Chapter III

DEVELOPMENT OF ANTIMALARIA ACTIVITIES 1946 - 1951

GENERAL REVIEW

After World War II, Taiwan was retroceded to China by Japan. It was then followed by the change of the Government Administration, resulting in a transitional period of adaptation and adjustment in the political system and official language as well as in the social and cultural life of the community. As far as malaria was concerned, the epidemic was not yet over and, besides, the former Japanese antimalaria stations were practically closed. There were no reliable statistical data to show the extent of the disaster; however, various parasite surveys conducted early in 1947 in northern, central and southern Taiwan revealed parasite rates of 20% - 40% among primary school children sampled.

In November 1946 the International Health Division of the Rockefeller Foundation, in collaboration with the Government, established a Malaria Research Center in Chaochou, southern Taiwan. Under the technical direction of the Rockefeller Foundation's Robert Briggs Watson, who was based in Shanghai at that time, a Field Research Center was established in Chaochou, with a resident malariologist -- J. Harland Paul -- and a visiting sanitary engineer -- J. C. Carter -- of the Rockefeller Foundation, an entomologist from the National Institute of Health - Nanking, three medical officers from the Taiwan Provincial Health Administration and eight locally recruited technicians and field personnel. Two branch research centers were added in the mid-1947 -- one in Shuili, central Taiwan, and the other in Keelung, northern Taiwan. Each branch research center was headed by a medical officer transferred from the Chaochou headquarters, with three to four technicians, either transferred or locally recruited. The activities in 1946 and 1947 principally concerned studies of local epidemiological conditions, including analyses of available Japanese records on malaria, malariometric surveys of the populations in the nearby villages and entomological observation of local anophelines. In 1948 the research activities were extended to include field trials with newly available drugs, residual house spraying and larviciding with DDT, and construction of automatic siphons to control stream-breeding anophelines.

At its initial stage in 1946 the Research Center established it laboratory in the former Japanese antimalaria station in Chaochou, and then moved to an old Japanese shrine offered by the Kaohsiung county government to the Rockefeller Foundation for its malaria research project. There were three houses of traditional Japanese style in the shrine compound. One was converted into a laboratory and the other two were modified for residential use.

In April 1948 the Research Center became one of the public health agencies of the Provincial Health Administration (PHA) and was named the "Taiwan Provincial Malaria Research Institute (TAMRI)." As work progressed and more staff were added, more space was required for the laboratory. A former Japanese police gymnasium, badly damaged when the town was bombed in 1945, was restored for use as TAMRI headquarters. This building served as the headquarters for the malaria eradication program until 1969 when TAMRI was moved to Taipei.

Fig. 4: Taiwan Provincial Malaria Research Institute (TAMRI)
Chaochou, Pingtung county (1948 - 1969)

Although TAMRI came into existence in April 1948, the Rockefeller Foundation continued its technical and financial support through 1949 when it withdrew from Taiwan. However, its fellowship assistance continued until mid-1952.

The Taiwan malaria eradication program owes much to the Rockefeller Foundation, which provided opportunities for training technical staff, introduced new technology and sowed the seeds for the creation of the entire malaria program.

RESEARCH PROJECTS (1946 - 1951)

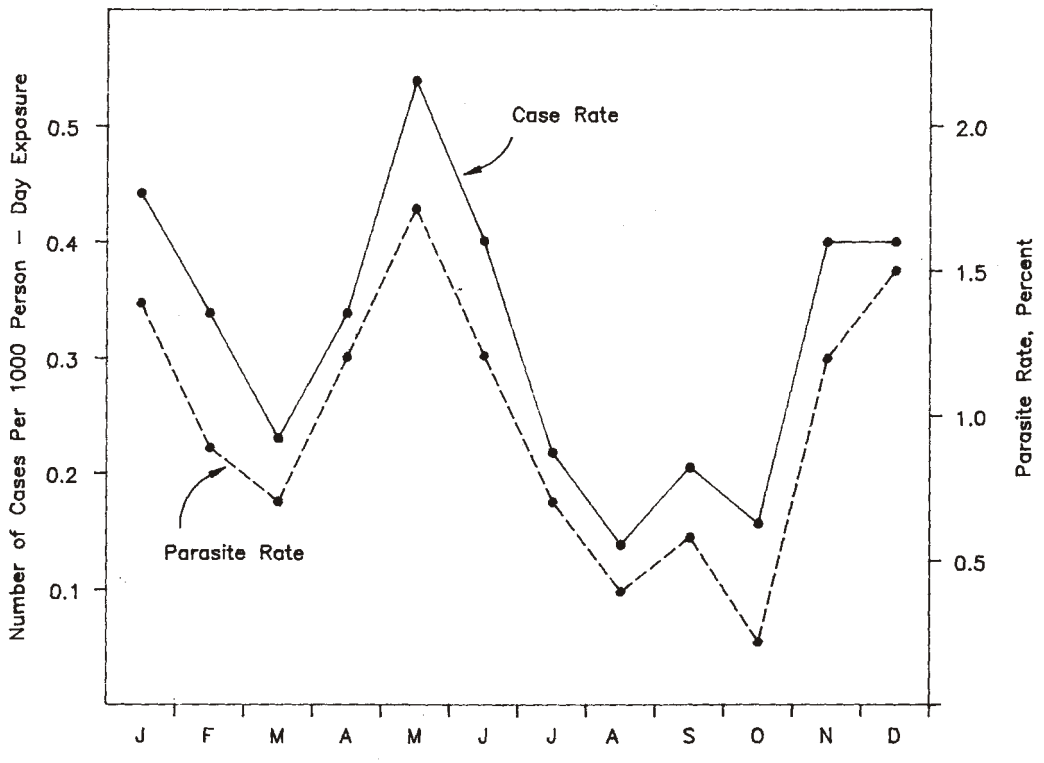
Observations on Malaria Prevalence

Studies were made on malaria prevalence around all three research centers. The observations emphasized examination of infants and of children up to 25 months old, examination of primary school children and analysis of available Japanese records.

Seasonal Prevalence of Malaria in Southern Formosa

(Watson, Liang, 1950)

On an average, 580 infants and children less than 25 months living in the vicinity of Chaochou, were examined monthly from March 1948 through March 1950. In common practice, infant infection rates are computed with data from infants less than 13 months old, but such rates are most often based upon one or more surveys in a year, less often upon monthly surveys of the same population. The broader age base of the data is justified by the fact that infants were examined at monthly intervals from birth; thus, the chance of an infection escaping attention was rather small. The results indicated that malaria transmission of all three common species of malaria parasites occurred every month throughout the year with peaks in May and December - January (Fig. 5).



The rates are computed for a composite year
from data collected from March 1948 through March 1950.

Fig. 5: New malaria infections of infants and
young children of Chaochou

Monthly surveys of the two primary schools near Chaochou showed the highest parasite rate in January and the second highest in June. Similar waves of prevalence also characterized the slide positivity rates of the Japanese records of 1937 - 1944. These waves apparently were closely correlated with the propagation of *Anopheles sinensis* and *Anopheles minimus* in the Chaochou area (Fig. 6).

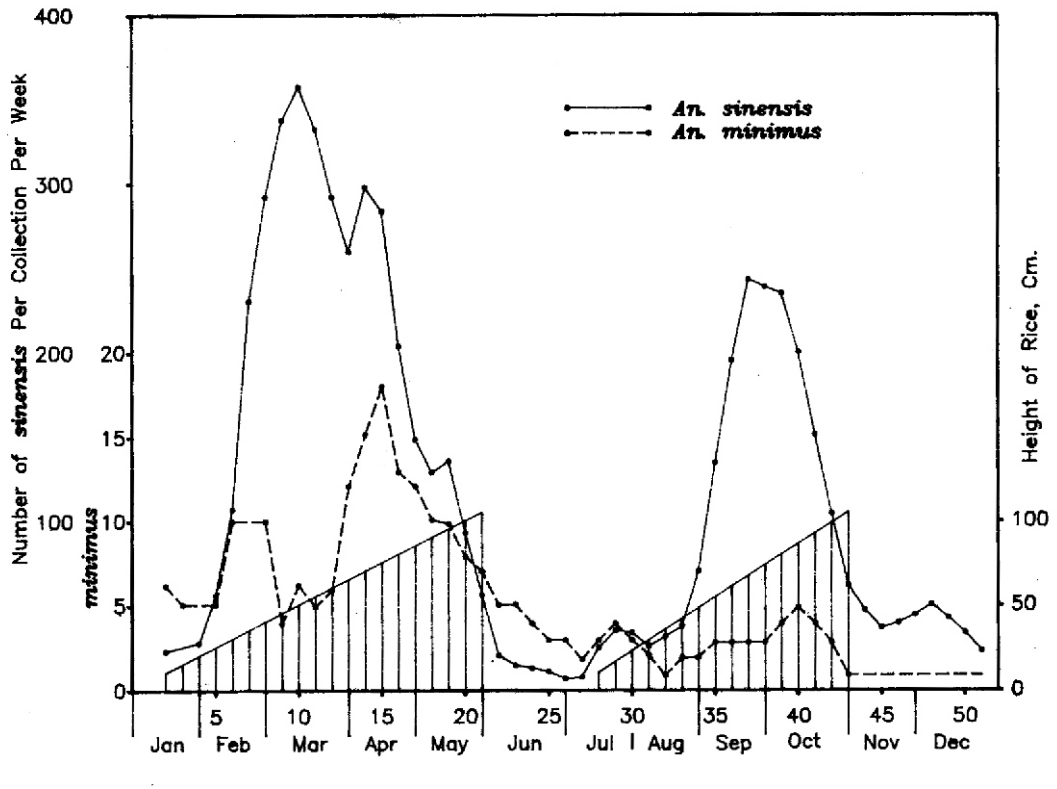


Fig. 6

Three weeks movig mean of density values for *An. sinensis* and *An. minimus*, from seven collecting stations in Chaochou township, 1949. The approximate heights of the rice crops are based upon measurements made in 1948.

Seasonal Prevalence of Malaria in Central Formosa

(Watson, Paul, Chow L.P. and Peng, 1950)

Studies were made in the vicinity of Shuili (central Taiwan) where malaria had been recognized as hyperendemic. Both *An. sinensis* and *An. minimus* were present, but the latter was considered to be the more important vector of malaria.

Monthly surveys were made at the Shuili primary schools from June 1947 through May 1948. Parasite rates increased during the summer months, reaching a peak (38.7%) in September 1947. Thereafter, they decreased to a low point (22.5%)

in March 1948. All three common species of malaria parasite were present, but *P. vivax* was predominant during the observation period (Table 7).

The analysis of the Japanese records for the period 1924 - 1938 revealed an increase of malaria prevalence from August to November. There was also noted an apparent cycle of prevalence about every 10 years.

Seasonal Prevalence of Malaria in Northern Formosa (Taiwan)

Although Studies similar to those done in central and southern Taiwan were made in the vicinity of the Keelung Research Center, no paper was published on this subject. Available records indicated only one annual peak of malaria prevalence in September – October. The spleen rate was 88.5% and the parasite rate was 22.9% among 170 school children examined in July 1948. During July – September 1947, 2,365 *An. minimus* were dissected; one gland and seven gut positives were found.

Northern Taiwan is rather hilly and has many small streams providing good breeding places for *An. minimus.* The coal mining villages in the vicinity of Keelung city were known to be highly malarious throughout the year.

Observation on Anopheline Mosquitoes

Seasonal Prevalence of Anopheline Mosquitoes in Southern Formosa
(Chang, Watson and Chow C.Y., 1950)

There methods were used to study the prevalence of anopheline mosquitoes at Chaochou. These methods consisted of weekly collections from cattle sheds, night catches of mosquitoes biting water buffalo and collections from an artificial pit. The observations were made during January 1947 - December 1949.

An. sinensis was the most prevalent species found at Chaochou. It was present throughout the year and had two peaks of prevalence associated with the two rice crops. It was believed at that time to be the principal vector of malaria on the southern plains of Taiwan. *An. minimus* was found in small numbers in comparison with the former species. It was found throughout the year with a prominent peak in April and May. At the time of the study, it was thought to play a relatively minor role in malaria transmission on the plains of Taiwan. Seven other species were also

identified, but they were not considered as important vectors of malaria in southern Taiwan.

Table 7

Seasonal Variation of Parasite and Spleen Rates and of Spleen Size in the Children of Shuili Primary School, as Determined by Monthly Surveys, June 1947 - May 1948

Months	No. Exam.	Spleen Rate (%)	Average Enlarged Spleen	Blood Films Positive For				Parasite Rate (%)
				vivax	*falciparum*	*malariae*	Mixed	
1947								
June	434	76.5	2.1	59	74	13	0	33.6
July	196	80.6	2.2	24	15	16	4	30.1
Aug.	335	71.0	2.2	46	25	41	7	35.5
Sept.	416	69.5	2.4	64	41	41	15	38.7
Oct.	614	70.4	2.4	74	54	51	15	31.6
Nov.	507	71.2	2.2	60	62	18	10	29.6
Dec.	575	68.1	2.1	52	71	26	17	28.9
1948								
Jan.	327	59.3	2.1	38	27	16	7	26.9
Feb.	539	63.0	2.2	67	25	23	9	23.0
March	644	55.1	2.1	70	28	39	8	22.5
April	614	57.3	2.1	57	44	43	7	24.6
May	640	54.5	2.0	71	52	49	3	27.3
All months mean	487	66.4	2.18	56.8	43.2	31.3	8.5	28.7

Natural Infection of Anopheline Mosquitoes With Malaria Parasites in Taiwan

As early as 1901 Kinoshita reported gland infection of 0.5% and stomach infection of 2.0% among *An. sinensis* collected inside human dwelling in Keelung (Morishita, 1976). Later, Anazawa (1931) reported seven species of *Anopheles* from Taichung infected with plasmodia, as shown in Table 8.

Table 8
Natural Infection of Anopheline Mosquitoes from Taichung (Central Taiwan)

Anopheles Species	Number Dissected	Stomach Infection	Gland Infection	Total	
				No.	%
sinensis	2,462	5	15	20	0.81
minimus	4,208	55	57	112	2.66
maculatus	246	-	1	1	0.41
tessellatus	104	-	2	2	1.92
ludlowae	949	1	5	6	0.63
annularis	946	-	2	2	0.21
splendidus	44	-	1	1	2.27
Total	8,959	61	83	144	1.61

Source: Anazawa, 1931

From January 1947 to December 1949, dissections were made of 60,915 anopheline mosquitoes of eight species (Chow C.Y., Watson and Chang, 1950). Only *An. sinensis* and *An. minimus* were found infected (Table 9). The other anopheline species were all negative, although the numbers dissected were relatively small. These findings concluded that *An. sinensis* and *An. minimus* were principal malaria vectors on the plains in southern Taiwan. However, the importance of *An. sinensis* as vector later became uncertain when the sporozoites on one of the eight gland-positive slides were reexamined and were recognized as crithidial forms of an unidentified species of trypanosome (see Chapter V for further details).

Table 9

Results of Dissections of 45,458 An. sinensis and 6,498 An. minimus from Three Locations in Taiwan, 1947 - 1949

Place	Source of Mosqutioes	*An. sinensis*				*An. minimus*			
		# Diss.	G1+	G+	Total	# Diss.	G1+	G+	Total
Keelung	Stable	691	0	1	1	95	1	1	2
	Houses	196	0	0	0	2,270	0	6	6
Shuili	Stables	3,728	0	0	0	667	2	0	2
	Houses	126	0	0	0	646	0	0	0
Chaochou	Stables	39,666	8	0	8	1,096	0	1	1
	Houses	159	0	0	0	1,340	0	0	0
	Pits or traps	892	0	0	0	384	0	0	0
Total		45,458	8	1	9	6,498	3	8	11

G1+=salivary glands infected; G+= guts infected; Diss. =dissected.
Source: Chow C.Y., Watson and Chang, 1950

EXPERIMENTAL MALARIA CONTROL

Field Trial of Chlorguanide (Paludrine) as a Suppressive and as a Therapeutic Agent in Southern Formosa

(Watson, Paul and Liang, March 1950; Paul, Watson and Liang, Dec. 1950)

The village of Sanhsing, situated about 1 km from Chaochou and with a population of 417, was kept under observation for 55 consecutive weeks while chlorguanide was administered to the entire population after proven cases of malaria had been treated with therapeutic doses. The objectives of this trial were to test the efficacy of chlorguanide as a suppressive and as a therapeutic agent and to determine the minimal doses under field conditions in southern Taiwan. The trial began in the last week of June 1947, during which period the weight of each person was recorded, a blood film was taken, and a spleen examination was made. Three different treatment schedules were used at different periods, the first two based on body weight and the third on age groups. A 100 mg adult dose seemed to be sufficient to prevent the occurrence of malaria symptoms, but insufficient to rid the

body of infection. In 55 weeks, the parasite rate was reduced from 18.2% to 3.8%, the spleen rate from 72% to 46%, and the average enlarged spleen (AES)[2/] from 2.16 to 1.56. It was concluded that suppressive doses employed were too small for satisfactory suppression of malaria under Formosan conditions. For treatment of clinical malaria, at a dose of 800 mg in three days for an adult, chlorguanide appeared to be the drug of choice at that time. During the study period, six *P. malariae* and two *P. falciparum* infections were found to be refractory to treatment with chlorguanide, but they were cleared up with quinacrine.

Fig. 7: Paludrine is distributed to villagers in Sanhsing village, Chaochou township, 1947
Source: JCRR

2/ ASE: Average enlarged spleen is calculated by multiplying the number of individuals in each spleen class (except class 0) by the class number, adding these products, and dividing the total by the number of those whose spleens are palpable (*also see* Chapter XIII).

A second field trial with chlorguanide was carried out during April 1948 - March 1949 in two more villages near Chaochou, with a population of 1,100 in one and 1,400 in the other. A third village, with a population of 400, was left untreated for comparison. In this trial, only suppressive doses were given and no attempt was made to give chlorguanide routinely to persons reporting sick with malaria, as was made in the previous trial. The drug was given in the same dosage (200 mg for an adult) once a week in one village and once every two week in the other village during an entire year. It was surprising to note that approximately the same results were obtained with administration of the drug at weekly and fortnightly intervals. It was concluded that the new synthetic drug should normally be reserved for treatment of malaria cases rather than for suppression programs.

Field Trial of Chloroquine (SN-7618-5) for Malaria Control in Central Taiwan

(Watson, Paul, Chow L.P. and Peng, 1950)

The employees of two power plants in a highly malarious area of central Taiwan, along with their families (about 400 persons), were treated with chloroquine during the last six months of 1947. The drug was administered as a suppressant and as a curative agent to persons with parasitaemia, with or without clinical illness.

Suppressive doses (5 mg/kg body weight) at weekly intervals gave good results in adults. Doses as low as 2.5 mg/kg to infants or to children also gave good suppression of parasitaemia. Giving smaller doses per week or increasing the interval between doses to two weeks, even when the dose was doubled, did not give adequate protection. It is believed that a suppressive program using chloroquine should be based upon administration of 5 mg/kg body weight to all persons, at weekly intervals.

Treatment of malaria cases with a total dosage of 40 mg/kg over a two-day period was followed in most instances by disappearance of parasitaemia in 24 hours. In infants and children, doses as low as 12 mg/kg gave satisfactory results.

Some of the adults complained of symptoms that might have been due to side effects of the drug, the most common of which was "dizziness."

The people were generally very cooperative, but there was evidently less interest toward the end of the study than at the start.

Control by Automatic Flushing of Streams

Malaria was hyperendemic in the hilly terrain of northern Taiwan, especially in the mining areas. Even in Keelung city, malaria was very serious in its outlying districts, where streams were abundant. One of the malarious districts, Shinyi, was selected to test flushing control measures using automatic siphons. The area was carefully studied for one year, July 1947 - July 1948, prior to the experiment and before the principal *minimus*-breeding streams were mapped. To provide protection within this area, five dams with eight automatic siphons were constructed on the main streams. They were put in operation from July to November 1948, the period with the heaviest breeding of *An. minimus*. Entomological evaluation showed a considerable decrease in larval density while the system was in operation, but after the discontinuation of the automatic flushing the larval density increased rapidly. Beginning in 1950, it was therefore decided to leave the siphons in operation throughout the year. Even though the larval densities in the main streams and the nearby rice fields were very low, the adult densities did not show any significant decrease. Furthermore, newly-infected infants were still being found (Table 10). A careful search revealed that there were many breeding places of *An. minimus* other than the main streams. It was then decided to make larvicidal applications in 1950 and 1951 to reduce the risk of new infection.

In conclusion, the automatic flushing control measure was not a solution to the malaria a problem in northern Taiwan for the following reasons:

* Flushing was not effective enough to reduce the anopheline population;
* Aside from the cost of construction and installation, the maintenance (e.g., cleaning of silt above the dam, repairing bank erosion of the dam, and removal of tree branches and other debris from the siphon box) cost was high;
* Heavy rainfall frequently flooded the streams, resulting in continuous flow through the siphons or clogging of the siphon boxes;
* Children frequently plugged the auxiliary pipes to make the siphon inoperative, so that they could have ample water for swimming; and
* Villagers were unhappy because they could not wash their clothes in downstream areas.

Table 10
Flushing Control and Impact on Malaria

Year	Control Measures	Spleen Rate* (%)	Parasite Rate* (%)	Number of Infants Positive**
1947	None used	84.6	38.5	--
1948	Auto flushing, July-Nov	88.5	22.9	1
1949	Auto flushing, July-Dec.	63.3	9.0	14
1950	Auto flushing and larviciding throughout the year	35.5	16.2	8
1951	Auto flushing and larviciding throughout the year	37.0	3.5	2

* On the average, 150 school children were examined at least once a year.
** On the average, 50 infants were examined monthly.

Larviciding

Larviciding with DDT was applied as a supplement to automatic flushing control in northern Taiwan during 1950 and 1951, as described above. In southern Taiwan, a total of 627 hectares (1,550 acres) of rice fields and other water surfaces around Chaochou was treated with DDT as a larvicide to protect more than 11,000 persons. DDT emulsion with camphor oil as a solvent and Triton X-100 as an emulsifier were used in this experiment. The dosages applied were 45 gm (0.1 lbs) of technical grade DDT per acre for rice fields and 181 gm (0.4 lbs) technical grade DDT for rivers and canals. The larvicide was applied on a 10-day cycle from January 30 to April 19, 1950, from August 22 to November 3, 1950, and from February 26- May 5, 1951. Although larviciding had produced a considerable reduction on adult anopheline populations and malaria parasite indices in treated areas, this measure was not considered cost-effective in rice growing areas of Taiwan. Along with other factors contributing to this decision was the realization that working conditions in paddy fields were excessively difficult for spraymen. Additionally, acceptable dosages of the insecticide were evidently not reaching mosquito breeding surfaces in maturing rice plantings.

It should also be recalled that in the 1950s the selective pressure of larviciding toward mosquito resistance, and potential environmental damage caused by DDT when applied as a larvicide, were not yet appreciated.

Fig. 8: Larviciding
Source: JCRR

DDT Residual House Spraying

DDT residual house spraying was carried out in many villages in the vicinity of Chaochou, Taichung and Keelung beginning in January 1948, May 1950 and October 1948, respectively. The population protected reached 26,000 by the end of 1951. Different dosages were applied, namely 0.5 gm, 1.0 gm and 2 gm technical grade DDT per m^2 of surface. Spraying was done twice a year.

The results of DDT house spraying were remarkable wherever applied. Six of the sprayed villages were selected for entomological observation using daytime

mosquito collections inside the houses and night catches with water buffalo as bait. Unfortunately, the only details available today the those in Tables 11 and 12.

Table 11

Daytime Mosquito Collections in Sprayed Houses

Village Sprayed	Date of Last DDT Spraying (day/monty/year)	Date of First Mosquito Found (day/monty/year)	Interval
Ssuchun	07/10/49	19/09/50	12 months
Neichong	19/09/49	09/03/50	6 months
Juifong	23/05/50	06/51	13 months
Ssulin	22/09/49	19/09/50	12 months
Chikuangchu	15/10/49	19/09/50	11 months
Uting	15/10/49	11/09/50	11 months

Table 12

Total Anophelines Captured in Sprayed and Unsprayed Villages
January 1950 - June 1951

Period	Night Catches		Daytime Catches	
	Sprayed	Unsprayed	Sprayed	Unsprayed
Jan - June 1950	- - - -	- - - -	22	6,635
July - Dec. 1950	2,325	3,361	3	4,129
Jan. - June 1951	1,261	3,663	24	11,670

Generally speaking, intradomiciliary house spraying does not necessarily reduce the mosquito population, but in Taiwan the anopheline population -- especially *An. minimus* density -- seemed to have been greatly affected by such spraying using DDT (Fig. 9).

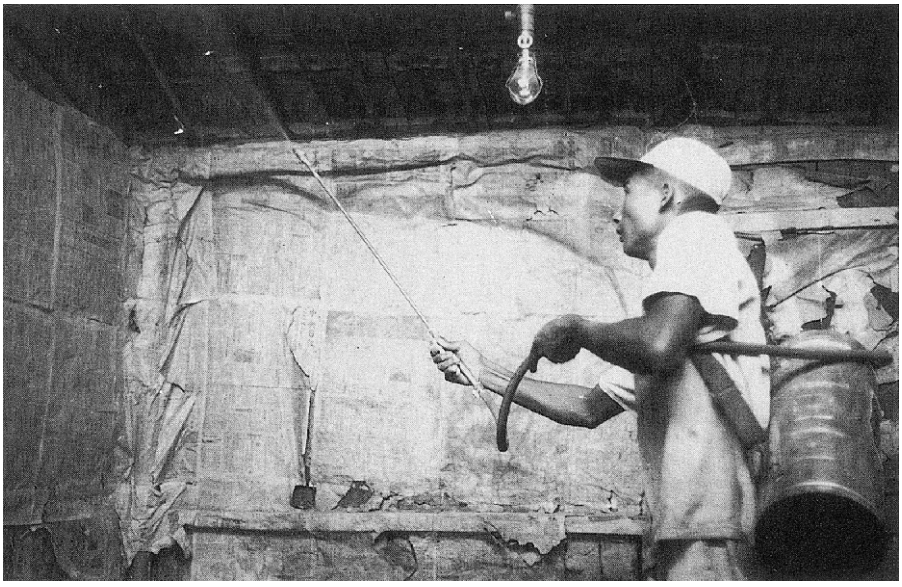


Fig. 9: Intradomiciliary spraying with DDT

In practically every village included in the house spraying program, there was epidemiological evaluation of the results, including a monthly infant survey and periodic spleen and blood surveys of the village people and/or of the school children. Unfortunately, after 40 years, the detailed records cannot be found. The information available today is often fragmentary. Nevertheless, some statistical data have been found in an annual report of TAMRI for 1951.

In the vicinity of Chaochou, 11 villages with a total population of 5,562 were sprayed during the period 1948 - 1950 at doses ranging from 0.5 gm - 1.78 gm of technical grade DDT per m^2. The parasite rate in the treated villages was brought down form 2.85% in December 1949 to 0.85% in December 1950; in nearby untreated villages, the corresponding rates were 2.43% and 2.83% for the same period.

In northern Taiwan, four coal mine villages with a total population of 4,676 were sprayed twice a year during the period 1948 - 1950, at doses ranging from 0.75 gm - 0.94 gm of technical grade DDT per m^2. In one of the four villages sprayed (Shenaokeng), the spleen rate fell from 93.3% in March 1948 to 49.0% in March 1951, and the parasite rate fell from 52.2% to 7.3% during the same period. The rate of new infant infections was 17.9% in 1948 and 0.8% in 1951 among an average of

30 infants examined every month.

As described above, some malaria control measures were tried in northern, central and southern Taiwan during the period 1946 - 1950,originally initiated by the Rockefeller Foundation's Malaria Research Center and later continued by TAMRI. While each control measure had its merits, DDT residual house spraying was confirmed to be the most effective and suitable malaria control measure applicable on a large scale. The cost, calculated on the basis of two applications per year at the dose of 1 gm technical grade DDT per m^2, was US$0.40 per capita.

TRAINING

Training of malaria personnel was one of the major activities of the Rockefeller Foundation's Research Center and the succeeding institution, TAMRI. To build a central malaria cadre, professional staff including three medical officers, an engineer and an entomologist were recruited and were given in-service training in research projects with the malariologists of the Rockefeller Foundation. Most of these professionals received further training abroad in tropical medicine and public health through the Foundation's fellowships during the period 1949 - 1951. To work in the three Research Centers, technicians were also recruited locally and enjoyed apprenticeships by working with the professionals.

On the other hand, training programs were extended to include antimalaria technicians at county and township levels. The first four-week training course was held in November - December 1947 for 17 county malaria supervisors who had served as microscopists during the Japanese period (Fig. 10).

During the period 1950 - 1951 TAMRI, with the financial assistance of JCRR, organized a series of four-week refresher training courses for 227 county and township microscopists (*see* Chapter V). These personnel were later incorporated into the network of basic health services and provided the backbone for the malaria eradication program.

Fig. 10: First training course for County Malaria Supervisors, 1947