2.8% in the dry season, March 1945, and to 0.91% during the rainy season, October 1945. Corresponding figures for untreated village were 4.7%, 1.5%, and 3.8%.[82]

Panama. Trapido [87] has reported on the residual spraying of dwellings with DDT in Panama, where *A. albimanus* is the principal vector. Cumulative parasite index for the year 1945, following initiation of spraying in October 1944, was 14.8% in a treated town compared with 52.0% for the same period in the untreated towns. Considering falciparum malaria only, the corresponding figures were 7.4% for the treated town and 29.4% for the untreated towns.

Trinidad and Tobago. An extensive malaria-control programme in Trinidad has been supplemented by an attempt to eradicate malaria from the Island of Tobago, where the principal vector is *A. aquasalis.* The major weapon in this eradication programme was the residual spraying of houses with DDT. This was supplemented, however, by larviciding with an oil containing 5% DDT. The programme was begun in January 1948. Though at the time of the published report for 1948 no definite conclusions could be drawn, it is claimed that a very considerable reduction in the total number of slides positive for malaria parasites had already resulted.[88]

TABLE I. REDUCTION IN SPLEEN- AND PARASITE-RATES IN BRITISH GUIANA AS A RESULT OF DDT TREATMENT

Index	Pre-treatment	Post-treatment in terms of months						
		6	12	18	24	30	36	42
Spleen-rate	71.6	46.5	32.0	28.2	17.9	12.2	8.0	4.0
Parasite-rate . . .	40.3	18.0	37.7	33.3	27.1	41.1	6.9	3.0

British Guiana. Initial experiments were started in British Guiana in 1945. Since then residual spraying with DDT has been extended and an

interval of 8 to 10 months was set between applications (150-160 mg per square foot (900 cm²). Without the use of larvicidal measures, residual spraying has eradicated *A. darlingi* from the coastal belt.[30] Falciparum infections rapidly decreased, in most places disappearing within 24 months. Table I shows an example of decline in spleen- and parasite-rates in East Indian children following treatment.

Venezuela. Gabaldon [26] indicated an average of 112 deaths from malaria per 100,000 population during 1941 and 1945 and 15 deaths per 100,000 during 1948. He attributes the reduction largely to DDT residual spraying of houses.

Chile. DDT was used as a residual spray in dwellings and out-houses, and was used as a larvicide from October 1944 onwards. Since April 1945, not a single indigenous case of malaria has been diagnosed. Chile is perhaps the only American country in which both malaria and anophelines have been eradicated.[58]

Brazil. There was a marked fall in the number of human malaria-parasite carriers and a very notable fall in the number of persons applying for treatment for malaria in the Doce River Valley following residual spraying of houses with DDT at the rate of 2 g per m². The first application was started in September 1946, and a second in January 1947. About 85% of all houses were treated.[10]

American tropics. Elmendorf [23, 24] reported on some field experiments in an unidentified country along the Atlantic seaboard of the American tropics in which DDT was used as a residual spray in one of four towns under observation. All four towns had a severe to hyperendemic incidence of malaria as measured by spleen and blood findings at the beginning of the experiment. In two of the towns, drastic reductions in the incidence of parasitaemia resulted from the use of drugs. In the third town, 5% DDT in diesel oil was applied by aeroplane once a week. No significant lowering of malaria incidence was noted until after 12 months, when 12.7% of the population were found to be positive as compared with 85.4% before treatment and 57.6% in a town with no control. In the fourth town, 5% DDT was applied as a residual spray at the rate of 300-400 mg per square foot (900 cm²). In this case, a single application resulted in a reduction of incidence from 92.1% in the preceding year to 15.6% after eight months, as compared with 57.6% in the untreated town at the same time.

Netherlands. Malaria has not been as serious in the Netherlands as it has in more tropical areas, and there seems to be no report of a malaria-control campaign using DDT. However, Swellengrebel & Kraan [85] have reported on 10 years of house-spraying with pyrethrum solutions to control malaria in North Holland. They claim that it has greatly reduced malaria in rural areas, though the results were unsatisfactory in urban areas. The

severe epidemic which started in 1944 was not felt in rural villages which were under control.

Spain. Lozano Morales [50] has reported on the use of benzene hexachloride in the hyperendemic zone of the Guadalquivir marshes. Benzene hexachloride was applied at the rate of 500 mg per m^2 three times during the 1947 season at 60-day intervals. This was followed by a drop in morbidity, reduction of incidence to the point where the only cases observed were relapses, the disappearance of pernicious types, and the total suppression of falciparum infection.

Sardinia. At the beginning of a DDT-spraying campaign in 1946 there were 17,186 cases of malaria in one district alone. During the first six months of 1948, the number in the same district was 457 of which only 31 were new.[66] The full story of the Sardinia programme yet remains to be told.

Italy. A DDT residual spray programme in southern Italy was begun in January 1945. By August 1945, the spleen index dropped from 43% to 25%, and the parasite index from 21% to 1%. Concurrently in the check area, the spleen index rose from 56% to 63%; the parasite index, from 18% to 41%; and the average size of the spleens examined increased.[1] A continuous search was made for new cases, but only one was found.[79] Antimalaria drugs were not considered an important factor in this reduction. At the Second World Health Assembly it was reported [101] that in Italy a marked decrease in general and infant mortality had been noted in those regions where DDT had been used. The cause of mortality was not mentioned but was presumably largely malaria.

Elba. DDT house-spraying at the rate of 2-3 g per m^2 was initiated on the Isle of Elba in September 1946. At the same time, larvae were attacked by means of paris green. By 1948, drastic lowering of malaria incidence had been obtained. In 1946 there were 201 primary infections and 323 relapses. In 1947 there were only 31 primary infections, though there were 362 relapses. In 1948 there were no primary infections and only 22 relapses.[12]

Greece. A DDT spraying programme was initiated in 1946 and after the first season the spleen-rates were half the previous rates recorded. The parasite-rates averaged 2.1% compared with 20.6% before initiation of the programme. In three non-protected areas the parasite-rates were higher than previously.[49] Hospital admittances for diagnosed malaria cases showed a satisfactory decline.[91]

Cyprus. The campaign for the eradication of anopheline mosquitos from Cyprus using DDT as the principal weapon was begun in 1946. Malaria incidences, as reflected in new cases and in blood and spleen indices, have been brought almost to extinction during the first two seasons,

though there had been a gradual decline since 1944 even in the untreated area of the island.[4] In 1944 there were 7,686 cases of malaria in Cyprus but in 1948 only 406 cases, of which 3 were of recent origin. In school-children, splenomegaly dropped from 32.4% to 10.6% and parasitaemia from 51.9% to 1.3% from 1944 to 1948.[75]

Palestine. A reduction in average size of spleens examined was noticed within a period of eight months subsequent to initiation of a DDT residual spray programme. The author believes the programme also reduced the composite incidence of typhoid, diarrhoea, dysentery, and conjunctivitis.[7]

Mauritius. The parasite index of the general population was reduced from 37.6% in August 1946, to 12.9% in June 1947, by residual spraying with DDT in kerosene between September 1946 and March 1947. On the latter date, the parasite index in the control village was 46.5%. Based on thick films, the parasite index was reduced by two-thirds in the general population and by one-half in schoolchildren.[86]

India. In the Kanara District, where *A. fluviatilis* is the vector, some previous control had been obtained by other means, but in 1946 residual spraying with DDT was initiated. At the end of the first year, cumulative spleen-rates in the sprayed and unsprayed villages were 14.4% and 72.2% respectively ; and parasite-rates 3.8% and 14.6% respectively. At the end of the second year, the spleen-rate in the sprayed villages declined to 11.6% and the parasite-rate to 2.7%. In the Dharwar District, where *A. culicifacies* is the vector and no previous control had been practised, at the end of the first year, cumulative spleen-rates in the sprayed and unsprayed villages were 19.6% and 28.3% respectively ; and parasite-rates 4.4% and 7.5% respectively. At the end of the second year the spleen-rate in the sprayed villages declined to 10.6% and the parasite-rate to 0.9%.[93, 94] Viswanathan [92] claimed that by the end of the third year of treatment in these two districts the use of DDT had not only greatly reduced morbidity but that malaria death-rates were greatly reduced and that the birth-rate was increased by about 5 per thousand. Effects on the death-rate due to diarrhoea and dysentery as well as the total elimination of plague were also claimed. Ramakrishnan et al.[65] reported on a pilot scheme for malaria control in the betelnut growing area in the Kanara District, where 2.5% DDT suspension and DDT-MKE emulsion in water were applied as indoor residual sprays on houses and cattle-sheds at the rate of 50 mg DDT per square foot (900 cm^2). Comparison between a small number of children (less than 100 in each area) in treated and in untreated areas of a village showed consistent reduction in spleen-rates and consistent reduction in parasite-rates in treated areas as contrasted with an increase in parasite-rate from 4.6% to 19.3% in untreated areas. The infant parasite-rate was maintained at zero in treated areas though it rose to as high as 9.1% in some untreated areas.

Malaya. Nair [57] reported that an expected seasonal increase of malaria in a hyperendemic village was kept in check by three residual sprayings of DDT.

New Guinea. A significant increase in the parasite-rate (all age-groups) and spleen size was recorded in an untreated village ; while in a DDT-treated village, a slightly decreased parasite index and no true increase in spleen size was found. In contrast with most other reported programmes, no decrease in falciparum malaria was noted in the sprayed village.[5]

New Hebrides. During December 1943, before the use of DDT, 41 primary malaria infections of military troops were reported. During November and December 1944 no new infections were reported. Yust [103] claims that this reduction in the incidence of malaria in military troops must be attributed in part to the use of DDT.

South Pacific. Downs et al.,[21] discussing the epidemiology of malaria in the South Pacific military campaign of 1942-45, conclude that " it is clear that early insect control measures (largely insecticidal) . . . can prevent malaria and other insect-borne diseases from jeopardizing the success of military campaigns in the tropics".

Summarizing, there has been, in general, a difference in results with different species of *Plasmodium.* Most frequently, falciparum malaria has been more affected by the DDT residual treatment than have the other types, but there have been some notable exceptions.

Perhaps it is only natural that only the successful campaigns would be described in publications, but the negative reports are conspicuous by their absence. The authors recently have learned that endemic malaria continues in Sicily at a high level in spite of an intensive residual DDT programme. *A. superpictus,* a mosquito that shows no special preference for houses, is the vector. Many of the people sleep out in the fields during the summer, thus leaving themselves exposed in a place favoured by the vector and where residual spraying offers no protection.

Results of malaria control by residual spraying are so promising that the WHO Expert Committee on Malaria has concluded that " even when local conditions appear to be unfavourable, the application of residual spray may be attended with conspicuous success. The committee would therefore urge that the method be given a preliminary trial in all antimalaria campaigns however unfavourable the local conditions appear to be." [102]

Yellow fever

If evidence on the effectiveness of insecticides in the control of malaria is too voluminous to review adequately here, objective epidemiological evidence in the case of yellow fever is at the other extreme, or essentially

non-existent. Anomalously, this is doubtless in part due to the fact that antimosquito campaigns have been such an effective aid to other control measures in reducing the incidence of yellow fever that epidemiological evidence is no longer available. That is to say that no highly endemic areas of urban yellow-fever now exist where it seems feasible to attempt an evaluated control-programme by means of insecticides alone. Whenever and wherever an outbreak of urban yellow-fever now occurs, it is immediately combated by all available means, including immunization, medication, and quarantine, as well as a variety of antimosquito measures. As a result, it has been difficult to evaluate any one weapon by itself. In the fight against yellow fever, insecticides alone are used as larvicides, as residual sprays, and as aerosols (especially in quarantine work). In fact, the use of insecticides has been of primary importance in several campaigns to eradicate the yellow-fever mosquito from certain areas. In the control of yellow fever in Brazil by means of vector eradication, insecticides were not stressed though they did play an important role.[80]

Dengue fever

A similar situation to that of yellow fever exists in the case of dengue fever. However, in the latter case there have been some recent epidemics of sufficient size to furnish interesting statistics. In no case have insecticides been relied upon completely, but both in the Hawaii epidemic of 1943-44 [31] and in the Madagascar epidemic of 1947 [54] insecticides were considered as major weapons.

Simmons [76] cites a spectacular example of the usefulness of DDT against this disease. An extensive epidemic of dengue on Saipan during August 1944 was terminated by spraying the occupied area with an oil solution of DDT from aeroplanes.

Encephalitis

The encephalitides are another group of mosquito-borne diseases which are in the category of yellow fever and dengue in that the incidence has not been large enough in man, or sufficiently concentrated, to provide valid epidemiological evidence of the importance of insecticides. In the epidemic of Japanese B encephalitis on Okinawa in 1945, there seems little doubt of the importance of mosquito-control measures (presumably largely DDT sprays, though the original reference has not been consulted) in breaking the epidemic. The incidence was greater in the northern mountainous wooded area, where mosquito-control measures were instituted late or were difficult on account of the terrain. The incidence on the island of Heanza fell abruptly two or three weeks after the introduction of intensive antimosquito measures.[56] There are conflicting reports from Okinawa and Japan which appear to be unpublished but which indicate that in certain areas DDT did not effectively control Japanese B ence-

phalitis, and this has been used as evidence of vectors other than mosquitos. Hammon et al. [36] in studying western equine encephalitis in California reported that a material reduction in the number of resting mosquitos in chicken-houses did not cause a significant decrease in the incidence of infection in the birds. These two cases are of considerable interest in that they imply that the failure to control a disease by use of an insecticide may provide useful information as to the vectors ; thus, if the insecticide in question is known to be highly effective against a suspected vector, its failure to control the disease may indicate the presence of other vectors which are not so susceptible to the method used.

Filariasis

The high endemicity of filariasis in native populations of certain tropical countries should afford an excellent opportunity to study the effect of insecticides on this disease. Apparently, the only carefully planned experiment of this nature so far published was carried out on the island of St. Croix, Virgin Islands. Even there the experiment was terminated prematurely by the superimposition of other control measures. However, during a 21-month period in which residual house-spraying with DDT was the only major control measure, the *Wuchereria bancrofti* infection-rate in schoolchildren dropped from 13.3% to 10.6% and the average microfilaria count fell from 74.1 to 45.8 per 0.04 ml of blood. The authors stated that " the differences are not quite statistically significant by conservative criteria," but they do not state what statistical tests were used nor what level of significance was chosen.[11]

Louse-borne Diseases

Three major louse-borne diseases—epidemic typhus, trench fever, and relapsing fever—may well be considered together because of their many similarities. They have all been associated with wars in the past, and epidemic typhus in particular has been considered as an unavoidable adjunct of war. During the second World War it was considered a foregone conclusion that epidemic typhus would be a major problem. The US Typhus Commission was organized to combat this threat. Extensive plans for gas chambers were made first. Then the development of MYL louse powder in 1942 [84] replaced the delousing chambers previously used. DDT louse-powder finally displaced practically all former methods of combating the louse-borne diseases. Its effectiveness in terminating the civilian typhus epidemic which threatened Naples late in 1943 won worldwide acclaim for this new insecticide. The number of cases dropped sharply within one month, and within two months the epidemic was broken after 1,404 cases of typhus had been reported in Naples alone.[13, 78, 97] DDT

proved so successful that during the war there were only 61 cases of epidemic typhus and 4 cases of relapsing fever in the US Army, and none of the latter was considered as louse-borne.[76]

Gear & Murray [29] reported that an epidemic of typhus in eastern Transvaal was successfully combated with DDT in 1945.

After two general dusting campaigns with DDT, no new cases of typhus were observed in the epidemic of 1945 in the native population of northern Nigeria.[55]

According to Hugonot,[43] DDT shares the honours with vaccination for making epidemic typhus practically unknown in the French Army during the Italian campaign.

Davis [18] reports that at the time of the liberation of Belsen there were 3,500 cases of typhus in this camp. All internees were heavily infested with lice, which averaged 100 per person. Within nine days, all inmates were dusted with DDT. The effect was dramatic; the decline in incidence of new cases was sharp, the last case commencing with fever two weeks after the first delousing had been completed. Snyder [77] has presented a history of louse-borne typhus in the Balkans, Germany, Iran, Italy, North Africa, Poland, and Spain. He reports that the incidence in 1945-46 was relatively low because of newer control-measures including DDT. Sande [72] described successful results obtained with DDT in combating louse-borne typhus in an endemic area in Spain. Outbreaks of this disease occur during the spring when there is a great influx of labourers.

Erzin [25] reports that an epidemic of typhus in Turkey during the war years 1942-44 was brought under control by the extensive use of DDT, vaccination, and public-health propaganda. DDT was used with great success during the typhus epidemic in Hungary during the period 1945-47.[104] Petrilla [62] says that the incidence of both typhus and relapsing fever in Hungary in 1946 decreased parallel with the more extensive use of DDT powders among other things.

Information on the control of louse-borne typhus by DDT during the second World War is well summarized in a group of three papers covering Europe [32], Japan [73], and the Mediterranean.[6]

In an epidemic of typhus fever in two Mexican villages, prompt and complete control was achieved by a combination of dusting of clothing with 5% DDT and treating of heads with phenyl cellosolve.[59]

Viel & Romero [90] call attention to the striking contrast between the ease with which one epidemic of exanthematic typhus in south Chile was controlled by the use of DDT and the elaborate organization needed to deal with an earlier one which occurred before DDT was available.

An epidemic of relapsing fever in Kenya was terminated rapidly by control measures that stressed the use of 5% DDT powder.[28]

The use of DDT dust essentially eliminated relapsing fever in isolated test villages in Tunisia in 1945.[35]

An epidemic of relapsing fever in Abadan (Persia) between November 1945 and June 1946 closely followed the degree of coldness of the weather until the application of DDT in January caused a drop in incidence.[9]

Flea-borne Diseases

Murine or endemic typhus

Davis [16] reported very encouraging results from DDT dusting in San Antonio, Tex., where he found only 4 human cases in treated premises and 10 in premises not yet treated as against 20 cases in the same area before treatment began, and 23 cases during the treatment period in an untreated area.

The number of reported human cases of murine typhus in the USA as a whole rose from 1,882 in 1940 to 5,401 in 1944. In 1945 a flea-control project was begun in 11 States using 10% DDT dust. In that year, the number of human cases was 5,193 ; in 1946, there were 3,365 ; and in 1947, there were 2,034, an overall decline of about 62%. About 1,200 cases were expected in 1948 [99] and 1,184 actually were reported in *Public Health Reports*. During 1946, the differential between the percentage decrease in cases in dusted counties and the percentage increase in undusted counties was 41.1%. In the first half of 1947 the differential was 56.4%.[98]

The incidence of human murine typhus fever was reduced significantly by DDT dusting in two special study counties in Georgia as shown by comparison with previous experience in these counties and by concurrent comparisons with data from an untreated county.[41]

During the five-year period ending in 1943, Chatham County, Ga. had the highest human incidence of typhus fever of any county in the USA. Continuing that trend, there were 132 cases in 1944 and 129 in 1945. Late in 1945 a carefully planned DDT dusting programme was put into effect. In 1946 the cases dropped to 15 and the number of cases did not exceed 10 in either 1947 or 1948.[14]

Plague

Gordon & Knies [33] using DDT reported the control of an epidemic in Dakar as early as 1944 and another in Casablanca in 1945.

Localized recrudescenses of plague in Ngamiland were eradicated by dusting 6,000 huts once every four months with DDT.[17]

Macchiavello [51, 52] reports, on the basis of his experience with an epidemic in Peru, that the application of DDT, followed by poisoning with 1080 (sodium fluoroacetate), promises to be the procedure of choice in the control of epidemics of bubonic plague. Pollock [64] has reported the control of an epidemic in Haifa in July 1947 using DDT alone. Dr Niyazi Erzin, in a private communication to the US Public Health Service, reported a successful campaign against this disease in Turkey.

Viswanathan [92] claims the elimination of human cases of plague in the Kanara and Dharwar Districts of India following use of DDT in a malaria-control programme during 1946, 1947, and 1948. There were cases of plague in rats, and in the adjoining Mysore State there was a plague epidemic during this period.

The Second World Health Assembly [100] approved the objective of the elimination of plague from the endemic areas or small foci where it has persisted for years, by the combined use of modern rodenticides and insecticides with residual action. By these means, it is claimed, sea- and airports, ships and aircraft, can be made plague-free and plague-proof so as to prevent international transmission of the disease.

Fly-borne Diseases

Enteritis

In the case of mosquito-, louse-, or flea-borne diseases, the relationship between the etiological agent and the vector appears to be so definite, and in many cases even obligatory, that it often appears to be only a matter of logic that appreciable reduction of vector populations must have an effect on disease incidence.

In the case of those diseases that are believed to be transmitted by the so-called filth flies, the conclusion is not so obvious. It is interesting that, though the role of flies in transmitting such diseases as enteritis has been suspected probably longer than any other arthropod-disease relationship, the objective evidence in terms of epidemiology has been strikingly absent until lately.

Berberian [7] expressed the opinion that the use of DDT in Palestine has reduced the composite incidence of typhoid and other fevers, and diarrhoea and dysentery. Viswanathan & Rao [94] also expressed such an opinion as regards diarrhoea and dysentery. Viswanathan [92] found a material reduction in deaths due to diarrhoea and dysentery during the years 1946 to 1948 in the Dharwar District of India where DDT spraying measures designed for malaria control included the spraying of cattle-sheds as well as home dwellings. Semple [74] noticed unusually few cases of dysentery and gastro-enteritis in Malta during a DDT residual spraying programme in 1945.

According to La Face,[47] Missiroli observed a decline in the incidence of infant diarrhoea in areas where houseflies had been controlled with DDT. It is claimed [63] that the use of DDT and benzene hexachloride, as aerosols, resulted in eradication of flies and termination within eight days of a dysentery epidemic in one Spanish village.

Apparently the only objective evaluation of the effectiveness of fly control on enteritis was that of Watt & Lindsay.[95] They found significantly less *Shigella* infections in infants in sprayed towns than in untreated towns.

This was directly correlated with fly abundance. When the two groups of towns were reversed as regards control measures (DDT spraying primarily), the fly abundance reversed within a matter of three weeks and so did the incidence of new *Shigella* infections within three months. Fly control had less effect on *Salmonella* infections, and there was abundant evidence that no degree of fly control could be expected to reduce infant diarrhoea below a certain level.

Cholera

Although no epidemiological evidence is presented, Ouchterlony [60] reports that DDT was used against flies in combating the epidemic of cholera that occurred in Egypt in 1947 and 1948.

Sandfly fever

Semple [74] reported an epidemic of sandfly fever in Malta in 1944 which was controlled by the use of 5% DDT in kerosene as a wall-spray. Three applications at the rate of 56 mg per square foot (900 cm^2) were used. Jacusiel [44] found some evidence indicating a decline in sandfly-fever incidence among troops in an area of Palestine as a result of widespread spraying of houses with DDT. Hertig [37] reports that the British promptly controlled sandfly fever in Greece by spraying their barracks with DDT. According to him, about 25% of the personnel of the United Nations Relief and Rehabilitation Administration (UNRRA) had sandfly fever in 1945, but in 1946 their quarters were sprayed and no cases at all were reported among some 2,000 employees.

Leishmaniasis

Hertig & Fairchild [39] controlled *Phlebotomus* in two large construction camps in Peru by the use of DDT residual sprays and found this to be followed by an almost complete cessation of new cases of cutaneous leishmaniasis. In Canea (Crete) a marked decrease of oriental sore had coincided with the application of DDT. The control of kala-azar in Canea is attributed to the reduction of the dog population rather than to DDT. The effect of DDT in maintaining the low level after the dog population returned to normal cannot be evaluated. [37, 38]

An increase in the incidence of kala-azar in Palermo has resulted in a campaign against the sandfly by means of DDT. D'Alessandro et al.[2] are optimistic but present no data on results.

Onchocerciasis

Epidemiological data are missing but Vargas [89] reports that repeated applications of DDT (1 to 5 parts per million) gave almost complete extermination of the simuliid vector. Similarly, a very successful campaign was carried out against *Simulium neavei*,[27] the vector of onchocerciasis,

ending in complete extermination of the insect, but no data on disease suppression is given. Doubtless, one reason for the lack of epidemiological evidence is associated with the very long incubation period, which means that there would be an unduly long delay between vector control and epidemiological effects.

Trypanosomiasis

African sleeping sickness is an outstanding example of a disease which has so far effectively withstood efforts for its control with insecticides. The habits of the vectors (various species of tsetse fly) are such that their control by insecticides has been very impractical, though efforts with DDT and benzene hexachloride applied as an aerosol have shown promise in local areas. Dutoit & Kluge [22] report 85% decrease in tsetse-fly populations in Zululand as a result of three applications by aeroplane of 5% DDT sprays. Such published results have been on too small a scale to have any influence on the disease as yet.

Bartonellosis

Hertig & Fairchild [39] found almost complete control of bartonellosis after using DDT residual sprays against *Phlebotomus* in two large construction camps in Peru.

Hemiptera-borne Diseases

Chagas' disease

Chagas' disease is another example of a disease which reasonably should be controlled by insecticides. However, the triatomas have been very resistant to DDT as well as to most of the older insecticides. Dias [20] says that the best method of eliminating triatomas still is to burn the infested huts. Nevertheless, pyrethrum sprays have given some worthwhile results and there is some evidence that the triatomas can be controlled adequately by the use of benzene hexachloride. Apparently, nothing has been published on the effect of such efforts on the incidence of Chagas' disease.

Mite-borne Diseases

Tsutsugamushi fever

Scrub typhus has been controlled to a marked extent by the use of chemicals. Repellents were used widely by the armed forces as a prophylaxis against scrub typhus and were presumably highly effective in this regard, though other methods of controlling the chiggers were combined with the use of the repellents in this connexion.[76]

Dibutyl phthalate as a repellent was found to be a valuable preventative of this disease. [81] Welt [96] reports an experimental use of dimethyl phthalate as protection against scrub typhus. Three groups of soldiers were used in these tests in a highly endemic area. One group received no dimethyl

phthalate, and they had the highest incidence of the disease. A second group had their clothes sprayed with the repellent and received some protection. A third group had their clothes impregnated with the compound and they had the lowest incidence.

Scabies

Benzyl benzoate was quite effective during the war in the treatment of scabies in American troops.[76]

Tick-borne Diseases

There appears to be no epidemiological evidence available as to the effectiveness of chemicals in the control of tick-borne diseases, though there are at least limited experiments under way in various parts of the world. Leon & de Leon [48] in describing relapsing fever in Ecuador suggest as prophylaxis the eradication of ticks and bedbugs with DDT. The evidence as regards bedbugs is based upon the absence of ticks and the scarcity of lice in certain areas where the disease abounds.

Miscellaneous Diseases

Diphtheria

A novel report from the literature is that cockroaches were found to harbour true diphtheria bacilli during a serious increase in the number of diphtheria carriers in a large hospital in the Netherlands. After a campaign for exterminating these pests (presumably with insecticides, and most probably with sodium fluoride), the number of new diphtheria infections dropped and finally stopped altogether.[34] It is obvious that the reported relation between diphtheria and cockroaches needs further confirmation.

Bilharziasis

Although bilharziasis is not an insect-borne disease, the chemical control of the cercariae of *Schistosoma* and of schistosome-bearing mollusca is sufficiently similar to the use of insecticides to justify mention of it here. Kuntz & Stirewalt [46] report that at practical field-rates of application, the laboratory findings indicated that DDT was not dependable against cercariae of *S. mansoni.* McMullen & Ingalls [53] report that the most efficacious compound which they tested was the dicyclohexamine salt of dinitro-*o*-cyclohexyphenol, known as K-604. Stirewalt & Kuntz [83] found a mixture of copper sulfate with various diesel oil solutions to be effective against schistosome-bearing mollusca in field tests.[a]

[a] Since the preparation of this manuscript, promising results in field tests with pentachlorophenates as molluscicides have been reported by Berry, E. G., Nolan, M. O. & González, J. O. (1950) *Publ. Hlth Rep., Wash.* 65, 939.

SUMMARY

The authors review the literature on the control of disease resulting from the use of insecticides.

Of the mosquito-borne diseases, it may be stated that there is a rapidly increasing volume of experimental data, some of it of unquestioned statistical significance, to indicate that DDT has been effective in controlling malaria. Most frequently, falciparum malaria has been more affected than other forms. As regards urban yellow-fever and dengue fever, although valid epidemiological evidence is not available, there should be little doubt as to the effectiveness of insecticides in the control of these diseases. In the case of epidemic encephalitis, an additional factor, that of unknown vectors, has established this disease as unique, in that failure to control it with specific insecticides may be used as evidence of the existence of unknown vectors. Filariasis is a disease which should certainly be susceptible to control by insecticides and, since it is of such widespread importance in tropical countries, it may be expected that more evidence will be available in the future.

Of louse- and flea-borne diseases, there is abundant evidence that typhus and plague have been greatly reduced by the use of DDT. DDT was first introduced in the control of epidemic typhus during the second World War. However, other methods of control, including immunization, have been so widely used that an objective evaluation of the importance of insecticides is difficult to obtain.

In the case of those diseases believed to be transmitted by filth flies, valid epidemiological evidence is not great. It is apparent that fly control cannot be expected to give more than partial control over enteric diseases such as diarrhoea

RÉSUMÉ

Les auteurs passent en revue la littérature concernant la lutte contre les maladies par l'emploi des insecticides.

En ce qui concerne les affections transmises par les moustiques, l'on peut affirmer, sur la base d'un ensemble sans cesse croissant de données expérimentales dont certaines présentent une valeur statistique incontestable, que le DDT s'est révélé efficace dans la lutte contre le paludisme. Le plus souvent, de meilleurs résultats ont été obtenus dans l'infection à *falciparum* que dans les autres formes. Pour ce qui est de la fièvre jaune urbaine et de la dengue, bien qu'on ne dispose pas d'informations épidémiologiques valables, il n'y a guère de doutes sur l'efficacité des insecticides comme moyen de lutte contre ces maladies. Le cas de l'encéphalite épidémique est tout à fait particulier, par suite d'un facteur supplémentaire : l'existence de vecteurs inconnus, que l'on peut considérer comme démontrée par l'échec de la lutte contre cette affection au moyen d'insecticides spécifiques. La filariose est une maladie que l'on devrait certainement parvenir à combattre au moyen d'insecticides ; étant donné sa grande fréquence dans les pays tropicaux, on peut prévoir qu'à l'avenir un plus grand nombre de données seront disponibles à son sujet.

En ce qui concerne les maladies transmises par les poux et les puces, de nombreuses indications montrent que la fréquence des cas de typhus et de peste a été considérablement réduite par l'emploi du DDT. C'est au cours de la deuxième guerre mondiale que le DDT a été utilisé pour la première fois dans la lutte contre le typhus épidémique. Toutefois, étant donné que l'on a aussi recouru largement à d'autres méthodes de lutte, dont la vaccination, il est assez difficile d'évaluer objectivement l'importance du rôle des insecticides dans ce domaine.

Il existe fort peu de renseignements épidémiologiques valables au sujet des maladies que l'on croit transmises par les mouches scatophages (mouches à ordures). Il apparaît que les mesures de destruction des mouches ne peuvent amener qu'une

and dysentery. Some epidemiological evidence exists as to effectiveness of insecticides in the control of sandfly fever, leishmaniasis, and bartonellosis. In the case of onchocerciasis, although insecticides have resulted in the control of the vector, no epidemiological evidence has been published on the effect on the incidence of the disease, probably as a result of the very long incubation period.

African sleeping sickness appears to be the one insect-borne disease against which insecticides have so far been of little value. Chagas' disease may be in this category but there is reason to believe that it is now succumbing to insecticidal measures. Scrub typhus is apparently quite adequately controlled through the use of repellents, but there seems to be little epidemiological evidence available in the literature.

diminution partielle de l'incidence des affections entériques telles que la diarrhée et la dysenterie. Certaines données épidémiologiques permettent d'affirmer l'efficacité des insecticides dans la lutte contre la fièvre à phlébotomes (fièvre de trois jours), la leishmaniose et la bartonellose. En ce qui concerne l'onchocercose, l'utilisation d'insecticides a été efficace pour combattre les vecteurs, mais l'effet produit sur la fréquence de la maladie n'a pas donné lieu à la publication de travaux épidémiologiques, en raison probablement de la très longue période d'incubation de la maladie.

La trypanosomiase africaine paraît être l'unique affection transmise par des insectes et contre laquelle les insecticides se sont avérés, jusqu'ici, de peu d'utilité. On pourrait peut-être en dire autant de la maladie de Chagas, mais il y a des raisons de penser que celle-ci cède actuellement du terrain devant l'action des insecticides. Le typhus tropical de brousse (« scrub typhus ») peut, semble-t-il, être efficacement combattu par l'emploi de produits répulsifs, mais l'on ne trouve que fort peu d'informations épidémiologiques sur ce sujet dans la littérature médicale.

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