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Control of insect vectors of disease

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THE CONTROL OF INSECT VECTORS
OF
DISEASE

Deane Alfred Petersen

Senior Thesis Presented to the College of Medicine
University of Nebraska
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INTRODUCTION

The field of preventive medicine has been gathering increasingly larger numbers of enthusiasts and an ever-widening scope of problems for study. The problems of controlling insects, both those detrimental to plants as well as those which disseminate disease, are not new, but have received more active attention since our armed forces have been exposed to and contracted many of the previously strange sounding diseases of the tropical and semi-tropical countries. The problem does not end with the control of the insect vectors in only those areas of operation where the diseases are endemic, for it has been found that many of these same vectors are a part of the fauna of our own United States. Immediately the problem is apparent: if these insects serve as vectors in the battle areas, will they and can they also serve a similar role here? Many of the returning veterans and prisoners of war will be infected and it is a serious question whether or not they will serve as reservoirs for these various diseases. Even if our native insects do not act as vectors for these diseases, the rapid means of transportation by air may import insects which are capable of transmitting the diseases. Individuals

who are infective stages of disease may also arrive by air transport.

International quarantine¹ in the past has been based upon evaluation of recent contacts of the traveler with quarantinable diseases - cholera, plague, smallpox, louse-borne typhus and yellow fever - and upon physical inspection upon arrival in order to detect the presence of symptoms of infection. This practice is presupposed accurate knowledge of the occurrence of disease in areas from which the traveler had departed and inferred that sufficient time had elapsed since exposure for the infection to have become apparent. In air travel, particularly during war, neither of these assumptions was valid. Furthermore, physical inspections at airports of entry and enroute, required disproportionate effort and time, frequently inconveniencing both traveler and quarantine personnel. The result was evasion, irritation, and a conviction of uselessness.

In the revised regulation, a different approach is adopted. War Department¹ policy requires all military personnel and all civilian personnel on duty with the army to be immunized against smallpox as a routine measure and against typhus fever, yellow

fever, cholera, and plague, whenever significant exposure may be anticipated.

The new regulation¹ requires that the "pilot of the aircraft will be notified in writing that all persons aboard, unless otherwise indicated, have met these requirements". Freedom from vermin and from quarantinable disease at the time travel is begun is ordinarily certifiable on the basis of normal medical care of military personnel.

No¹ animal or plant product likely to convey disease or subject to quarantine or other restrictive regulations, and no living plant or animal - will be carried across national boundaries by an airplane under the jurisdiction of the Army, except upon specific permit.

Much confusion¹ in the past has resulted from varied routines in disinsectization of aircraft. The revised regulation provides for disinsectization only once during each span of flight in which there is danger of the transmission of insects, or in accordance with civil requirements. Spraying should be with the aerosol-pyrethrum bomb after full loading of the plane and with all openings of the cabin closed. This is in agreement with the recommendations

of international groups also studying this problem and permits concentration of effort at one time, to combine effectiveness with least objectionability. It is not anticipated that disinsectization will be needed in flight or upon landing except, as in Brazil, where civil regulations require such measures.

Recalculation¹ of requirements permits reduction of approximately 50% in the amount of spray to be released in all types of aircraft. Since this provides a less irritating spray, the end-result should be greater acceptability and over-all effectiveness of the procedure. Spraying should be carefully timed, and proportionately devoted to cabin, cockpit, and other spaces requiring disinsectization.

It is not to be expected that the family physician be an entomologist or an engineer. He should however, be able to recognize the diseases and the vectors in his region and to perform reliable microscopic studies when the need arises. He should be alert to recognize dangerous conditions such as inadequate screening, larvae in the rain barrel, and adult mosquitoes on the wall of the sick room, and be in frequent and friendly communication with public health officials.

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Even where sufficient biologic knowledge exists, control may fail to be established because of economic, social and political conditions. In many diseases, the mechanism of transmission is largely understood, but adequate preventive measures are not yet available.

Control does not necessarily require the complete extirpation of a vector, but rather the reduction of the vector below a critical level of density. Control measures once established must usually be retained as a permanent institution. Preventive measures are rational only when based on exact knowledge of transmission mechanisms.

Riley and Johannsen² divide arthropods into three separate groups as to methods of transmission of disease. First, simple carriers which incidentally serve as transporters of disease to the healthy. As an example they site the case of the house fly and typhoid fever. Second, are the direct inoculators to which the species of insects with biting or piercing mouth parts belong, and whose mouth parts are contaminated, innoculating the bacteria directly into the next victim. The horse flies and anthrax are cited here for examples. The third major group are those

arthropods which are essential hosts of the disease "germs", and at least one part of the life cycle of the organism is undergone in the insect. Two well-known examples of such an arrangement are the anophelid mosquito to malaria, and the cattle tick to Texas fever. This group in itself may disseminate infection in at least three different ways: first by infecting man or animals who ingest it. Dipylidium caninum in the cystericeroid stage occurs in the dog louse or in dog or cat fleas and by accidentally ingesting the infected insect the vertebrate becomes infected. Hymenolepis diminuta undergoes part of its life-cycle in various meal-infesting insects and is accidentally taken up by its definitive host. Another is Dracunculus (Filaria) medinensis which is received through swallowing, in drinking water, the crustacean Cyclops containing the larvae of this worm. The second method of dissemination is by infecting man or animals on whose skin or mucous membranes the insect host may be crushed or may deposit its excrement. The causative organism may then actively penetrate or be inoculated by scratching. An example is the causative organism of typhus fever deposited by the body louse. The third method of dissemination is by direct inoculation

by its bite as happens in the case of malaria and the mosquito, and Texas fever and the cattle ticks.

From this short discussion it can be seen that to understand only the disease process in man is not sufficient, but if we are to prevent infection, which is fully as important as treatment, we must understand not only the life history and habits of the organism itself, but also something of the life-history and characteristics of the insects that serve as a part of the life cycle or as carriers.

It is not enough to find an insect capable of transmission of the disease organism, but Koch's postulates must be proved. When an insect is suspected of being a host, proof must be sought through experimental laboratory work in attempts to discover whether the suspected insect, after having bitten a patient, is capable of infecting susceptible animals or persons through biting; or whether the salivary glands, or the crushed body of the insect, or the contents of its gastro-intestinal tract, or its expelled feces, are capable of transmitting the disease to susceptible animals when inoculated.

The problem of control of insect vectors resolves itself basically into a phase of public health

Like all public problems, our health officers must be adequately supported by an intelligent public opinion. They can gradually develop the desire for cleanliness of person, of home, or private and public buildings, of all operations concerned with the disposal of garbage and wastes, of farming operations and so forth. Until we can instill into the great body of our citizens, the desire for cleanliness in all things, we can hope for very little progress by the passage of drastic sanitary laws which, difficult to enforce, ofttime defeat the ends they were intended to serve. Education of the public must come first. This can be accomplished by a planned campaign in the newspapers, by the board of health, by school authorities, by posters, by talks and radio addresses, by lantern slides, and movie films.

The possibility of our being sent as medical officers to countries where the diseases and insect vectors are endemic is not remote. Therefore, it is our duty to recognize the problems that are to be facing us and to prepare ourselves to meet these problems. It is with this concept in mind that I present this thesis. I realize that all angles of some problems not been covered, and that other sections contain mu

detail. I have attempted to extend those facts that seem to me to be of most general interest and practical importance.

The separate section written on dichlore-diphenyl-trichlorethane may appear to be out of place and might well be used as a separate thesis topic; however, because of the recent enthusiasm shown by the public and investigators and its close relationship to my problem, I have included a section on D.D.T.

INSECT MORPHOLOGY

A brief review of the anatomy and characteristics of an insect is necessary both for the purpose of definition and for study of a means to attack the offensive types.

The body of an insect is composed of a head, a thorax, and an abdomen.

The head⁷ is provided with eyes, simple or compound, or both, two antennae or feelers, and the mouth parts including the maxillary palpi. The structure of the mouth parts varies depending on the feeding habits of the insect which may be masticatory or suctorial and may be adapted to piercing or cutting the skin and sucking blood.

The thorax⁷ is divided into three segments; the prothorax, mesothorax, and metathorax. Each segment is divided into two main portions: the tergites, or nota, forming the dorsal part; the sternites, the ventral part. The lateral surfaces are known as the pleura. From both sides of each sternite there arises a leg, making three pairs of legs in all. Each leg is composed of a coxa, trochant femur, tibia and tarsus. From each side of the mesothorax and metathorax there arises a wing, making two pairs of wings in all. This however, is not true of

all members of the Class for in the Order Diptera there is but one pair of well developed wings, the second pair or hind pair being rudimentary; in some of the Hemiptera there are merely vestiges of one pair of wings only, while in the Orders Siphonaptera and Anoplura wings are entirely wanting.

There⁷ is no osseous system. The hard chitinous integument, the exo-skeleton, which invests the body of the insect serves not only as a protective covering to the soft parts, but as an attachment for muscles, as well as to maintain rigidity.

There⁷ is no vascular system. The blood, which is colorless, circulates in the body cavity and is kept in circulation by passing through a thin-walled pulsating aorta located in the extreme dorsal part of the abdomen and thorax.

There⁷ is no lung or gill. Air is taken in through stigmatic openings located on the sides of the thorax and abdomen. It is carried to the most remote parts of the body by a system of branching tracheae which have their origin at the stigmatic openings.

The central nervous system⁷ is represented by a chain of ganglia running close to the ventral wall, from the head through the thorax and into the

abdomen. The first or largest ganglion, the brain, is located in the head and is pierced by the esophagus. The special senses are well developed.

The kidneys⁷ are represented by the Malpighian tubules which empty into the intestines.

The digestive system,⁷ the salivary glands and the reproductive organs are well developed. The salivary glands and their ducts have no connection with the alimentary tract, other than the buccal cavity.

The number of segments⁷ of the abdomen varies. There are normally ten; the terminal segments being modified to form the accessory organs of generation. Each segment is composed of a tergite dorsally and a sternite ventrally. They are connected to each other by a soft membrane. The membrane connecting the tergite with the sternite contains the opening of the tracheae and is called the pleural membrane.

The body⁷ of an insect is furnished with setae (hairs and bristles), and at times with spines, and perhaps with spurs.

Depending on the species, an insect⁷ in its life cycle may undergo a complete or a gradual metamorphosis. The former requires four stages; namely - egg, larva, pupa, and imago or adult. Growth occurs

in the larval stage; the larva shedding its old skin as it increases in size, a new one having formed to take the place of the old. The larva is active and voracious. When fully grown it turns into a pupa in which stage the insect ceases to eat and is usually quiescent, but may be active as in the case of mosquitoes. It is in the pupal stage that the wonderful changes take place which transform the lowly worm-like larva into the fully developed, highly organized adult insect.

The gradual metamorphosis⁷ is somewhat different. The young emerge from the egg looking not unlike the adult except in size, color, and hardness. They eat the same food as the adult. These immature forms grow by successive moultings similar to the larval stage of the complete metamorphosis.

The sexes⁷ are not differentiated until the final moult which results in a fully formed and fully grown insect. These immature moulting forms correspond to the larval and pupal stages of the complete metamorphosis.

There⁷ are a number of Orders in the class Insecta which are of no interest in preventive medicine even though economically they may be of great importance

HISTORY

The history of insect-borne disease extends back before the time of Christ when there was a belief that mosquitoes were concerned in the transmission of malaria.

At the time of Herodotus, a contemporary of Hippocrates (4th Century B.C.), all over Egypt the population was annoyed by mosquitoes. The following description of means of dealing with this nuisance is of considerable interest as it contains the first reference to a mosquito net.

"The³ contrivances which they use against gnats, wherewith the country swarms, are the following: In the parts of Egypt above the marshes, the inhabitants pass the night upon lofty towers, which are of great service, as the gnats are unable to fly to any height because of the winds. In the marsh country, where there are no towers, each man possesses a net instead. By day it serves him to catch fish, while at night he spreads it over the bed in which he is to rest, and creeping in, goes to sleep underneath. The gnats, which, if he rolls himself up in his dress or in a piece of muslin, are sure to bite through the covering, do not so much as attempt to pass the net".

One² of the most remarkable of the early suggestions was by the Italian physician, Mercurialis, who lived from 1530 to 1607, during the period when Europe was being ravaged by the dread "black death", or plague. He wrote: "There can be no doubt that flies feed on the internal secretions of the diseased and dying, then, flying away, they deposit their excretions on the food in neighboring dwellings, and persons who eat of it are infected." Mercurialis had no conception of the animate nature of contagion and his statement was little more than a lucky guess.

In the medical literature of the eighteenth century there are scattered references to flies as carriers of disease. Edward Bancroft⁴ in 1769 wrote about "yaws": "It is usually believed that this disorder is communicated by flies who have been feasting on a diseased object, to those persons who have sores, or scratches, which are uncovered; and from many observations, I think this is not improbable, as none ever receive this disorder whose skins are whole." As early as 1587, Souza suspected⁵ flies of spreading yaws (Framboesia). It was years later when Castellani⁵ in 1907, demonstrated that flies do play a part in the dissemination of this disease--obtaining the organism

(Treponema pertenu) from sores and passing it on to the well.

In 1848², Josiah Nott of Mobile, Alabama, published a remarkable article on the cause of yellow fever, in which he presented "reasons for supposing its specific cause to exist in some form of insect life." While Nott's ideas regarding the relation of insects to yellow fever were vague and indefinite, it was almost contemporaneously (1854) that the French physician Louis Daniel Beauperthuy argued in the most explicit possible manner that yellow fever and various others are transmitted by mosquitoes. He thought the mosquitoes brought the disease from decomposing matter and injected it into man and this was long before the discovery of pathogenic bacteria by Pasteur. Beauperthuy not only discussed the role of mosquitoes in the transmission of disease, but he taught, less clearly, that house flies scattered pathogenic organisms. Some believe Doctor Beauperthuy may be regarded as the father of the doctrine of insect-borne disease.

Filariasis

In 1863 Demarquay⁵ discovered the larval nematode in cases of chyluria; they were later seen by

Wucherer in other cases and Lewis in 1872 discovered that the blood of man is the normal habitat of this filarial worm. Doctor Patrick Manson in 1866 went to Formosa and Amoy, China (1871) where he investigated everything that came his way. He found filariae abundant in the blood of his Chinese patients, established the "periodicity" of their appearance in the peripheral circulation and in 1879 published the first account of an insect, Culex fatigans (the house mosquito of the tropics), serving as the intermediate host in the developmental cycle of any parasite. He believed the females died soon after laying the eggs, and the disease to be propagated in man by drinking the water in which infected mosquitoes died. In 1900 Low discovered the true method. In 1890 Manson returned to London and in 1893 he evolved his mosquito theory of malaria. Ronald Ross continued the work and later made his epoch making discovery in 1897 and 1898.

In 1891 Manson⁵ reported a new filaria in the blood of natives from the Congo and Old Calabar, naming it Filaria sanguinis hominis major (later known as Microfilaria diurna). On account of its diurnal periodicity, Manson predicted that some blood-sucking, day-feeding fly would be found to be the intermediate

host. From talks with the natives of Old Calabar he suggested that the "mangrove flies", Chrysops dimidiata and Chrysops spp. would prove the correct flies. In 1912 Leiper confirmed this prediction and Kleine (1915) worked out the plan of transmission in detail.

Fedschenko (1869)⁵ demonstrated that Cyclops (Crustacea) were intermediate hosts of the famous "fiery serpent" of Moses, the dragon worm, Dracunculus medinensis. Manson 1894 confirmed this work.

Thus the advances in the general field of parasitology and the clarifying of the conception of the role of intermediate hosts in the life cycle of some of the grosser forms paved the way for the discoveries which have revolutionized the control of some of the most devastating diseases of man and animals.

Malaria

No traditions⁶ have been handed down to us concerning the knowledge of malaria of the ancient Egyptians. In contrast, the material from Greek sources is extremely rich. The legend of the philosopher Empedocles of Agrigentum (about 550 B.C.), who delivered Selinus in Sicily from a plague by draining the marshes, or by turning two rivers into them,

proves how early the Greeks rationally associated malaria with swamps.

The Hippocratic writings⁶ (4th Century B.C.) abound with information concerning malaria. For 2,000 years little was added. Some of the most important insights of the Hippocratic writers were even forgotten for example, that children are the main sufferers in endemic areas. This was only rediscovered by Robert Koch in 1899. The Hippocratic writers knew of the periodicity of these fevers; they spoke of tertians, and quartans, and mentioned the benign character of the latter. They described the stages of the attack (chills, fever, perspiration), symptoms such as splenomegalia and bilious complexion, and sequelae like oedema and cachexia. The Hippocratic writers noticed the seasonal character of the disease, and the detrimental consequences of wet spring and dry summers. They stated the relation between marshes and fevers. It is true they misunderstood this influence and thought fevers were caused by drinking marsh water.

The same knowledge⁶ of malaria is reflected in Plato and Aristotle and in later Greek medical authors such as Aretacus and Galen.

As clinicians,⁶ the Romans were never any-

thing but imitators of the Greeks, but as engineers they have left their mark in history. Vitruvius, the great architect and military engineer of Augustus, observed that certain transmitting mosquitoes cannot breed in salt water.

Little of importance⁶ occurred until Sydenham (1624-1689) in 1676 recognized the value of Peruvian bark (cinchona) as a specific against malarious fevers and who was one of the first to establish the rules for the use of the drug. Richard Morton (1635-1698), who, in his Pyretologia (1692), gave, in addition to Galenic theories, not only a wealth of clinical observations and valuable indications for treatment with the bark, but first proposed the differentiation of fevers on the basis of their yielding to cinchona. It was thus possible to identify not only the typical tertians and quartans, but a great number of "continuous" or remittent fevers as malarious and different from other "remittent" fevers like typhoid.

Giovanni Maria Lancisi⁶ (1654-1720) was mainly interested in the cause of the periodic fevers and his main purpose their prevention. He thought the disease-producing emanations of swamps were of two kinds: animate ("worms") and inanimate. He

probably came closer to answering the malaria riddle than any who came before him. The differentiated theories of Lancisi on the manner in which swamps produce fevers gained no ground. The crude theory that poisonous vapor or miasma emanating from swamps (mal' aria = bad air) is the culprit, remained the general explanation of the disease in the medical profession up to the end of the nineteenth century.

As far back as 1847 Meckel² called attention to the fact that the spleen of patients dying of malaria presented a characteristic pigmentation and it was soon seen that the pigment was to be found in the red blood corpuscles in cases of the disease. Thirty years later Laveran in 1880 working in Algeria, demonstrated that this pigmentation was contained in a living parasitic organism in the red blood cells of his patients. More than ten years was required before Laveran's organism was accepted as the causal agent of disease.

In 1883 A.F.A. King³ in America also propounded a mosquito malarial theory.

Ross⁵ continued his work and in 1897 recorded his great discovery that "dappled-winged" mosquitoes served as the definitive hosts of species of Plasmodium. His results were fully confirmed by Bastianelli,

Bignami, and Grassi (1898 and 1899), Manson (1898), and Sambour and Low (1900). This discovery by Ross is undoubtedly one of the great landmarks in medical history for it has led to the reduction, and can lead to the elimination of the most widespread and devastating of human diseases.

Piroplasmiasis

The first great advance in the study of the relation of arthropods to protozoal diseases was made in 1889 when Smith and Kilbourne² discovered that the dread Texas fever, or Red-water fever, of cattle was caused by an intracorpuseular protozoal parasite, Piroplasma bigemina, and when very soon afterward the demonstrated that this organism was transferred from animal to animal solely by the cattle tick, Boophilus annulatus.

Trypanosomiasis

In 1895 Bruce⁵ discovered Trypanosoma brucei, the causative agent of Nagana or Tsetse fly disease of cattle in Zululand and demonstrated the Tsetse fly, Glossina morsitans, could transmit the disease from the sick to the well. In 1909 Kleine proved the developmental cycle in the fly and showed the true methods of transmission. In 1901, Forde,

in West Africa, observed a parasite in the blood of a European patient suffering from Gambian sleeping sickness; later Dutton (1902) recognized it as a trypanosoma and described it as Trypanosoma gambiense; Castellani (1903) and Bruce and Nabarro (1903) proved this trypanosome was the causative agent of sleeping sickness and that Glossina palpalis was the transmitting fly. In 1910 Stephens and Fantham described Trypanosoma rhodesiense as the etiological agent of Rhodesian sleeping sickness while Kinghorn and Yorke (1912) proved that Glossina morsitans was the transmitter. In South America, Chagas (1909) demonstrated that a trypanosome, Trypanosoma cruzi; was transmitted by a bug, Triatoma megista. This parasite is the etiological agent of South American trypanosomiasis or what has been called Chagas's disease.

Yellow Fever

While these African⁵ investigations were being developed, the American Army Yellow Fever Commission, consisting of Reed, Carroll, Lazear, and Agramonte, made a still more remarkable discovery. They demonstrated in 1900 that yellow fever can be transmitted only through the agency of the "tiger mosquito" or yellow fever mosquito (Stegomyia fasciata,

Aedes calopus, Aedes argentens now known as Aedes aegypti). Though Carlos Finlay, a Cuban physician had as early as 1880 propounded a mosquito theory for yellow fever, it must ever redound to the glory of this band of devoted workers that, due to their discovery, one of the most deadly of human diseases could now be controlled or even eliminated. In 1928 Bauer, proved that three other species of mosquitoes were capable of transmitting yellow fever. Since that date some seven additional species of mosquitoes have been shown capable of transmitting yellow fever.

Plague

In 1894, Yersin and Kitasato⁵ independently discovered the causative agent, Bacillus pestis, of plague, and Yersin demonstrated that the disease in man was identical with a plague-like disease of rodents. Simond (1898) suggested that fleas were agents in the dissemination of plague and his experiments showed that he was on the right track. In 1903-1904, Verjbitski demonstrated that fleas act as vectors of the plague bacillus but his results were not published until 1908. The development of the plague bacillus in the gut of the rat flea was independently discovered

by Liston (1905) and the role of fleas play in the epidemiology of plague fully determined by the British Plague Commission (1907-1908). Finally Bacot and Martin (1914) demonstrated the method of transmission of the plague bacilli by fleas.

Dengue

Dengue⁵ or breakbone fever, was shown by Graham (1902) to be mosquito-borne and his results were confirmed by Ashburn and Craig (1907). Though the mosquitoes with which these investigators were supposed to have worked have since been shown not to be true vectors, yet their discovery was of great importance. The true vectors have since been shown to be Aedes aegypti and Aedes albopictus.

Pappataci Fever (Three-day fever or sandfly fever)

Pappataci Fever⁵ was shown by Doerr, Franz, and Taussig (1909) to be transmitted by a sandfly, Phlebotomus papatasi. Oraya Fever, Verruga Peruviana, or Carrion's disease, a disease of rather high mortality in parts of South America, was demonstrated by Townsend (1913-1914) to be transmitted by Phlebotomus verrucarum and his results have been confirmed by Noguchi and his

associates (1929). Phlebotomus spp. have also been incriminated as vectors of Kala-azar, Oriental Sore, and Espundia.

Various recurrent fevers in man have been shown to be tick or louse-borne. Ross and Milne⁵ (1904) first demonstrated that the tick, Ornithodoros moubata, is the vector of African relapsing fever caused by Spirochaeta duttoni. These conclusions were confirmed and extended by Dutton and Todd (1905) working independently in Africa. Since then various species of ticks (Argasidae) and lice (Pediculus humanus) have been shown to be natural transmitters of the different relapsing fevers of man. Mackie (1907) working in India first demonstrated the part played by lice (Pediculus corporis) in the dissemination of relapsing fevers.

Tsutsugamushi Disease

Tsutsugamushi disease⁵, Kedani fever, Flood fever, Japanese River fever, and so forth, a serious disease in Japan, China, Formosa and other parts of the Far East, was first diagnosed as a distinct disease by Balz and Kawakami in 1879. Kitasato (1891-1893) as a result of his observations, decided that the bites of a red mite played a role in the causation of the

disease. The mite theory of the transmission of the disease has since been fully confirmed by the work of Tanaka (1899), Kitashima (1909) and Miyjima (1918), Miyjima and Okumura (1917) and others. The etiological agent has been isolated by Nagayo and his associates (1931) and described as a Rickettsia, R. orientalis.

Rocky Mountain Spotted Fever

Rocky Mountain spotted fever was definitely proved by Ricketts⁵ (1906) to be transmitted to man by a tick Dermacentor andersoni Stiles. His results have been fully confirmed by various later workers and Wolbach (1916, 1919) determined the causative agent to be Dermacentroxemus rickettsi.

Typhus Fever

Though the head and body lice (Pediculus humanus variety capitis and variety corporis) have been closely associated with man in all his long career, it⁵ was not until 1909 that Nicolle, Comte, and Conseil working in Tunis, demonstrated the role played by the body louse (corporis) in the spread of the much dreaded typhus or jail fever. These results were confirmed by Ricketts and Wilder (1910) working

independently in Mexico. Da Rocha-Lima (1916) discovered the causative agent and named it Rickettsia prowazeki. During the World War I (about 1915) a peculiar disease dubbed "trench fever" appeared among the troops of the contending armies and was definitely proved by various workers to be disseminated by the head and body lice. Topfer (1916) described what is considered the causative agent as Rickettsia quintana.

Tularaemia

A peculiar plague-like disease⁵ of rodents was investigated by McCoy (1911) and the etiological agent, Bacterium tularense, was isolated and described by McCoy and Chapin (1912). In 1911, Pearse, in Utah, described a peculiar disease of man under the title of "Insect Bites" and this disease later became known as "deer-fly fever". Francis (1919-1920) recognized the identity of "deer-fly fever" of man and the plague-like disease of rodents and named the disease Tularaemia. Francis and Mayne (1915) demonstrated that the deer-fly Chrysops discalis (Tabanidae), was the transmitting insect. Since then a large number of insects and ticks have been shown to be able to transmit the disease in nature.

Onchocerciasis

Blacklock⁵ (1926) determined that Onchocera volvulus passes part of its life cycle in black flies (Eusimulium damnosum, Family Simuliidae) while Hoffman (1930) and Strong (1931) demonstrated that Onchocera caecutiens undergoes a developmental cycle in at least three species of black flies.

Mechanical Carriers

Very early the filth-loving flies, in the mind of the common people and the physicians were associated with disease outbreaks. An abundance⁵ of flies during the summer presaged an unhealthy autumn, wrote Sydenham (1666), and since his time a long series of physicians and others called attention to the abundance and dangers from filth-loving flies. Veeder (1898) called more specific attention to the house fly while Reed, Vaughan, and Shakespeare (1900) outlined the role of the house fly may play in the spread of typhoid fever. Since then the importance of filth-loving flies as possible disseminators of disease-producing organisms has been well established and recognized. Doctor L. O. Howard² in this country was actively interested in all phases of the subject

of insect-borne disease, and is responsible more than any other man, for the awakening of the public to a realization of the dangerous possibilities of transmission of disease by the house fly.

MALARIA

Control of malaria depends fundamentally upon the prevention of bites by anopheline mosquitoes. The fight against the anopheles sometimes failed due to misconceptions concerning the habits of the mosquito. In 1826,⁹ when the first naval hospital was commissioned at Pensacola, Florida, an eight foot brick wall was built around the compound in order to keep out mosquitoes. It seems that people in those days believed that the mosquitoes could fly no higher than that.

The numerous species of anopheles vary in their susceptibility to infection with plasmodia. They vary no less widely and significantly in their habits. Generalized statements are not only inadequate, but they are definitely detrimental to successful control. Success in mosquito abatement depends upon exact knowledge of the species of mosquitoes in the particular region to be placed under control, of the habits of each particular species or subspecies, and of the appropriate methods for the abatement of each species. There¹⁰ are almost 200 species in the genus Anopheles, but only 17 have any great importance as vectors of malaria.

The eggs¹⁰ of the mosquito are produced in

large numbers and are deposited in water. The character of the site chosen for oviposition tends to be constant for a given species and is a fundamental determinate of control measures. Thus Anopheles quadrimaculatus, the common vector of malaria in the southeastern United States, breeds in swamps, pools, lakes or stagnant or impounded water. Accordingly, the control of malaria in the domain of Anopheles quadrimaculatus required such measures as drainage of swamps and the application of larvicides to reservoirs. In Malaya where Anopheles maculatus breeds in running water on cleared land, an entirely opposite technic was requisite. Dams were constructed, streams being converted thereby from sluggish pools which discharge over small water falls. Although the swamp is traditionally feared as a hotbed of malaria, in regions where the vector is not paludic, swamp areas may actually be safe. In each region detailed knowledge of the habits of the local vector is indispensable. For this reason the control of malaria usually requires the collaboration of the malariologist, the entomologist and the engineer.

The eggs¹⁰ of the anopheline mosquito are frequently hardy enough for hibernation. Under

proper environmental conditions they hatch, yielding actively motile, voracious, air-breathing, aquatic larvae. These molt four times as they grow, then change into aquatic nonfeeding pupae, and finally into adults. Certain species habitually produce but one brood each year; most species breed repeatedly in any one season. At all stages the rate of development is greatly dependent on conditions of temperature, humidity, salinity, acidity, and so forth. The external form of the larvae is highly distinctive for a given species and is as important for the epidemiologist as for the taxonomist. Through a knowledge of larval morphology it becomes possible to identify the breeding sites of each species in a given area. Great attention is also paid to the morphologic traits of the adult, reliance being placed chiefly on the venation and the color pattern of the wings and on the structure of the terminal abdominal segments. Within the limits of a similar anatomic form, subspecies may exist. These subspecies sometimes exhibit marked behavioral individualities in the transmission of malaria. This is notably true of the common European species Anopheles maculipennis, which includes at least seven subgroups, recognizable by egg markings and characterized by

important ecologic differences.

The mosquito¹⁰ transmits malaria by virtue of its habit of sucking blood. With respect to this fundamental property, certain significant limitations exist. The males of all mosquito species lack the mechanism for drawing blood and hence have no direct role in the transmission of malaria. Many species of anopheline mosquitoes avoid man and ordinarily subsist on the blood of other animals, including common domesticated mammals. Other species exhibit differing degrees of preference. A few dangerous varieties show marked predilection for human blood. In mosquitoes which have fed on blood, the source of the blood meal can be studied profitably by means of the precipitin test. This procedure makes it possible to determine feeding proclivities.

Mosquitoes¹⁰ likewise differ in the tendency to frequent or to avoid the habitations of human beings and of animals. This trait, like many of the traits which have been mentioned, is apt to be constant for a given species in a given area, but need not be constant for any one species in all areas of occurrence.

The flight range of mosquitoes has been the subject of much divergence of opinion. Valuable data

have been accumulated by the liberation and recapture of adult mosquitoes permanently stained with aniline dyes. The¹¹ effective flying range of malaria mosquitoes rarely exceeds a mile in the tropics, but is apt to be more than this in temperate zones or under exceptional conditions of wind or terrain in the tropics. Most of the flying and biting occurs at night.

It is evident from the foregoing considerations that the control of malaria is necessarily local and regional. To an equal degree, the control of malaria is also social. In the choice of the methods to be employed in a given area, the malariologist not only must consider geographic and entomologic minutiae, but must understand the economic and social relations of the disease in the area under examination, since these relations limit his effectiveness or may nullify it altogether. In the southern¹⁰ United States, for example, malaria is chiefly a disease of poverty-stricken rural communities. Consequently, the more expensive methods, such as drainage, will often be impossible, and indeed the purchase of atabrine or quinine may be beyond the reach of most persons. Similarly, it will be futile to recommend screening for dilapidated leaky dwellings which can scarcely support a roof.

The social¹⁰ aspects of malaria are also seen in the relations between the occurrence of the disease and the activities of man. Thus, malaria has accompanied the irrigation of sugar cane fields in the West Indies, the cultivation of rice in Portugal (but not in all countries), the production of rubber in Malaya, the construction of levees along the Mississippi river, the reclamation of land in the Netherlands and the construction of the famous Burma road.

Prior¹⁰ to engaging in the actual choice of control measures in his allotted territory, the epidemiologist will execute a malaria survey and an anopheline mosquito survey. These are intended to reveal the quantity, type, severity and distribution of the malaria; the identity, density, location and habits of the vectors, and incidental information about the distribution and habits of the human population. Where several species of Anopheles are present, it is often necessary to concentrate on the principal vector. Unless the facilities are unusually good, it is also necessary to disregard mosquito species which are merely pests, such as culicine mosquitoes. Where detailed maps are unavailable, these must be made. Geographic and especially climatic conditions must also receive careful attention.

Among¹² the most important means employed in the control of malaria among our armed forces are the elimination of mosquitoes by destroying their breeding places, and by killing them with insecticides, and the interposition of barriers which will prevent them from biting troops. When complete protection against mosquitoes is not possible, certain drugs such as atabrine, given regularly, are valuable to prevent immediate sickness from malaria. Antimosquito measures employed to control malaria are, in general, also applicable to the prevention of other mosquito-borne diseases such as dengue and filariasis.

Personal¹² protective measures include the wearing of protective clothing, use of bed nets and repellents, and the taking of suppressive drugs such as atabrine and quinine. Except when the bed is suitably protected by a bed net, which is inspected daily for rents, individuals must wear long trousers and long-sleeved shirts buttoned to the neck with sleeves rolled down from dusk until dawn. Trouser legs should be encased in boots or leggings.

Environmental¹² control includes mosquito proofing of buildings, draining and filling of mosquito breeding places, and spraying and larviciding,

all of which have their greatest usefulness at permanent bases and semi-fixed installations.

Camps¹² should not be located within flight range of large breeding places of mosquitoes or of native villages which provide a reservoir of infection. Native workers are not allowed to live on the military reservation or within a mile of military quarters.

Mosquito-proofing¹² of buildings is one of the most effective measures in reducing malaria. Not only sleeping quarters, but also washrooms, latrines, mess halls, day rooms, post exchanges, theaters, and all other buildings where personnel may congregate indoors during the evening should be tightly screened. The diameter¹¹ of wire and of the apertures are important. In general it is not safe to use screening which has apertures larger than 0.0475 inch (0.121 cm) in diameter. Heavy grade copper wire screening, having sixteen meshes to the inch (about forty to the centimeter), has a wire diameter of 0.0150 inch and a mesh diameter of 0.0475 inch, but regular sixteen mesh wire screening has apertures measuring 0.0512 inch (0.130 cm) which will not exclude all malaria vectors and will not keep out members of the Aedes genus. Standard eighteen mesh wire screening has a wire diameter of 0.0090 to

0.0100 inch (0.023 to 0.025 cm) and a mesh which is 0.0456 inch (0.116 cm) in diameter. Proper routine maintenance of screening is essential, with prompt repair of rents and tears, and discovery and blocking of new cracks and knotholes.

One¹² of the most effective means of breaking up the cycle of malaria transmission is the destruction of the adult mosquito. The aerosol insecticide dispenser, containing pyrethrum or D.D.T. in solution, is used for spraying all types of enclosures such as barracks, billets, tents, bomb shelters, trenches, foxholes, jungle shelters, mosquito bars, jungle hammocks, and gun emplacements, as well as aircraft and ships. Pyrethrins¹³ are contact poisons and kill all species of mosquitoes and certain other insects by destructive action on the central nervous system. The sprays are non-toxic to man and lower animals. Pyrethrins rapidly disintegrate by photochemical catalytic reaction when exposed to sunlight and oxygen. In selling containers, Pyrethrum extracts will maintain their potency for a year or more, even in the tropics. If a Pyrethrum spray fails within three minutes to kill all additional mosquitoes with which it comes in contact, it no longer contains the standard amount of

Pyrethrins and is not suitable for use. Pyrethrum is commonly supplied in containers holding a mixture of 20 to 1 concentrate sesame oil and liquid freon¹⁴ (freon 12 is non-toxic, non-inflamable dichlorofluoromethane under 85 pounds pressure). The Quartermaster dispenses this in 18 oz. (532 cc) mixture of liquid freon (freon 12) with .08% wax free Pyrethrins and 6% sesame oil. The sesame oil is a synergist or activator and enhances the killing power of Pyrethrins. The vapor pressure of the solvent produces the necessary spraying pressure which does not decrease as long as a drop of liquid is present in the closed container. When freon 12 containing the insecticide is sprayed, it forms a fine mist from which the solvent vapors immediately, leaving the Pyrethrum and sesame oil suspended in the air as a cloud of fine droplets causing an aerosol. When aerosol dispensers are not available, liquid spray dispensed from flit-gun type sprayers should be used to kill adult mosquitoes inside buildings. D.D.T. residual spray applied to tents, screens, and the walls and ceilings of buildings leaves a residue which kills mosquitoes and other insects which alight or crawl on the treated surfaces. This toxic effect persists for from two to three months

Most mosquito repellents¹³ have had one or both major defects; a transitory or weak effect, and a risk of poisoning by absorption of the skin especially when the repellent had to be used liberally during extended periods. For example, diethylene-glycol is a mosquito repellent, but is reported to be toxic when absorbed through the skin and apt to damage kidney and liver tissue if used freely for a considerable time. There are two excellent repellents known as "612 Everready", and dimethylphthalate (also called "Skat"). It may be stated that repellents will give good protection against mosquitoes for about four hours after liberal application even when the subject is sweating. A third repellent "Indealone" is better than the average cream, but is less effective than the two liquids.

Control¹² of mosquito breeding is accomplished either by draining or filling the breeding areas, or, when this is not possible, by treating them with chemicals which kill the larvae before they can transform into adult mosquitoes. Drainage⁷ plus clearing debris and plants from the border of streams and ponds, straightening edges and deepening channels so that a free and more rapid flow of water may be

had, are important measures in the control of the Anopheles mosquitoes. Drainage is applicable to ponds marshes, lakes, puddles and ditches in which water has become stagnant. Temporary puddles can be controlled by oiling, road ditches should be cleaned and channels leveled out. Old wells, cisterns and the like should be filled, oiled, or treated by chemicals. Streams should be straightened and cleaned and made free of vegetation at the edges. The obstructions to the flow of water should be removed. Drainage ditches should have clean-cut sloping edges, steep banks, and uniform grade and width, a straight course and kept free from weeds, stones, sticks, or anything that might impede the flow of water. When bends are necessary, sharp bends should be avoided. The bottom should be narrow so that the flow of water will be rapid instead of slow. As few ditches as possible should be dug. The main drainage ditch should be dug first and the laterals built on as they are needed. The laterals should enter the main ditch at an acute angle or a curve in order to lessen the deposit of silt or sand at the junction.

Not all foliage along the banks of streams and ditches is to be considered a hindrance in the control of malaria mosquitoes. It¹⁵ was noted that

the breeding of Anopheles culicifacies was more intense in canals whose banks were devoid of shrubs and creepers, than in those where there was a dense marginal growth of certain plants. Ipomea bilaba, a fast growing creeper, is sometimes planted along the embanked portions of a canal to strengthen the bends; it acts as a sand-binder. It appears to reduce mosquito breeding. Experiments made with other plants showed Vitex negundo to be useful. It is quick growing perennial shrub with lateral branches and thick quinque-foliate leaves, which provide shade and mechanical obstruction to the oviposition of mosquitoes. It is easily propagated by cuttings. Significantly fewer larvae were found in a section of canal whose banks had been so planted than in a control section similar in all respects save its banks' vegetation.

Earth⁷ ditches may be expensive to maintain and to reduce the ultimate cost of maintenance as well as to make drainage more effective, it may be advisable to give them a permanent lining of cement. A rough base of concrete (1:3:5) may be laid on the bottom of the ditch about $1\frac{1}{2}$ inches thick and extending for about 6 inches up the side or 3 inches above the normal water line for small ditches. This should be covered with

$\frac{1}{2}$ inch of cement and sand (1:1). This lining should be "U" shaped, not "V" shaped. In large ditches 24 inches or more in width, the lining should extend higher and be thicker. The lining should also extend higher at the bends or key walls should be built. Seepage holes should be provided above the key wall. A lining of concrete 2 inches thick reinforced with chicken wire is satisfactory or a rough lining of flat stones sealed roughly with cement mortar may be used.

Sub-soil drainage⁷ is another method of drainage in which the level of the ground water is lowered permitting surface pools to be absorbed more quickly. Drain tiles of 3 to 12 inches in diameter and 1 to 2 foot lengths are used. All drains are spaced 50 to 150 feet apart and laid up and down the slope. Drains should be 2 to 4 feet deep. The deeper it is the more area drained and the fewer drains needed. A grade of 12 inches to 400 feet should be laid and each piece of pipe should touch the other. The joints should be loose. Drains should be covered with earth. Sub-soil drainage has the advantage over surface drainage of being more easily maintained, because it is self cleaning, needs little attention, and no oiling, besides there is no water exposed in which mosquitoes may breed.

The outlet should be guarded by metal rods to prevent entrance of small animals. Such drains should never be used to collect house drainage in which there is much sediment.

Vertical drainage⁷ is a method of draining surface water into a well dug or bored through the upper impervious stratum to a porous water bearing stratum below.

Where drainage is not economical or practical filling all depressions holding water may be used. This is particularly true of small collections of water in hoof-prints, household water containers, tin cans, old automobile tire casings, coconut shells, road ruts, shell holes, and bomb craters. Shallow parts of ponds should be filled so it is easier to care for the deeper parts. Sawdust, shavings, rubbish, ashes, cinders, and the like, serve satisfactorily for material to use to fill in.

Impounded water⁷ should be kept as high as possible when mosquitoes are not breeding. Before breeding season begins the level of the water should be lowered so that all brush and land vegetation which has accumulated along the edges at high water will be killed when the water falls. During the breeding

season, the water should be kept as low as possible, unless to do so uncovers growth otherwise submerged.

To be effective in controlling mosquito breeding, larvicides must be reapplied at intervals of from a week to ten days. Three¹² types of larvicide are in common useage at the present time: D.D.T., oil, and Paris green. Oil itself (diesel or fuel oil number 2, or used crankcase oil) is an effective larvicide. The oil⁷ kills larvae by plugging the breathing tube when they come to the surface to breathe, thus asphyxiating them. It also acts as a chemical poison and as deterrent against egg laying. Oil solutions may be applied to water surfaces by hand sprayer, knapsack sprayer, power sprayer, or by merely pouring it on the surface. Vegetation is a barrier, rain may wash the oil away, and the wind may blow the film to shore. When using diesel oil number 2,¹² from 10 to 30 gallons are required per acre of water surface for complete coverage with a uniform stable oil film. When 5 per cent D.D.T. in oil is used, only 1 to 2 quarts per acre are required. It is usually necessary to spread oil once a week. Continuous oilers are useful where the oil will be dispersed by currents, as in streams or ditches. It must be pointed out that contin-

uous oilers require a good deal of attention, generally use more oil than would be dispensed for the same area from a knapsack sprayer, and are often unreliable. A gunny sack of oil soaked sawdust or waste anchored to the bottom of the pond, or drip cans for streams and ditches may be used. A flow of ten to twenty drops per minute for a square foot of surface is usually sufficient. A wick may be used to regulate the flow.

Paris green¹³, an aceto-arsenite of copper, is a microcrystalline powder. Its color should be emerald green with at least 50% arsenious oxide. Solubility should exceed 3%. Paris green should pass a 300 to 325 mesh sieve. The later has a mesh opening measuring 0.043 mm. As mixed readily in the field, Paris green should kill all second, third, or fourth stage larvae in a laboratory jar in two hours. It¹² is highly effective against anopheline larvae. Although the specific gravity of Paris green powder is greater than that of water, it usually remains on the surface for at least several hours. The longer it floats, the better it is as an anopheline larvicide. The usefulness of Paris green depends on the fact that it is a gut poison for larvae. This especially true for Anopheli

larvae and when Paris green floats long enough in still water, it will be ingested by Aedes and by some Culex larvae which feed some of the time at the surface. Paris green has its greatest use against Anopheles larvae. It¹² is frequently the larvicide of choice for the treatment of rice fields where oil solutions might injure the plants. Dust mixtures are prepared with diluents such as powdered soapstone, slaked lime, or road dust. The required dilution of Paris green varies from 5 to 10 per cent by volume for hand-operated dusters and from 1 to 2 per cent for hand casting. When dusted from airplanes, 25 per cent mixtures are usually employed. Paris green mixtures can be applied to ponds, lakes, and larger streams with rotary dust blowers by putting the dust blowers by putting the dust into the air from the windward side so that it will form a cloud and be carried out over the water. From 1 to 3 pounds of Paris green are generally required per acre of water surface.

If Paris green¹³ and other larvicides are not available, phenothiazine makes an effective substitute, either dust directed or used in water. It is less suitable than Paris green but floats better.

Nitre cake⁷ is an efficient larval poison

poison when used in the concentration of one part for every 100 parts of water. It is used in old wells, cisterns, fire buckets, small stagnant ponds and other small bodies of water where there is no danger in poisoning persons or animals.

In¹² some areas stream-breeding anophelines may be controlled by periodically sluicing the stream. A small dam is built to impound water which can be suddenly released to flush away the larvae. Where irrigation water in rice fields or canals is a source of breeding, effective mosquito control is sometimes possible by interrupting the supply of water so that the fields become just dry enough each week to remove the surface film of moisture without drying the roots of the plants. Periodic fluctuation of the water level in ponds and reservoirs is sometimes very effective in controlling mosquito breeding by preventing growth of shore-line vegetation favorable to the larvae. It¹⁶ has been found that the breeding of Anopheles albimanus can also be eliminated by increasing the relative salinity to about 75% sea water. Anopheles albimanus breeds abundantly in certain brackish coastal lagoons in Puerto Rico. This degree of salinity can best be maintained in marginal areas of lagoons by tidal action

produced by an adequate sea connection. It has also been observed that a very troublesome plant, widgeon grass (probably Ruppia maritima) stopped spreading and was largely eliminated. It grows in dense mats in the brackish water making a particularly favorable habitat for Anopheles albimanus.

Natural² enemies of the larval mosquitoes can also be used to some advantage in limiting their numbers and in special pools. One of the oddest natural enemies is the plant called the bladderwort which traps large numbers of the larva. Aquatic bugs such as the Ranatra, Nepa, Notonecta, and Zaitha, dragon-fly nymphs, adult and larval water beetles, Hydrophilus, Dytiscus, all destroy large numbers of the aquatic forms of the mosquito. The adult toads and frogs also clean up their share of the larval and adult forms of the mosquitoes. Salamanders, Diemictylus viridescens help by consuming many mosquitoes. The top minnows⁷ or mummichogs (Poeciliidae), the sun fishes (Centrarchidae) and the minnows (Cyprinidae) are all useful in the control of mosquitoes in certain ponds. The fish must be of small size to get into small places and both the old and the young must feed on mosquito larvae. They should multiply rapidly and be able to live under a great many

conditions. Goldfish and tadpoles are of value to limit the larvae in lily pools and other ornamental pools. Other natural enemies² of adult mosquitoes include the lizards which enter houses freely in the tropics and are not insignificant in mosquito reduction, spiders, birds such as the nighthawks and swallows, a parasitic nematode, Paramermis canadensis, which inhibits the development of the Aedes vexans; and the bats used in Texas are all helpful in diminishing the mosquito incidence.

In many cases⁷ it is possible to set up biological barriers to the mosquito. Malarial mosquitoes will suck blood of animals, even preferring animal blood to human blood. Piggeries may be established well removed from human habitations, but between such habitations and the source of mosquito breeding. In this way, many of the mosquitoes seeking blood will be intercepted by the piggeries and will not reach human habitations. It is possible to build pig pens so that they will act as mosquito traps, that is, mosquitoes enter but cannot leave and they may be killed from time to time by fumigation.

If mosquito control¹⁷ is to be successful, some organization must be responsible and be equipped

with the necessary authority and means. It is possible to use existing political organizations for this purpose, but the practical difficulties are at times considerable, as few existing political entities match in their boundaries the mosquito infested areas which should be treated as units. For that reason, different types of organizations have been established by laws in various states. New Jersey made it compulsory for counties to establish a mosquito abatement organization with an appointive state official, an ex-officio member of the commission, in each county. California has districts, but they are not compulsory and some districts are too small and have such restricted funds as to be rather ineffective in their operations.

It¹⁸ is firmly believed that any military malaria control program will fail unless it has the intelligent and active support of the men and officers of the force for which it is intended. Camp areas are visited frequently and local control problems discussed with line officers as well as with medical officers. Participation for the officer and men means first and preeminently the acquisition and constant practice of good malaria discipline. Good malaria discipline implies a willingness and an ability to utilize individu-

ally and collectively all anti-mosquito measures available.

Education of the public is necessary before their interest and cooperation can be expected. There¹⁷ are four main points to be emphasized in this campaign: first, that the mosquitoes constitute a health menace or a considerable handicap to the comfort and development of the community; second, that it is worth while to spend money to remove this menace or handicap; third, that the mosquito nuisance can be satisfactorily controlled; and fourth, that the cost of abolishing the mosquito will be reasonable. The means of education can and should take several forms; newspaper publicity, speeches, radio talks, motion pictures and slides, exhibits, informative pamphlets, house to house inspections, and generalized tours of inspection.

The perfection¹⁷ of detail of mosquito control may not be as important as continuity of effort. Except in a few unusual cases a sustained attack, year after year, will produce better ultimate results than an intense attack in one year followed by comparative neglect and inaction.

In order to summarize the whole problem of control of mosquitoes, the following is a classification¹⁷

of mosquito abatement methods:

Against aquatic stages

I. Mechanical

- a. Drainage
 - 1. Open
 - 2. Subsurface
 - 3. Vertical
- b. Pumping
 - 1. Surface water
 - 2. Subsurface (well) water
- c. Diversion of water
- d. Channeling of streams and sloughs
- e. Filling low areas
- f. Restriction or control of excessive use or needless abuse of irrigation water
- g. Miscellaneous
 - 1. Screening or mosquito-proofing cisterns, wells, and water containers
 - 2. Removal or destruction of unnecessary artificial water containers
 - 3. Removal of protective vegetation or floatage
 - 4. Repair of leaks or defects in water supply, plumbing, or drainage systems
 - 5. Tree surgery

Against adult mosquitoes

I. Mechanical

- a. Screens, nets, special clothing
- b. Deterrents, fans and punkaks, exposure to wind
- c. Trapping
 - 1. Bated traps
 - 2. Light traps
- d. Hand catching and killing
 - 1. Active season killing
 - 2. Winter killing
- e. Removal of houses or villages beyond the flight range

Against aquatic stages

II. Toxic

- a. Petroleum derivative oils
 - 1. Direct refinery products

2. Treated oils for increased toxicity or increased spreading capacity.
3. Restrained waste oils
- b. Larvicides
 1. Emulsions
 - Pyrethrum
 - Cresylic or phenolic acid
 2. Soluble poisons
 3. Solids (powdered)
 - Paris green
 - Phenothiazine
 - Gesarol (D.D.T.)
- c. Toxic gases

Against adult

II. Toxic

- a. Sprays
- b. Fumigants
- c. Chemical repellents

Against aquatic stages

III. Naturalistic

- a. Chemical
 1. Changing salt (Na Cl) content of the water
 - Salinifications
 - Freshening
 2. Pollution with decaying vegetation (herbage packing) with sewage or wastes
 3. Stagnating
- b. Physical
 1. Drying by agricultural use or by special planting
 2. Natural fills (silting)
 3. Setting water in motion
 4. Intermittent drying
 5. Fluctuating water levels
 6. Flushing or sluicing
 - Automatic
 - Hand operated
 7. Constant level flooding
 8. Controlled reflooding and redraining
 9. Agitation
 - Volumetric
 - Surface, especially by wind
 10. Shading to exclude sunlight

11. Clearing to expose to sunlight
12. Muddying
- c. Biological
 1. Introduction of natural enemies
 - Predatory fish
 - Other aquatic predators
 2. Changing flora and fauna to unsuitable or competitive types
 3. Elimination or destruction of aquatic food supplies (copper sulfate as an algicide)

Against adult mosquitoes

III. Naturalistic

- a. Chemical
 1. Administration of drugs like sulfur which cause odorous perspiration
 2. Creating repellent barriers of odorous plants
- b. Physical
 1. Clearing, destruction or removal of shelter
 2. Creation of plant barriers to flight
 3. Rendering dwellings, especially bedrooms, unattractive to mosquitoes
- c. Biological
 1. Introduction of natural enemies
 - Predatory
 - Crepuscular birds, etc.
 - Parasites
 2. Deviation by animals
 3. Minimizing available harborage for winter hibernation

THE MORE COMMON OR MORE GENERALLY TYPICAL BREEDING PLACES OF THE MOST IMPORTANT SPECIES OF ANOPHELES MOSQUITOES TRANSMITTING MALARIA IN VARIOUS REGIONS AND THE PRINCIPAL CONTROL METHODS WHICH MAY BE EMPLOYED

Modified and Enlarged by Harold Farnsworth Gray from a Diagram Originally Devised by Sir Malcolm Watson (Further Modifications by Division of Preventive Medicine, Bureau of Medicine and Surgery, U. S. Navy, 1943)

REGION	Brackish water swamps, pools and marshes, usually open to sunlight	Fresh water swamps, usually open to sunlight	Fresh water swamps, pools, shaded. Water under jungle or swamp vegetation	Large rivers, fast or slow, grassy edges (stream bed pools)	Small streams, ditches, seepages, moderate current, grassy sides, clear water	Hill streams, free from grass, very slow current, clear water	Hill streams, free from grass, rapid current, clear water	Irrigation channels, with bays or sockets, grassy sides, average current	Shallow seepage, clear water, from irrigation or streams	Reservoirs, impounded water, ponds, bays, lakes	Rain water pools, especially if containing algae. Rock pools	Springs, small pools, hoof-prints	Rice fields	Open wells	Tanks in open air, or dark wells in houses	Artificial containers, cans, coconut shells, gourds, boats, etc.
South Pacific Islands	<i>A. punctulatus moluccensis</i>	<i>A. punctulatus moluccensis</i> <i>A. p. punctulatus</i>	<i>A. punctulatus moluccensis</i>	<i>A. punctulatus moluccensis</i>	<i>A. punctulatus moluccensis</i>	<i>A. punctulatus moluccensis</i>					<i>A. punctulatus moluccensis</i>	<i>A. punctulatus moluccensis</i> <i>A. p. punctulatus</i>				<i>A. punctulatus moluccensis</i>
Netherlands Indies	<i>A. sundanicus</i> <i>A. subpictus</i>		<i>A. umbrosus</i> (also in brackish water)		<i>A. maculatus</i> (in sunlight) <i>A. br-birostris</i>	<i>A. minimus flavirostris</i> <i>A. maculatus</i> (in sunlight)	<i>A. maculatus</i> (in sunlight) <i>A. kochi</i>	<i>A. aconitum</i>		<i>A. kochi</i>	<i>A. subpictus</i> (usually polluted)	<i>A. leucosphyrus</i> <i>A. hyrcanus sinensis</i>				
Philippine Islands					<i>A. minimus flavirostris</i> <i>A. maculatus</i>	<i>A. minimus flavirostris</i>	<i>A. minimus flavirostris</i>							<i>A. minimus flavirostris</i>		
Malaya	<i>A. sundanicus</i>		<i>A. umbrosus</i>		<i>A. maculatus</i> (? <i>A. barbirostris</i>)	<i>A. maculatus</i>	<i>A. maculatus</i>	<i>A. aconitum</i>		<i>A. philippinensis</i>			<i>A. annularis</i> (fuliginosus) <i>A. minimus</i> <i>A. philippinensis</i>	<i>A. umbrosus</i>		
Burma	<i>A. sundanicus</i>				<i>A. minimus</i> <i>A. maculatus</i>	<i>A. maculatus</i>	<i>A. maculatus</i>	<i>A. minimus</i>		<i>A. philippinensis</i>						
India	<i>A. sundanicus</i>	<i>A. annularis</i>		<i>A. superpictus</i> <i>A. jeyporensis</i>	<i>A. minimus</i> <i>A. fluviatilis</i>	<i>A. superpictus</i> (Baluchistan)		<i>A. culicifacies</i> <i>A. minimus</i>		<i>A. philippinensis</i> (in open ponds)	<i>A. culicifacies</i> <i>A. stephensi</i> <i>A. minimus varuna</i>	<i>A. culicifacies</i> <i>A. annularis</i>	<i>A. stephensi</i> <i>A. minimus varuna</i>	<i>A. stephensi</i> <i>A. minimus varuna</i>	<i>A. stephensi</i>	<i>A. stephensi</i>
Ceylon				<i>A. culicifacies</i> (in sand pools)	<i>A. minimus</i> <i>A. fluviatilis</i>								<i>A. minimus</i> <i>A. culicifacies</i> <i>A. annularis</i>	<i>A. culicifacies</i> <i>A. minimus varuna</i>	<i>A. stephensi</i>	
Thailand, Indo-China		<i>A. tessellatus</i>		<i>A. culicifacies</i> <i>A. jeyporensis</i>	<i>A. minimus</i> <i>A. culicifacies</i> <i>A. maculatus</i> <i>A. barbirostris</i>	<i>A. minimus</i> <i>A. maculatus</i>	<i>A. maculatus</i>	<i>A. culicifacies</i>		<i>A. minimus</i> (?)			<i>A. minimus</i> <i>A. culicifacies</i> <i>A. hyrcanus sinensis</i>	<i>A. culicifacies</i>		
China		<i>A. tessellatus</i>		<i>A. jeyporensis</i>	<i>A. minimus</i> <i>A. maculatus</i>	<i>A. minimus</i> <i>A. pattoni</i>	<i>A. maculatus</i>	<i>A. minimus</i> <i>A. hyrcanus sinensis</i>			<i>A. subpictus</i>		<i>A. hyrcanus sinensis</i> <i>A. minimus</i> <i>A. pattoni</i>			
Near East	<i>A. sacharovi</i> (elutus)			<i>A. culicifacies</i> <i>A. superpictus</i>	<i>A. culicifacies</i> <i>A. superpictus</i>						<i>A. gambiae</i> <i>A. superpictus</i>	<i>A. sergenti</i>			<i>A. stephensi</i> <i>A. claviger</i>	<i>A. stephensi</i>
North Africa	<i>A. maculipennis labran-chiae</i>	<i>A. algeriensis</i> <i>A. pharoensis</i>		<i>A. superpictus</i>	<i>A. superpictus</i>			<i>A. multicolor</i>				<i>A. sergenti</i>	<i>A. maculipennis labran-chiae</i>			
Central and South Africa		<i>A. funestus</i> <i>A. nini</i> <i>A. bargreavsi</i>		<i>A. funestus</i> <i>A. nini</i> <i>A. bargreavsi</i>	<i>A. gambiae</i> <i>A. funestus</i>				<i>A. gambiae</i> <i>A. funestus</i>	<i>A. gambiae</i> <i>A. moucheti</i>	<i>A. gambiae</i> <i>A. funestus</i>	<i>A. gambiae</i> <i>A. funestus</i>	<i>A. gambiae</i>	<i>A. gambiae</i>	<i>A. funestus</i> <i>A. gambiae</i>	
Italy, Balkans, Spain	<i>A. maculipennis labran-chiae</i> (also var. <i>atropurpureus</i> in Spain and Portugal) <i>A. sacharovi</i> (elutus)			<i>A. superpictus</i>	<i>A. sacharovi</i> (elutus) <i>A. superpictus</i>	<i>A. superpictus</i>						<i>A. sacharovi</i> (elutus)	<i>A. maculipennis labran-chiae</i>			
Russia, Eastern Europe	<i>A. sacharovi</i> (elutus)	<i>A. maculipennis messeae</i> <i>A. m. maculipennis</i>		<i>A. superpictus</i>	<i>A. sacharovi</i> (elutus) <i>A. superpictus</i>	<i>A. superpictus</i>			<i>A. maculipennis maculipennis</i>			<i>A. sacharovi</i> (elutus) <i>A. m. maculipennis</i>				
South America		<i>A. albimanus</i> <i>A. albimanus</i>		<i>A. pseudo-punctipennis</i> (pools, algae) <i>A. darlingi</i>	<i>A. argyritarsis</i>						<i>A. albimanus</i>	<i>A. tarsimaculatus</i>				
Central America West Indies	<i>A. tarsimaculatus</i>	<i>A. albimanus</i>	<i>A. punctimacula</i>	<i>A. pseudo-punctipennis</i> (pools, algae)							<i>A. albimanus</i>	<i>A. tarsimaculatus</i>				
Southern North America											<i>A. quadrimaculatus</i>					
Western North America					<i>A. punctipennis</i>					<i>A. maculipennis freeborni</i>			<i>A. maculipennis freeborni</i>			

EFFECTIVE MOSQUITO CONTROL MEASURES WHICH ARE APPLICABLE TO THESE TYPE BREEDING PLACES

Open marsh ditching. Dykes, tide gates and ditches. Filling (hydraulic and natural). Increase salt content of water by flooding with sea water. Decrease salt	Drainage. Natural and artificial fill. Enclosure by dykes, with flooding plus larvicidal fish. Pollution with decaying vegetation. Oiling. Paris green. Pyrethrum larvicide.	Drainage. Natural and artificial fill. Clearing to let in sunlight. Pollution with decaying vegetation. Oiling. Paris green. Pyrethrum larvicide.	Channelizing of river stream. Controlled silting of stream bed sides. Clear away or poison grass. Oiling. Paris green. Pyrethrum larvicide.	Subsoil drainage. Open drainage with dense shade. Flushing. Oiling. Larvicidal fish. Paris green.	In Malaya, dense shade, flushing, oiling, subsoil drainage. Elsewhere flushing, channelizing of stream bed. Oiling. Paris green.	Flushing. Continuous drip oiling. (Dense shade against <i>A. maculatus</i>)	Intermittent irrigation. Reshape canal banks. Clear vegetation away. Larvicidal fish. Oiling.	Restriction of excessive use of irrigation water. Canal and ditch lining to reduce seepage. Larvicidal fish. Vertical drainage. Pump out low	Clear reservoir bottoms of all vegetation before filling. Fluctuating water levels. Larvicidal fish. Clear vegetation from banks. Oiling. Paris green.	Drainage. Filling. Oiling. Paris green. Pyrethrum larvicide.	Subsoil drainage. Drainage. Oiling. Paris green. Pyrethrum spray on springs used for drinking water.	Intermittent drying. Carefully level paddies before planting. Keep banks clear of vegetation. Muddying water. Larvicidal fish. Pyrethrum	Fill in, if not in use. Cover with mosquito-proof cover. Larvicidal fish? Pyrethrum spray. Oiling with a light oil such as kerosene.	Mosquito-proof covers or screens. Frequent change of water with surface disturbance. Larvicidal fish. Pyrethrum spray. Oiling with a light oil.	Remove, empty and/or destroy useless containers, shells, cans, gourds, etc. Empty water out of tanks periodically. Cresylic acid larvicide. Oiling.
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YELLOW FEVER

Yellow fever¹⁰ is an acute disease due to infection with a specific filtrable virus of small size (17 to 25 millimicrons). On epidemiologic grounds it is necessary to distinguish two types, urban yellow fever and jungle yellow fever. In these two types, the infecting agent is the same and the clinical and anatomic features are the same, but the dissemination, incidence, and technic of control are significantly different.

Until recent years¹⁰ urban yellow fever existed both endemically and epidemically in the sea-coast cities of tropical and subtropical America, with sporadic extension as far north as Philadelphia, New York and Boston. The last North American outbreak was that of 1905 in New Orleans. Nowadays yellow fever is met in South America and in an extensive area in West Africa. It has not occurred in the Orient.

In the urban variety¹⁰ the virus is conveyed to man by the bite of the mosquito Aedes aegypti. It is believed that both the virus and this mosquito were introduced into the western world from Africa as concomitants of the slave trade.

The nonimmune human¹⁰ being who is bitten by

a yellow fever mosquito passes through an incubation period of three to five days; he becomes infective to mosquitoes at least six hours prior to the onset of symptoms and continues infective during the first three days of illness. The mosquito becomes infective about twelve days after biting an infected person and remains infective for the rest of its natural life, a period of one or more months. In view of these facts it is possible for a man who has been bitten by a mosquito in Brazil to travel to the United States by airplane and infect Aedes mosquitoes before recognizable symptoms of yellow fever develop. It is also possible for infected mosquitoes to be transported by airplane or ship and to create epidemic outbreaks or endemic foci.

Aedes aegypti¹⁰ is found between the latitudes 40 degrees north and 40 degrees south in a zone extending irregularly around the world. This fact signifies that yellow fever can be transmitted to part of the United States (where indeed it has repeatedly occurred) and to such vast territories as India and Australia (where it has never succeeded in establishing itself). The disease can extend annually during warm weather to areas beyond the limits of

continuous mosquito infestation; such extensions are regularly terminated by frost. In previous centuries much of the transmission was mediated by sailing ships which offered numerous places -- such as water casks -- in which mosquitoes might breed or take shelter. For this reason, also, outbreaks of yellow fever were repeatedly observed to start in seacoast towns, the initial cases appearing in houses near the waterfront.

Aedes aegypti¹⁰ is predominantly domestic in its habits. It breeds by preference in artificial containers, especially those associated with human habitation, that is, rain barrels, tin cans, flower vases, holy water fonts in churches, heaps of discarded automobile tires, rubbish, cemetery urns, cisterns, pools which form between agave leaves, and so forth. Such situations are usually free from the natural enemies of the mosquito. The species also breeds in tree holes. In African villages Aedes aegypti has often been found in small collections of rain water which have gathered in and around the shrines of the local divinity.

The eggs¹⁰ are extremely hardy, being especially resistant to desiccation. The developmental cycle from egg to adult takes nine and a half to

eighteen days. The virus is not transmitted from one generation of mosquitoes to another.

Human beings who survive yellow fever are permanently immune. Since the presence¹⁰ of immune bodies can be detected by means of the mouse protection test, the test can be made to yield valuable information as to the past occurrence of the disease in a human or animal population. Indeed, the test is a priceless supplement to clinical observation, since it permits the detection of mild subclinical disease and aids in the diagnostic exclusion of such conditions as Weil's disease. Significant data are also collected through the use of viscerotomy. This is a punch technic by which small pieces of hepatic tissue can be removed post mortem for microscopic examination; in patients with yellow fever midzonal necrosis of the liver is encountered.

The control¹⁰ of yellow fever has been greatly complicated by the discovery that the disease is endemic in huge areas of South America in which Aedes aegypti does not exist. This fact compelled a search for new vectors and additional hosts. Investigations have now disclosed that the virus will survive under experimental conditions in certain mosquitoes of the genera Aed

Mansonia, Psorophora, and Wyeomyia. Indeed, several species, such as Aedes fluviatilis, Aedes scapularis, Culex fatigans and certain anopheline mosquitoes, have been shown capable of transmitting the virus by their bites. A few species of jungle mosquito (Aedes leucocelaenus, Haemagogus capricorni and certain species of sabethine mosquitoes) have been found naturally infected. It is likewise of great importance that many wild monkeys captured in endemic zones have been found immune, presumably as a result of previous infection; on at least one occasion fatal yellow fever has been observed in wild monkeys. No less than twenty-five simian species are susceptible to yellow fever, as are red squirrels, voles, hedgehogs and other small mammals.

Yellow fever¹⁰ acquired in the jungle is definitely susceptible to transmission to Aedes mosquitoes and in one recorded instance has led to an urban outbreak.

The control of yellow fever is dependent on the control of Aedes aegypti. This¹⁷ involves the systematic detection, inspection and reinspection of all possible breeding places, especially small containers, street vaults, sewer inlets and catch basins,

storm drains and street gutters, defective plumbing, such as house drains, leaky water pipes, improperly or unconnected refrigerators, building sumps, wet basements, abandoned buildings, barrels, buckets, tin cans roof gutters, breeding inside houses, ornamental garden ponds, reservoirs and ponds, sewage treatment works, air bombed areas, vases, cisterns, and rubbish heaps. Be-cause of the unobtrusiveness of the mosquito, great care and ingenuity may be demanded. In rural areas, the control measures should be particularly centered around the cesspools and privies, liquid manure tanks, liquid wastes from dairy drains and canneries, watering troughs, wells and cisterns, rain and fire barrels, streams, ditches, springs, tree holes, cemetery urns, duck clubs and impounded water anywhere.

The drainage technics described in the section on malaria are usually not necessary against yellow fever. A fundamental¹⁰ requisite is the introduction of piped water supplies and closed sewage systems. Small collections of water must be emptied weekly or screened or treated with larvicides. Houses must be screened and carefully mosquito-proofed. Since travelers and foreigners who enter an endemic area are apt to be nonimmune, it is advised that they avoid residing

in close proximity to the homes of the natives. All patients⁴ with yellow fever and all persons suspected of having it must be isolated immediately in screened buildings; all adult mosquitoes found in these and other habitations should be destroyed. The patients' homes should be fumigated.

In the control¹⁰ of urban yellow fever, it is not necessary to destroy every single individual of Aedes aegypti in a given area. It is sufficient to reduce the mosquito density below a critical level. This level depends on such factors as the density of the population, the percentage of immune persons, immigration of nonimmune persons and immigration of actively infected persons. If the proportion of immune persons is high, a comparatively large number of mosquitoes will be necessary to prevent the disease from dying out. On the other hand, if the proportion of immune persons is low, or if a group of nonimmune persons has suddenly entered the area of endemicity, a smaller number of Aedes aegypti will suffice to produce a high case rate. Mass migrations of people and especially military operations thus favor the development of out-breaks. Similar principles obtain in the epidemiology of malaria and many other infectious diseases.

For reasons already given, all ships¹⁰ and airplanes arriving from endemic areas should be subjected to examination for mosquitoes. Airplanes are usually sprayed with insecticides. Unvaccinated persons are kept under the surveillance of government authorities for the unexpired remainder of the incubation period.

Perhaps¹⁰ the most valuable method for the immediate control both of urban and of jungle yellow fever is vaccination. The vaccine consists of living yellow fever virus, known as strain 17D, which has been attenuated through many generations of tissue culture.

Although¹⁰ it has not yet been possible to extend vaccination to all the native populations of Africa, great and increasing progress has been made. In Central Africa, in regions where Aedes aegypti is scarce, Aedes simpsoni has newly been incriminated as a vector of jungle yellow fever. The wide prevalence of this mosquito threatens the spread of the disease into East Africa, India and Australia. In this connection, government officials have quite properly emphasized the disinsectization of aircraft, special antimalari airdromes being constructed for the purpose. Obviously it will be a long time before such control measures as vaccination or piped water supplies can be introduced

into remote African villages. Until this can be done, the menace of yellow fever will continue to live.

DENGUE

Dengue¹⁰ is a brief acute disease due to infection with a filtrable virus conveyed to man by Aedes aegypti and also by Aedes albopictus. The disease has occurred in vast epidemics in Athens, Greece, Formosa, Australia, and other countries. Great outbreaks have occurred in the southern United States (1905, 1922, 1934), especially in the Gulf States. A dengue-like fever was observed in California in 1934 and 1935.

The incubation period¹⁰ is believed to be between five and nine days. Virus is found in the blood during the last day of the incubation period and for three to four days thereafter, although the clinical course often lasts as long as ten days. After biting an infected human being, the mosquito cannot transmit the disease until eight to eleven days have passed. After this, the mosquito is infective during the rest of its life.

Immunity¹⁰ to dengue is inconstant and apparently brief. A high case rate is characteristic of dengue. Probably no disease except influenza spreads so rapidly and widely through a population. The mortality rate is estimated as between 1 in 1,000 and 1 in 5,000. Monkeys captured in nonendemic areas

are susceptible to infection with the virus; monkeys captured in endemic areas are often immune, presumably as a result of previous infection. It can be inferred that the monkey constitutes a natural reservoir of the virus.

From¹⁰ the foregoing introductory statements it will be observed that dengue has certain elements in common with yellow fever, especially as regards causation, incubation and transmission. Herein lies the chief epidemiologic significance of the disease. Where dengue has occurred, yellow fever can also occur; Aedes aegypti will serve as a vector for either. Hence the emergence of large outbreaks of dengue in Georgia, Florida, Louisiana, Puerto Rico, Australia and India is a warning that yellow fever might also obtain foothold in these areas.

There¹⁰ is at least one epidemiologic fact however, which modifies this generalization. Every outbreak of yellow fever leaves in its wake a large number of immune survivors, who are unable to infect mosquitoes. Consequently, the subsequent persistence of the disease requires a high density of infected Aedes. Dengue apparently produces no such intense and durable immunity. Hence, the virus of dengue can be kept alive by comparatively small numbers of mosquitoes.

Therefore, the control of dengue requires a much more drastic reduction of Aedes densities than is necessary for the control of yellow fever.

The disease¹⁰ is of military importance to the United States and Great Britain. The virus could easily incapacitate an army in a short time; the acute symptoms, moreover, are sometimes followed by protracted weakness and indisposition. Dengue recently occurred during the memorable defense of Bataan peninsula in the Philippine Islands.

At present¹⁰ no satisfactory method of immunization exists. The prevention of dengue, therefore, depends on measures directed against Aedes aegypti and Aedes albopictus.

RICKETTSIAL DISEASES

There¹⁰ are three main categories. The first, or typhus, group predominantly louse-borne, includes classic European endemic and epidemic typhus; Brills's disease; the widespread flea-borne murine typhus of southern and southeastern United States; the ship typhus of Toulon; urban, or shop, typhus of Malaya, and Mexican tabardillo. Trench fever¹⁰, an unwelcome visitor in the first World War, presumably belongs in the same category. The second, or spotted fever, group contains the tick-borne diseases--both the western and the eastern strains of Rocky Mountain spotted fever, Sao Paulo exanthematic typhus, fievre boutonneuse of the Mediterranean region, South African tick fever, Kenya fever and the newly described petechial fever of Tobia in Columbia. Australian Q disease and nine mile fever of Montana should probably constitute a special subdivision of the spotted fever group. The third group, borne by mites, includes tsutsugamushi fever, Sumatran mite fever and the so-called "rural typhus" of Malaya.

The rickettsial diseases¹⁰ vary widely in virulence. Thus in American murine typhus, the mortality rate is as low as 3 per cent, whereas the mor-

RICKETTSIAL DISEASES AND THE VECTORS AND ANIMAL RESERVOIRS OF THE CAUSATIVE ORGANISMS

DISEASE	ORGANISM	VECTOR	RESERVOIR
<u>Typhus Group</u>			
Classic, or epidemic, typhus (and Brill's disease)	R. prowazeki	Pediculus humanus (man to man) Xenopsylla cheopis (rat to rat and rat to man)	Rodents, man
Murine, endemic typhus	R. prowazeki	Xenopsylla cheopis	Rat, mouse
Ship typhus of Toulon, Manchurian typhus, Urban (shop) typhus of Malaya Tabardillo	var. mooseri	Pediculus humanus	
Trench fever	R. quintana	Pediculus humanus	Man
<u>Spotted Fever Group</u>			
Rocky Mountain spotted fever	D. rickettsi (R. rickettsi)	Dermacentor andersoni (western) Dermacentor variabilis (eastern) Haemaphysalis leporispal-	Tick (hereditary) numerous mammals

DISEASE	ORGANISM	VECTOR	RESERVOIR
<u>Spotted Fever Group (Con'd)</u>			
Sao Paulo typhus		Amblyomma cajennense	
Fievre boutonneuse	R. conori	Rhipicephalus sanguineus	Dog
South African tick fever		Rhipicephalus sanguineus Amblyomms hebraeum	
Kenya fever		Rhipicephalus sanguineus	Dog
Australian Q fever	R. burneti	Haemaphysalis humerosa (bandicoot tick)	Bandicoot
Montana X fever and nine mile fever	R. diaporica	Dermacentor andersoni	
<u>Tsutsugamushi Fever Group</u>			
Tsutsugamushi fever	R. akamushi (R. orientalis)	Trombicula akamushi	Vole (Microtus)
Malayan rural typhus		Trombicula deliensis	Rat

tality of classic European typhus is estimated at 30 to 50 per cent and that of Rocky Mountain spotted fever has approached 80 per cent in limited areas. Rickettsial diseases likewise vary in the degree of immunity which they produce. Many subclinical infections probably occur.

It¹⁰ is true that the vectors of rickettsial diseases are at present largely uncontrollable except in special circumscribed areas. For this reason, preventive measures nowadays are directed chiefly toward (1) avoidance of vectors, (2) reduction of mammals which either convey the vector or act as reservoirs of infection, (3) specific immunization and (4) general hygienic precautions.

The table, based on those of Wolbach¹⁹ and of Murgatroyd,²⁰ presents a classified list of rickettsioses and indicates the vectors and the animal reservoirs.

Typhus

Classic, or European, typhus is an acute infectious disease produced by Rickettsia prowazeki. This organism is conveyed from man to man by the louse Pediculus humanus. In the writings of Jarcho¹⁰ it is stated that typhus is transmitted from rat to rat by the important rat flea, Xenopsylla cheopis, and

the rat louse, Polyplax spinulosa; and from rat to man by Xenopsylla cheopis. The chief natural reservoirs of the disease are rodents and man; probably all rodents are susceptible, as well as monkeys, dogs, cats and opossums.

Unlike¹⁰ mites and ticks, lice are true insects: they constitute the order Anoplura of the class Insecta. They are small and wingless and have clawed legs and relatively large eyes. The human body louse, Pediculus humanus corporis, lives by preference in the inner layers of human clothing and sucks blood frequently, day and night. Changes in the temperature or the activity of the host cause the louse to migrate in search of other hosts; this favors propagation of the disease. The blood of the human patient with typhus is infective from the third to the tenth day of illness. Rickettsias acquired by the louse take up their residence in the epithelium of the insect's alimentary canal and are passed on to new hosts by the bite of the louse and by its highly infective feces. The duration of infectivity in the louse is uncertain.

In view of these principles¹⁰ it will readily be understood that European typhus tends to spread during the winter, especially when large numbers of

people exist in close confinement in unclean places accessible to rats and lice. Conditions of this sort regularly prevail in time of war, and it is a matter of historic fact that typhus followed the armies of Charles V, Gustavus Adolphus, Napoleon Bonaparts and Nicholar II. The mortality has often reached or exceeded 50 per cent.

Brill's disease,¹⁰ a mild sporadic congener of European typhus, has been encountered in the cities of the Atlantic seaboard. On epidemiologic grounds, the late Dr. Hans Zinsser²¹ ingeniously surmised that Brill's disease represents the delayed recurrence of infections acquired in Europe. It remains to be seen whether this concept will stand the test of time; recent immunologic evidence²² adduced by Plotz has been confirmatory.

Clearly distinguishable¹⁰ from louse-borne European typhus is the so-called endemic, or murine typhus, a disease caused by Rickettsia prowazeki var. mooseri and carried by the rat flea. This infection is now known to occur in almost all the Southern and Southeastern states. It is fortunately mild and differs from European typhus in that the peak of incidence occurs in the late summer and the autumn. Recently it

has shown a tendency to spread from its habitual urban strongholds into the small towns and the countryside; this spread is probably due to migration of the brown rat. Many other native rodents are susceptible, and the disease has been detected in the field mouse. Of late the peanut-growing districts of Georgia and Alabama have suffered a high incidence. A severe outbreak recently occurred in Nashville, Tennessee. The reservoir of murine typhus is the rat.

The so-called "ship typhus" of Toulon,¹⁰ the urban (shop) typhus of Malaya and the typhus of Manchuria probably belong in the category of murine typhus, as does the much severer louse-borne Mexican tabardillo.

The specific prevention of typhus is based on the control of the louse, the flea and the rat. Field mice and perhaps other rodents may have to be included.

The old saying,²³ "No lice, no typhus" is unchanged. To stop infection is to stop lousiness among the general community, not to kill a few infected lice. A typhus case in a louse-free community is no danger.

The use of powders²⁴ and sprays against body lice is by no means new. For at least three centuries

men have worn bags of herbs, impregnated their clothing, dusted on insecticides, or carried copes of pungent chemicals in the hope of warding off vermin.

The control of lice can be accomplished by eight cardinal rules of cleanliness and delousing. Avoid⁵ all contact with lousy persons and their effects, avoid overcrowding, bathe at least once a week, using plenty of hot water and soap and rub dry with a rough towel, underwear should be worn at all times and a complete change should be made at least once a week, the head should be carefully shampooed at frequent intervals; combed and brushed at least once a day and kept clean at all times, avoid unclean bedding, especially blankets, inspect head and body at frequent intervals, especially if you have been exposed to contacts with lousy individuals, and in case of infestation, vigorous treatment should be adopted at once.

Head lice⁵ may be removed by hand picking and combing. Heat the comb to a pleasantly warm temperature and lice will abandon their places at the bases of the hairs and can be removed more quickly. Frequent washing and combing will eliminate a mild infestation. In severe infestations, the hair should

be clipped short and the head shaved followed by a hot bath and plenty of soap and a complete change of clothing. Three other methods include; equal parts of kerosene and olive oil are used to wash the hair, next morning wash the hair with soap and water, then treat with vinegar or 10% acetic acid. Repeat this for two or three successive nights. A second method is to wash the hair, soak a large towel in a 10% tincture of larkspur (Delphinium) and wrap about the head like a turban for 6 to 8 hours; wash and repeat if necessary. The third method is to pour a 2½% solution of phenol or carbolic acid over the head, especially the nape of the neck and behind the ears. Continue this for ten minutes. Drain the hair (do not wring it out), and wrap the head with a flannel cloth or towel for an hour.

The pubic louse⁵ is eliminated by removal of perianal and pubic hair followed by hot bath and change of clothing. In heavy infestations, spray the region with 95% alcohol 2 or 3 times and fan dry, then remove the hair. The cast off clothing (shirt and fork of trousers) should be dipped in alcohol, allowed to dry, and not used for about two weeks.

The laundering of clothes requires careful attention. The clothes⁷ should be washed fifteen min-

utes at 131° F. in heavy suds and a light load, rinsed three times, three minutes each in water at 131° F., then extracted and dried in a tumbler for fifteen minutes at 140° F. until dry, and finally ironed.

The most troublesome of the three types of lice is the body louse. In the epidemics²⁵ of the last war, the chief methods of delousing were by heat and to a lesser extent by fumigation. Hot air treatment has made more rapid and reliable progress by the use of air circulation systems. For fumigation, many alternatives have been proposed instead of the dangerous hydrogen cyanide formerly used--methyl bromide here in the United States, methylallyl chloride in Britain, trichloroacetonitrile in Germany, and methyl formate in Russia.

A fumigant²⁶ for delousing clothing must have the following properties; it must be toxic to lice in a short time, even at low temperatures, it must be penetrating, non-injurious to clothing and not dangerous to man (that is, the clothing must be wearable directly after fumigation without danger from skin irritation or inhalation). Methyl bromide adequately fulfills these requirements.

Either²⁶ of two methods may be used, a

demountable chamber of $\frac{1}{2}$ inch plywood, and a bag method for use in the field. The former should be of 330 cu. ft. capacity and take over 50 barrack bags of clothing assembled on three shelves. One end, which forms the door, is closed against sponge rubber gaskets. Then the fumigant is introduced into the circulating system blown by a fan from a gasoline motor. After the fumigation, the residues are blown out of an exhaust.

For the field method,²⁶ bags of duck or sateen rendered gastight with ethyl cellulose or neoprene are used. These hold one soldier's uniform and blankets. They are sealed by folding over the margin three times and tying with tapes. An ampoule of methyl bromide is introduced with the clothing, and it is broken when the bag is closed. After fumigation, the clothing is turned out in a well-ventilated place, and it can be worn after five minute's airing.

Methyl bromide²⁶ is not free of all risks for bad burns have resulted from splashes of the liquid when used in fire extinguishers. Also the vapor has a delayed toxicity; and it is possible to acquire a lethal dose without being unduly affected at the time. Although hot air and fumigants are effective in kill-

ing lice, they made little headway in combating general lousiness in a large group of people living under difficult conditions, because the deloused people soon became reinfested. The need has been for some treatment which would keep the lice away, but no suitable insecticide was known which would insure more than two days freedom from them. This need for a louse-proofing agent was realized and two partial answers, evolved. One was a very finely ground insecticide, 'AL 63', which by clinging to dusted underwear protected wearer from reinfestation for five or six days. The other remedy was to spray the underwear with organic thiocyanates which killed lice and prevented reinfestation for a month. The thiocyanates could also be used on an anti-lice belt woven so as to attract lice which were then killed by the impregnated drug. Unfortunately the thiocyanates caused smarting of the skin if the wearer began to sweat profusely. As the result of experimentation, the American army first adopted a fine dust, 'MYL',²⁷ somewhat like the British AL63, but more efficient. This MYL contained pyrethrum which was scarce and wanted for other purposes. It²⁸ was developed by the U.S. Department of Agriculture, but the exact formula has not yet been revealed. In the meantime, the Russians²⁴ developed

two synthetic compounds: a powder containing diphenylamine, and clothing impregnated with the chemical bis-ethyl-xanthogen. The diphenylamine dust was successfully used among the civilian population in Moscow in the winters of 1941 and 1942. The powder is about as insecticidal as AL63. Garments impregnated with bis-ethyl-xanthogen, which is of the same order of effectiveness as the thiocyanates, were widely worn in Bessarabia when the Russian troops were there.

All these insecticides²⁵ developed in different countries suffer from more or less serious disadvantages. But the new synthetic compound, dichlorodiphenyltrichlorethane seems at last to give trouble-free protection from lice. For combating lousiness it can be used in two principal ways. As a powder diluted with kaolin or pyrophyllite it can be rubbed into underwear and will give protection from lice for two or three weeks. It is even effective when blown up the sleeves or down the necks of dressed people, and was largely applied in that way in Naples under General Leon Fox. The speed of this treatment accounts for his astonishing peak number of 73,000 people treated in one day.

Very early in the war, the danger of prisoners of war acting as transmitters both of insects especially lice and disease was recognized by the medical depart-

ment and elaborate steps for prevention were taken. Colonel Daniel L. Borden²⁹ describes a port where prisoners in large numbers are returned aboard our cargo ships. These ships are brought into the piers and are guarded on all sides by Coast Guard cutters manned by guardsmen with "tommy" guns to prevent any possible escape over the sides. Prisoners are then marched off the ships onto the pier, which is roped off in such a manner that they may be segregated and thoroughly searched. It is an amazing sight to see the types and kinds of articles that are removed from these prisoners of war. Any material found on the prisoners, such as knives, bottles which may be broken and thus used for escape purposes, and metal contraptions of any kind are removed and placed in salvage cans. All tobacco and matches are confiscated to prevent possible sabotage on the piers or train. All personal belongings such as pocketbooks, money, and toilet articles are then placed in a small bag furnished to and then to and then carried by the prisoners. All heavy clothing, overcoats, blankets, life preservers, etc. are taken from the men and put into a separate load. This heavy material is trucked away where it is sterilized as a separate unit.

The men²⁹ then are all marched in groups by their own noncommissioned officers to the fenced-in disinfection station. Needless to say, the pier embarkation area is thoroughly guarded by armed military police all equipped with "tommy" guns slung over their shoulders for instant use. Most of the military police selected for this guard duty speak either German, Italian, or both languages. In evidence on the pier and in the disinfection station are large directional signs written in English, German, and Italian.

Upon arrival²⁹ in the disinfection station, the prisoners are marched in groups of about fifty into a room where they are told exactly what is to be done to them from the moment they begin their disinfecting process to the time they arrive at the concentration camp. This lecture of instruction is given to separate groups namely German, and then Italian. In other words the prisoners are not mixed but are always carried through in groups of their own nationality under the command of their own noncommissioned officers.

The men²⁹ are then passed into a room where they disrobe and are given a fish net bag in which they place their personal clothing. With their bagged valuables and shoes in one hand, and their fish-net bag

containing their personal clothing in the other, they pass by a window, turn in their property and are given in return an identification tag number for the material which they deposited. This tag is worn like a dog tag around the neck and stays with the man throughout his delousing process. He is now entirely naked, devoid of all of his belongings, except his identification tag. He then passes along the line and must walk through three separate basins containing calcium hypochlorite for the control of ringworm, thence into the wash room where there are about thirty showers running, controlled by a master valve. A cake of ordinary laundry soap is given him as he passes along and he is required to stay under his shower, with supervised soaping and bathing, for a period of five minutes.

While passing through this procedure,²⁹ his clothes have gone into a steam sterilizer or methyl bromide fumigation chamber and his pack of valuables and shoes have been dusted with delousing powder so that all of these articles will have been sterilized by the time he is through his disinfecting process.

From the showers he is given²⁹ clean towels and after drying himself completely, he is again passed through a foot bath into another room where all the

hairy portions of his body is sprayed with an insecticide spray delousing material which cleans all lice and destroys nits. This spraying apparatus is an electrically controlled compressed air spray which strikes the man with considerable force thoroughly dusting his head, chest, axillae, pubic and anal regions. This spraying causes the insecticide powder to impregnate the air in the room. This problem is solved by an enormous electric fan installed in the roof which sucks the powder-laden air into the great outdoors.

After the man²⁹ has had a complete spraying, he is then examined individually by a rubber-gloved medical officer. If any lice, living or dead, are found, he is shunted off into another room where with electric clippers all the hair on his body is removed. This includes the hair of his head, chest, axillae, and pubic region. The hair is removed over hoppers and immediately burned.

Men with scabies²⁹ are treated in the same manner and given sulfur ointment as a control measure.

He²⁹ now passes along the line and picks up his deloused valuables and his clothes which have in the meantime been sterilized with steam under pressure. If the man by any chance has come to this country

without underclothing or with improper outer clothing, he is given ordinary prisoner garb supplied by the quarter master.

The only variation²⁹ from the above routine was extended prisoners who were brought in sick. These men were deloused by our corpsmen and were not required to go through the process already described. In other words they were deloused in bed by spraying and if necessary, clipping the hair. Whether well or sick, every prisoner arriving in this country is deloused. All personnel of the medical department who have come in contact with prisoners at the port of embarkation are required to pass through the delousing process after they have completed their tour of duty.

The control of rats requires a skillful persistent campaign, which must include rat proofing, poisoning and trapping. The details are readily available in numerous special treatises. The principal rat poisons¹⁰ are red squill, barium carbonate and strychnine. A mixture of strychnine, saccharin, oats and molasses has proved extremely useful. Fumigation can be accomplished by means of methyl bromide, hydrocyanic acid, carbon disulfide or sulfur dioxide and should be entrusted to persons specially trained. A

dead rat should be regarded as presumably infected and should be handled with appropriate caution.

A valuable and inevitable advance in the control of typhus has been the development of vaccines. One of the earliest vaccines¹⁰ is that of Weigl, who inoculated lice per rectum with rickettsias and subsequently emulsified the intestines in phenolized solution of sodium chloride. This vaccine is apparently effective but cannot be prepared quickly in large quantities. More satisfactory is the technic of Ruiz Castaneda,³⁰ who injected live rickettsias intranasally into mice and rats. This produces rickettsial pneumonia, from which the organisms are readily recoverable in large numbers. The rickettsias are diluted in a solution of formaldehyde and sodium chloride to a standard concentration of 1,000,000,000 per cubic centimeter. The vaccine is injected subcutaneously in doses of 0.5 cc., 1.0 cc. and 1.0 cc. at weekly intervals. Since the duration of the resultant immunity is as yet unknown, annual revaccination is advised by the manufacturer.

Another important typhus vaccine is that of Cox,³¹ who was able to cultivate many varieties of rickettsia in the yolk sac of the developing chick embryo. The Cox³¹ vaccine now commercially available is a suspension of rickettsias of the type causing

European epidemic typhus, grown in the yolk sac and killed with phenol and solution of formaldehyde. The dose is tentatively set at 3 cc., divided into three doses which are administered subcutaneously at intervals of five days.

Circular Letter 1 62, from the Office of the Surgeon General of the United States Army (issued Nov. 28, 1942), states:¹⁰ "At the present time, typhus vaccination is required for all military personnel stationed in or travelling through Asia, Africa, Europe (including the British Isles), and the mountainous regions of Central and South America (including Mexico, but excepting Panama). It should be recognized that vaccination alone is not adequate for the prevention of typhus... The vaccine approved at this time consists of a suspension of killed epidemic typhus rickettsiae prepared by the yolk sac culture method... The initial vaccination will consist of three injections of the vaccine, 1 cc. each, administered subcutaneously, with intervals of from seven to ten days between injections. A stimulating dose of 1 cc. of typhus vaccine should be administered every four to six months as long as serious danger of infection is present."

An interesting amplification of the yolk sac

method has been devised by Zinsser, Plotz and Enders.³² Minced embryonic tissue or macerated yolk sac taken from eggs on the fourth day following inoculation is used to inoculate large quantities of normal minced chicken tissue from ten days embryos. The tissue thus inoculated is distributed in large amounts of agar surfaces in Kolle flasks. The flasks are kept for a week at 37 C., and a rich yield of rickettsias is obtained. By this method, one bacteriologist and two technicians can prepare 1 liter of vaccine, enough for three hundred complete immunizations, in one week. The technical details and the effectiveness of this interesting method require evaluation.

European investigators¹⁰ have experimented with the use of attenuated live rickettsias, but this method has generally been avoided in America.

As yet there is no conclusive proof that any vaccine extant can be relied on to produce high degrees of immunity to typhus.

The second major group¹⁰ of rickettsial diseases consists of the tick-borne spotted fevers. In accord with taxonomic principles, ticks are not regarded as insects. They are placed in the class Arachnida, order Acarina. The larva has three pairs of legs, the adult four pairs. The ticks concerned in the

spotted fever are the wood tick, Dermacentor andersoni (western United States); the common dog tick, Dermacentor variabilis (eastern United States); the widespread rabbit tick, Haemaphysalis leporis-palustris. There are many other probable and potential vectors, as well as innumerable animals which can act as reservoirs of infection. Thus the control of the arthropod vectors is at present almost hopeless, and it is not astonishing that Rocky Mountain spotted fever has been encountered in nearly every state in the Union and in Canada. Virulent strains are not confined to the Western states.

Areas of brush have been burned in the attempt to lessen the density of ticks and of their mammalian hosts. The usual methods of rat control and rodent control are a necessary adjucant. Slight progress¹⁰ has been made by the introduction of avian and lepidopterous enemies of the tick. Ticks may be removed from cattle and other domestic animals by dipping in arsenical solutions (0.2 per cent arsenious oxide) or in petroleum, and by rotation² of pasture areas and hand-picking of individual animals.

Much can be accomplished by individual hygienic measures. Those persons¹⁰ who occupy infest-

ed areas should wear leggings or puttees to prevent ticks from crawling up within the trouser legs. Clothing should be removed and carefully inspected twice daily, and ticks found in clothes or on the skin should be removed systematically and destroyed. Tick bites may be treated with tincture of iodine or with a silver nitrate stick. Care should be exercised in the selection of camp sites. Campers⁵ should avoid sitting or sleeping on tick-infested ground. The use of hammocks is to be recommended. It is perhaps needless to add that patients with Rocky Mountain spotted fever or suspected of having it should be isolated from contact with ticks.

A vaccine¹⁰ has been prepared which is effective against Dermacentroxenus rickettsii (Rickettsia rickettsii), the cause of Rocky Mountain spotted fever. Larvae of Dermacentor andersoni are inoculated, raised to the adult stage, ground and suspended in a solution of formaldehyde and sodium chloride. Vaccination should be repeated annually. Similar vaccine has been prepared against Sao Paulo typhus, the spotted fever of Brazil. Topping³³ has had success in the treatment of infected laboratory animals with the serum of immunized rabbits.

The recent studies³⁴ of Trager have revealed the possibility of immunization against the tick vectors themselves.

Australian investigators¹⁰ have reported a rickettsiosis known as Q fever, caused by Rickettsia burneti and carried by the bandicoot tick, Haemaphysalis humerosa. The reservoir animal is the bandicoot. A high percentage of infection has been encountered among foresters and abattoir workers. Closely related to Australian Q fever is nine mile fever of Montana, caused by Rickettsia diaporica and conveyed by the wood tick, Dermacentor andersoni. According to Cox,³⁵ it is possible to prepare a polyvalent vaccine effective against both Rocky Mountain spotted fever and nine mile fever.

Tsutsugamushi Fever

The third major rickettsial group¹⁰ includes tsutsugamushi fever (also called Japanese river fever, or kedani), Malayan rural typhus and Sumatran mite fever. Immunologic studies have demonstrated strong bonds of similarity in the diseases of this group. Thus, Kouwenaar concluded that Sumatran mite fever belongs to the tsutsugamushi group and that Malayan scrub typhus is merely a variant;

Malayan shop typhus, however, is probably murine typhus. Similarly, Lewthwaite and Savor,³⁶ on the basis of cross protection tests, concluded that Sumatran mite fever is not a disease sui generis but is identical with tsutsugamushi disease. Heaslip³⁷ reported 54 cases of tsutsugamushi fever occurring in Queensland, Australia.

The causative organism,¹⁰ known as Rickettsia akamushi or Rickettsia orientalis, is conveyed to man by the hexapod larvae of mites, Trombicula akamushi and Trombicula deliensis. It is important to recognize that only the larvae are actual transmitters of the infection. Adult mites do not attack animals but are capable of transmitting the rickettsias through their eggs.

Mites¹⁰ are taxonomically akin to ticks. Rickettsial vectors are placed in the family Trombididae (harvest mite) of the order Acarina. A common host of Trombicula akamushi is the vole; the rat is the important host of Trombicula deliensis.

Tsutsugamushi fever¹⁰ has an average mortality rate of 40 per cent. Control depends on measures adopted against the vole--a kind of field mouse--and against mites. The latter are minute animals. They

require to be picked from the skin with the point of a needle; saponated solution of cresol (1 per cent) is also employed. Protective clothing should be worn, and flowers of sulfur or powdered naphthalene should be applied to the underclothing. Flit[#] (essentially an extract of pyrethrum in a deodorized kerosene base an invaluable tropical panacea, may be sprayed over the shoes, stockings and trousers. Since the mites attack from the ground, it is sometimes advisable to moisten the ground with water, after which an emulsion of kerosene (1: 100) is applied. The mites which occur in the United States are not as yet known to be rickettsial vectors.

Kawamura and others³⁸ have attempted to protect human beings against virulent tsutsugamushi fever by means of live strains possessing little virulence. Sumatran strains have been grown on chorioallantoic membranes.

PLAGUE

Plague¹⁰ is a disease of rodents which afflicts man incidentally. It is enzootic and epizootic in rats, mice, ground squirrels, chipmunks and prairie dogs; in the tarabagan, or marmot, of Manchuria; in the gerbil of South Africa; in the South American cavy, and in the Russian suslik. Pasteurella pestis, the causative agent, is not readily transmitted among these animals by ordinary contact, and the spread of the bacillus from rodent to rodent, from rodent to man, and from man to man is usually accomplished by fleas.

Fleas¹⁰ are true insects, of the order Siphonaptera. They are laterally compressed, wingless bloodsuckers and range between 1.5 and 4 mm. in length, males being smaller than females. Although individual species of fleas manifest certain preferences as to species of host, this preference is not absolute. Hence, the flea is well fitted for conveying disease from one species of mammal to another, and a single mammalian host may simultaneously harbor several kinds of fleas.

In the act of biting,¹⁰ the flea ingests a maximum of 0.5 cubic millimeters of blood, which may contain a maximum of 5,000 plague bacilli.

The ingesta form a mass, in which actual bacterial multiplication occurs. The flea now proceeds to suck blood from other mammals but does not at first infect them. Ultimately the bacterial mass increases until it is large enough to produce obstruction of the flea's proventriculus. When this happens, any subsequent biting is accompanied by regurgitation of blood contaminated with plague bacilli, which enter the bitten host. Although the rat flea does not customarily defecate while feeding, the feces are infective. Thus plague bacilli may be transmitted from flea to mammal in several ways; (1) by the contaminated mandible of the flea, (2) by proventricular obstruction and regurgitation, (3) by rubbing pulicine feces into the skin--especially if an infected flea has been crushed-- and (4) through the rodential habit of biting the flea.

Of the numerous types of fleas¹⁰ which are capable of transmitting plague, the most efficient is the oriental rat flea Xenopsylla cheopis. The superiority of Xenopsylla cheopis is attributed to anatomic arrangements conducive to obstruction of the proventriculus. Yet it must be inferred that at best even Xenopsylla cheopis is a relatively inefficient vector, capable of biting innumerable individuals without

necessarily infecting them. For this reason, it is probable that the perpetuation of plague requires a high pulicine density. Any estimate of flea populations should include not only the fleas found on rodents, but the fleas encountered in the burrows of rodents. After acquiring the plague bacillus the flea does not become infective until a variable interval (five to one hundred and thirty days) has elapsed.

Plague¹⁰ is thought to have been introduced into the United States at the start of the 20th century; presumably it was conveyed from China to San Francisco. The disease is now firmly established in wild rodents of all the Western states. In this connection, certain facts require to be emphasized; (1) the Western states, California, Colorado, Idaho, Montana, New Mexico, North Dakota, Oregon and Washington constitute one of the great plague areas of the world, (2) plague in rodents may be clinically and anatomically inapparent, (3) uninfected rodents may carry infected fleas, hence bacteriologic studies of rodents must be combined with the inoculation of pools of captured fleas, (4) in endemic zones many of the rodents manifest specific resistance, (5) although few cases of human plague have occurred in the United States, the stage is now set for a severe

outbreak, (6) greatly to be feared is an eastward spread of infected wild rodents toward urban areas heavily infected with domestic rats, for example, the Mississippi valley, (7) the pneumonic form of plague does not require a vector, but is spread directly by droplet infection, (8) rarely the plague bacillus has been found in the throats of carriers, (9) predatory birds, such as the borrowing owl, occasionally carry infected fleas.

The control¹⁰ of plague depends principally on rat control, which has been described in the section on typhus. Equal vigilance is necessary with regard to wild rodents, such as ground squirrels, wood rats and prairie dogs. Burrows and rat holes should be treated with a fumigant, preferably methyl bromide, and the fleas found on the rodents and in the burrows should be chloroformed and a suspension of them injected into guinea pigs; bacteriologic study of rodent tissues alone is often inadequate. Fumigation is the only procedure which will control both rodent and flea. Recently the use of a kerosene torch ("flame thrower") has been advocated.

Rat proofing¹⁰ must include not only homes, but warehouses, freight cars and especially ships.

The rat is a hardy traveler and has strewn disease around the world. In the rat proofing of ships attention must be paid especially to the elimination of inaccessible corners and hideaways in which rats may elude fumigation. A thoroughly rat-proofed ship does not often require to be fumigated.

In the control of fleas, general measures of personal hygiene may be supplemented by delousing techniques. It is recommended that bedding be kept from contact with the floor and the use of carpets be avoided.

The most important measure in flea control is strict cleanliness. Dirty corners,⁵ unclean rugs, and carpets, dusty cracks and crevices, greasy kitchens, uncared-for and unkempt bathrooms and toilets, closets used as dumping places for dirty clothing, cellars littered with rubbish and filth, and other uncared-for places where the eggs of fleas, undisturbed can hatch and the larvae obtain sufficient food and moisture, serve as constant sources for flea multiplication. Cleanliness is the only remedy for such situations.

Destruction of stray cats and dogs⁵ and maintenance of pets in a clean condition with clean living quarters will practically assure the householder of freedom from fleas.

To destroy the fleas⁵ on cats and dogs, cleanse these animals in a 3% solution of creolin (4 tablespoonfuls to each gallon of water) in warm water. Carefully work the solution into the hairs especially around the head and neck, by means of a stiff brush. Leave in the solution for 5 to 10 minutes then remove, drain off the solution and in the case of cats and thin skinned dogs wash with soap and water.

Other methods⁵ recommended are rubbing of finely powdered naphthalene and closing the house for one day. Sodium fluoride (powder) is sometimes used. It is also effective against cockroaches. Sprinkle on the floors and cracks and corners. Leave for a day or two then sweep it up. After either of these treatments, wash the floors with hot soapsuds or a 5% solution of formalin to destroy eggs and larvae. Thoroughly clean the cellar and spray with kerosene or crude petroleum if possible. More recently than any of these methods, D.D.T. powder has been used to kill not only the fleas on the animal but also those that are present in the house.

Fumigation⁵ with hydrocyanic acid gas or sulphur fumigation are also effective.

Palliative devices⁵ to trap adult fleas have been used. Sticky fly paper on broom sticks with a suspended wire cage around to protect the paper from touching the floor and rolled along will catch many. The putting of fly paper on the legs and walking across the floor will catch many also. These are only palliative and good to determine the kind of flea present.

The actual presence of human plague requires many additional precautions. Patients¹⁰ with plague and those persons suspected of having it should be isolated strictly, and visiting should be discouraged. Attendants and bacteriologists should wear masks, or preferably complete head covers, and gowns and gloves. The patient's homes should be fumigated, and indeed native quarters may have to be burned. Fomites may be treated with steam, 1:1,000 solution of mercury bichloride, saponated solution of cresol or a 2 per cent concentration of solution of formaldehyde U.S.P.; these measures are directed against bacteria and insects simultaneously. Since the plague bacillus has been known to persist for at least three weeks after subsidence of symptoms, convalescent patients should be isolated conscientiously.

Strong¹⁰ originally demonstrated the immunizing

value of live cultures of avirulent plague bacilli. Such cultures were also used by Otten¹⁰ in recent large scale trials in Java.

All of these measures are no substitute for the undramatic and unremitting work of plague control. This includes continuous surveys of infected rodents and vectors, international interchange of information and quarantine. The last-named measure should be maintained for at least seven days from the date of the last possible exposure or the completion of disinfection.

Fleas² are important also because they are intermediate hosts to Dipylidium caninum, Hymenolepis diminuta and the parasite of kala azar.

TULAREMIA

Tularemia is an infectious disease of man caused by Bacterium tularense (Pasteurella tularensis). The malady¹⁰ has been observed in all parts of the United States and in Japan, Russia, Scandinavia and Central Europe. A single attack immunizes permanently.

For the most part tularemia¹⁰ is conveyed to man by direct contact with the tissues of infected mammals, especially wild rabbits, but also squirrels, opossums, coyotes, deer, red foxes, ground hogs, skunks, beaver, cats, dogs and birds. Hence, the disease is common among hunters, trappers and butchers. Frequently infection is the result of a wound incurred in the cleaning or cooking of a wild rabbit; the bacteria may, however, penetrate the unbroken skin. Domestic pet rabbits are usually uninfected. Outbreaks have resulted from the contamination of water by rats and other animals. Laboratory infections are common.

Arthropods¹⁰ are important in conveying tularemia from one small mammal to another; they thus maintain infection in the animal reservoir. Without this mediation it is probable that tularemia would tend to die out among animals. Less often arthropods transmit tularemia to man directly.

The vectors¹⁰ concerned are ticks (Dermacentor andersoni, Dermacentor variabilis and Haemaphysalis leporis-palustris) and deer-flies (Chrysops discalis).

It is probable that deer-flies are merely mechanical transmitters of tularemia, whereas ticks show genuine infection of intestinal epithelium and the body cavity. Ticks can infect by biting and by defecation; they can also transmit the bacilli through their eggs. Ticks which are in contact with sheep often become entangled in the wool, hence shearers may become infected.

Mosquitoes¹⁰ are potential mechanical transmitters of the tularemia bacillus, but probably not vectors under natural conditions. Arthropod transmission of tularemia would seem to be more important in the western states than in the East.

The immediate prevention¹⁰ of tularemia depends chiefly on care in the handling of small mammals, especially wild rabbits. Rubber gloves should be used, and even the smallest cut or abrasion in the skin should be cleansed and disinfected meticulously. Rabbit meat should be cooked with unusual thoroughness, uncooked residues being burned. The possibility of water-borne outbreaks cannot be ignored.

For the control of tularemia¹⁰ in wild animals

constant surveys are necessary. These should include autopsy and bacteriologic study of tissues and injection studies of ticks and suspected vectors. Such studies are most profitably oriented by the reports of the disease in human beings. The importation and transportation of wild rabbits should be restricted by statute

The control of ticks has been discussed in the section on rickettsial disease. A notable accessory vector¹⁰ is the widely distributed rabbit tick Haemaphysalis leporis-palustris. This creature does not bite human beings, but serves to perpetuate the tularemia bacillus among rabbits and may transfer infection from wild rabbits to gallinaceous birds.

The control of tabanid flies¹⁰ requires separate consideration. Under the order Diptera (two-winged flies) taxonomists have disposed the families Tabanidae (horseflies), Culicidae (mosquitoes), Muscidae (true flies), Psychodidae (sandflies), Simuliidae (black flies) and Oscinidae (eye flies). Each of these families demands at least a modicum of attention from the medical entomologist.

The family Tabanidae¹⁰ includes horseflies, deer-flies and gadflies. These are large-eyed insects with thick, sturdy bodies from 10 to 25 mm. long.

They are vigorous fliers and vigorous, persistent bloodsuckers. The larvae tend to occur in marshy or muddy places; hence a principal type of control measure is drainage.

Drainage¹⁰ should be supplemented by the use of repellents, especially those which contain fish oil. In the transmission of tularemia, the most important tabanid species is Chrysops discalis, the deer-fly. This insect remains infective for at least fourteen days after biting an infected rabbit.

RELAPSING FEVER

Human relapsing fever¹⁰ exists in two principal forms--the louse-borne infection of Europe and Asia, and the tick-borne infection of Africa and America. In all types, the causative organisms are spirochetes of the genus Borrelia. In the matter of nomenclature great confusion prevails, since certain authors have assigned specific titles to various local strains. The names Spirochaeta obermeieri, and Treponema recurrentis have been used for the louse-borne European organism, whereas the tick-borne African and American organisms are known as Borrelia duttoni, Borrelia novyi, Borrelia venezuelensis, and so forth, although it is as yet uncertain that these species are all different.

European relapsing fever¹⁰ is transmitted by the body louse, Pediculus humanus corporis. During the first World War the disease raged epidemically and tended to accompany or follow epidemic typhus. In the control both of typhus and of relapsing fever, control of the louse is essential. The technics have been described in the section on typhus.

In the United States, relapsing fever¹⁰ occurs in the West chiefly and is transmitted by ticks of the genus Ornithodoros, which belong to the family

Argasidae. In contrast to the ticks of the family Ixodidae (which are vectors of rickettsias), the argasids show little sexual dimorphism. They are nocturnal, and intermittent feeders and are notably long lived. The capitulum (a modified head) is situated ventrally; hence, when inspected from above, the argasids appear headless. In California, Oregon, and Nevada, Ornithodoros hermsi is known to be the vector of relapsing fever, whereas Ornithodoros turicata is the vector in Texas, Arizona and New Mexico. Ornithodoros parkeri is a probable vector in Colorado, California, Montana, Utah and Washington. Ornithodoros talaje, Ornithodoros venezuelensis and Ornithodoros moubata convey the disease in other parts of the world.

Ornithodoros hermsi¹⁰ is infective by its bite, at all stages of larval and adult development. Once infected the tick remains so for life and may transmit the spirochete to its progeny. The infectivity of the feces is not admitted by all students of the subject.

The eggs¹⁰ of Ornithodoros hermsi are often laid in crevices in the walls of houses, especially in mountain cabins. For this reason, certain of these cabins have become known as foci of relapsing fever.

Indeed, relapsing fever in California is to a great degree a disease of vacationists, since the disease prevails chiefly in the higher mountainous parts of the state and in the summer months. This limitation may be due to the fact that the wild rodents, chipmunks and tamarack squirrels, which are the probable animal reservoirs of California relapsing fever, are likewise limited to the higher regions.

In Texas¹⁰ the disease is chiefly rural. The local vector, Ornithodoros turicata, has been found in dry, sandy country, on the floors of dry caves and in old, uninhabited houses; the mammalian reservoir in Texas includes armadillos, opossums and rodents. Ornithodoros turicata has been known to transmit relapsing fever after five or more years of starvation.

The mammalian reservoirs¹⁰ of American relapsing fever are too vast and diverse to be controlled; hence the only feasible measures are those which are directed against ticks. Such technics have been described in the section on Rocky Mountain spotted fever. Special care should be given to the disinfection of dwelling places in the endemic area. Crevices in walls should be sprayed and treated systematically. The loose structure of most summer cabins is usually not conducive

to successful fumigation. Bedding, mattresses and sleeping bags should be steamed or sprayed. Cabins should be made proof against chipmunks, squirrels and similar animals which may carry the spirochetes. Infected persons should be isolated.

It will be evident from the foregoing statements that the control of tick-borne relapsing fever is not well developed and that troops operating in Africa may run the risk of acquiring the disease. Although direct attack¹⁰ on tick vectors is not feasible by present methods, much can be accomplished by avoidance of native habitations. Soldiers should not enter huts and should not store equipment in them. Encampments should not be established in immediate proximity to villages. Insect repellents³⁹ applied liberally to the skin and clothing provides partial protection against ticks. D.D.T. louse powder should be used especially in the presence of epidemics of relapsing fever.

COLORADO TICK FEVER

Under this term Topping, Cullyford and Davis¹⁰ have called attention to a febrile ailment clinically similar to dengue, but displaying well marked epidemiologic differences. The cause is unknown. The disease has long been familiar to physicians in Colorado and neighboring states. Evidence strongly favors transmission by the tick Dermacentor andersoni, the control of which has been discussed in the section on Rocky Mountain spotted fever.

PAPPATACI FEVER

This disease, also called phlebotomus fever and sandfly fever, is a virus disease which superficially resembles dengue. The causative agent⁴¹ is believed to have a diameter of about 160 millimicrons; it has been isolated from the circulating blood and cultivated on chorioallantoic membranes. The disease occurs in the Near East and in the Mediterranean area, especially in Egypt, Palestine and Greece. It has also been observed in Argentina.

Transmission⁴¹ is accomplished by small hairy flies of the family Psychodidae, genus Phlebotomus, especially Phlebotomus papatasi and perhaps other species. These are tiny gnats of crepuscular habit. The eggs are deposited in damp cellars, latrines, caves, tree trunks and the crevices of walls. The blood-sucking female and the harmless male pass with ease through the interstices of ordinary mosquito netting. Some authors believe that Phlebotomus does not fly more than 10 feet (305 cm.) above the ground; others deny this. The insect becomes infective the tenth day after biting an infected human being. Patients are infective during the first and the second day of the fever.

Control⁴¹ measures include the fumigation of cellars and latrines, the demolition of old ruinous walls,

the filling of crevices and the repair of cracked plaster work. Camp sites⁴² should be located on open, elevated, dry, sandy ground when feasible and as far from native dwellings and domestic animals as possible. The area within a radius of 50 to 100 yards of sleeping quarters should be cleared of rubble, detritus, gardens, vegetation, and needless earthen walls or banks. When such measures are impracticable, the area should be sprayed with D.D.T. residual spray. Ordinary screens and bed nets do not exclude sandflies. Occupants of buildings may be effectively protected by the application of D.D.T. residual spray to the inner walls, ceilings, and fixtures and to the inside and outside of screens and doors, including a foot or two of the outer wall around their casements. Additional protection may be secured by spraying twice daily with an aerosol dispenser or other available insecticide. After sundown, long-sleeved shirts and full-length trousers should be worn. Insect repellents should be used on exposed parts of the body.

During an epidemic⁴³ of sandfly fever which occurred among U. S. troops in Egypt, the value of dimethylphthalate was tried as a repellent against the vector of this disease and found to be satisfactory and

is recommended as a method for the control of sandfly fever.

Electric fans⁴¹ may be employed to blow adult sandflies away. Prophylactic vaccination has not as yet proved successful. Antilarval measures, such as saturating the ground with gasoline, have likewise accomplished little.

LEISHMANIASIS

Infections produced by protozoa of the genus Leishmania are divided into three categories.

Kala-azar,⁴¹ the most important of the three, is a generalized leishmaniasis (caused by Leishmania donovani or Leishmania tropica) of the reticuloendothelial system. The disease is characterized by hepatosplenomegaly, leukopenia and continued fever; it has often been confounded with malaria. Kala-azar occurs in the Mediterranean area, the Balkan states, North China and parts of India and Africa. The pathogen is almost certainly conveyed to man by sandflies, chiefly Phlebotomus argentipes, Phlebotomus major var. chinensis and Phlebotomus sergenti. Ticks may perhaps act as occasional vectors, especially Rhipicephalus sanguineus. The natural reservoir includes dogs and Chinese hamsters.

Important⁴¹ epidemiologic differences exist between Mediterranean visceral leishmaniasis and that encountered in India; the problem is further complicated by the recent discovery of a grave form of the disease in Brazil and Argentina. According to extensive observations by Chagas, Brazilian visceral leishmaniasis is predominantly sylvatic or rural, and rodents or

carnivores may be suspected of constituting the natural reservoir.

Preventive measures⁴¹ include prompt isolation and treatment, disinfestation or even destruction of sandfly-infested houses and the exclusion or destruction of dogs. It is emphasized that even dogs which appear normal may have large numbers of Leishmania in the deeper layers of the skin. In endemic areas all stray dogs and all sick dogs should be destroyed. The control of sandflies has been described in the section on pappataci fever. The European custom of housing animals in the lower stories of human habitations should be suppressed. Manure heaps, a favorite breeding place for Phlebotomus, should be kept at a distance from farmhouses. Mediterranean kala-azar is predominantly a disease of small children, and much can be accomplished by having children sleep under fine netting (interstices less than 0.5 mm).

Oriental sore,⁴¹ an ulcerating granulomatous leishmaniasis of the skin, occurs in the Mediterranean area, the Near East, India and South and Central America. Phlebotomus papatasi has been suspected as a vector of the disease, and dogs may constitute the natural reservoir. Preventive measures resemble those employed against kala-azar, namely, strict personal

hygiene, the exclusion of dogs and the control of sandflies. The stable fly Stomoxys calcitrans may prove to be an accessory vector.

American leishmaniasis (espundia)⁴¹ is a mutilating nasopharyngeal leishmaniasis believed to be conveyed by species of Phlebotomus. It occurs in Mexico, Panama and South America. The disease is said to be especially common among gum pickers and other forest laborers. Preventive measures consist of prompt treatment (injections of a compound containing antimony or arsenic or berberine sulfate) and the use of protective clothing and insect repellents. Benedek⁴⁴ has reported a case allegedly autochthonous in Chicago. Attempts at preventive vaccination have not yielded definite results.

BARTONELLOSIS

In the narrow Andean ravines⁴¹ of Peru, physicians and travelers have long recognized two endemic diseases, verruga Peruana and Oroya fever. These are now known to be, respectively, the local and the general manifestation of infection by Bartonella bacilliformis. The malady is limited to a zone extending between the latitudes two degrees north and thirteen degrees south, and altitudes between 500 and 3,000 meters. Recently observers have encountered the disease in Colombia and in Ecuador. The vector is a sandfly, Phlebotomus verrucarum. In the present state of knowledge adequate control is impossible. In endemic regions nocturnal travel should be reduced to a minimum and protective clothing should be worn. No satisfactory method of immunization is available; Kikuth⁴⁵ has devised an ingenious combination of compounds containing arsenic and antimony, known as Sdt 386B (18 per cent arsenic and 20 per cent antimony). This drug is said to be effective in ridding the blood of Bartonella.

TYPANOSOMIASIS

This disease⁴¹ produces the dreaded African sleeping sickness (caused by Trypanosoma gambiense and Trypanosoma rhodiense), conveyed principally by the tsetse flies Glossina palpalis and Glossina morsitans, respectively. A large number of mammals, including antelopes, oxen, goats and sheep, act as reservoir hosts. In November, 1941, a male tsetse fly was found on an airplane going from Africa to Brazil.

Control measures are directed chiefly against the flies. In order to prevent infection,² the sick should be segregated into regions where there are no flies, but this is unsuccessful when animals act as reservoir hosts. Systematic treatment of patients with various arsenicals, of which the most favored are atoxyl, tryparsamide, and Bayer's 205 (Germanin) are being used. Efforts are made to get a complete census of the natives and to require a medical examination and health passport for any native leaving infected regions. Avoidance of flies in endemic regions by locating and avoiding the fly belts, careful screening of houses, and protection of body against bites of the tsetse flies are important. Clearing the jungle along the water courses for some yards beyond the natural range of

flight (at least 300 yards) around villages has proved practicable and important. Agricultural practices should be carried out making the conditions unfavorable for fly development. Such things as systematic burning of grass, supplemented by catching of flies in unburnt areas by the use of various traps are helpful. It has been suggested that the systematic destruction of the big game in these areas would be helpful. Before any scheme of this sort is carried out, a careful study of the habits of the tsetse involved is important for some feed on batrachians and reptiles, while Glossina tachinoides thrives where man is almost the only host. In these areas such a plan of destruction would be foolish and wasteful. Because of the difficulty of controlling the vector, entire native populations have been removed from endemic areas.

Chagas' disease,⁴¹ the American form of trypanosomiasis, is a much less remote threat to the national health. The causative organism, Trypanosoma cruzi, is conveyed to man by reduviid bugs, especially Triatoma megista. These are popularly known as cone-noses, assassin bugs or kissing bugs. Adults are characterized by an elongated or conical head, large eyes and long, thin antennae. Several species of ticks

are vectors in the laboratory. The natural reservoir of infection is known to include the armadillo, the dog and probably certain rodents. Chagas' disease occurs in South America, Central America and Mexico. Inasmuch as reduviids of the genus Triatoma inhabit the southern states and the West, Hegner⁴¹ predicted a northward extension of the disease into the United States. This prophecy has received partial fulfilment in the work of Packchanian,⁴⁶ who found triatomas in Texas that were naturally infected with Trypanosoma cruzi. From the work of Brumpt⁴⁷ and others, it seems probable that Triatoma conveys the trypanosome not by biting, but by defecating on the skin or in the eye of the human victim.

The reduviid bugs⁴¹ deposit their eggs on the ground, on vegetation and in houses. Attempts have been made to destroy eggs by ploughing or oiling the ground near human habitations. More feasible measures are the improvement of domestic cleanliness, the exclusion of armadillos and rodents; the destruction of animal burrows and the use of mosquito nets and screens. Houses too dilapidated to be screened may be destroyed.

FILARIASIS

The term filariasis comprehends a group of diseases caused by nematode worms and transmitted to man by blood-sucking insect vectors. Filariasis⁴¹ due to Wuchereria bancrofti is widely distributed through the subtropical and the tropical regions of both hemispheres. The disease exists in the West Indies and in South America. Manson-Bahr lists twenty-four species of mosquito (including eight culicine species, eleven anopheline species and three aedine species) in which complete development of the nematode larva has been observed. Prophylaxis involves control of the local mosquito vector, destruction of breeding places, sanitation of stagnant pools, filling of tree holes and removal of protective vegetation. Patients should be compelled to sleep under nets or in screened houses. Since filariasis is often asymptomatic, examination of the blood is essential in any survey of the disease.

Infection⁴¹ with Loa loa occurs in West Africa and the Congo region. The vectors are mango flies of the genus Chrysops, which belongs to the family Tabanidae (horseflies). The control of tabanids has been described in the section dealing with tularemia.

Onchocerciasis,⁴¹ a third filarial disease, is beginning to receive the attention which it well deserves. The malady prevails over a wide area in West Africa and in South America and the mountains of Guatemala and Mexico. In the last-named country, onchocerciasis has shown a distinct tendency to advance northward; the migration of Mexican laborers could easily establish the disease in suitable insects within the United States.

The vectors⁴¹ are black flies (gnats) belonging to the family Simuliidae--Eusimulium avidum, Eusimulium ochraceum and Eusimulium mooseri. Important African vectors are Simulium damnosum and Simulium neavei.

According to Strong,⁴⁸ destruction of the larvae is difficult, since breeding occurs widely in almost all rapidly flowing streams in the endemic areas. Reduction has been attempted by control of marginal vegetation, the removal of logs, oiling, and so forth. In Guatemala the human patient constitutes an important reservoir of infection. Subcutaneous filarial tumors should be excised promptly; adult worms are thus removed, and the number of microfilarias is thereby reduced. Tumors which cannot be removed can sometimes be treated

advantageously by the injection of mercury bichloride solution. It is believed that wild animals, such as the antelope, may constitute part of the reservoir of onchocerciasis in Africa.

YAWS

This granulomatous disease⁴¹ resembling syphilis occurs in Africa, the Pacific Islands, Ceylon, India and South America. It is estimated that there are 80,000 cases in the Pacific regions of Colombia. The disease also occurs in the West Indies, especially in Jamaica, Haiti, and Santo Domingo. In Puerto Rico the disease is at the point of disappearance, although it is possible that a few cases can still be found in the northwest corner of the island in the vicinity of Isabela. Yaws is caused by a spirochete, Treponema pertenue. Transmission is attributed to small eye flies of the family Oscinidae (Chloropidae), genus Hippelates; for example, Hippelates pallipes (Jamaica) and Hippelates flavipes (Haiti). These insects have been found in large numbers on the cutaneous lesions and have been known to crawl under scabs in order to feed. They fly from one person to another and regurgitate "vomit drops" on the skin. These drops may contain large numbers of spirochetes, which are thus transmitted mechanically. The eye fly is not a bloodsucker. The relative importance of insects and of direct contact in the transmission of

yaws remains to be ascertained.

Hippelates⁴¹ breeds in decaying organic matter, especially dung. The control of this insect is not well developed. Trapping and the removal of organic debris have been suggested.

Patients suffering from yaws should be urged to keep the lesions well covered and to seek prompt treatment; personal contact should be kept at a minimum. The use of compounds⁴¹ containing arsenic and bismuth causes rapid regression of the granulomas. Nevertheless, the actual eradication of yaws has proved difficult.

VIRUS DISEASES OF THE NERVOUS SYSTEM

A comparatively new addition to the roster of human ailments is equine encephalomyelitis, a disease⁴¹ caused by one of the smaller filtrable viruses (20 to 35 millimicrons). Among human beings the disease has stricken adults and children and has shown maximal incidence in summer and early autumn. Of the five extant virus strains, two are known to occur in the United States. These are the so-called western and eastern varieties, the domains of which are separated by the Appalachian mountains; this geographic classification is of steadily weakening validity. At least ten species of aedine mosquitoes are capable of transmitting one or more of the North American strains. The list includes Aedes aegypti, Aedes sollicitans, Aedes vexans and Aedes taeniorhynchus. Recent studies by Hammon⁴⁹ and collaborators have shown that Culex tarsalis is an important natural vector of the western virus of equine encephalomyelitis and of the St. Louis encephalitis virus. The Rocky Mountain wood tick,⁴¹ Dermacentor andersoni, can transmit the western equine virus to mammals and to its own acarine progeny. The assassin bug Triatoma sanguisuga can transmit this virus to guinea pigs. Many birds are susceptible;

for example, chickens, prairie chickens, turkeys, ducks, and probably act as reservoirs of the virus.

Equine animals⁴¹ have been immunized by means of virus grown on chick embryos and inactivated by solution of formaldehyde. Beard and collaborators⁵⁰ have employed a bivalent chick embryo vaccine consisting of a mixture of formaldehyde-treated embryo tissue diseased with the Eastern virus and similar tissue diseased with Western virus. This vaccine produced antibodies in human beings. It is suggested that persons exposed to infection be given two courses of vaccination, one year apart. In the opinion of Fothergill,⁵¹ however, the present low incidence of the disease does not justify the use of the vaccine by human beings, except for occasional persons whose occupations cause unusual exposure to the disease.

Several of the aforementioned aedine species breed chiefly in salt marshes and may be controlled by such devices as drains, dikes and tide gates. Aedes aegypti is a domestic mosquito and has been discussed in the section on yellow fever. In the absence of extensive engineering installations, the use of mosquito nets and the simple hygienic technics must not be neglected.

Culex tritaeniorhynchus and Culex pipiens⁴¹

are incriminated as the vectors of Japanese encephalitis. In the case of spring-summer encephalitis of Russia transmission by Ixodid ticks (Ixodes persulcatus) has been established; the reservoir of the disease probably consists of ticks and sylvan rodents.

Several years ago Webster, Clow and Bauer⁵² showed that Anopheles quadrimaculatus could be infected with the virus of St. Louis encephalitis. More recently Hammon⁴⁹ and collaborators have demonstrated that both St. Louis virus and the virus of western equine encephalitis are transmitted by Culex tarsalis. This mosquito breeds in ponds, irrigation seepage, barnyard drainage and sewage; it feeds on man, horses, cows and ducks. Culex pipiens⁴¹ has been shown to be an experimental vector of the St. Louis virus. This virus has also been transmitted experimentally by the tick Dermacentor andersoni. Observations⁵³ of antibodies in the serums of mammals and birds suggest that suburban and rural barnyard fowl may constitute an important reservoir of both the St. Louis and the western equine virus. These facts point the way to rational preventive measures.

With regard to poliomyelitis, much less

definite information is available. The discovery of the causative virus in sewage and in the stools of persons recently convalescent tends to place poliomyelitis among the intestinal diseases, such as typhoid and dysentery. Recently the virus has also been detected in flies, especially Musca domestica, caught near privies and sewers. Much further study is necessary before the transmission of the disease can be described and rational measures of prevention devised.

Although flies may not be concerned in the transmission of poliomyelitis, they have been incriminated as mechanical carriers of many other diseases and a brief discussion of some of the possible methods of control will be helpful.

Flies of house fly variety are known to be carriers² of typhoid fever, infantile diarrhea, cholera, bacillary and amoebic dysentery, anthrax, leprosy, various types of ophthalmia, trachoma, and tuberculosis. They may ingest and disseminate cysts of various intestinal protozoa and the eggs of certain helminths.

In the control of flies, basically sanitary measures are of most importance. These sanitary measures should include⁵ an efficient sewage

disposal system so that the proper receipt, treatment, and discharge of all sewage wastes is cleanly managed with no opportunity for fly breeding to occur, a garbage collection system that compels the individual householder to thoroughly sterilize the cans each week or all wastes to be thoroughly dried and placed in cans securely wrapped in paper. Collections of garbage should be made once or twice a week, depending on the climate. The final disposal of garbage should be by incineration or sanitary dumps where the garbage is covered with ashes. Clean garbage wagons, washed and treated with disinfectants and deodorants each day after the close of work is also a good plan in the control of flies. Finally an alert, well-trained sanitary corps is to deal promptly and effectively with all problems arising from the disposal of wastes.

In rural areas the problem of manure disposal is of some magnitude. Daily disposal² is best being sure all corners, drains, stables, dump carts and the like have no left overs. The collected manure is hauled out and spread thinly on the fields daily or at least every other day. This increases not only the value of fertilizer but adds to the attractiveness and

safety of the farm. Compost heaps are made after frost and before thawing in which the manure is stacked evenly with closely compacted sides and edges. Chemical treatment of manure with kerosene, lime, chloride of lime, iron sulphate, and others have been used but none have met the situation. Hellebore⁵ applied in the quantity of $\frac{1}{2}$ pound to 10 gallons of water is sufficient to treat 10 cubic feet or 8 bushels of manure. The solution is sprayed on the manure with a hand pump. Borax used in the quantity of one pound for 16 cubic feet of manure, then wetted down with water has also been used. Coal tar oil or creosote oil at the rate of 100 cubic centimeters per horse per day can be used. It is also good to spray on dead carcasses. These and several other chemicals have been tried, but are not practicable unless the expense of time and chemicals is a slight consideration.

About the barnyard, one of the most common methods of destroying the adult flies is by trapping them and then burning or some other method of disposal. Several different types and variations of traps are to be seen on the different farms, but the most common or basic type is the use of a screen cylinder² with a frame of barrel hoops and lathes with a wire screen

cone inserted in the bottom. Molasses and water (1:3), or bread and milk make good bait and is placed at the bottom of the cone. The whole trap sits a few inches off the stand or ground so that the flies have free access to the bait. As the flies leave the bait dish, they fly against the cone and follow it up to the opening leading into the closed screen cylinder thus trapping themselves. Very few ever find the small opening in the tip of the cone and escape once they are within the cylinder.

Adult flies² may be killed by poison, catching them on sticky fly paper, or by sprays or fumigation. An effective poison is a teaspoonful formalin to a pint of water or dilute milk. The slogan "Swat that fly" should not be taken too literally for it can be disgusting and more unsanitary than to let them roam. Fly paper is not so unsanitary but is quite messy and not too efficient. When flies are abundant in a room, elimination by fumigation with sulphur or calcium cyanide is effective but should be done by trained experts. Spray made up of pyrethrum powder dissolved in kerosene ($\frac{1}{2}$ pound to a gallon of kerosene) is used. Other mixtures include kerosene and carbon-tetrachloride and kerosene (89.6%), carbon tetrachloride

(7%), and methyl salicylate (3.4%). The new 5% D.D.T. spray has found great favor among the users.

The most direct method² of protecting food and drink from flies and contamination, is by screening. Particular care should be taken in stores, restaurants, and dairies, as well as about the private home. The windows that are opened should be tightly screened as well as a built-in screen porch with the door at one end away from the kitchen or entrance door. Flies that get into this porch can be periodically and frequently exterminated by spraying or swatting.

Destruction⁵⁴ of adult flies by the use of insecticides, traps, and swatting should receive close attention, especially in sick wards, kitchens, mess halls, and latrines. D.D.T. should be used to kill adult flies by applying as a residual spray and to control fly breeding in organic wastes by applying as a spray or powder.

Maggot traps⁵ are constructed so that the manure is piled upon a lattice framework above a shallow tank whose bottom is covered with one inch or so of water. As the maggots migrate to the bottom of the heap, as is their custom, they drop into the water and drown. The water can be covered with a layer of fuel

oil to prevent mosquitoes and to hurry the killing of the maggots. This is about the only successful method of controlling the maggots.

One of the most important measures for preventing the spread of disease by flies is the abolition of the common box privy. Inexpensive and single sanitary privies have been designed for use where there are not modern sewer systems.

Disinfection of discharges from patients suffering with diseases especially typhoid fever and cholera, is important. Quicklime (not air-slaked lime), in quantity equal to the discharge and allowed to act for two hours is effective. Chloride of lime, carbolic acid, or formalin may be used, but are more expensive.

Coggeshall⁵⁵ and others have shown that lymphocytic choriomeningitis can be transmitted to guinea pigs by the bites of Aedes aegypti. The tick Dermacentor andersoni has been infected experimentally. Milzer⁵⁶ has confirmed the experimental transmission of the virus by Aedes aegypti and has been able to infect mice⁵⁷ and guinea pigs by the feeding of infected mites (Atricholaelaps glasgowi).

Bedbugs have been⁵⁸ accused of spreading syphilis, relapsing fever, typhus, trypanosomias, and

are said to be the causative agents of some asthma. The control of bedbugs in the home can be one of the most exasperating tasks that a homeowner has to do. Wooden bedsteads⁷ should be discarded, and the bedding washed and boiled or treated with live steam in a sterilizer. The house itself is the next problem. Fumigation is the best solution. Sulfur may be burned at the rate of four pounds for every 1,000 cubic feet of space. The house must be left tightly closed for three to four hours, and precautions must be carefully taken to prevent a fire destroying the property. Hydrocyanic acid gas may be used at the rate of one ounce for every 100 cubic feet of air. The house must be closed for twelve hours, then the windows opened from the outside for several hours. This method should not be used by a novice, for it is dangerous and specially trained crews are able to carry out the details more easily. Other commercial forms of gases are also used. Heating the rooms to 130° F. for three to four hours is a good method for the control of bedbugs. Kerosene and gasoline can be sprayed around the cracks and corners, but the danger of fire prohibits its use to a large extent. With the advent of D.D.T. many of these problems will be easily solved. D.D.T. has been

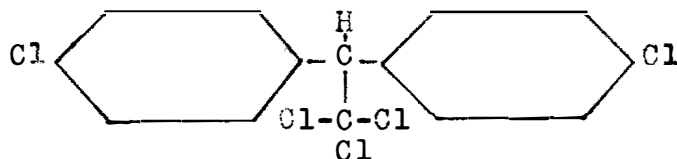
found to be very effective used either as a spray or powder against bedbugs.

In the case of toxoplasmosis, a little known disease, recent evidence⁵⁹ and ⁶⁰ also points toward arthropod vectors.

DICHLORE-DIPHENYL-TRICHLOROETHANE (D.D.T.)

D.D.T.⁶¹ was first synthesized by a German chemist O. Ziedler in 1874. The insecticidal properties were first known by Paul Müller in Switzerland when he reported his work on moths, flies and plant lice.

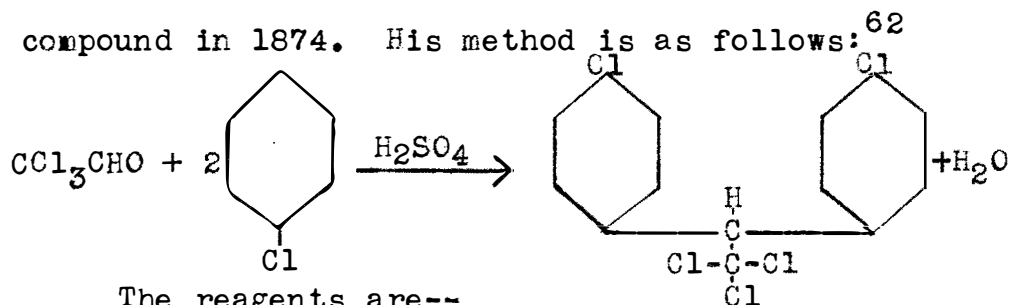
The compound, called "D.D.T." by an alphabetically-minded public and press, is really misnamed;⁶² or better, multi-named, as there are a number of possible isomers that would have the formula of Dichlore-Diphenyl-Trichloroethane. It is properly called 1,1,1, Trichlore-2,2, Bis (p-chlorophenyl) Ethane. It has a molecular weight of 354.497, being $(C_6H_4Cl)_2CH.CCl_3$ or $(C_{14}H_9Cl_5)$ and has the following structural formula:



Although D.D.T.⁶³ is chemically unreactive and stable to long boiling with water, it readily loses hydrochloric acid to alcoholic alkali or on heating to form bis (4-chlorophenyl)-BB-dichlorethylene. This compound as well as 4:4-dichlorobenzophenone and bis (4-chlorophenyl) acetic acid are almost inactive both

as contact and stomach insecticides, indicating that the CH_2CCl_3 group is associated with insecticidal activity.

There are several methods of preparation of D.D.T. but most of the present methods are merely variations of Othmar Zeidler's original preparation of this compound in 1874. His method is as follows:⁶²



The reagents are--

- (1) Chlorobenzene M. W. 112.5
- (2) Sulfuric acid--concentrated
- (3) Ethyl alcohol--95%
- (4) Chloral, anhydrous M. W. 147.5. For each gram of chloral hydrate, add 3.84 grams of concentrated H_2SO_4 (about 2 cc.) in a separating funnel. Shake, allow to stand until separated and draw off the acid. Keep the anhydrous chloral protected from moisture until used.

The procedure is to treat one mole of chlorobenzene with $\frac{1}{2}$ mole of chloral in the presence of concentrated H_2SO_4 (about 600 grams) and stir in a moisture free system until reaction is complete. Then separate by pouring into a large volume of water, wash well, and take up residue in boiling alcohol, place in an ice box and filter off the needle-like crystals.

These needles should melt at 105 degrees Centigrade.

A second method of making D.D.T. is as follows:

This method can be divided into two separate procedures.⁶⁴ The first requires the following reagents:

- (1) Chlorobenzene M. W. 112.5
- (2) Chloral hydrate M. W. 165.42
- (3) Concentrated sulfuric acid
- (4) Alcohol-ether mixture for each 75 moles of 95% ethyl alcohol, add 25 moles of ether and mix.

The procedure is to heat 16.65 grams (0.1 mole) of C., a mixture of 16.65 grams (0.1 mole) of chloral hydrate, 22.5 grams (0.2 mole) of chlorobenzene and 200 mls. of concentrated H_2SO_4 . Shake the mixture vigorously every ten minutes until the two layers disappear (about $2\frac{1}{2}$ to 3 hours) and then let stand twelve to twenty-four hours until crystals form. Then remove the sulfuric acid by filtration through a fritted glass filter and wash the crystals with water to remove sulfuric acid, and finally recrystallize from alcohol-ether mixture. Again the melting point of the product should be 105 degrees Centigrade.

The second procedure using this method requires the same reagents as the first. There are only minor variations in the procedure.⁶²

Again heat 16.65 grams (0.1 mole) of chloral hydrate, 22.5 grams (0.2 mole) of chlorobenzene with 200 mls. of sulfuric acid in an oil bath, keeping the mixture stirred at a temperature of 105 degrees Centigrade for eight to ten hours. Then allow it to cool somewhat, pour into a large volume of cold water, stir thoroughly and allow to cool. Finally wash several times with water to remove sulfuric acid and recrystallize from the alcohol-ether mixture.

Still a third method⁶⁵ of preparing D.D.T. requires the following reagents:

- (1) Chloral hydrate, Chlorobenzene, and Concentrated sulfuric acid as in previous methods
- (2) Fuming sulfuric acid-20% oleum
- (3) Sodium bicarbonate-solid

The procedure to be followed is to place in a 500 ml., round bottom, three-neck flask, equipped with an efficient mechanical stirrer and a thermometer, 350 grams of sulfuric acid, 50 grms. of fuming sulfuric acid, 45 grams (0.2 mole) chlorobenzene and 34 grams (slightly over 0.1 mole) of chloral hydrate. Stir the mixture rapidly to keep the material well-dispersed and at the end of an hour the D.D.T. should separate as a fine granular solid and the temperature rises to 45 degrees Centigrade. Continue stirring for an additional

one-half hour. After this the reaction mixture is poured, with stirring, into two liters of a 1:1 mixture of ice and water and the solid product which separates is collected on a funnel with suction and washed well with cold water. This precipitate is transferred to a beaker containing 500 mls. of boiling water, causing the D.D.T. to melt. The mixture is stirred well and allowed to cool, causing the D.D.T. to solidify. The wash water is removed by decantation and the process repeated two times, adding sodium bicarbonate with stirring to the last washing until neutral to litmus to insure removal of traces of acid. The crude product melts at about 90 degrees Centigrade and should weigh 50 grams, corresponding to 70% of the theoretical yield.

Pure D.D.T.⁶² occurs as white, fine needles. An odor of fresh apples has been attributed to the pure material by several writers. The crude, commercial material occurs as a granular, slightly sticky powder, varying in color from white to grey and having an odor of chlorobenzene.

The melting point⁶² of the pure material is 105 degrees Centigrade. The commercial material usually melts in the range of 88 to 90 degrees Centigrade.

This is due to various other products in the crude material and according to Gunther,⁶⁶ it has the following composition:

p-p ¹ Isomer	18%
o-c ¹ Isomer	6%
Oily by-product	2%
Unidentified solids	2%
Volatile material	1%
Ash	1%.

No figures of an exact nature are available for the solubility of this compound in water, data variously being given in indefinite terms as "insoluble , slightly soluble, almost insoluble". It is also listed as being insoluble in dilute mineral acids and dilute alkalies, including ammonia. The following solubilities are taken from Gunther⁶⁶ who compiled them from various sources.

Temperature⁶² not stated; grams of D.D.T. soluble per 100 grams of solvent.

Benzene	106
N-butyl alcohol	8
Tertiary-butyl alcohol	4
Chloroform	96
Cyclohexanol	8
Cyclohexanone	100
Ether	45
Ethyl acetate	68
Ethyl alcohol 99.5%	4
Kerosene (vaporizing)	11
Liquid paraffin	4
Orchard and spray oil	5
Petroleum ether (40-60 degrees Centigrade)	6

Petroleum ether (100-160 degrees Centigrade)	10
Tetrachlorethane	56
Tetralin	52
Toluene	48
Temperature ⁶² not stated; grams of D.D.T.	

soluble per 100 mls. of solvent.

Dimethylphthalate	31
Freon (12)	2
Fuel oil No. 2	10
Indalone	29
Kerosene (crude)	5-8
Kerosene (purified)	2-4
Sesame oil	10
Triton	20
Tung oil	10-14
Xylene	56

There is little doubt that this compound would be serious to man if ingested in any quantity. It will also cause dermatitis in sensitive persons. It has been suggested that the sensitivity lies in the solvent not the D.D.T. itself. To date no fatalities have been recorded in the literature so any lethal dose estimate would have to be drawn from work on experimental animals. The mode of ingestion and the absence or presence of solvents for D.D.T. would be prime factors in this regard. Smith and Stohlman⁶⁷ have given the following interesting figures. The lethal dose in rats administered in a one to five per cent olive oil solution is 150 mgm. per kg.; in rabbits 300 mgm. per kg. Compared to phenol, similarly ad-

ministered, D.D.T. was found to be more than three times as toxic as phenol in rats and probably twice as toxic in rabbits.

Death in animals⁶⁷ was found to be delayed for several days, symptoms consisting of "hyperexcitability, generalized fine and coarse tremors, spasticity progressing to the flaccid type of paresis of the extremities" but do not come on for several hours. Symptoms from progressive doses in series of rabbits of an average weight of about two kilograms were as follows:

50-100 mgm. per kg.	hyperexcitability
159-200 mgm. per kg.	tremors
300- mgm. per kg.	tremors and paralysis.

The effects in experimental animals are cumulative. For a detailed discussion of pathological findings in animals poisoned with D.D.T., the interested reader is referred to the articles by⁶⁸ R. D. Lillie and M. I. Smith and by⁶⁹ A. A. Nelson, J. H. Draize, G. Woodard, O. G. Fitzhugh, R. B. Smith and M. O. Calvery. It has been shown that the chemical is toxic for animals by ingestion or inunction; effects on the central nervous system, liver damage, and dermatitis are some of the manifestations. D.D.T. has been found in the liver, kidney, central nervous system, blood, and urine of exposed rabbits and rats.

It is⁶³ possible that the toxicity of D.D.T. is due to its chemisorption at vital centers, with interference with essential enzyme systems. In view of its chemical inertness, however, for example, no evidence of compound formation between D.D.T. and either the 'acceptor' phenolic hydrogen of the naphthols or the 'donor' nitrogen of the naphthylamines was obtained from melting point curves--the alternative hypothesis of the intracellular decomposition of D.D.T. is preferred. As the ethylene derivative is nontoxic although presumably sharing the permeativity of D.D.T., the toxicity of the latter is ascribed to the hydrochloric acid simultaneously produced either by elimination or reduction.

The insecticidal activity⁶³ of a compound to which this hypothesis is applicable would then depend on the ease with which hydrochloric acid is produced, provided that the compound is stable enough to survive translocation to its site of action. Preliminary work has shown that some other compounds, for example, certain chlorinated cyclic polymethylenes and non-aromatic substituted ethanes susceptible to this decomposition are insecticidal, whereas related compounds from which hydrochloric acid elimination is not

possible are inactive.

On the other hand, diphenyl trichlorethane⁶³ loses hydrochloric acid readily to alkali yet is relatively non-insecticidal. An additional factor, lipid solubility of the molecule as a whole, is therefore operative. The chlorophenyl groups of D.D.T. would be expected to confer high lipid solubility and thus high permeativity. The more polar dihydroxy derivative and its diacetate, with lower lipid solubilities, are less insecticidal than the dimethoxy analogue of D.D.T.

For the estimation of D.D.T. in possible cases of poisonings with this agent, Smith and Stohlman⁶⁷ have worked out a method of extracting the D.D.T. from blood, urine, feces, and tissue. Briefly, the D.D.T. is extracted with acetone, or ether, evaporated and the residue is taken up with absolute alcohol. The solution is treated with metallic sodium, refluxed, treated with charcoal and filtered. The sodium chloride derived from the action of sodium ethylate on D.D.T. is titrated by Volhard's procedure. There are other processes used in this toxicological examination.

There is a paucity of information concerning the toxicity of D.D.T. for humans, and no serious effects resulting from it have yet been reported in human beings.

It is thought however, that inhalations of heavy concentrations may be harmful for man. In a series of studies⁷⁰ on men of the Mediterranean theater who spent six hours daily, six days a week actually spraying, none showed any signs or indications of toxicity. Though provided with respirators, they often failed to utilize these protective devices. They were generally careful, however, to wear protective clothing as gloves, coveralls, and hats, and to bathe each evening on completion of duty. The period of time over which these subjects were exposed to the insecticide varied from one week to four and one-half months. The 50 men used approximately 15,000 gallons of 5% D.D.T. in kerosene representing 5,100 pounds of 100% commercial D.D.T.

To get back to the physical and chemical properties of D.D.T.; recent work⁶² indicates that D.D.T., particularly the crude material, is not very stable, especially toward heat, alkalies and certain catalytic salts and minerals.

Gunther⁶⁶ gives the following explanation as regards the instability of the crude product toward heat. As can be seen from the analysis, the commercial or crude D.D.T. contains 18% of the o,p-isomer which begins to split off hydrogen chloride at temperatures as low

as 50° C. (122° F.).

This decomposition⁶⁶ exerts an autocatalytic action, as the hydrogen chloride thus split off in turn causes more to be cleaved. A temperature of 80° C. (176° F.), causes a 90% loss of insecticidal activity within 24 hours and that when used on fruit trees, a leaf temperature of 52° C. (125° F.) and over, and a fruit temperature of 57° C. (135° F.) and over, causes D.D.T. to lose its potency very quickly, two weeks being more than sufficient, as a rule, to eliminate toxic effects completely. As a control, during the winter months, little, if any, of the toxic effects were lost over several months period.

Under no circumstances⁶⁶ should D.D.T. be mixed with alkalies, as this is perhaps the easiest way to destroy the compound. The mixing of D.D.T. with soaps and other alkaline detergents for use as sprays is to be avoided.

It⁷¹ has also been found that certain metals and salts hasten decomposition, anhydrous ferric and aluminum chlorides, iron, iron oxides, and certain minerals, as Fuller's Earth, catalytically decompose D.D.T.

The decomposition⁶² of D.D.T. by ultraviolet

rays does not seem to be definitely established, but is an interesting possibility to keep in mind when under the impression that one D.D.T. spraying will last indefinitely in areas exposed to strong sunlight.

The practical uses for D.D.T. are unbounded, or only limited by its possible toxicity and harmfulness to useful insects. It can be used as a powder⁷² diluted with kaolin or pyrophyllite, and such powders will protect against lice⁷³ for six to eight weeks wearing of the garments, and six to eight launderings before losing efficiency. The powder can be blown up the sleeves or down the necks of dressed persons, which was done in the control of typhus outbreak in Naples. Another way⁷² of using it is to impregnate undergarments with it by dipping them in a solution containing D.D.T. in a volatile solvent or in aqueous emulsions containing it. Both methods are good for either cotton or woolen garments.

Annand⁷⁴ and his co-workers report the favorable results of their tests of the action of D.D.T. on the bedbug, the house and stable fly, ticks and fleas of dogs, goat lice, "German" cockroaches (Blattella germanica), ants and termites and larvae of

the house fly and numerous plant pests. D.D.T. in antimosquito campaigns has played an important part. Beds⁷⁵ sprayed with kerosene solution containing 10% D.D.T. and 5% of cyclohexanone killed bedbugs for 104 days. By way of brief sidelight, encouraging results⁷² against caterpillars of the tomato moth, and against the grain weevil and the apple blossom weevil are reported.

It was found⁷⁶ that D.D.T. became firmly absorbed on a surface so that walls are effective against stable flies and house flies for two months by spraying a suspension of powder of 5% D.D.T. Investigators then tried to incorporate it in paints, but oil and varnish paint prevent D.D.T. from exercising its insecticidal effect because of the strongly absorbed oil film. With oil-bound water-paint, it continues to exert its insecticidal action. Experiments performed on house flies showed that after two months, the paint had not lost its insecticidal properties. In a room painted with 0.5% D.D.T. in oil-bound water-paint, 90% of house flies were killed overnight as compared to none in a control room. Experiments with oil and resin media show evidence

that in certain continuous film-forming media, D.D.T. retains its insecticidal effect.

When D.D.T.⁷⁷ solution is sprayed on interior surfaces, a residue is left which is toxic to insects alighting on the treated areas for several months. This characteristic of D.D.T., in which lies its extraordinary value is referred to as residual effect. Only brief contact by the insects with a treated surface is required to give a lethal dose. A preparation can be obtained by making a 5% solution of Larvicide, D.D.T., powder, dissolving in kerosene.

D.D.T. as a residual spray may be applied by a number of methods. Where available,⁷⁷ a gasoline engine compressor type of paint-spraying unit will offer an easy and effective means of application.

The unit may be mounted on a truck, jeep, or other means of conveyance to facilitate mobility. Knapsack sprayers, and the flit-gun type of hand sprayer also offer satisfactory means of application. Solutions of D.D.T. may be applied by hand, preferably using a paintbrush, where other equipment is not available. This method is the most economical means of application on wire screens, mesh surfaces,

for malaria and other disease organisms. Killing of mosquitoes in native houses destroys the insects at the time they become infected, thus breaking the chain of transmission. Other insects coming in contact with the residue of D.D.T. will also be destroyed, thereby offering additional results in the control of flies, bedbugs, roaches and other insect disease vectors and pests. When spray is not available, D.D.T. dusts may be used but they are not considered as efficient as the spray for use indoors as a residual insecticide.

D.D.T.⁷⁷ in five per cent solution in diesel oil or kerosene distributed out-of doors has not only direct killing effect on adult mosquitoes resting in vegetation and other hiding places, but also may exert residual action on insects that later fly into and rest in treated areas. Barrier zones may be established around bivouac areas, gun emplacements, observation posts, outdoor motion picture theaters, and other gathering places. Temporary reduction of the mosquito population is obtained with a dosage of one quart of five per cent solution (0.1 pound of D.D.T.) per acre. Dosages of two to four pounds of D.D.T. per acre have given residual action for two to three

weeks. Heavy rainfall and other weather factors may have an adverse effect on residual action.

Investigations by Simmons and Clapp⁷⁸ showed that D.D.T. residues from a xylene-D.D.T. spray mixture undergo a slow, gradual deterioration and lose about 25% effectiveness in the laboratory during the first twelve weeks after application. Mortality of adult Anopheles quadrimaculatus mosquitoes from D.D.T. residues occurs mainly within the first twenty-four hours after exposure, although some additional kill occurs in the twenty-four to forty-eight period. Adults incapacitated or knocked down by the D.D.T. rarely recovered. The exposure period necessary to kill 80% of the adult mosquitoes at any given time after spray application must be approximately doubled to kill the remaining 20%. Exposure time necessary to kill all the test insects at one week after treatment was 75 minutes, at four weeks, 100 minutes, at eight weeks, $2\frac{1}{2}$ hours, at 12 weeks, $3\frac{1}{2}$ hours, and at 20 weeks, 4 hours. Very little difference was encountered under laboratory conditions in mortalities after identical exposure periods to residues of 50 to 300 mg. of D.D.T. per square foot during the first twelve weeks after application. At twenty-four

weeks after application the results from 100 to 300 mg. D.D.T. per square foot residues were very similar. The concentration of D.D.T. within the range of 100 to 300 mg. per square foot did not materially affect the rate of deterioration of the residue. The nature of the solvent used in the D.D.T. spray mixtures appeared to influence the effectiveness of the residues at equal concentrations. Xylene, tetralin, PD-544B, PD-544C, Terposol No. 3, kerosene, and gas condensate have been the most promising solvents to date. Direct sunlight and the beating action of the rain caused accelerated deterioration of D.D.T. residues exposed to exterior weather condition. Many charts were shown to prove these facts.

Spraying of D.D.T.⁷⁹ from aircraft has opened a new era in insect control. A technic of application is now available which allows D.D.T. to kill insects in three ways: coming through the air in fine particles, it affects them in flight; striking the water it forms a surface film or emulsion fatal to larvae; remaining on vegetation or other surfaces, it leaves a residue which will kill adult mosquitoes or flies that alight thereon.

Spraying D.D.T.⁷⁹ from airplanes will

accomplish the following objectives; practical elimination of mosquito and fly adults and mosquito larvae within twenty-four hours, treatment of large areas in a minimum of time, access to areas difficult or impossible to reach with ground treatment, reduction in the number of personnel otherwise necessary to carry out ground treatment.

The time⁷⁹ relationship is especially important in controlling insect-borne diseases on beachhead areas. It takes from four to eight hours for D.D.T. to reduce the mosquito population effectively. If an invasion were to take place at dawn and D.D.T. were sprayed at that time, or during the previous night, the material would be effective by nightfall, when the anopheles would otherwise start to bite. It would therefore render possible some relaxation in malaria discipline.

One cargo-carrying airplane⁸⁰ properly fitted with simple equipment and carrying a capacity load of D.D.T. dissolved in kerosene or diesel oil No. 2, can effectively reduce a mosquito population covering a 2,000 acre area in less than twelve minutes of flying time. Application of D.D.T. over the same area at weekly intervals for one month will reduce

mosquito population so effectively that it is difficult for one accustomed to months of detailed planning, back-breaking drainage projects, and constant oiling and dusting operations to believe that the insecticide alone is responsible.

Mosquito larvicidal operations on the ground require from thirty to sixty days to become effective, so far as annoyance and transmission of disease is concerned. Aerially distributed D.D.T. produces almost immediate, though temporary, relief from such insects. It⁸⁰ is not recommended that airplane insecticide operations supplant all other mosquito control. The length of time a military installation is to be in use is an important criterion in planning the total mosquito control program.

In case of emergency⁸⁰ or in areas where it is necessary to control fly or mosquito vectors of human disease with limited time, personnel, or funds, D.D.T. released from the air will produce results which might otherwise be impossible.

The problem of transportation of insects by airplanes may be solved with the advent of D.D.T. A single application⁸¹ of D.D.T. to an airplane should be effective in the control of mosquitoes and other

pest insects. The presence of D.D.T. deposit would be an additional safeguard where aerosol was applied indifferently. Even the aerosol bombs can be made to contain D.D.T. and thus add more protection. Such a bomb⁸² would have the following ingredients: 3% pyrethrins, 3% D.D.T., 5% cyclohexanone, and 5% lubricating oil in Freon 12. Although data⁸¹ have accumulated on the effect of D.D.T. in buildings and tents, its use in the airplane presents a special problem. Residual treatments of D.D.T. may not be effective against untreated cargo and baggage. The most satisfactory treatment appears to be 20% concentration applied as a semifog spray.

For larvicidal purposes,⁸³ D.D.T. is supplied as commercial grade D.D.T. and as a 10% mixture of micronized D.D.T. with talc known as Laricide, D.D.T., powder, dissolving, and Laricide, D.D.T. powder, dusting respectively. In these forms, D.D.T. can be prepared for application as a larvicide either as an oil solution or as a dust. Oil solutions of D.D.T. make highly effective larvicides, and only a few quarts of solution are required to treat an acre of water surface, as compared with sixty to twenty gallons when ordinary oil is used alone.

To prepare⁸³ a 5% (weight/volume) solution, D.D.T. (Larvicide, D.D.T., powder, dissolving) is dissolved at the rate of seven ounces D.D.T. to one gallon of oil. Petroleum products such as kerosene, fuel oil, diesel oil, and waste crankcase oil are satisfactory as solvents. The mixture should be stirred at intervals until all of the D.D.T. is in solution, which may require twenty-four hours. Solution may be hastened by placing the mixture in the sun. For control of mosquito larvae, it is recommended that oil solutions of D.D.T. be applied at such a rate as to give 0.2 pound of D.D.T. per acre. This amount of D.D.T. is contained in two quarts of 5% oil solution. The treatment should be repeated every six to nine days. In order to obtain complete coverage it is often advantageous to use equivalent amounts of D.D.T. in more dilute solution (1 or 2 per cent). This is particularly true when spreading properties are diminished in the presence of an algal scum or heavy growth of surface vegetation. Under ideal circumstances larger doses of D.D.T. up to five pounds per acre may give residual effects up to three weeks. This dosage is not recommended, however, where wind, rain or other

inclement circumstances are likely to break up or remove the surface film. Dosages of D.D.T. greater than 0.2 pound per acre may kill fish and be harmful to wild life.

However, Lackey and Steinle⁸⁴ show that fish, crayfish, tadpoles, and large organism generally seem to suffer no direct effect from a concentration of 0.1 pound per acre, which represents 0.3 p.p.m. in the first three inches of water, if the average depth is greater than the three inches. An over-all concentration of 0.25 p.p.m. from which escape is impossible produces some mortality of fish, crayfish, tadpoles, and large organisms generally in the field. Under laboratory conditions, concentrations of 0.1 p.p.m. are lethal to fish, tadpoles, and Daphnia in twenty-four hours. The age and size of crayfish apparently make a difference in susceptibility. The large individuals were not killed at 20.0 p.p.m. in the laboratory. Chlamydotheca, a relative of Daphnia, 3 mm. in length, was not killed by 20.0 p.p.m. of D.D.T. Protozoa and algae are unaffected by concentrations up to 1.0 p.p.m.

Concentrations⁸⁴ as high as 1.0 p.p.m. become non-toxic in less than six days to the above

organisms in shallow waters. None of the carriers or dispensing agents used for D.D.T. have proved toxic at concentrations used.

No pupal⁸⁵ mortality has been noted in field tests with D.D.T. larvicide. Laboratory tests have shown that little mortality of pupae has taken place until the solvent concentration were high enough so that solvent checks produced equivalent mortality.

The same methods⁸³ of mosquito larviciding as employed with oil alone may be used to dispense the D.D.T. oil solution, except that smaller volumes are applied. Sprayer, insect, knapsack type, plunger type, cylindrical shape, three gallon capacity, an engineer item, is a practical and economical apparatus for applying D.D.T. oil solutions to ditches, small ponds, or other collections of water which can be reached by the spray. Large power sprayers may be employed to oil extensive areas such as the borders of lakes or, in some instances, swamps. A fog type of spray is required when five per cent D.D.T. oil solution is dispensed, utilizing wind currents to distribute the material. Continuous act on flit-gun sprayers are suitable for dispersal of D.D.T. solutions. Decontamination sprayer or other types of oil sprayers, with

the spray nozzle modified or adjusted to produce a fine spray are generally satisfactory. In treating streams, standard mechanical methods of the drip can type can be used. For large-scale area control, specially equipped aircraft may be employed to spray oil solutions of D.D.T. Application at the rate of from 0.2 to 0.4 pound of D.D.T. per acre will give good kill of larval mosquitoes as well as of adults.

For control⁸³ of anopheline mosquitoes one to five per cent D.D.T. in dust can be used very much in the same manner as Paris green dust. Any available finely divided material - such as soapstone, condemned flour, or road dust - may be used as a diluent. D.D.T. dust mixture may be applied with a hand rotary duster at the rate of 0.2 pound of D.D.T. per acre. When the dust is distributed by hand casting the stock dust should be mixed with fifty parts of diluent in order to make it easier to maintain a rate of distribution of 0.2 pound of D.D.T. per acre. In general, oil solutions are more satisfactory for routine use than dust preparations.

D.D.T.⁸⁶ has proved to be a very satisfactory larvicide for the control of Aedes aegypti. The composition of the container, whether glass, wood, rubber,

or metal does not markedly effect the residual action of D.D.T., even in the presence of rust, and moderately heavy dosages in these containers have remained effective against larvae of A. aegypti for six months or longer when exposed to both summer and winter weather of Savannah, Georgia. The larvae became morbid very rapidly, but may not die before seventy-two hours.

D.D.T.⁸⁴ has been effective in an emulsifiable solution, or as a wettable powder that may be dusted into wet or dry containers. D.D.T. in concentrations as high as 1 p.p.m. in water does not appear to be repellent to ovipositing Aedes aegypti females, nor does D.D.T. in xylene appear to be ovicidal. Fire barrels were treated with a concentrate consisting of D.D.T. 35%, Triton X-100, a proprietary emulsifier manufactured by the Rohm and Haas Company, Philadelphia, Pennsylvania, and five per cent xylene. One cubic centimeter was used for a fifty gallon barrel for these studies.

Tarzwell and Stierli⁸⁷ show that D.D.T. does not repel mosquitoes, but after varying periods of exposure to it, they become irritated and move usually toward the light. Results secured to date

indicate that D.D.T. is more effective against male mosquitoes than it is against females. In unoccupied buildings, treatments of 200 mg. of D.D.T. per square foot killed a high percentage of the mosquitoes which entered the building for a five month period after treatment. Results showed that D.D.T. residues are effective against mosquitoes in unscreened houses, as many dead mosquitoes were found on the floors of such buildings after they had been sprayed with D.D.T. In occupied houses treatment with 100 to 200 mg. of D.D.T. per square foot did not give as high percentage of kills as was obtained in unoccupied houses. This was due in large measure to the fact that in occupied buildings, only a portion of the available resting places was treated when only the walls and ceilings were sprayed. Safe resting places were provided by untreated furniture, exposed clothing, pictures, and the like. The D.D.T. was especially effective against flies, bedbugs, and the native cockroaches, and occupants of treated houses were able to discontinue the daily use of commercial sprays after D.D.T. treatment. In treating occupied houses all possible surfaces should be carefully and thoroughly sprayed, even though such treatment prolongs the actual spraying time.

Twenty-nine paired⁸⁷ releases of mosquitoes in specially prepared rooms indicated that mosquitoes exposed to D.D.T. residues on walls and ceilings have a definite behavior pattern. After varying lengths of exposure, depending on temperature, dosage, and age of the residue, they become irritated and began to fly around the room and move toward the light. The resistance of individual mosquitoes to D.D.T. varied greatly, necessary exposures ranging from fourteen minutes to over two hours. Kills of 100% were obtained in $4\frac{1}{2}$ hours or less under normal conditions. The toxicity resulting from a single spraying with 200 mg. of D.D.T. per square foot in vacant rooms gave good kills for a period of more than eleven months. The knockdown time increased with the age of treatment and somewhat longer for the smaller dosages. Temperature greatly influenced the rate of knockdown: the higher the temperature, the more rapid the effect of the D.D.T.

Simmons and his staff⁸⁸ has published many of their techniques and apparatus such as traps which they used in their studies on D.D.T. as an insecticide for mosquitoes which may be of some value in further study.

It⁸⁹ was estimated that the average cost of treatment, exclusive of overhead, was \$1.20 per average house containing 1,750 square feet, for crews with power equipment in similar urban areas was estimated to be \$1.39 per house.

The significance of D.D.T. as an insecticide can best be assessed by comparing it with other insecticides used. Pyrethrum⁹⁰ has the outstanding feature of a quick knockdown. Its defects are that as ordinarily applied as a pyrethrum kerosene spray, it is not persistent, and that to some skins it is an irritant. Rotenone, lacks the rapidity of action of pyrethrum, is not suited for application in kerosene but is more effective as a dust. In this form it is more persistent than pyrethrum and does not cause skin irritations. Synthetic insecticides such as the organic thiocyanates and iso-butyl-undecylenamide more nearly approach rotenone than pyrethrum in their insecticidal action-they lack the knockdown action; they are more toxic to man and animals and the thiocyanates have a persistent unpleasant odor which quite seriously limits their use. D.D.T., while lacking the rapid action of pyrethrum, has all the good insecticidal qualities of rotenone and the synthetics.

In pure form it is practically odorless and it is remarkably persistent. When sprayed on walls at a suitable concentration, D.D.T. kills any fly alighting on them up to a period of several weeks; a bed sprayed with D.D.T. is fatal to bedbugs for 300 days, and clothing dusted with it is safe from lice for a month even after several launderings.

DISCUSSION

Like most preventive public health problems, insect control must be brought to the attention of the public in such a way that its value to the individual as well as the group can be easily realized. The problem is not one of only passing or seasonal interest, but measures decided upon must be carried out and advanced every day of every year. As has been stated, a persistent effort is often of more value than periodic enthusiasm. The cooperation of all concerned must be gained for the stubbornness or ignorance of a few can cause the failure of the whole plan. Interested persons and organizations must be employed as the controlling leaders in the campaign against the insects.

Before any attack can be made, it is necessary to know something of the size and habits of the enemy. This is also true in the campaign against the insects. Careful studies must be made in the particular locality to determine the kind of mosquito or other insect carrying the disease, then the habits of breeding, of migration, and any other pertinent facts about its life history and habits that could be used in control measures. After these facts have been

gathered, the environment must be studied to determine the measures that would be practical, necessary and proper to control the insect vector. After these things have been done by an entomologist, the public health officer, or medical officer in the armed forces, is to make recommendations as to what should be done. The engineering department in turn carries out the doctor's recommendations.

After reviewing the literature on the control of insect vectors, one finds that the older method of drainage, oiling, sprays, and repellents are still useful along with the new chemical preparations. There will be many times when the D.D.T. mixtures and solutions will not be obtainable and these old procedures will be the only available means of combating the insects. Therefore, it is not enough to know just one method of insect control. The insects themselves may respond differently to different measures and a study of the local vector become important. In some diseases, vaccination is an important means of providing protection to the individual. This is not possible in all diseases such as the protozoan and metazoan and has not been worked out completely in other diseases.

Mosquito control is based mainly upon the control and elimination of the larvae and the breeding places of the adults. Drainage, oiling, and filling are still recommended and used in conjunction with the chemical larvicides. In general the control of the adults had not been successful until D.D.T. was initiated. The prevention of disease borne by mosquitoes is performed by the individual with the use of repellents, protective nets and screening. Segregation and isolation of persons who have the diseases is useful to prevent the infection of the insect vector. If the possibility of controlling any of the insect vectors is remote, attention must be turned to the elimination of the reservoir host of the disease organism.

Whenever large groups of people are in close contact with one another without the benefit of adequate bathing and laundering facilities; as in time of war, the problem of pediculosis and typhus begins to expand rapidly. The prevention of typhus is based on the control of the louse, the flea, and the rat. Elaborate plans have been worked out for the treatment of persons and their clothing infested with lice. A description of one of these plans is included. Again

D.D.T. has been of great usefulness during World War II in the control of human lousiness. Rat control must include rat proofing, poisoning, and trapping. The problem of flea control is important in preventing epidemics of plague and murine typhus. Various methods of fumigation, spraying, and careful cleaning have been described to eliminate the fleas, but recent studies have shown D.D.T. to be effective not only in ridding a house of fleas, but also against the fleas on pets.

Although ticks are not true insects, they represent the vectors of a group of diseases known as the spotted fevers. To prevent tick bites one should merely avoid contact with the shrubbery on which the ticks await their victims. Protective clothing and repellents are also helpful. Vaccines are used to prevent the development of the diseases. Mites are akin to ticks and are guarded against in the same manner. The actual control of the insect vector themselves is difficult because of their widespread presence and the abundance of animals both wild and domestic on which they may feed.

Flies are divided into two general groups; the biting types and the filth-bearing types. The

former types are difficult to control for their larvae are found in a larger variety of places such as mud, damp cellars, latrines, caves, tree trunks, and crevices of walls. The adults of the sandflies are so small that screening and netting are ineffective. Fumigation, clearing of debris, protective clothing and repellents are of most importance in preventing bites from these flies. The latter type of flies breeds in filth almost entirely and for this reason cleanliness and distance are about all that is necessary to control them. Those adults that do come near are barred by screens and killed by sprays. The importance of flies as vectors of poliomyelitis is doubted by many investigators, but their proved guilt as vectors of other diseases still makes control of utmost importance.

Finally a miscellaneous group of "bugs" including the reduviid bugs which carry the trypanosome of Chagas' disease and bedbugs which are probably more important as pests than actual disease vectors are included in the discussion. Improving the standard of living and the housing of the people is most important in the case of the reduviid bugs, and to some extent in the case of bedbugs also. Bedbugs

choriomeningitis, and toxoplasmosis among others. The field is in much need of more intensive investigation and experimentation. From time to time, newly recognized disease entities will undoubtedly be discovered and traced to insects already in the United States or to some of those which will almost surely be imported by airplanes in baggage or shipments. Many of the discharged service men and women will be coming back home with some of the diseases that can be transmitted by our domestic insects. With the rapid means of transportation by air, the week's voyage by ship can no longer be considered adequate time of incubation.

SUMMARY

1. Before any control measure can be begun against a proved insect vector of disease, a careful survey of the environment and life cycle of that insect must be made. At times a census of the insects and infected reservoir hosts is necessary.

2. Mosquito control is launched chiefly against the larvae and breeding sites. Drainage, oiling, filling, and the use of chemical larvicides are of main importance. The airplane has become an important factor in covering large areas and reaching inaccessible breeding areas quickly and effectively spraying them. D.D.T. has proved itself to be very effective even in small quantities against both adult and larval forms.

3. Various repellents and combinations were tried to ward off the bites of mosquitoes and other insects. Dimethylphthalate was found to be most useful and effective by the United States Army.

4. Louse control is closely allied to the cleanliness of the individual. Frequent bathing and changing of the clothing from the skin out is important in preventing lousiness. Where facilities are few and large groups are in need of treatment,

elaborate delousing stations are set up. During the war in Italy, large crowds of people fully dressed were deloused by dusting D.D.T. down the necks and arms of their clothes.

5. Tick control is largely ineffective. Individuals should avoid heavily infested areas, wear protective clothing, and frequently inspect the clothing and body for ticks. Vaccination, of persons who expect to enter tick areas, for the spotted fevers, is recommended.

6. Mites are repelled by flowers of sulfur, powdered naphthalene and protective clothing. Mites occurring in the United States are not as yet known to be rickettsial vectors.

7. Strict cleanliness is the most important measure in flea control. Pets should be bathed frequently in a 3% solution of creolin and soap and water. D.D.T. has been used effectively to kill not only the fleas on the animal, but also those present in the house.

8. The larvae of biting flies (horseflies, deerflies, and gadflies) tend to occur in marshy or muddy places; hence, a principal type of control measure is drainage. Fish oil repellents are effective

for protection against bites. Residual D.D.T. spray in houses is effective against sandflies.

9. Ordinary house flies are best controlled by cleanliness about the yard and with disposal of refuse. The maggots are difficult to control but the adults are prevented from entering the house by screens. Those that do get in are easily killed with pyrethrum or D.D.T. spray, poison, swatting and fly paper.

10. D.D.T. is found useful in ridding a house of bedbugs. Formerly, heat, fumigation and spraying with kerosene were used.

11. D.D.T., the newly discovered insecticide is reported to be effective against both the adults and mosquito larvae, lice, flies, bedbugs, and many other insects, both harmful and beneficial as well. Methods of making the substance, a short report of the possible toxicity, methods of application and effectiveness, and a brief comparison of the action of D.D.T. to three other valuable insecticides, are the main points covered in this discussion of dichlore-diphenyl-trichloroethane.

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