EPIDEMIOLOGY
AND CONTROL OF
VECTOR-BORNE DISEASES

Training Guide — Insect Control Series

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INTRODUCTION

It is much easier to control a disease that is understood than an unknown malady. No longer do malaria, yellow fever, plague, and typhus occur in devastating epidemics in this country, or in many other parts of the world. These great achievements are the result of cooperative efforts by the entire public health team in attacking the weak points in the cycles of these diseases. Much of this success has been due to years of patient work and research in working out the reservoir of these sicknesses; in isolating the causative agents of these vector-borne diseases; in identifying the vectors and studying their life histories; and in understanding the complex host-parasite interrelationships that result in disease, inapparent infection, or immunity. Public health workers must have an appreciation of the complicated interrelationships of all these factors, often called the natural history or epidemiology of disease, in order to apply control measures intelligently. Therefore, this training guide has been organized with sections on epidemiology, reservoir, parasite, vector, host, the host-parasite relationship, and control.

I. EPIDEMIOLOGY

How does a particular disease enter or appear among a group of people? How then does it spread and persist? What are its cycles and fluctuations, its everyday and its exceptional manifestations? How does it recede and disappear?

These and many other questions are dealt with by epidemiology which, freely translated, means:

the study of, or the science of, illness . . . . . logos
as it rests upon . . . . . epi
the people . . . . . demos

Epidemiology, therefore, is the sum of everything known about a disease as it affects a community rather than a person. It is often called the natural history of disease.

A physician is concerned with individuals, while
An epidemiologist studies and works with aggregations.

Each has some knowledge and practice in the other's domain, but each has unique methods, prescriptions, and responsibilities. Usually, the work of the epidemiologist begins with the physician's report.

"Epidemiology, at any given time, is something more than the total of its established facts. It includes their orderly arrangement into chains of inference which extend more or less beyond the bounds of direct observation. Such of these chains, as are well and truly laid, guide investigation to the facts of the future." W. H. Frost in Winslow (1943, p. 267).

"Epidemiology deals with the large scale phenomena of infectious disease, not only with epidemics, but also with the more or less constant prevalence of disease in human communities." Burnet (1953, p. 24). Examples: malaria, encephalitis, and plague.

Historically, epidemiology in the modern sense began in the 1800's with the working-out of the man-to-man cycles:

Diseases involving mainly two living factors:

HOST AND PARASITE

1. Air-borne diseases - as measles by Panum in 1847:
2. Water-borne diseases - as cholera worked out by Snow in 1854;
3. Food-borne diseases - as typhoid worked out by Sedgwick in 1892;
4. Venereal diseases - as gonorrhea worked out by Neisser in 1879; and
5. Contact diseases - as pediculosis and scabies, known for centuries.

Many of the most serious and important human diseases fall into this category, for man is the most important reservoir of diseases affecting mankind. The first three listed above are often grouped together as the vehicle-transmitted diseases, i.e., diseases transmitted by inanimate carriers.

Towards the end of the 19th century, and at the very beginning of the 20th century, great progress was made with the epidemiology of the true vector-borne diseases in which man is the vertebrate host and an arthropod such as a mosquito, flea, or tick, is the invertebrate vector.

Diseases involving mainly three living factors:

HOST, PARASITE, AND VECTOR

Filariasis - Sir Patrick Manson, 1878-1879
Malaria - Laveran, Ross, Grassi, and co-workers, 1880-1915 and later
Yellow Fever - Finlay, Reed, Gorgas, Carter, and others, 1880-1915
Typhus - Nicolle, 1909

These are commonly grouped as the vector-borne diseases, i.e., diseases maintained and transmitted by animate carriers. Although in the broadest sense of the definition, vector-borne diseases may include those transmitted from man to man, or from vertebrates to man, general usage in the United States usually restricts the vector-borne diseases to those maintained and transmitted by arthropods and/or rodents to man.

In the 20th century, intensive research by many investigators has lead to a better understanding of many diseases of other animals which occasionally and accidentally occur in man, i.e., the zoonoses, diseases of animals transmissible to man. These are:

Diseases involving mainly four living factors:

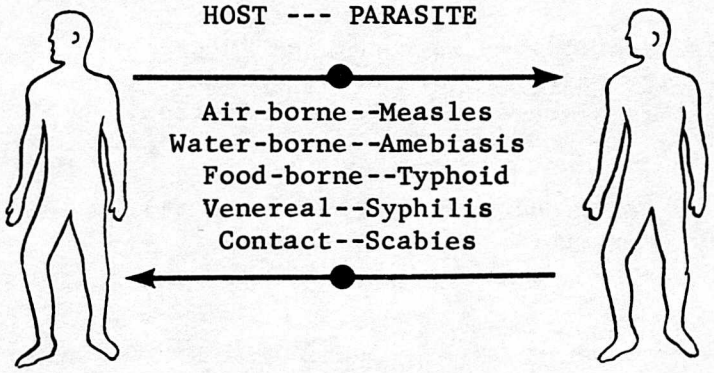
HOST, PARASITE, VECTOR, AND RESERVOIR

Plague	Murine Typhus
Tularemia	Encephalitis
Spotted Fever	And many other diseases

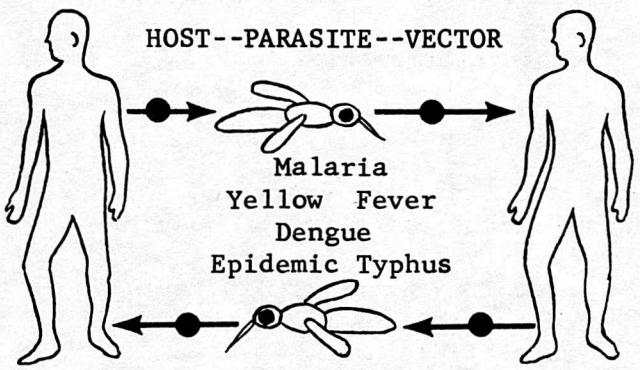
In these diseases, the vertebrates are normal hosts (or from the human viewpoint, the reservoir of the disease) while man and his animals are abnormal and accidental hosts, usually dead ends in the chain of infection.

PRIMARY FACTORS

Most communicable disease in U. S. involve MAINLY TWO LIVING FACTORS



Many insect-borne diseases involve MAINLY THREE LIVING FACTORS



AUXILIARY FACTORS

PHYSICAL (OR ENVIRONMENT)

- Climate
  - Rainfall and humidity
  - Temperature
  - Sunshine and cloudiness
  - Wind direction and velocity
- Relief
- Soils
- Hydrography

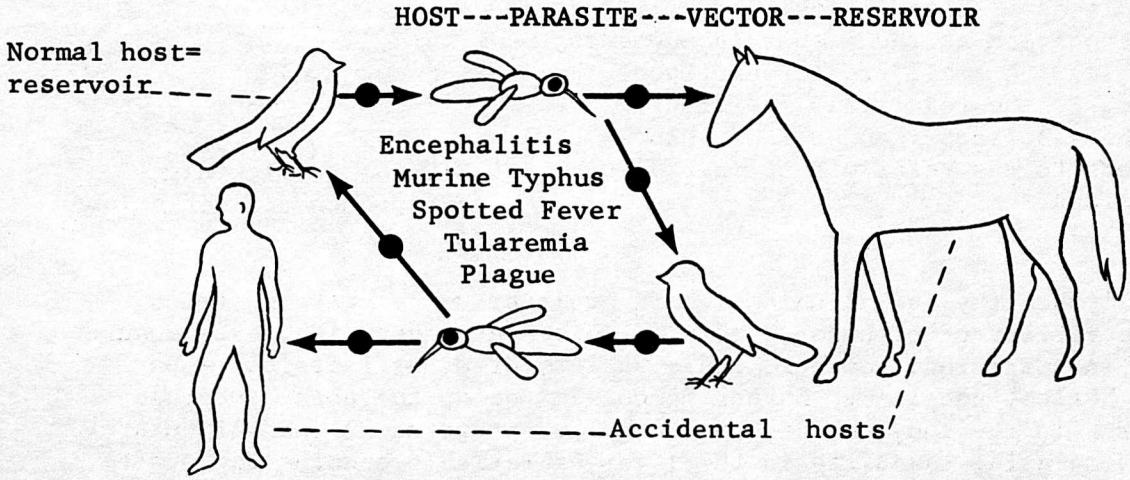
HUMAN (OR SOCIAL)

- Population distribution and density
- Standard of living
  - Housing
  - Diet
  - Clothing
  - Sanitation
  - Income
- Religious customs and superstitions

BIOLOGICAL

- Vegetable life
- Animal life
- Parasitism, human and animal
- Prevalent disease
- Dominant blood groups

Many vector-borne diseases involve MAINLY FOUR LIVING FACTORS



These are the zoonoses, i. e., diseases of animals transmissible to man. Human and domestic animal cases are often accidents, "dead ends" in chain of infection

Figure 1. Factors in the transmission of communicable disease.

II. HOST-PARASITE: HOST-VECTOR RELATIONSHIPS

The host-parasite and host-vector relationship is a complex interplay of four primary factors, namely reservoir, parasite (or causative agent of disease), vector, and host which result in disease, inapparent infection, or immunity, as shown in Figure 2.

1. Man
2. Animals
3. Free-Living

RESERVOIR

(+) Environment: Extrinsic (+) Factors Intrinsic (+) Factors

X PARASITE X VECTOR X HOST = DISEASE and/or IMMUNITY

(-) Environment: Extrinsic (-) Intrinsic (-)

Figure 2. Diagram of host-parasite: host-vector relationships.

A. Infections versus Disease

Infection - the presence of parasites in the body; the entry and development, or multiplication, of an infectious agent in the body.

Disease - an illness due to a specific infectious agent or its toxic products, arising through transmission and multiplication of that agent or its products from reservoir to susceptible host.

There can be infection without disease, but no disease without infection. Infection is not synonymous with infectious disease; the result may be inapparent infection or manifest disease. Epidemiologists aptly describe this condition as the iceberg phenomenon, comparing the small projecting tip of the iceberg to the relatively few clinical cases, and the vast submerged bulk of unknown proportions to the reservoir of inapparent infections.

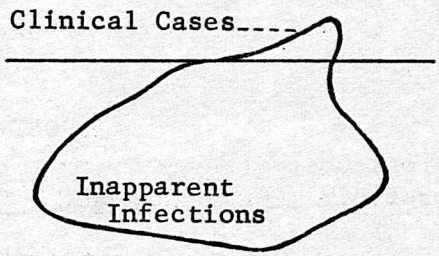


Figure 3. "Iceberg phenomenon" of infectious disease.

Normally healthy individuals live in equilibrium, a state of truce, with a variety of pathogens, some of which can cause disease as changes occur in nutrition, weather, and a variety of other factors. Apparently healthy people may harbor Demodex mites on the nose, tubercle bacteria in the lung, enteric bacteria and protozoa in the alimentary canal, malarial parasites in the liver or reticulo-endothelial system, filarial worms in the lymph nodes, and athlete's foot fungi between the toes. Are apparently healthy people ever really completely free of some of these parasites?

III. RESERVOIR

A. Reservoir - Sum of all sources of infection: natural habitat of the parasite.

B. Sources

1. Human - malaria, urban yellow fever, dengue, epidemic typhus - the greatest success in the control of human diseases transmitted by insects has come in the group in which man is the vertebrate reservoir and only one species of insect was the vector in a particular area.

2. Arthropods - ticks and spotted fever, chiggers and scrub typhus, a very peculiar type of infection chain in which there is transovarial transmission of the pathogen from parent to offspring.

3. Vertebrates - the zoonoses; rodents and plague, birds and encephalitis. The major problems in vector-borne disease control lie in this group where it is impossible to kill or control all animals acting as reservoirs of the disease.

4. Free-living - soil, feces, contaminated with Shigella bacteria causing diarrhea and dysentery, Salmonella causing typhoid.

C. Human Sources - (Some diseases as malaria and dengue are peculiar to man).

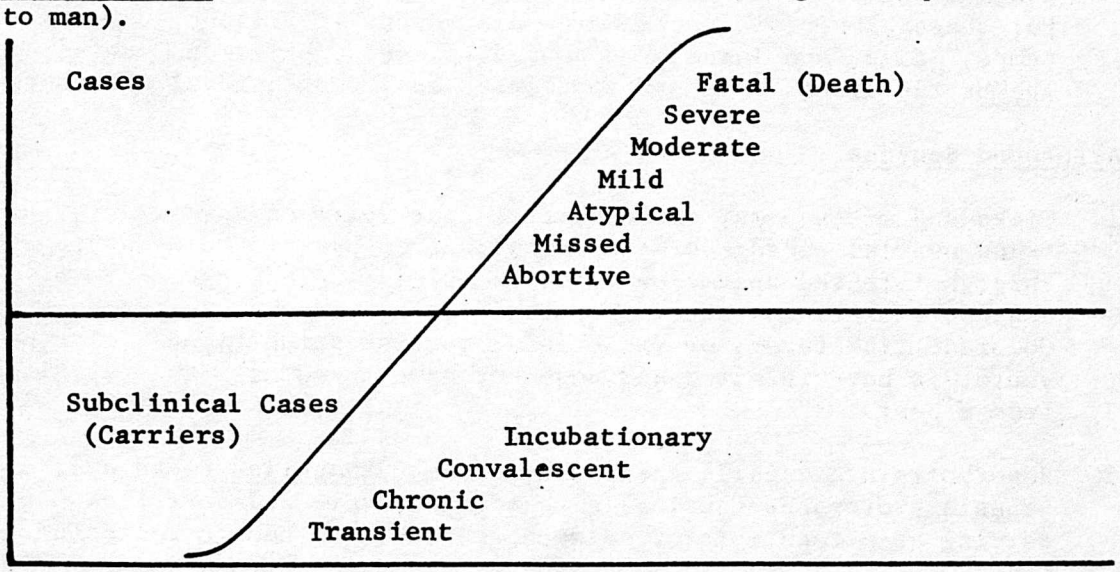


Figure 4. Spectrum of disease (transient carrier to fatal case).

In an epidemic the moderate, severe, and fatal cases (Figure 4) are often easily located and reported. On the other hand the mild, atypical, and abortive cases are the important ones epidemiologically because they are the sources of infection for new cases - they keep the epidemic smoldering. In the case of virus diseases such as yellow fever and dengue, the

virus is circulating in the peripheral blood (and hence is available to infect additional mosquitoes) only during the first few days of the disease. Yellow fever and dengue have been introduced repeatedly into the United States and other areas by carriers in which the virus was incubating before clinical signs of diseases were evident. Similarly, malaria has been introduced many times into uninfected areas by carriers in the transient, chronic, convalescent, or incubationary stages of the disease, or by people in whom malarial attacks were abortive, missed, atypical, mild or moderate (Figure 4).

It has been observed many times that an epidemic resulted simply because of a shift of the curve to the right (Figure 4) when nutrition declined, environmental sanitation broke down, and there was increased crowding and stress due to shifting populations. Under such conditions, atypical or mild cases of disease became moderately severe to severe (Figure 4), and while moderate and severe cases ended in death. It has often been observed that epidemic disease is associated with wars. This is not surprising when one considers that armies, when occupying territory to which their personnel are not native, are exposed to diseases for which no resistance has been acquired. This exposure, coupled with poor nutrition, fatigue, crowding and stress is ideal for the propagation of an epidemic among the large "herd" of "non-immunes." For these same reasons epidemics also occur in prisoner-of-war camps, jails, and large groups of displaced populations behind the battle lines, or in support areas following natural disasters.

D. Arthropod Sources

1. Ticks and mites - may serve as true reservoirs of infection with trans-ovarial passage of the parasite from parents to offspring through infected sperms or eggs; examples: relapsing fever spirochetes, rickettsiae causing spotted fever, virus organisms causing Colorado tick fever, or rickettsiae causing scrub typhus. The vector is born infected and does not have to acquire the parasites from a host.

2. Reservoirs are usually species specific: Boophilus ticks and Babesia protozoons causing Texas cattle fever, and soft ticks serving as a reservoir of spirochetes causing endemic relapsing fever.

E. Vertebrate Sources

1. Mammals - may act as reservoirs of many diseases such as plague, tularemia, murine typhus, relapsing fever, and Chagas' disease.

2. Man is an abnormal host, e.g., Audy (1958) has written that a particular host may harbour a parasite without maintaining it, for example: scrub typhus or encephalitis in man. The virus does not develop to a high enough level (titer) normally for man to serve as a source of infection to the arthropod.

3. Birds, either resident or migratory, can serve as reservoir of encephalitis viruses. The size of the small bird nestling population may be one of the important factors in determining the human hazard of encephalitis.

F. Size of reservoir (determines chance of spread).

1. In many diseases epizootics in the animals hosts precede epidemics in humans. Examples - tularemia outbreak in wild rodents in Oregon in 1958; dead rats before plague outbreaks; dead monkeys indicated advancing wave of jungle yellow fever in Central America; dead birds sometimes precede human or horse encephalitis outbreaks.

2. Transient reservoir. Seasonal pattern of cases - Yellow fever in summer and early fall when Aedes aegypti mosquitoes are active.

3. Permanent reservoir. The Russians under the stimulation of the work of Pavlovsky call this the "nidality of disease" - the focus of infection. Epidemiologists, for example, watch for Eastern encephalitis in eastern Massachusetts near certain tamarack-cedar bogs; for St. Louis encephalitis in the Mississippi-Ohio or Rio Grande Valleys; for Western encephalitis in Kern County, California. Spotted fever seems endemic in the Bitterroot Valley in Montana where the infected Rocky Mountain wood tick occurs in numbers. The best example of extreme localization of disease was reported by Walker (1961). Cases of relapsing fever occurred in the same log cabin in a park in California 20 years apart, presumably maintained by chipmunks and soft ticks in this cabin for 20 years.

G. Proximity of Reservoir.

1. In World War II, U. S. military found it desirable to segregate military personnel from civilian workers who might be carriers of malaria in the Caribbean, and from natives in the South Pacific who might have filariasis. In Hawaii, the majority of the dengue cases in 1944 were in Honolulu where non-immunes and Aedes aegypti lived in close proximity, few were found on the military bases where reasonable Aedes aegypti control and lack of carriers in the incubationary stage were present.

IV. THE PARASITE (OR CAUSATIVE AGENT OF DISEASE)

A. Parasite - A small organism living in or on, and at the expense of, a large one.

Students should be cautious in using the terms parasite and agent. An infected oriental rat flea may be a true ectoparasite on a rat. At the same time it is a vector of true internal parasites or endoparasites such as plague bacteria or rickettsiae causing murine typhus. The same problem arises in using the term agent, which can refer to causative or parasitic agent of disease, or can mean agent, carrier, or vector of disease-causing organisms.

B. Types of Parasites (Man attacked by many)

1. Viruses - yellow fever, dengue, encephalitis



2. Rickettsiae - spotted fever, typhus, rickettsialpox



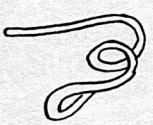
3. Bacteria - plague, tularemia



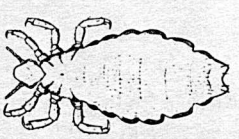
4. Spirochetes - relapsing fever



5. Protozoa - malaria, Chagas' disease, amoebic dysentery



6. Helminths - filariasis, broad fish tapeworm, Asiatic lung fluke



7. Arthropods - scabies, pediculosis, myiasis, chigoe flea infestations.

C. Specificity - Usually considered that one disease and only one is produced by each parasite. However, malaria mimics many diseases and "dengue" can be caused by very different viruses. Hence, the physician and public health worker must rely on reputable laboratories for correct diagnoses of the parasites in order to conduct effective disease control programs.

D. Dosage - The number of parasites necessary to initiate disease varies with virulence of the parasite and resistance of the host.

In general the larger the number of parasites, the greater the chance of infection. A bite of one infected mosquito may introduce enough parasites to initiate clinical attacks of malaria, yellow fever, dengue, or encephalitis. On the other hand it may require the bites of thousands of mosquitoes, and the injection of many filarial worms, to bring about a clinical case of filariasis, especially elephantiasis. According to Boyd (1941) malaria can be induced by intravenous inoculation of as few as 10 trophozoites of Plasmodium vivax, the threshold of infection or pyrogenic level. In his patients there was usually no malarial fever unless there was at least 1 parasite to 100,000 red cells, i.e., 50 parasites in 1 cm. of blood, or 150,000,000 parasites in a man weighing approximately 150 pounds.

E. Virulence - This is a complex property which combines infectivity, invasiveness, and pathogenicity (Frobisher, 1962, p. 351).

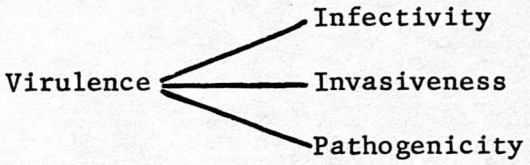


Figure 5 - Factors in Virulence

a. Infectivity, or the ability to initiate and maintain an infection in the host. This depends on the ability of the parasite to establish an initial "beach head" in the host by evading or overcoming local defensive mechanisms: skin barriers, phagocytes, or antibodies. With normal precautions, laboratory workers can study plague, typhoid, or shigella organisms with minimal risk. On the other hand, it is a rare person who can work for a long time with Q fever, tularemia, or brucellosis without contracting infection. Burnet (1953, p. 399) has written "if we had enough information, we could probably express the differences in the form that if one living organism of typhoid fever is taken into the body, the chance of its initiating infection is 1 in 1000, but if one Q fever Rickettsia lodges in the lung, there is 1 chance in 3 that it initiates infection. The numbers are pure guess, but the ratio is approximately correct".

b. Invasiveness, or the power to progress farther into the host from the initial infection. Parasites may grow in superficial tissues, as Scabies and Demodex mites; in deeper tissues or sinuses, as fly maggots; in the lymph, as in buboes and swollen lymphatics found in plague or tularemia; others may invade the blood stream, causing viremia, bacteremia, rickettsemia, septicemia or blood poisoning. After parasites have entered the blood stream they may be carried to other organs, such as the liver, spleen or bone marrow.

c. Pathogenicity, or the ability to injure a host once an infection is established. The principal cause of pathogenicity of most parasitic micro-organisms is toxicity. Many toxins liberated by bacteria affect nervous tissue, heart muscle, or kidney tissue. Strains of parasites vary from highly virulent to avirulent.

V. ARTHROPOD VECTORS OF DISEASE

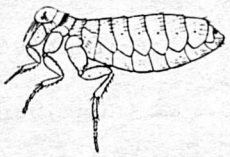
A. Vector - the living carrier of dissemination or inoculation, or both, of the causative agent of disease.

B. Groups of Arthropod Vectors: (largely six orders)

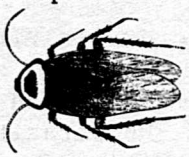
1. Order Diptera-flies & mosquitoes



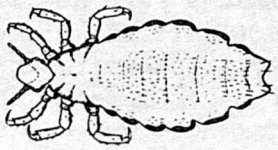
2. Order Siphonaptera-fleas



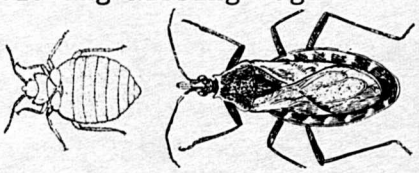
3. Order Orthoptera-cockroaches



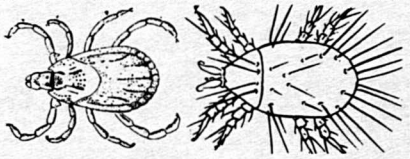
4. Order Anoplura-sucking lice



5. Order Hemiptera-true bugs including kissing bugs



6. Order Acarina-ticks & mites



In the control of vector-borne diseases, frequently the most important questions in any initial survey and later control programs are:

a. What are the vectors of the disease?
b. What are the reservoirs of the disease?

Here a detailed knowledge of the species is involved, frequently requiring the services of an expert taxonomist.

C. Methods in which Vectors are Involved in the Transmission and Propogation of Parasites - The classification of methods by which arthropods transmit vertebrate infections below follows the general outline of Huff (1931).

1. Mechanical transmission - the parasite neither changing nor multiplying significantly on or within the arthropod vector.

Flies and cockroaches - on feet and body hairs, as typhoid and bacillary dysentery;
Tse-tse flies - on contaminated mouthparts, as African sleeping sickness;
Stable flies - on contaminated mouthparts, as anthrax;
Deer flies - on contaminated mouthparts, as tularemia;
Flies and cockroaches - enteric bacteria passing through alimentary canal, as in bacillary dysentery.

2. Biological transmission - the parasites multiplying, often changing or passing through a cycle, in the arthropod vector which serves as an essential host and part of the transmission cycle.

   Propagative - the parasites multiplying within the vector but undergoing no cyclical change.
   Maturation - mosquitoes with encephalitis and yellow fever viruses;
   Multiplication - ticks with spotted fever rickettsiae in gut; fleas with plague bacteria in gut.

   Cyclo-developmental - the parasites undergoing cyclical change within the vector but not increasing in numbers; mosquitoes with filarial worms.

   Cyclo-propagative - the parasites undergoing both cyclical change and multiplying within the vector; mosquitoes with malarial parasites; kissing bugs with trypanosomes causing Chagas' disease.

D. Methods by which Vectors Transmit Parasites

   a. Biting - mosquitoes and malaria, yellow fever, dengue, encephalitis with injection of agent into blood stream.

   b. Regurgitation - fleas and plague organism from "blocked fleas."

   c. Scratching-in of infective feces - fleas and murine typhus; lice and epidemic typhus; kissing bugs and Chagas' disease with portals of entry as skin, eyes, nose, or mouth.

   d. Contamination of host with body fluids of infected vectors - i.e., lice with spirochetes of relapsing fever liberated only by crushing insects, or soft ticks and relapsing fever spirochetes in coxal fluids.

E. The Important Factors in the Arthropod Element of the Transmission Cycle are:

   1. Ability to become infected - only Anopheles mosquitoes can become infected with the malarial parasites.

   2. Ability to transmit the pathogenic agent to a susceptible host - some species of Anopheles are better transmitters than others.

   3. Willingness to bite man repeatedly - A. gambiae versus A. quadrimaculatus or hyrcanus; Aedes aegypti versus Culiseta melanura; Xenopsylla cheopis versus "wild rodent fleas."

4. Survival rate - live long enough to become infective to man; Anopheles gambiae versus culiciefacies, importance in stable and unstable malaria (MacDonald, 1957).

5. Domesticity - close association with man:

Aedes aegypti - yellow fever and dengue
Anopheles gambiae - malaria
Body louse - epidemic typhus
Xenopsylla cheopis - plague and murine typhus

F. Indices of Vector Necessary for Transmission. (dependent on level of infection in reservoir)

MALARIA

In Puerto Rican native villages between 1920-44 - transmission of malaria when populations of A. albimanus rose above 1 per bait trap per night.

In Puerto Rican military installations (screened) during 1942-1944 - little or no transmission until populations of A. albimanus rose above 5 per bait trap per night.

In the United States during World War II at military camps - index of satisfactory control was arbitrarily set at about 10 female A. quadrimaculatus per night in resting stations.

YELLOW FEVER

Often stated that transmission stopped when less than 5 percent of the premises were infested with yellow fever mosquito (Aedes aegypti).

MURINE TYPHUS

Little transmission when index of oriental rat flea (Xenopsylla cheopis) dropped below 1 per rat, or when Rickettisia typhi was found in less than 25 percent of rats. When flea index and rickettsial infections rose above these figures, there was a tendency to "spill over" into human population.

PLAGUE

When plague is established in commensal rodents, the critical index for plague transmission to humans seems to be about 1 or 2

oriental rat fleas per rat. When indices are above 1 or 2 fleas per rat, plague epidemics have occurred in San Francisco, New Orleans, and Thailand. In San Francisco, Meyer (in Dubos, 1958, p. 418) reported the following:

> In 1907, 27 of 1,000 rats (2.7%) were infected with plague. There were 56 human cases and 25 human deaths.
>
> In 1908, 1.1% of rats infected. There were 2 human cases and no deaths.
>
> Many other factors may be involved in plague transmission as discussed by Kartman, et al. (1958)

G. Effects of Environment.

1. Temperature

a. Yellow fever and dengue outbreaks in United States usually occurred in summer and extended into fall until cold weather or frost killed infected yellow fever mosquitoes.

b. According to McDonald (1956) "Malaria is not transmitted except at temperatures exceeding 15°C. and this temperature must be maintained for a month or more for it to become established even when potent vectors are present...in consequence the extreme limits of malaria in the northern hemisphere lie within the July 15°C. isotherm." The parasites develop within the mosquito in a relatively short temperature gradient...parasite development is indefinitely prolonged below 19°C. for P. falciparum and below 15°C. (57°F.) for P. vivax. High temperatures are lethal for the parasite, the proportion surviving decreasing rapidly at temperatures over 32°C. (90°F.)...Within the limits thus set the rate of development is a function of temperature."

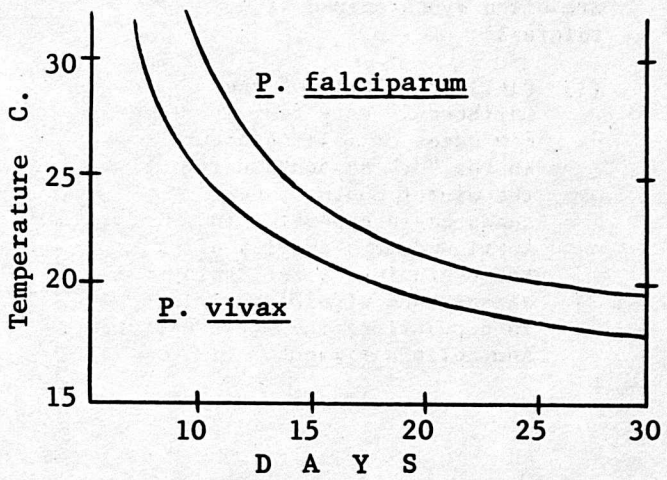


Figure 6. Time-Temperature relationship of P. falciparum and P. vivax in Anopheles mosquitoes.

c. Similar data has been worked out for yellow fever by Davis (1932, see Bates, 1949, p. 220).

Aedes aegypti became infective with Asibi strain of yellow fever virus as follows:

37°C.(98.6 F.)	4 days
36	5
31	6
25	8
23.4	11
21	18
18°C.(65 F.)	not at 30 days

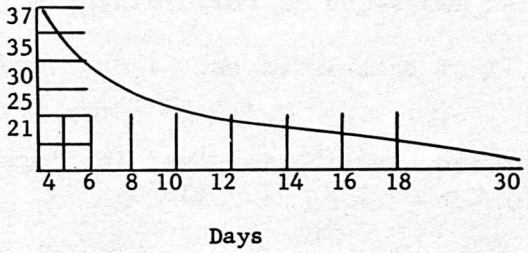


Figure 7. Time-temperature relationships of yellow fever virus in Aedes aegypti.

d. In the hot dry tropics, malarial parasites develop in Anopheles mosquitoes until the temperature reaches 90°F. (32°C.). Above 32°C. there is marked decrease in parasite development in the mosquitoes, and also in the number of new cases of malaria. (Daggy, 1959).

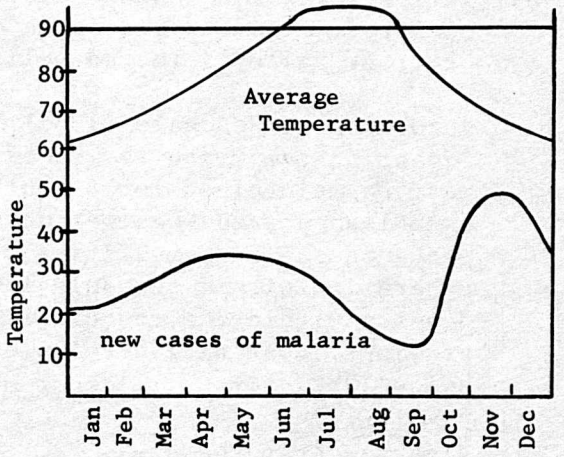


Figure 8. Oasis malaria (Daggy, 1959)

2. Rainfall

a. Seasonal outbreaks of malaria are often synchronized with rainfall.

(1) Flatland malaria of the Caribbean. Very few new cases of malaria occur in the "dry season" during the winter months. New cases begin appearing in April and May, shortly after the beginning of the "rainy season" and significant rises in populations the major vector, Anopheles albimanus.

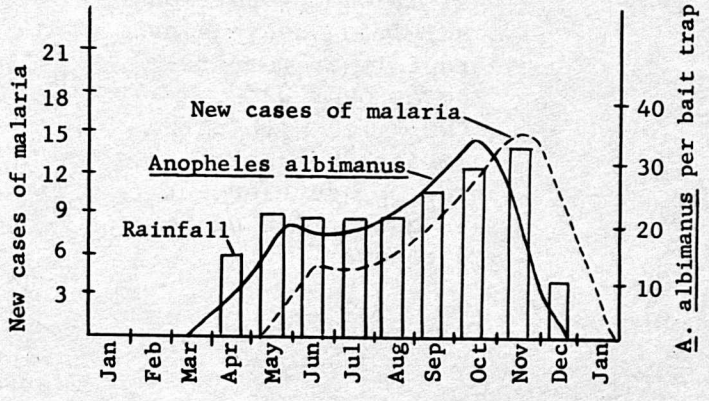


Figure 9. Flatland Malaria in Caribbean

(2) Mountain malaria of the Andes -- Populations of A. pseudopunctipennis increase as rainy season ends and brookpool breeding places stabilize. The malaria season is correlated with the "dry season".

(3) In the United States with encephalitis.

(a) Heavy rainfall, high water table, and increased irrigation may increase breeding places of Culex tarsalis and are sometimes associated with epidemics of Western and St. Louis encephalitis.

(b) High rainfall tends to maintain the swamp breeding places of Culiseta melanura and Mansonia perturbans, suspected endemic vectors of Eastern encephalitis. Example, no cases of Eastern encephalitis in Massachusetts in 1957 coincident with most severe drouth in many years. When swamps were filled with water in 1958 and populations of the epidemic vectors, Aedes sollicitans and Aedes vexans, were very high in 1959, the New Jersey epidemic of Eastern encephalitis occurred.

(c) Low rainfall tends to produce pooling in streams conducive to high populations of Culex pipiens-quinquefasciatus and outbreaks of St. Louis encephalitis in Mississippi-Ohio valleys and the Rio Grande valley in Texas.

H. Detailed Knowledge of the Natural History or Ecology of the Vector.

Much of the success in the control of insect-borne diseases has resulted from detailed studies of the ecology of the important vectors, for example:

1. Yellow fever and dengue control programs concentrate on elimination of the larval breeding places of the Aedes aegypti or on control of infected adults.

2. Malaria campaigns have been based on detailed knowledge of the breeding places of important vectors: A. quadrimaculatus in impounded waters, A. gambiae in small sunlit pools, A. bellator in bromeliads; or on the habits of the adults -- the house-resting A. quadrimaculatus or sacharovi versus A. bellator which feeds mostly out-of-doors.

3. A better knowledge of the ecology of sylvatic plague has resulted from studies of all groups of small native rodents, so that today in the West more attention is being given to the small nocturnal rodents, such as Microtus and their fleas, than to the more conspicuous diurnal animals such as prairie dogs and ground squirrels and their fleas which formerly were given top priority.

4. In the study of jungle yellow fever -- attention has focused particularly on the day-time feeding Haemagogus and Sabethes rather than on the night-biting Anopheles and Culex.

VI. HOST

A. Host - one who receives and entertains another; any living animal or plant affording subsistence and lodging to a parasite.

B. Types of hosts. In many vector-borne diseases the parasites pass through a life cycle in two or more hosts of different species. Animals in which the parasite attains maturity or passes its sexual cycle are primary or definitive hosts; those in which the parasite is in the larval or asexual stage are secondary or intermediate hosts.

Type of Host	Disease	Disease
Primary Host or Definitive Host For sexual forms	Malaria in Mosquito	Filariasis in Man
Secondary Host or Intermediate Host For asexual forms	Malaria in Man	Filariasis in Mosquito

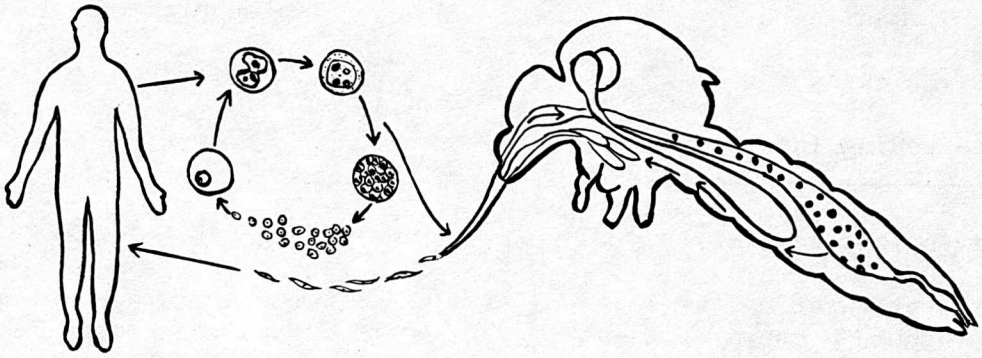
It is not possible to apply these definitions strictly to diseases caused by viruses, rickettsiae, spirochetes, bacteria, or leishmaniae which have no sexual forms. Chandler and Read (1961) prefer to use the terms definitive for the vertebrate host and intermediate for the invertebrate host, or even more simply vertebrate and invertebrate hosts.

C. Intrinsic and Extrinsic Incubation Periods of Disease-Causing Organisms.

In many vector-borne diseases the parasites develop in two hosts. The intrinsic incubation period is the time interval between injection of the parasite into the vertebrate host (usually man) until clinical signs and symptoms of the disease are evident. The extrinsic incubation period is the time interval required between acquisition of the parasite by the invertebrate host and the development of infective forms (in the case of rickettsiae, one-celled micro-organisms and helminths) or concentrations (in the case of viruses) of the parasite.

The intrinsic and extrinsic incubation periods of disease-causing organisms vary greatly with the number of parasites, temperature, humidity, nutrition, season, and other factors. A knowledge of

the incubation periods of disease-causing organisms in both man and vectors is essential in investigating epidemics of, or in controlling, vector-borne diseases.



Intrinsic Incubation Period in Man

Extrinsic Incubation Period in Vector

Figure 10 - Intrinsic and Extrinsic Incubation Periods in Man and Vector.

Disease	Average Intrinsic Incubation Period in Man	Average Extrinsic Incubation Period in Vector
Vivax Malaria	10-14 days	10-14 days at 20°C. in Anopheles
Yellow Fever	3-6 days	8-12 days in Aedes aegypti
St. Louis Encephalitis	5-15 days	2-3 weeks in Culex quinquefasciatus
Bubonic Plague	2-6 days	15-45 days X. cheopis
Typhus	6-15 days	5-9 days in Pediculus
Chagas' Disease	7-14 days	6-15 days in Triatoma

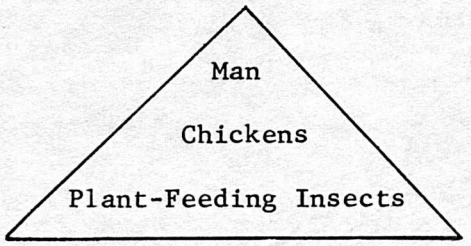
VII. HOST-PARASITE RELATIONSHIPS

A. Symbiosis - the living together of dissimilar organisms whether as forms of parasitism, harmless commensalism, or beneficial mutualism - Philip (1958) or Steinhaus (1946). The partners should be called symbiotes not symbionts according to Philip (1958).

B. Parasitism - this condition results from a small organism living on or in, and at the expense of, a larger one (Chandler and Read, 1961).

C. Pyramid of Numbers - Audy (1958) visualizes this as a pyramid of numbers with two classic examples following:

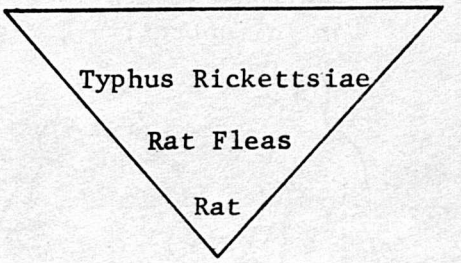
PREDATOR-PREY RELATIONSHIP



Living off capital

One large predator may be supported through a chain of lesser predators by many small herbivores.

HOST-PARASITE RELATIONSHIP



Living off interest

Large numbers of increasingly small organisms feed on relatively fewer but larger hosts.

Figure 11

D. Parasite-Host Reactions.

When a parasite invades a host, one of several reactions may occur:

1. The parasite may die quickly: example, schistosome dermatitis;

2. The parasite may survive but without causing any obvious symptoms of disease; however, its presence may cause a host reaction (inapparent infection) which may prevent re-infection or superinfection: example, malaria;

3. The parasite may survive and cause disease, with or without a host reaction which may or may not cure the disease, prevent re-infections or super-infections; example, malaria or Chagas' disease; or

4. The parasite may kill the host: example, plague (Cameron, 1956, p. 231).

Many parasitologists have expressed their opinion that in the long-established, well-adapted host-parasite relationship, the host is not seriously injured. Zinsser (1934) has expressed his opinion that the murine typhus-rat flea cycle is an old and long-established relationship because the rickettsiae do not kill the host, while the epidemic typhus-louse cycle is a recent development because the Rickettsia prowazeki of epidemic typhus kill the lice. Many virologists believe that the arthropod-borne viruses, in general, do not kill their mosquito hosts and that these relationships are therefore long established. On the other hand, it is well-known that after feeding on people with a large number of microfilariae in the blood, mosquitoes are killed by the helminths. This mosquito-filarial worm relationship may therefore be a relatively recently established host-parasite association.

E. Susceptibility versus Resistance.

Susceptible - a host not possessing resistance against a particular pathogenic agent and for that reason liable to contract the disease if exposed to the specific parasite.

Resistance - the sum total of body mechanisms which interpose barriers to the progress of invasion of parasitic agents. There are two main aspects of such resistance: non-specific and specific resistance.

F. Non-Specific Resistance.

Non-specific resistance is not directed against any particular disease but against infection in general.

a. Genetic aspects. Species or racial resistance to disease. Man is not susceptible to hoof-and-mouth disease, rinderpest, or fowl pox; while lower animals do not suffer from measles, syphilis, or gonorrhea. Negroes are not as susceptible to yellow fever as people of other races; similarly, negroes are not as susceptible as members of the white race to Plasmodium vivax and falciparum. Therefore, in negroes P. malariae is used to obtain high fever in treating neurosyphilis.

b. Physical and Chemical Barriers to Infection

The skin rids itself rather quickly of surface bacteria. Acetic acid in perspiration is quite toxic to many bacteria. Tears not only contain a bactericidal substance, but wash invading organisms through the tear duct into the nasal cavities. The nose is lined with ciliated epithelial cells which urge parasites toward the pharynx. Sticky mucous membranes trap parasites which are either coughed up or swallowed. In the mouth suction and

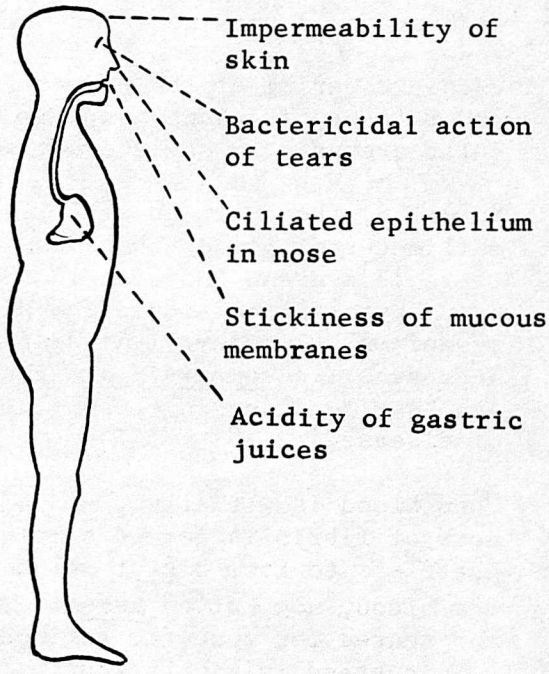


Figure 12 Physical and chemical barriers to infection

drainage sweep foreign matter and parasites into the gullet. In the stomach most bacteria and protozoa are destroyed by the strongly acid digestive juices.

c. Antimicrobial factors of blood and cells.

Blood is a complex fluid consisting of:

1. Plasma - a yellowish transparent liquid;
2. Red cells (erythrocytes) which carry oxygen from the lungs to tissues;
3. White cells (leukocytes) which in some cases act as scavengers and "policemen" in the blood; and
4. Platelets, which appear to aid in clotting of blood.

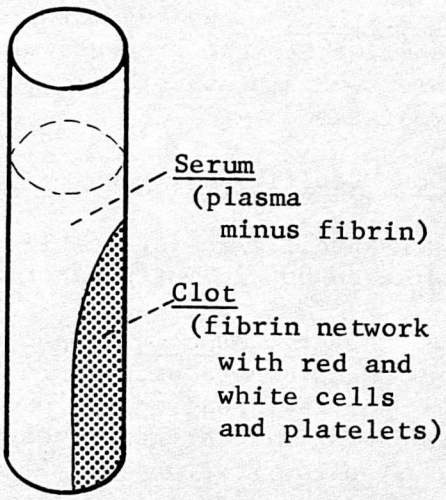


Figure 13. Tube with clot which enmeshed almost all the cells and squeezed out the clear serum.

Normally, there are about 5 million red cells per cubic millimeter of blood in men and about 4.5 million in women. In some vector-borne diseases, such as malaria, the number of red cells may drop to a million or less with profound anemia. Some arthropod venoms, and some toxins, cause rupturing of the red cells and release of hemoglobin. Such cells are said to have been "laked" or hemolyzed.

Normally, there are about 7,000 to 9,000 leukocytes per cubic millimeter of blood. However, in many bacterial infections there is a great increase in the number of white cells (leukocytosis) to aid in combating the disease-causing microorganisms. In many virus diseases the number of white cells decreases (leukopenia). Reliable laboratory data on blood examination is an invaluable aid in diagnosis and treatment of disease.

When blood is withdrawn, and allowed to stand, an elastic network of fibrin is formed enmeshing red and white cells and platelets to form a clot which squeezes out the fluid part of the blood, now called serum. This serum can be drawn off, and tested for specific antibodies which are stable enough to withstand refrigeration.

These antibodies aid in combating infection by combining with foreign parasites, or their products, in blood or in tissue

d. Special Mechanisms - Phagocytosis by Leukocytes and Reticulo-Endothelial System.

Parasites may be destroyed by white cells floating in the blood. In addition, special white cells (phagocytes, macrophages or histiocytes) are "built into" the linings of blood vessels particularly in the liver, spleen and bone marrow. They are part of the reticulo-endothelial system whose function in part is to destroy pathogens and dead cells by a process known as phagocytosis. (literally, cells eating cells, or the process by which cells ingest and digest other cells, micro-organisms, and foreign particles). This action is the basis of the cellular theory of immunity proposed by Metchnikoff and the French School (see also, Von Behring and the German School, p. 22).

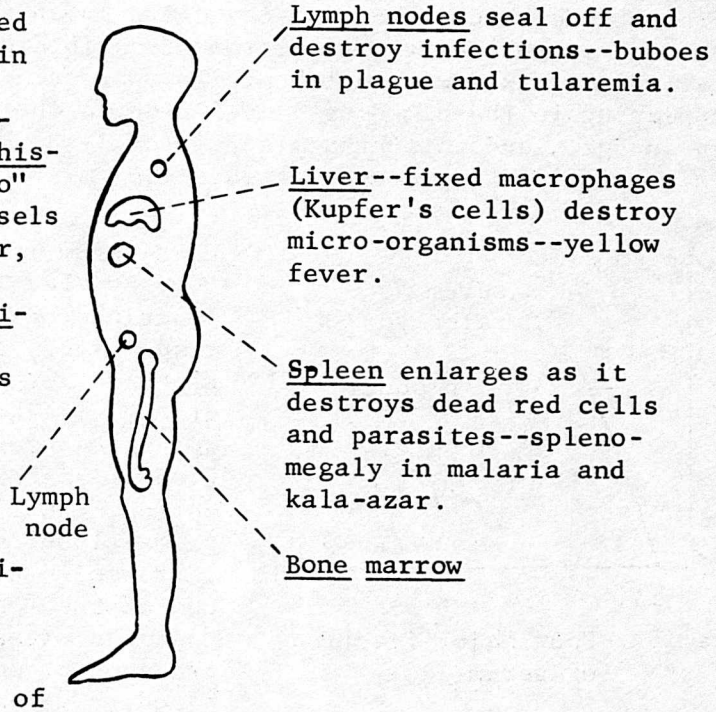


Figure 14 - Phagocytic mechanisms

In many infections the white cells try to dispose of foreign particles by ingesting and destroying them, or by giving off enzymes that will kill, destroy, or digest them. These white cells may themselves be killed. For example, the white creamy material in boils and infections is made up largely of dead white cells (pus cells). White cells help destroy plague and tularemia bacteria sealed off in lymph nodes (buboes). In the liver of people immune to yellow fever, fixed phagocytes help destroy new virus injected by mosquitoes. In malaria and kala-azar the protozoan parasites may destroy so many red cells that the spleen becomes overworked and enlarged trying to "clear" the blood of the dead cells - splenomegaly.

G. Specific Resistance.

Attacks by parasites are frequently countered through the development of antibodies and antitoxins. This idea is the humoral theory of Von Behring and the German School. Stated in simplest terms, it proposes that to each action of the parasite, there is a reaction by the host. The parasite itself, or its products, contain antigen - a substance which, when injected into human tissues or the blood stream, stimulates the formation of antibodies that react specifically when mixed with antigen. In contrast, antibodies are substances appearing in the blood or body fluids as the result of stimulation by an antigen, and which react specifically with the antigen. Antibody is a modified fraction of gamma globulin.

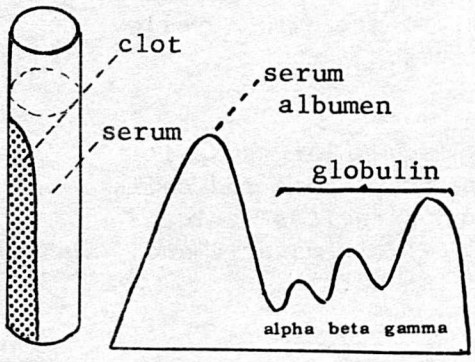


Figure 15. Four major fractions of serum

When serum is studied in the laboratory by electrophoresis, four main fractions can be demonstrated known respectively as serum albumen, alpha globulin, beta globulin, and gamma globulin. Each protein moves at its own speed toward the positive electrode. Following infection or immunization, there is an increase in the gamma globulin fraction, due to an increase in the amount of antibody. One of the most certain ways of diagnosing a disease is to determine the presence of specific antibodies in the blood. Two samples of blood are collected, one during fever, and the other during convalescence. The paired sera from the same patient are called acute and convalescent sera. They may be tested for a variety of antibodies produced by disease-causing organisms. There are:

Agglutinins - as in the Weil-Felix test for rickettsiae, or the Widal test for typhoid;
Precipitins - as in plague, anthrax, or the Kahn test for syphilis;
Complement-Fixing - as in rickettsial diseases or the Wasserman test for syphilis;
Neutralizing -as in yellow fever, encephalitis, and many virus diseases;
Opsonins - which "butter-up" invaders as malaria parasites so that phagocytes can ingest them more easily;
Antitoxins - as in diptheria.

There is a time sequence in the appearance and disappearance of these antibodies. Complement-fixing antibodies appear early following infection but do not last long; neutralizing antibodies appear later but may last for years. The longest well-authenticated period of protection by neutralizing antibodies of an arthropod-borne disease known to this writer is that reported by Sawyer (1931). An 82-year-old-man who had survived the Norfolk, Virginia, epidemic of yellow fever in 1855 still had neutralizing antibodies in his blood in 1930, a period of 75 years.

H. Immunity Against Infectious Disease.

1. Naturally acquired immunity may be of the

   Passive type - due to antibodies in the newborn child of a mother who has recovered from the disease. These provide protection for the first few months: example, yellow fever; or of the

   Active type - due to antibodies resulting from natural disease or subclinical infection with yellow fever, plague, typhus, or encephalitis. Long-lasting immunity.

2. Artificially acquired immunity may be of the

   Passive type - use of serum or gamma globulin to lessen the severity of reaction to parasites while the body builds its own protective antibodies: example, measles treated with gamma globulin, or typhus with hyper-immune serum experimentally, or of the

   Active type - with protective antibodies resulting from vaccines to give initial protection and periodic "booster shots" to maintain high level of immunity: examples, yellow fever, and epidemic typhus.

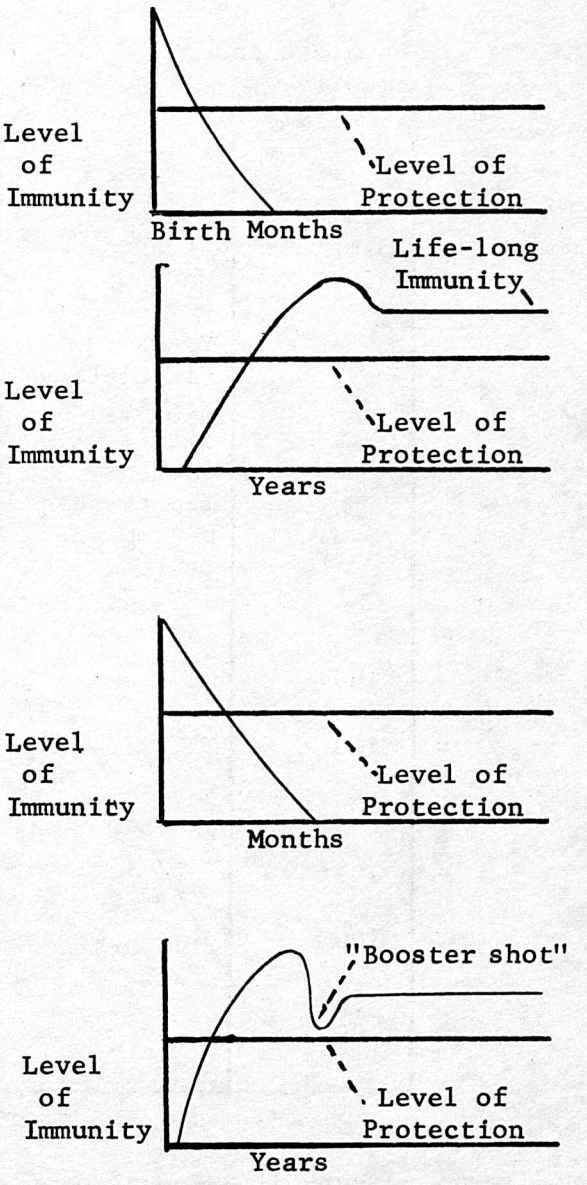


Figure 16. Immunity against infectious disease.

I. Sequence of Events in Virus Infections.

In many infectious diseases, particularly virus diseases, there is a regular sequence of events as follows:

Most Infectious Diseases	Important aspects of virus Diseases Immunologically
1. Vague symptoms	
2. Onset - gradual or abrupt	Virus circulates freely, little antibody; insects can become infected.
3. Illness or fever	Increasing amounts of antibody developed; insects do not become infected.
4. Convalescence	Development of protective antibodies
5. Immunity	Development of resistance

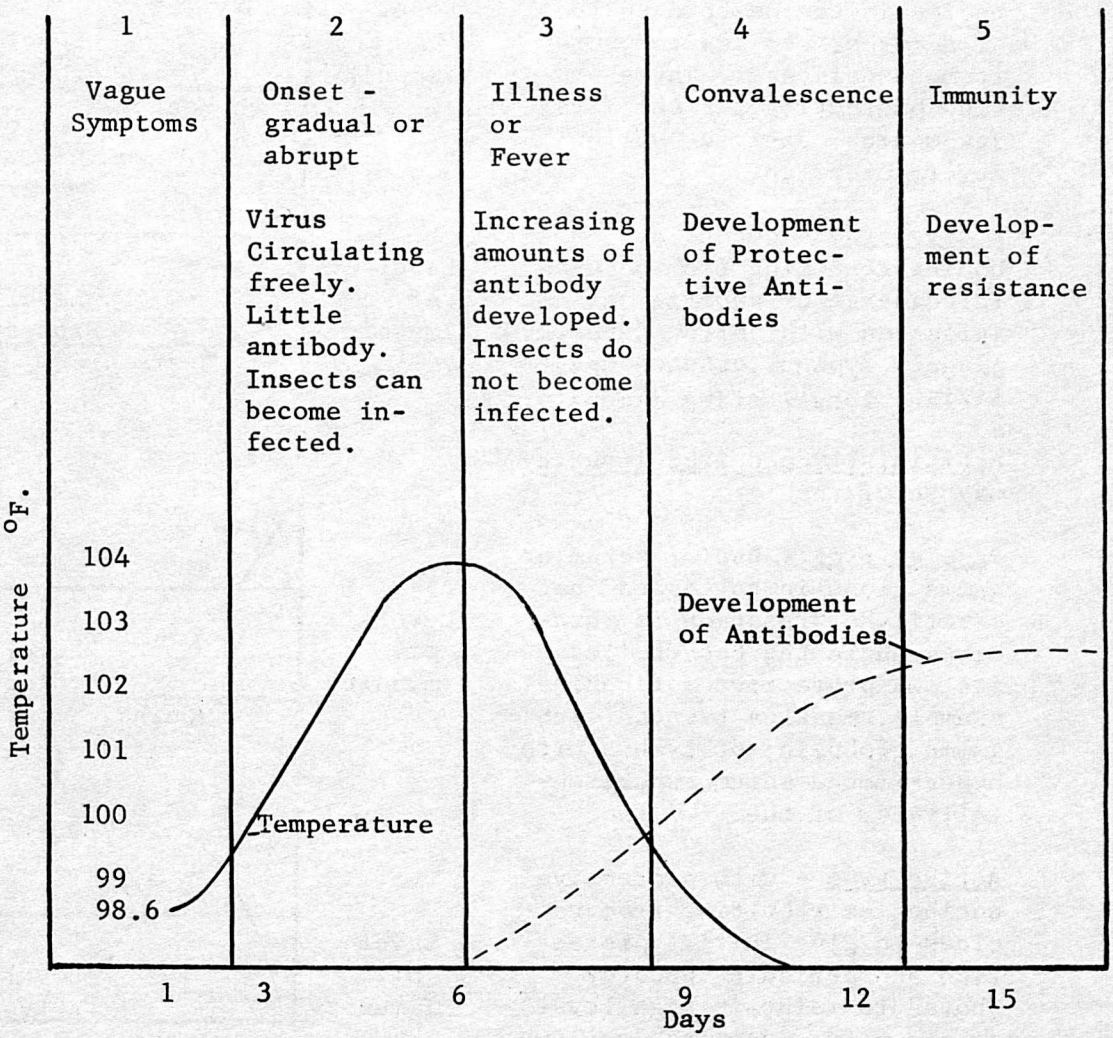


Figure 17 - Sequence of events in typical virus disease.

J. Sequence of Events in Typical Malaria Infection.

In malaria, the parent sexual cells (gametocytes) do not appear in the host during the early stages of the developing disease, but may be present both during clinical attacks and long afterward, particularly during relapses. Therefore, mosquitoes may become infected by ingesting gametocytes for months or years after the first severe attacks of the disease.

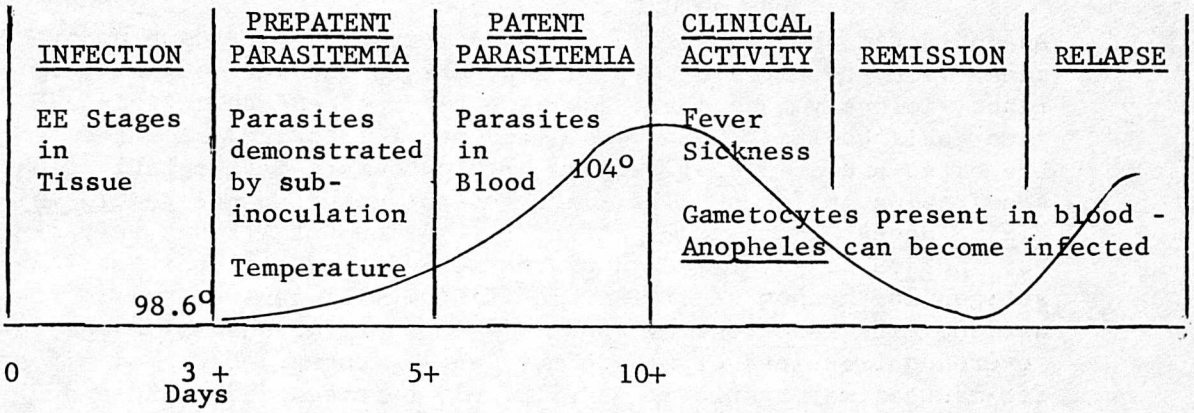


Figure 18. Typical diagram of malaria infection

K. Special Aspects of Immunity

A number of aspects of immunity deserve special consideration in any course devoted to the epidemiology and control of vector-borne diseases.

1. A large proportion of the population in an endemic area may have had a particular disease, recovered, and be immune. Strangers, however, fall easy victim to the disease; examples; sandfly fever in the Mediterranean, malaria in much of the tropics, and scrub typhus in Southwest Pacific.

2. Epidemics tend to "burn themselves out" from diminution of reservoir of susceptibles - as with dengue or yellow fever on islands with limited populations. Those previously exposed are unaffected because of long-lasting immunity due to persisting antibodies: those affected that live will not get the disease during the next epidemic.

3. Vaccines can be produced which have entirely changed the control procedures: killed and/or live avirulent vaccines for:

   a. Yellow fever
   b. Epidemic typhus
   c. Rocky Mountain Spotted Fever
   d. Plague

   There is not yet a suitable vaccine for St. Louis encephalitis or scrub typhus.

4. Laboratory tests utilizing antigen-antibody reactions are used to confirm cases and to determine areas previously infected, often with inapparent, non-clinical cases. These tests include the following:

   a. Weil-Felix test
   b. Complement-Fixation (C-F) test
   c. Haemagglutination tests
   d. Mouse-protection tests

5. Anaphylactic Shock - A significant number of people develop hypersensitivity to certain soluble antigens to the degree that they react violently when small doses of the antigen are introduced into their bodies. Some venoms and other materials excreted by the bites and stings of certain arthropods are particularly good sensitizing antigens. The first contact with the antigen (sensitizing dose) causes no significant reaction but after a refractory period of several days or weeks, reintroduction of the same antigen in the now sensitized individual will cause a severe reaction. The reaction may appear in the form of wheals (hives) or severe contractions of smooth muscles may ensue. Death within a few minutes may result in an extremely hypersensitive individual (anaphylactic shock) unless adrenalin or some powerful antihistamine is administered quickly.

L. Epidemics.

An epidemic or outbreak is the occurrence in a community or region of a group of illnesses of similar nature, clearly in excess of normal expectancy and derived from a common or from a propogated source. Thirty years ago, a dozen cases of malaria in southern United States would not have been considered an epidemic; today, two or more cases would. In the United States today, one case of plague, yellow fever, or epidemic typhus either is considered an epidemic, or as a potential epidemic meeting the requirements in respect to reporting of an epidemic (American Public Health Assoc., 1960).

Epidemics may be Classified as:

pandemics
long term epidemics
short term epidemics
irregular epidemics

Pandemics, world-wide epidemics, of which plague is a classic example.

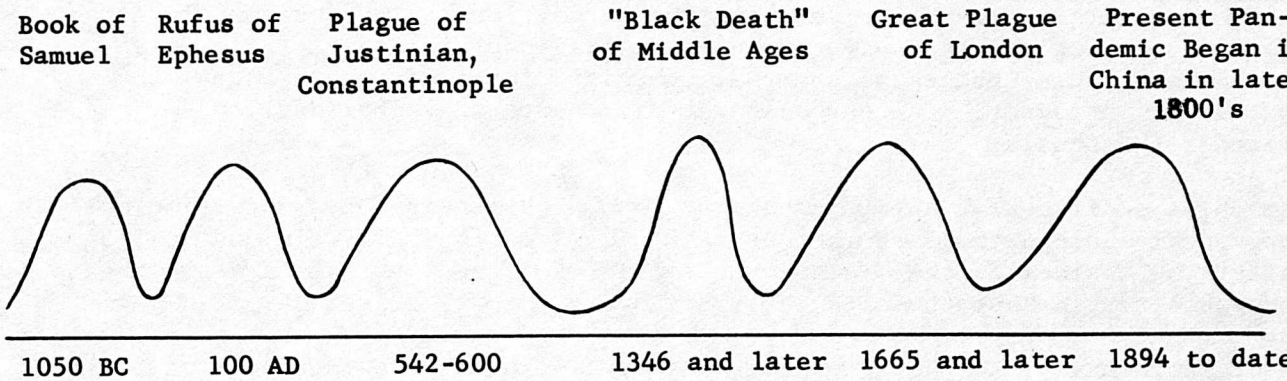


Figure 19. Some recorded pandemics of plague.

Similar long-term epidemic cycles have been recorded on 5, 8, or 20 year cycles for malaria, tularemia, and some other vector-borne diseases--the rises and falls perhaps due to the combination of factors such as immune status of host and reservoir, numbers of vectors, and environmental influences.

Short-term, seasonal, or cyclical epidemics of short amplitude occur. Examples:

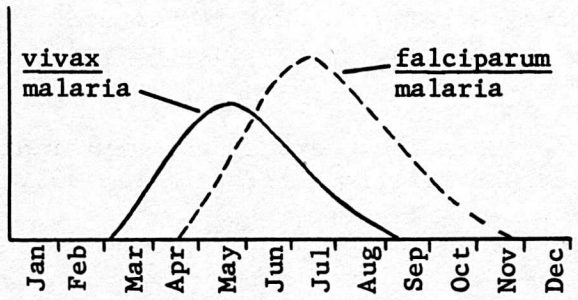


Figure 20. Malaria tends to be a warm season disease in U.S.: vivax often in spring-early summer; while falciparum occurs in summer-early fall, i.e. aestivo-autumnal.

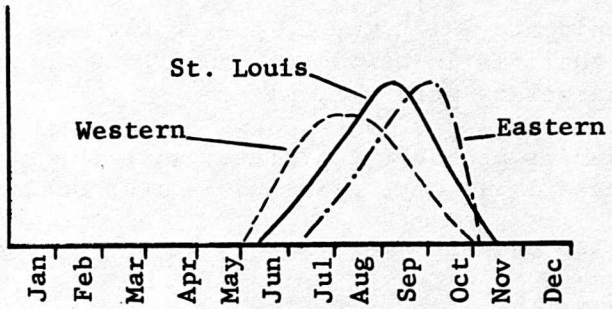


Figure 21. Encephalitis tends to be a summer and early fall disease in U.S.

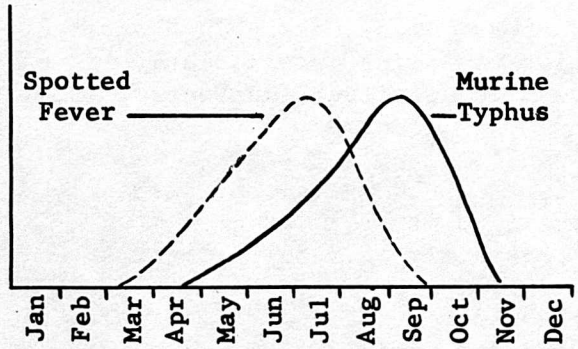


Figure 22. Spotted fever tends to be a spring-summer-disease and murine typhus a summer-early fall disease.

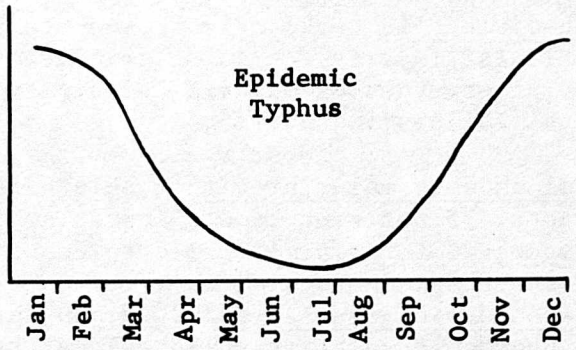


Figure 23. Epidemic typhus tends to be a winter disease.

Irregular epidemics may be due to any factor, or combination of factors, which facilitates transmission above the normal level. The extent of the epidemic varies considerably depending on previous history of the disease in the area, disturbance of communal immunity, introduction afresh of the parasite, introduction afresh of a vector, change in vector density, or weather (MacDonald, 1957).

Examples of irregular epidemics absent from a community for a long time, or previously unreported, are the outbreak of yellow fever in Trinidad in 1954 after the absence of the disease since 1914, and the outbreak of eastern encephalitis in Massachusetts in 1938 (Rivers, et al. 1959).

A dramatic example of an irregular epidemic following the introduction of the parasite into an area is the malaria outbreak originating at Lake Vera, California in 1952-1953. A veteran of the Korean War slept outdoors near Campfire girls' camps while he was having a relapse of malaria. Anopheles mosquitoes which acquired the infection from him later transferred the malarial parasites to at least 35 Campfire girls.

An irregular epidemic which followed the introduction of a vector into an area include the huge outbreak of very severe malaria in Brazil in 1938 attributed primarily to importation of a very efficient African malaria vector, Anopheles gambiae (MacDonald, 1957).

An epidemic which may be due to changes in vector density is that of Eastern encephalitis in New Jersey in 1959 when populations of Aedes sollicitans and Aedes vexans were very high.

Epidemics probably correlated with changes in weather include the huge outbreak of malaria in Ceylon in 1934-35, or Western encephalitis in California in 1952.

Disease may be classified as epidemic, endemic, or sporadic.

Epidemic disease results from a sudden or unusual disturbance in the host-parasite relationship so that more than the average number of clinical cases appear in a community. How much above "the average number" the incidence must be before it is regarded as epidemic disease is a matter of judgment and previous experience. The greater the fear of the disease, as of encephalitis, the smaller the number of cases needed to justify the term "epidemic".

Endemic disease is constantly present to a greater or less degree in a district or particular locality. In malaria eradication campaigns, particularly in the tropics, four types of malaria endemicity have been described (MacDonald, 1957, p. 80) as follows:

Holoendemic malaria, with a spleen rate in the 2-10 age group constantly over 75 per cent, and a low spleen rate in adults;
Hyperendemic malaria, child spleen rate constantly over 50 per cent, adult spleen rate high;
Mesoendemic malaria, child spleen rate 11-50 per cent; and
Hypoendemic malaria, child spleen rate 0-10 per cent.

Sporadic disease -- one to several cases of a disease in an endemic area, but no more than the average expected. Example, a few cases of malaria in an endemic area.

M. Typical Age Patterns of Disease

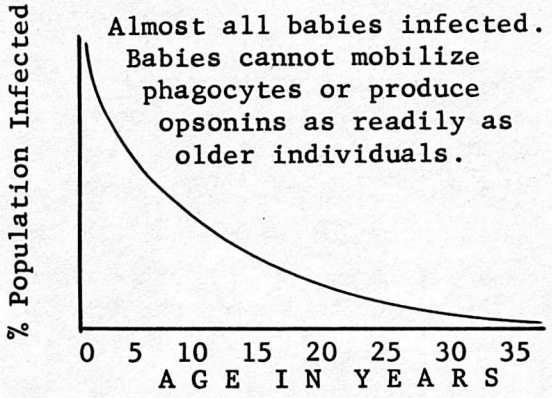


Figure 24. Malaria in an endemic area.

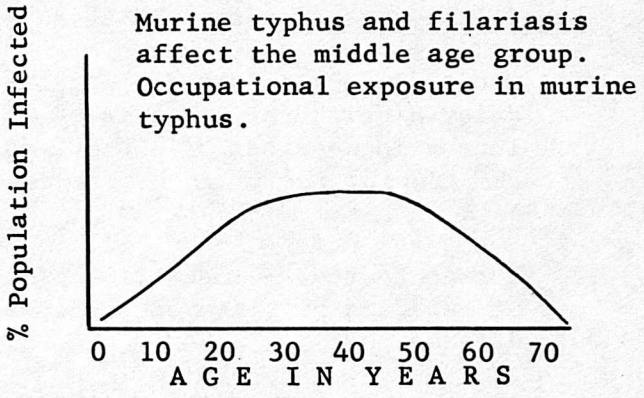


Figure 25. Murine typhus and filariasis.

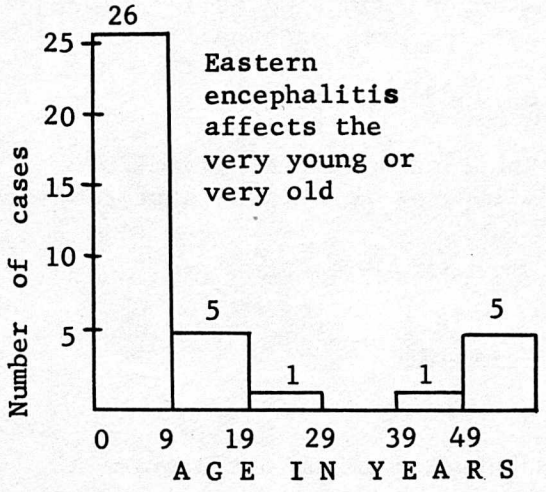


Figure 26. Eastern encephalitis in Massachusetts, 1938. (Feemster, 1938)

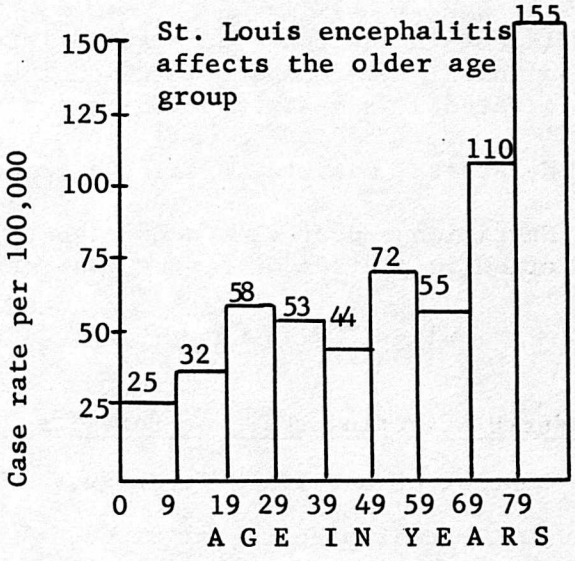


Figure 27. St. Louis encephalitis--St. Petersburg, Florida, 1962. (Unpublished preliminay data)

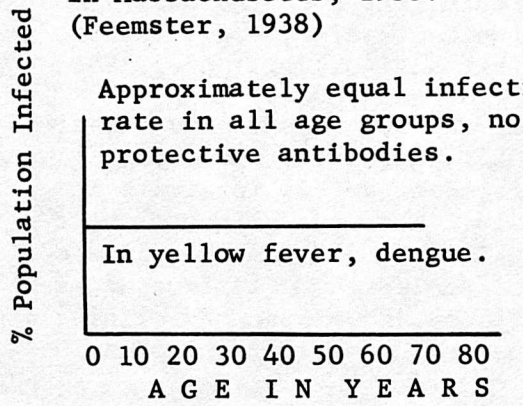


Figure 28. Epidemic of arbovirus disease--no previous exposure.

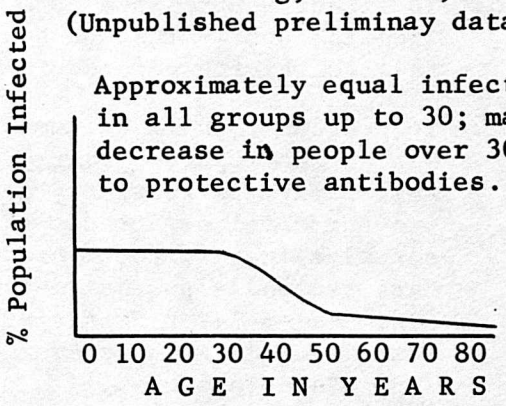


Figure 29. Epidemic of arbovirus 30 years previously.

N. Special Aspects of Arthropod-borne Infections.

1. Short or long incubation periods - i.e., although normally vivax malaria develops in man in 10-14 days, with some strains of vivax incubation periods of 200-300 days occur; some people may live in the tropics for years before developing clinical cases of filariasis or onchocerciasis.

2. Superinfection - imposition of a second infection on a first before it has died out, commonly occurs in malaria, filariasis, and Chagas' disease.

3. Premunition - immunity which depends upon a persistent latent infection as in malaria, filariasis, or some rickettsial infections. This is somewhat like tolerance, with a connotation of immunity to superinfection by the same strain of parasite.

4. Latent infections - persisting infections which give rise to no clinical symptoms and in which the pathogen cannot be easily demonstrated - as malaria or Chagas' disease, perhaps encephalitis.

5. Relapses - malaria, Brill's disease versus epidemic typhus.

6. Nutrition - poor diet conducive to typhus and malaria epidemics, often in periods of famine, war, flooding, or in prisoners or soldiers.

VII. CONTROL OF VECTOR-BORNE DISEASES

A. Measures Affecting the Host-Parasite Relationship.

1. Control of parasites by drugs.

   a. To control clinical disease - as broad spectrum antibiotics to control a variety of vector-borne diseases.

   b. To effect suppressive cure - the elimination of the parasite from the host - through suppressive medication, e.g., use of salt containing chloroquine or other anti-malarial drugs.

   c. To prevent clinical attacks of the disease (suppressive treatment or chemophrophylaxis) - as chloroquine and other new anti-malarials routinely administered at weekly intervals to prevent clinical attacks of malaria. These drugs often inhibit actual illness without preventing infection. Many people who have stopped suppressive treatment on leaving malarious areas (and had no later chance of infection), have soon had clinical attacks of malaria, presumably due to the development of a suppressed infection.

      (1) The usefulness of this method is high. Sometimes it is the only practical method of disease control in hyperendemic areas where vector control is impractical.

(2) Limitations -

(a) Development of resistant parasites - as malarial parasites resistant to pyrimethamine; and

(b) Development of sensitivity of host to antibiotics and chemicals, as to penicillin and atabrine.

2. Immunization - making the host insusceptible to parasites by vaccination as in yellow fever, plague, or rickettsial diseases such as epidemic typhus or spotted fever.

3. Eradication of certain ectoparasites by insecticides - in control of scabies and sucking lice.

4. Disinfection - as laundering of clothing from people infested with lice or scabies; or use of chemicals in buildings inhabited by patients with highly infectious or contagious diseases such as plague or Q fever.

B. Measures Affecting the Host-Parasite-Vector Relationships.

1. Reduction of total numbers of vector by:

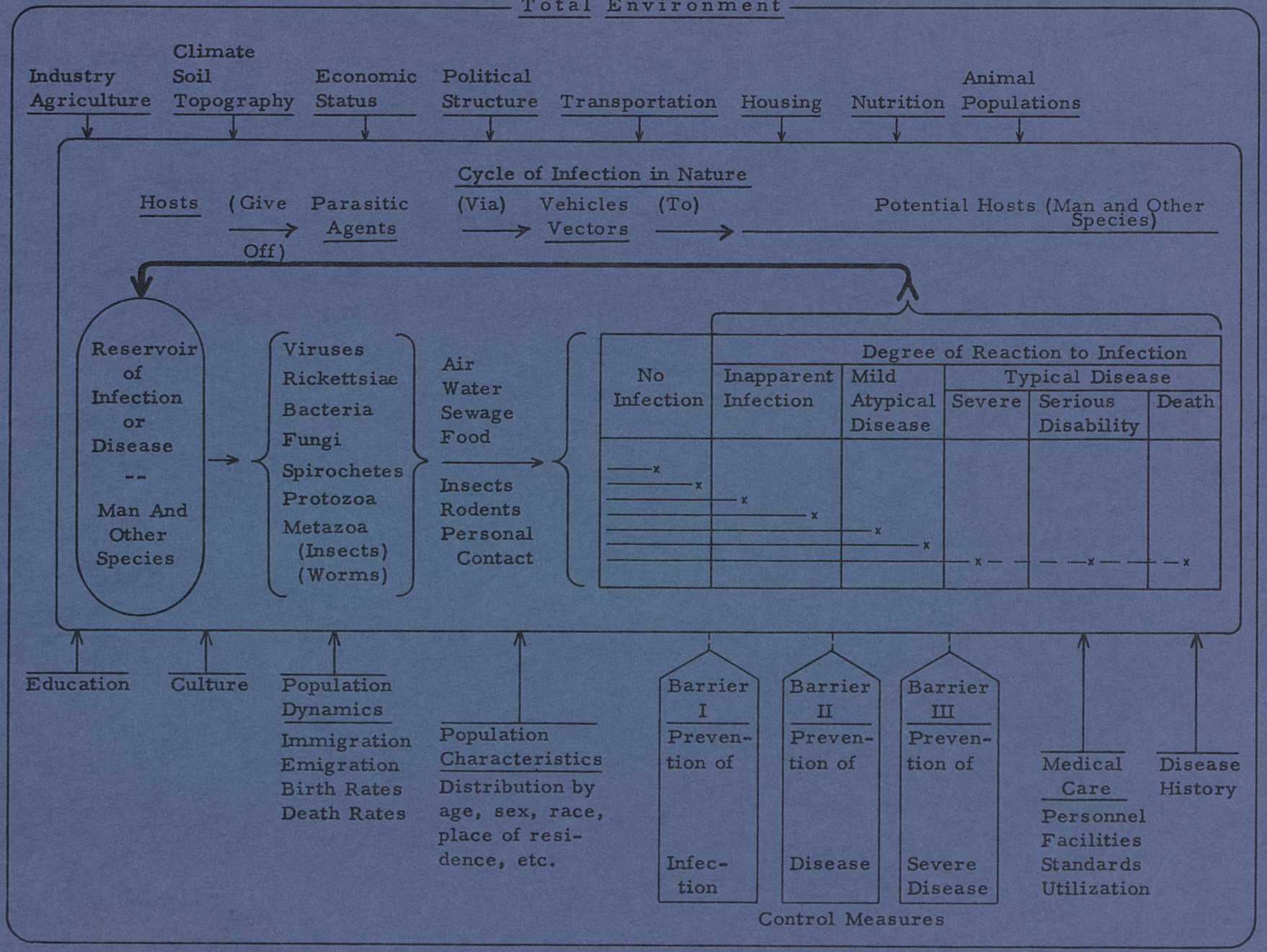
a. Insecticides - as larvicidal or adulticidal programs in malaria, encephalitis, yellow fever, epidemic typhus or plague.

b. Environmental sanitation -- reduction of vector breeding places and harborages, as by drainage to reduce mosquito breeding places; or better storage, collection and disposal of refuse to reduce amount of food and harborage for flies and cockroaches.

2. Prevention of infection in vectors:

a. Physical barriers between infected hosts and vectors - as screening of rooms or use of bed nets to prevent mosquitoes from having access to yellow fever or dengue patients, particularly during the first few days of the diseases when the viruses are circulating in the peripheral blood; and isolation or quarantine of patients with plague or epidemic typhus, or contacts of such cases.

b. Chemical barriers preventing infection of vector - as pyrimethamine which delays development of gametocytes of malaria in man, thus making it difficult for mosquitoes to become infected after feeding on such patients (MacDonald, 1957, p. 155).


Total Environment
Industry
Agriculture
Climate
Soil
Topography
Economic
Status
Political
Structure
Transportation
Housing
Nutrition
Animal
Populations
Cycle of Infection in Nature
Hosts
(Give Off)
Parasitic Agents
(Via)
Vehicles
Vectors
(To)
Potential Hosts (Man and Other Species)
Reservoir of Infection or Disease -- Man And Other Species
Viruses
Rickettsiae
Bacteria
Fungi
Spirochetes
Protozoa
Metazoa
(Insects)
(Worms)
Air
Water
Sewage
Food
Insects
Rodents
Personal Contact
Degree of Reaction to Infection
No Infection
Inapparent Infection
Mild Atypical Disease
Typical Disease
Severe
Serious Disability
Death
Education
Culture
Population Dynamics
Immigration
Emigration
Birth Rates
Death Rates
Population Characteristics
Distribution by age, sex, race, place of residence, etc.
Barrier I
Prevention of
Infection
Barrier II
Prevention of
Disease
Barrier III
Prevention of
Severe Disease
Control Measures
Medical Care
Personnel
Facilities
Standards
Utilization
Disease History