Reprinted from 2,(?)
THE PROCEEDINGS OF THE FOURTH INTERNATIONAL CONGRESSES ON TROPICAL MEDICINE AND MALARIA. Washington, D. C., May 10-18, 1948

SANDFLIES OF THE GENUS *PHLEBOTOMUS*—A REVIEW OF THEIR HABITS, DISEASE RELATIONSHIPS, AND CONTROL

MARSHALL HERTIG, *Gorgas Memorial Laboratory, Panama, Republique de Panama*

Introduction.—Sandflies of the genus *Phlebotomus*, represented by about 300 species, are widely distributed in both hemispheres in the tropics, the subtropics, and in parts of the temperate zone as well. Their habitats are extraordinarily diverse and include cultivated fields, deserts, villages, large cities, jungles, and mountain valleys, and range from sea level to at least 11,000 feet. *Phlebotomus* sandflies are notorious pests of man in certain areas but their chief importance medically lies in their role as vectors of a number of diseases: pappataci or sandfly fever in the Old World; bartonellosis in a small section of South America; and the whole group of the leishmaniases in both hemispheres.

Habits and biology.—In reviewing the habits and biology of sandflies we shall not attempt a detailed account but rather emphasize those points particularly related to disease transmission and control.

The whole group is remarkably uniform in general appearance, life-cycle, and habits. All species suck blood, mostly of warm-blooded animals, although a few attack reptiles and amphibians. Like mosquitoes, only the females bite. With few exceptions, sandflies are nocturnal or crepuscular, leaving their hiding places in late afternoon or evening and returning usually before sunrise. Certain important flight habits will be mentioned later in connection with control.

Breeding places are typically in damp, loose soil with organic debris. They are never aquatic and never continuously wet, in contrast with the aquatic and semiaquatic breeding places of mosquitoes and *Culicoides*. They are dark, accessible through cracks or other openings, and usually protected from rain and run-off. Typically they are found under large stones, in the crevices of stone walls and old masonry, at the base of hollow trees and tree buttresses, in animal burrows and deep soil cracks. Burrows and soil cracks are especially important in desert and semiarid regions.

The larvae and pupae are notoriously hard to find, which makes the actual demonstration of any particular breeding place rather diffi-

836683—49

cult. It is usually necessary to resort to washing the soil and debris through graduated screens, followed by flotation with salt or sugar solutions. There is surprisingly little known about the young stages in nature, even of those species most studied as disease vectors. There is urgent need of detailed ecological study throughout the whole sandfly group, and especially in the matter of the breeding places.

We are dependent almost entirely on the capture of adult sandflies for our information about species and distribution, and as a source of experimental material. The daytime resting places are relatively easy to demonstrate. They include the same situations as the breeding places, and in addition a variety of others, such as caves, shallow hillside excavations, hollow trees, together with houses, stables, and other animal shelters where sandflies may remain after seeking a blood meal.

In houses, sandflies eventually make their way to the darker corners near the ceiling, where they may remain often in plain sight throughout the day. Whether they remain in a building or not depends on its construction. A dark structure such as one of masonry, or adobe, with few openings may harbor many, while those loosely made of cane, sheet metal or boards often have no sandflies during the day even though they may enter and feed freely at night. If there are open fires, few sandflies remain indoors. Some species do not enter houses at all.

It is necessary to know where and how to look for sandflies. Searches should be made with tobacco smoke, which causes the sandflies to move and thus to reveal themselves. The slight narcotizing effect makes them easy to capture, which is most conveniently done with a suction tube. At night, sandflies may be taken in the act of biting man or domestic animals, or by means of animal-baited traps, or light traps, or with adhesive or oiled paper placed in strategic spots.

Sandflies are easily reared, and most of our information about the young stages is derived from such laboratory cultures. Eggs are laid 4 to 5 days after a blood meal in batches of 20 to 50 with a maximum of 70. They hatch in 7–10 days. The 4 larval instars require usually a minimum of 3 to 4 weeks and often as much as several months. Pupation takes about 10 days. Thus, the total life-cycle is hardly ever less than 2 months and is frequently longer. This slow development is one of the sandfly's weak points, which may be exploited in control. Although in the laboratory females usually die after oviposition, with good technique they may live several weeks, refeeding and laying eggs several times. In nature, refeeding at least once and probably oftener has been shown to be a normal process in the case of several species (1, 2). This point, together with the longevity of the sandfly in nature, has not yet been well studied and is of importance in relation to disease transmission. Just as in the case of the malaria parasites, *Leishmania*, for example, requires some time to develop to the infective stage.

In climates with a cold season, hibernation takes place apparently in the fourth larvel instar. So far as known there are no overwintering adults. In the tropics sandflies are usually found the year round, but in the temperate zones the sandfly season generally begins in late spring and is usually over by mid-autumn. In some regions the season is relatively short and sharply defined. Thus in north China, in spite of a long warm spring, there are few sandflies before the first of June. Furthermore, in the case of the Chinese sandfly, *P. chinensis*, supposed to be the principal vector of kala-azar, the species appears to be partly single-brooded and decreases sharply after the middle of July. In any case the limited season, in some regions where sandfly-borne diseases are serious, greatly simplifies the problem of control.

Disease relationships.—For each of the known *Phlebotomus*-borne diseases the transmission problem constitutes a series of long and fascinating chapters, which are still not complete for any one of them. They have several features in common. In each case there is uncertainty as to the source of the sandfly's infection. In the case of sandfly fever there is the problem of the overwintering of the virus. For bartonellosis and the leishmaniases the reservoirs are imperfectly understood. In dealing with the several transmission problems we shall limit ourselves to certain general considerations, principally in connection with those phases which are still in doubt.

Sandfly fever is of minor public health importance to local populations but is potentially critical for armies composed of nonimmunes. It is known to extend from the Mediterranean to the Orient but has not yet been identified in the Pacific Islands or in the New World. This virus disease is transmitted by biting during the sandfly season. The disease is usually associated with *P. papatasii* throughout the wide range of this extraordinarily versatile species. Outside its range the vectors are not well understood. Investigators in the Mediterranean (3), and in Russia (4), have secured transmissions by the progeny of infected females, while others (5) have failed. Since no animal other than man is known to be susceptible, and in the absence of any demonstrated carriers or of any hibernating adult sandflies, the overwintering of the virus in the sandfly larva remains a good possibility which needs further study.

Bartonellosis (Carrión's disease or verruga peruana), a disease of man limited to certain parts of Peru, Ecuador, and Colombia, has been transmitted to rhesus monkeys by the bites of wild-caught *P. verrucarum* (2). There remain unsolved, however, the problems not only of the reservoir, but of the development of *Bartonella* in the sandfly. Wild sandflies frequently exhibit a phenomenon unique in the history of insects as disease vectors, namely, massive infections of the tip of the proboscis with organisms of unknown origin and nature (2). Since both sexes are equally concerned, these infections are not derived from the blood meal. Two such infected females have yielded cultures of *B. bacilliformis*. It is still to be determined whether or not these proboscis infections have any relation to the transmission of bartonellosis. The reservoir is still an open question. One naturally infected field mouse, *Phyllotis* sp., has been found out of many examined, but attempts to infect this and other rodents have failed. While human carriers may total 5 to 10 percent of the local population (6), transmission from person to person is still to be demonstrated. Furthermore, the speed with which the disease may be contracted in a very sparsely populated region seems to us to call for a reservoir other than man.

The history of *Phlebotomus* and the transmission problems of the leishmaniases comprise one of the most unusual chapters in medical entomology. During nearly two decades the sandfly (an insect known to be in reasonable accord with the epidemiology), which is capable of developing the flagellates of *Leishmania* and providing an apparently suitable mechanism of infection and known to harbor the infection in nature, nevertheless persistently refused to transmit the infection in the laboratory, with a few reluctant and perhaps doubtful exceptions. However, in 1940 and 1941, the seventeenth and eighteenth years of this period of heartbreaking sandfly stubbornness, there appeared reports that kala-azar in India (7) and oriental sore in Palestine (8) had been transmitted a number of times and with "ridiculous ease," to quote one of the authors (8). The difference between final success and previous failure apparently lay in providing the sandflies with certain substances not given in earlier experiments, namely, in India, the sugar and other substances derived from raisins, and in Palestine, salt. These and later transmissions removed the last doubt as to the ability of *Phlebotomus* to transmit these two leishmaniases. In all likelihood there could be demonstrated a similar ability to transmit other species and strains of leishmaniasis. At any rate, the vast body of evidence which has now accumulated justifies proceeding on the broad assumption that all the leishmaniases are transmitted by *Phlebotomus* unless proven otherwise. The problem has become, then, one of continuing the investigation of other factors, along with *Phlebotomus*, underlying the epidemiology of the leishmaniases in all their bewildering variety of terrain, climates, cycles, and vagaries of distribution. One phase of this problem of immediate importance appears to us to be the matter of reservoirs.

In the case of Mediterranean and Asiatic kala-azar especially, there is a tendency to regard dogs or man, or both, as the sole reservoirs. However, the distribution of kala-azar, and other leishmaniases as well, is curiously and sharply restricted and spotty within endemic regions. Even in the immediate vicinity of permanent foci, kala-azar may be absent in spite of the joint presence of a supposedly good vector and the highly mobile, supposed reservoirs, dogs and people. We find it difficult, for example, to reconcile the epidemiology of kala-azar in north China with man and/or dogs as the sole reservoirs (9). The disease is predominantly rural and may halt abruptly at the edge of a city, while the sandflies do not. It has been repeatedly brought out in connection with nearly all the leishmaniases that they are characteristically rural rather than urban, and hence associated with open fields, natural vegetation and fauna. In some cases the disease is acquired in normally uninhabited or sparsely inhabited regions, as *chiclero* ulcer in the forests of Yucatan, *espundia* in the jungles of South America, oriental sore in the salt desert near the Dead Sea.

We do not mean to imply that the reservoir problem has been overlooked or neglected, but rather that certain currently accepted solutions do not explain completely the observed epidemiology. There is one outstanding instance in which the epidemiological picture appears to be reasonably complete. In semidesert areas of Turkmenistan with a high endemic rate of oriental sore, sandflies are found breeding in the burrows of rodents, in which the gerbils especially, as well as the sandflies, show a high rate of infection with *Leishmania tropica* (10). Some such series of relationships seems to us to be called for in many other situations. It can not be denied that dogs in particular, along with man, in addition to being joint victims, may also take an active part in the leishmaniasis cycle, but wherever the concept of man and dogs as primary and sole reservoirs fails to fit completely the epidemiology, some other reservoir or some other factor is still to be searched for.

Control.—In the matter of controlling *Phlebotomus*, the advent of DDT has suddenly changed the whole situation from the melancholy state of no control at all to the brighter one of a method which has proved effective and economical wherever it has been tried. In connection with sandfly fever in Italy in 1944 it was found that whenever barracks or billets were treated with residual DDT, sandflies disappeared and new cases of sandfly fever ceased (11). In Palestine near the Dead Sea, controlled experiments showed that spraying the interiors of houses gave virtually complete protection against *Phlebotomus* (11). Their flight habits make sandflies peculiarly vulnerable to residual DDT. Generally characterized as weak fliers, sandflies advance by means of short flights, alighting on various objects in their path. Before entering a structure in search of blood or shelter, they usually alight on the outer walls and then with short, hopping flights, broken by long pauses, make their way to windows or other openings. Once inside they may spend even more time resting on the walls before attempting to feed. In effect, DDT transforms such surfaces into lethal barriers.

The effectiveness of house-control has been established by its invariable success wherever it has been tried, involving various types of dwellings, stables, and even tents, in several countries and with various species of *Phlebotomus*. With the objective of extending the method so as to achieve area-control, i. e., protection outdoors as well as indoors, we (12) began in 1945 control studies in the sandfly-verruga zone of Peru. The same leisurely, dawdling flight habits which lead sandflies to destruction in sprayed houses, are also exhibited whenever they leave or enter a shelter or breeding place, a process repeated nearly every night of their adult lives. If the surfaces associated with shelters and breeding places can retain residual DDT, i. e. if they are of stone, cement, or wood, these vitally necessary places become death-traps. In Peru the principal outdoor shelters and breeding places in our experimental areas were stone walls laid without cement.

We found that treatment of all stone walls within a radius of only 60 yards reduced the local sandflies sharply, although the effect was neither complete nor uniform. However, the combined spraying of houses, animal shelters, and nearby stone walls reduced the sandfly population to negligible numbers, an effect which persisted for at least a year and a half. The effect was extremely localized and sharply defined, since places just outside the sprayed areas continued to have sandflies in normal abundance. Practical trials in 2 large construction camps were carried out. The program became chiefly one of spraying all buildings, with some outdoor stone walls, every 3 or 4 months. Control of sandflies was virtually complete, and the sandfly-borne diseases, cutaneous leishmaniasis in one case, bartonellosis in the other, practically ceased. In attempting to analyze these results in terms of sandfly bionomics, it appeared that the local sandfly population, vulnerable to DDT at practically every phase of adult life, had been dealt a devastating stroke from which recovery was very slow. The long life-cycle delays replacement of a depleted population even after the direct effect of the DDT has worn off.

Large-scale trials are still necessary to give the answer to a number of important problems. A valley-wide DDT program is now being carried out in Peru, with both sandfly-borne diseases and malaria as primary objectives. The current results are highly satisfactory. It is obvious that any residual DDT-malaria project in a sandfly area is also a sandfly-control project. It is of prime practical importance to determine whether the single measure of spraying houses and animal shelters, carried out over wide areas, can knock out the local sandfly population. The tremendous DDT campaign in Greece during the past 2 or 3 years, in addition to the spectacular results in malaria control, has also greatly reduced the sandflies, according to fragmentary, informal reports. It is to be hoped that the Greek and other malaria campaigns may be more exactly evaluated in terms of sandfly control.

It is our opinion that sandfly control with DDT is ready for practical application, provided always that the experimental approach is maintained. Our Peruvian work was in the tropics with sandflies abundant the year round. In temperate zones, where so many of the serious sandfly problems are located, and where the sandfly season lasts only 4 or 5 months, the situation seems made to order for control with DDT. A preseason application, lying in wait for the overwintering generation and able to operate with maximum initial toxicity, could conceivably ruin the summer generations or prevent them altogether.

Desert and semiarid regions where sandflies are dependent on animal burrows or deep soil cracks, are special cases where residual DDT could hardly be utilized. We know of no area-control studies directed against sandflies in such situations, but it occurs to us that DDT dusts might prove effective, applied from the air or from the ground. It is possible that some of the wettable DDT formulations designed for agricultural purposes, if sprayed on desert vegetation, would have a satisfactory residual effect.

It is to be hoped that practical large-scale trials and the adaptation of control methods to special situations will not long be delayed. We have a new and powerful weapon and may look forward with confidence to the effective control of *Phlebotomus* and the sandfly-borne diseases.

References

(1) Adler, S., and Theodor, O.: Proc. Roy. Soc. ser. B, 108: 464–480, 1931.
(2) Hertig, M.: Am. J. Trop. Med. Suppl. vol. 22, No. 5, 1942.
(3) Whittingham, H. E.: J. State Med. 32: 461–469, 1924.
(4) Moshkovsky, S. D., et al.: Med. Parasitol. Moscow, 6: 922–937, 1937, abstract in Trop. Dis. Bull. 41: 565, 1944.
(5) Sabin, A. B., Philip, C. B., and Paul, J. R.: J. A. M. A. 125: 603–606, 1944.
(6) Weinman, D., and Pinkerton, H.: Proc. Soc. Exper. Biol. & Med. 37: 596–598, 1937.
(7) Smith, R. O. A., Halder, K. O., and Ahmed, I.: Indian J. M. Research 28: 585–591, 1940.
Smith, R. O. A., Halder, K. O., and Ahmed, I.: Indian J. M. Research 29: 799–802, 1941.
(8) Adler, S. and Ber, M.: Indian J. M. Research 29: 803–809, 1941.
(9) Young, C. W., and Hertig, M.: Am. J. Hyg. 9: 227–246, 1929.
(10) Various papers reporting work of Russian expeditions in Turkmenistan 1937–39, summarized in Trop. Dis. Bull. e. g., 39: 538, 1942.
(11) Hertig, M., and Fisher, R. A.: Bull. U. S. Army Med. Dept. No. 88, pp. 97–101, 1945.
(12) Hertig, M., and Fairchild, G. B.: Am. J. Trop. Med. 28: 207–230, 1948.

U. S. GOVERNMENT PRINTING OFFICE: 1949