Chapter 2
Dynamics of Arthropod-Borne Diseases

2.1 Mechanical vs Biological Transmission of Pathogens

Transmission of etiologic agents by arthropods is a complex phenomenon, and generalizations are difficult to make. Just because an arthropod feeds on a diseased host does not ensure that it can become infected, nor does it ensure (even if disease agents are ingested) that ingested pathogens can survive and develop. There is considerable misunderstanding about this. When bitten by a tick, people think of Lyme disease (or something similar), often insisting that their physician prescribe an antibiotic prophylactically. Little do they realize that there are many tick species and not all are capable of disease transmission (1). Further, they fail to realize that not every tick in nature (even within a vector species) is infected. Depending on the disease and area of the country, the presence of an infected tick can be like a needle in a haystack.

Arthropods capable of transmitting disease organisms to vertebrate hosts are called vectors (2). For example, mosquitoes in the genus *Anopheles* are vectors of malaria organisms. Interestingly, no other mosquitoes are able to acquire and transmit the parasites. Other mosquitoes certainly feed on diseased humans but fail to become infected. Myriad factors affect the ability of arthropods to acquire, maintain, and ultimately, transmit pathogens. An understanding of arthropod–pathogen interactions is crucial to preventing and/or managing vector-borne diseases. First, a distinction must be made between mechanical and biological transmission and their various modes (Table 2.1).

2.1.1 Mechanical Transmission

Mechanical transmission of disease agents occurs when arthropods physically carry pathogens from one place or host to another host – often via body parts. For example, flies and cockroaches have numerous hairs, spines, and setae on their bodies that collect contaminants as the insects feed on dead animals or excrement (Fig. 2.1). When they subsequently walk on food or food preparation surfaces, mechanical

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Table 2.1 Modes of pathogen/parasite transmission[a]

Mode of transmission	Example
Mechanical transmission	Pathogens on cockroach bodyparts
Biological transmission	
Transmission by eating vector	Fleas: dog tapeworm
Transmission during/after bloodsucking	
Proliferation in gut and transmission in feces	Kissing bugs: Chagas' disease
Proliferation in gut and transmission by bite	Fleas: plague
Penetration of gut and transmission by bite	Mosquitoes: malaria

[a]Adapted from Lane and Crosskey (6)

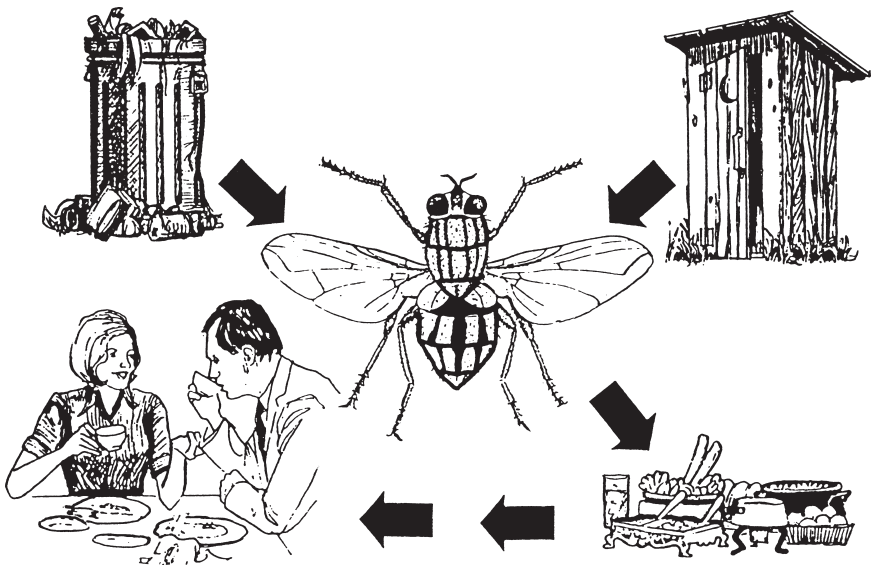

Fig. 2.1 Example of mechanical transmission of disease agents (CDC figure)

transmission occurs (3–5). Mechanical transmission may also occur if a blood-feeding arthropod has its feeding event disrupted. For example, if a mosquito feeds briefly on a viremic bird and is interrupted, a subsequent immediate feeding on a second bird could result in virus transmission. This would be similar to an accidental needle stick. The main point about mechanical transmission is that the pathogen undergoes no development (cyclical changes in form and so forth) and no significant multiplication. It is just there for the ride.

2.1.2 Biological Transmission

In biological transmission, there is either multiplication or development of the pathogen in the arthropod, or both (6, 7). Table 2.2 provides a detailed list of many

Table 2.2 Arthropod-borne or caused human illnesses

Disease	Pathogen	Type	Primary vector	Common name
Yellow fever	Flavivirus	Virus	*Aedes aegypti*, *A. africanus*	Yellow fever mosquito
Dengue fever	Flavivirus	Virus	*Aedes aegypti*	Yellow fever mosquito
Malaria	*Plasmodium* spp.	Protozoan	*Anopheles* spp.	Mosquito
Filariasis	*Wucheria bancrofti*	Nematode	*Anopheles* and *Culex* spp.	Mosquito
Rift Valley fever	Phlebovirus	Virus	*Culex* spp.	Mosquito
West Nile Virus	Flavivirus	Virus	*Culex pipiens*, *C. quinquefasciatus*	Northern/southern house mosquito
St. Louis encephalitis	Flavivirus	Virus	*Culex pipiens*, *C. quinquefasciatus*	Northern/southern house mosquito
Eastern equine encephalitis	Flavivirus	Virus	*Culiseta melanura*	Mosquito
LaCrosse encephalitis	Bunyavirus	Virus	*Ochlerotatus triseriatus*	Tree-hole mosquito
African sleeping sickness	*Trypanosoma brucei gambiense*, *T. brucei rhodiense*	Protozoan	*Glossina* spp.	Tsetse fly
Epidemic relapsing fever	*Borrelia recurrentis*	Spirochete	*Pediculus humanus*	Body louse
Epidemic typhus	*Rickettsia prowazekii*	Rickettsia	*Pediculus humanus*	Body louse
Trench fever	*Bartonella quintana*	Bacterium	*Pediculus humanus*	Body louse
Leishmaniasis	*Leishmania donovani*, *L. braziliensis*	Protozoan	*Phlebotomus*, *Lutzomyia* spp.	Sand fly
Sand fly fever	Phlebovirus	Virus	*Phlebotomus*	Sand fly
Onchocerciasis "river blindness"	*Onchocerca volvulus*	Nematode	*Simulium* spp.	Black fly
Endemic (murine) typhus	*Rickettsia typhi*	Rickettsia	*Xenopsylla cheopis*	Rat flea
Plague	*Yersinia pestis*	Bacterium	*Xenopsylla cheopis*	Rat flea
Tularemia	*Francisella tularensis*	Bacterium	*Chrysops discalis*, *Dermacentor variabilis*, *D. andersoni*	Deer fly, Tick
Cutaneous anthrax	*Anthracis bacillus*	Bacterium	*Chrysops* spp.	Deer fly
Loa loa	*Loa loa*	Nematode	*Chrysops silacea*, *C. dimidiata*	Deer fly, mango fly
Chagas disease	*Trypanosoma cruzi*	Protozoan	*Triatoma* spp.	Kissing bug
Tick-borne relapsing fever	*Borrelia* spp.	Spirochete	*Ornithodoros turicata*, *O. hermsii*, *O. parkeri*	Soft tick
Babesiosis	*Babesia microti*	Protozoa	*Ixodes scapularis*	Black-legged tick
Colorado tick fever	Reovirus	Virus	*Dermacentor andersoni*	Rocky Mountain wood tick
Ehrlichiosis – HME, HGA	*Ehrlichia chaffeensis*, *E. ewingii*, *Anaplasma phagocytophilum*	Bacterium	*Amblyoma americanum*, *Ixodes scapularis*, *Dermacentor variabilis*	Lone star tick, black-legged tick, American dog tick

(continued)

Table 2.2 (continued)

Disease	Pathogen		Primary vector	Common name
Lyme disease	*Borrelia burgdorferi*	Spirochete	*Ixodes scapularis, I. pacificus*	Black-legged tick
Q fever	*Coxiella burnettii*	Rickettsia	Many tick species	Hard tick
Rocky Mountain-spotted fever	*Rickettsia rickettsi*	Rickettsia	*Dermacentor andersoni*, *D. variabilis*, *Amblyoma cajennense*	Rocky Mountain wood tick, American dog tick, Cayenne tick
Tick-borne encephalitis	Togavirus	Virus	*Ixodes* spp.	Hard tick
Rickettsial pox	*Rickettsia akari*	Rickettsia	*Liponyssoides sanguineus*	Mite
Scabies	–	–	*Sarcoptes scabiei*	Mite
Scrub typhus	*Orientia tsutsu gamushi*	Rickettsia	*Leptotrombidium* spp.	Mite

of these vector-borne pathogens. Biological transmission may be classified into three types. In *cyclodevelopmental transmission*, the pathogen must undergo a cycle of development within the arthropod vector, but no multiplication. For example, the filarial worm causing Bancroftian filariasis, when first ingested by mosquitoes, is not infective to a vertebrate host – it must undergo a period of development. *Propagative transmission* means the pathogen must multiply before transmission can occur. There is no cyclical change or development of the organism – plague bacteria in fleas, for example. Finally, in *cyclopropagative transmission*, the pathogen must undergo both cyclical changes and multiplication. The classical example of this is malaria plasmodia in *Anopheles* mosquitoes.

Biological transmission reflects an evolutionary adaptation of the parasite into a cyclic event between vertebrate host and arthropod vector. This involves several factors, including the arthropod feeding on the right host, feeding in such a way (or time) that the parasites, circulating in the peripheral blood of the host animal, are ingested, and a mechanism for getting into a new host – often by penetrating the gut wall of the arthropod and subsequently migrating to a site for reinjection. All of this becomes a fine-tuned system operating efficiently for countless generations.

Take plague as an example of the complex interplay of factors affecting disease transmission (2). *Yersinia pestis*, the causative agent, is essentially a disease of rodents that occasionally spills over into the human population (Fig. 2.2). The enzootic cycle (established, ongoing among animals) is primarily mechanical, with the rodent hosts being relatively resistant. In the epizootic cycle (occasional outbreaks or epidemics), susceptible rodent populations become infected, resulting in mass die-offs. Fleas on epizootic hosts become heavily infected with bacilli and regurgitate into feeding wounds. There may also be other modes of transmission during epizootics, such as cats eating infected rodents, becoming pneumonic, and

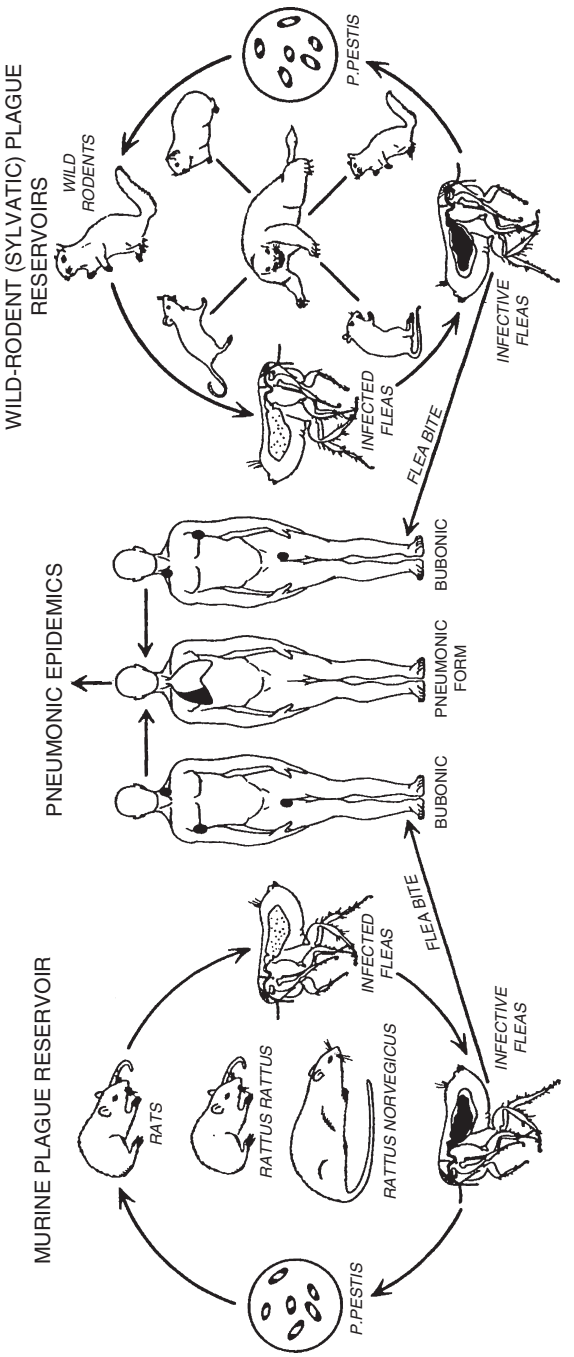

Fig. 2.2 Plague life cycle (CDC figure)

directly infecting humans by coughing. Obviously, the worst-case transmission scenario is development of primary pneumonic plague in humans (transmission by coughing), resulting in tremendous case numbers.

Since vector-borne diseases are dynamic and quite complicated, basic research into arthropod vectorial capacity is of great importance. Here basic research tremendously aids the medical community. By identifying animal hosts and which arthropod species are "competent" vectors (*see* Vector Competence) and targeting control measures toward those species, disease transmission can be interrupted, leading to abatement of the epidemic. Interruption of the transmission cycle is especially important for viral diseases (mosquito-borne encephalitis, for example), which have no specific treatments. I personally have been involved in eastern equine encephalitis outbreaks where the only hope of stopping the appearance of new cases was to identify the vector species in the area and direct specific mosquito control measures toward them.

2.2 Vector Competence

Vector competence refers to the ability of arthropods to acquire, maintain, and transmit microbial agents (1). As mentioned, not all arthropods are vectors of disease agents. Even blood-feeding arthropods are not always vectors. Insects, ticks, or mites may "pick up" a pathogen with their blood meal, but the pathogen must overcome many obstacles before being transmitted to another host. In many cases, the gut wall must be bypassed, the pathogen must survive (and even develop) in arthropod tissues, such as hemolymph, muscles, or the reproductive system, and finally, must penetrate the salivary glands for injection into a new host. Note: in some cases, transmission occurs without the pathogen making its way into the salivary glands (*see* Table 2.1). In the meantime, the arthropod itself must live long enough for all of this multiplication/movement/development to take place. An ideal vector then would be one providing a suitable internal environment for the pathogen, be long-lived, have a host feeding pattern matching the host range of the pathogen, feed often and for extended periods, ingest large amounts of blood in each life stage, and disperse readily (2). Of course, no arthropod possesses all these characteristics, but some have varying degrees of them. In a specific region or season, there are primary vectors, which are the main arthropods involved in the transmission cycle of a given disease, and secondary vectors, which play a supplementary role in transmission, but would be unable to maintain the disease in the absence of primary vectors (7).

Both intrinsic and extrinsic factors affect vector competence. Intrinsic factors include internal physiological factors and innate behavioral traits governing infection of a vector and its ability to transmit an agent – things like duration of feeding, host preferences, whether or not there is transovarial transmission, and so forth. Extrinsic factors include number of host animals, their activity patterns, climatic conditions, genetic variation in the infectivity of the pathogen, and so on.

Competition between microorganisms inside a vector may also affect vector competence. This has often been referred to as the "interference phenomenon" (1, 7, 8). A good example occurs in ticks. Burgdorfer et al. (9) reported that the tick *Dermacentor andersoni* from the east side of the Bitterroot Valley in western Montana contained a nonpathogenic spotted fever group (SFG) rickettsia, which they named the East Side agent. East Side agent was ultimately described as a new species, *Rickettsia peacocki* (10). This rickettsia, closely related to the causative agent of Rocky Mountain spotted fever (RMSF), *Rickettsia rickettsii*, is rarely present in tick blood (hemolymph), and is readily missed by the standard tick testing method – the hemolymph test. The rickettsiae are confined primarily to portions of the ticks midgut and, most importantly, the ovaries. *R. peacockii* is maintained in the tick population through transovarial transmission and infected ticks are refractory to ovarian infection with *R. rickettsii*. However, these ticks are susceptible to experimental infection with *R. rickettsii* and may transmit the infection horizontally (stage to stage). Thus, ticks infected with *R. peacockii* and infected experimentally with *R. rickettsii* are unable to transmit *R. rickettsii* to their progeny. In effect, infection of the tick, *D. andersoni*, with *R. peacocki* blocks the subsequent ability of the ticks to transmit *R. rickettsii* transovarially. Other experiments have also demonstrated that tick ovarial infection with one rickettsial species precludes secondary infection with other rickettsiae (11). This "interference phenomenon" provides an explanation for the curious long-standing disease situation in the Bitterroot Valley. Most cases of RMSF have occurred on the west side of the valley where *D. andersoni* is abundant; on the east side, *D. andersoni* is also abundant and is reported to bite local residents, yet few locally acquired cases occur there. With *R. peacockii* in the area, *R. rickettsii* cannot be maintained transovarially – it can only be maintained transstadially. Thus, long-term maintenance cannot be sustained. Burgdorfer et al. (9) say that transovarial interference of *R. rickettsii* in *D. andersoni* ticks may also be mediated by other nonpathogenic SFG rickettsia, such as *Rickettsia montana* and *Rickettsia rhipicephali*. Most ticks in nature infected with rickettsial organisms harbor nonpathogenic species. Thus, transovarial interference may have epidemiologic significance – it may explain why ticks collected from various geographic regions are not infected with two or more species of SFG rickettsiae (8).

2.2.1 Incrimination of Vectors: A Complicated Issue

To illustrate the difficulty in incriminating vectors of a specific disease, the following discussion on malaria in the western United States is provided as an example. Much of this discussion is from McHugh (12), Porter and Collins (13), and Jensen et al. (14).

Concerning malaria in the western United States, we must first consider what criteria the mosquito must fulfill to be proven to be the primary, or at least an important, vector of the human malaria parasites:

It must be a competent vector of the parasites.
Its geographic distribution must match the transmission pattern.
It must be abundant.
It must be anthropophilic.
It must be long lived.
Field collections should demonstrate a measurable proportion of the mosquito.
Population infected (usually about 1%).

Anopheles freeborni (sensu latu) is certainly well known through laboratory transmission studies as a competent vector of a number of *Plasmodium* species including *Plasmodium falciparum* from Panama and Zaire, *Plasmodium vivax* from Vietnam, and *Plasmodium malariae* from Uganda to name a few. Does this mean *An. freeborni* is a vector of those malarial parasites in those areas? Of course not, the mosquito does not occur there. That is, it does not fulfill the second criterion.

What about *An. freeborni* in the western United States? Because this species is a competent vector, is widely distributed, and is often abundant, it is frequently cited as the most likely suspect vector. However, it turns out that *An. freeborni* is a catholic feeder and not particularly anthropophilic. Several studies in California found only 1–3% of several thousand field-caught females had fed on humans. Longevity studies of this species indicated a daily survivorship of about 0.72–0.74 for female *An. freeborni*. Based on this estimate, an initial infected bloodmeal on day 3 post emergence, and an extrinsic incubation period of about 12 d, the probability of a female living long enough to be infective would be on the order of 0.0072 or less.

What about the last criterion – finding infected mosquitoes in field collections? There have been only a very limited number of isolations of any human malaria parasite from any species of *Anopheles* collected in the western United States. Dr. Bill Reeves at UC Berkeley gave an anecdotal report of oocysts on the gut of *An. freeborni* collected in California during the mid-1940s, and he also reported infected *An. freeborni* from New Mexico at that same time. However, as will be discussed below, changes in nomenclature and our understanding of mosquito systematics, not to mention the failure to provide a specific determination of the parasites involved, make it impossible to ascribe much significance to these reports.

Considering these data, particularly host selection (i.e., low rate of human feedings) and survivorship (i.e., low), *An. freeborni* may be overrated as a potential vector. Perhaps another species may be responsible – such as *Anopheles punctipennis*. If one visits a number of locations where autochthonus cases of malaria have occurred in California, he or she will be struck by the fact that most cases were acquired in riparian settings. This habitat is more typical of *An. punctipennis*. It turns out that Gray back in the 1950s published several insightful reviews drawing the same conclusion (15, 16). Gray reported that *An. punctipennis* was actually more common than *An. freeborni* at the site of the famous Lake Vera outbreak of malaria in the early 1950s and was the probable vector. Recent evidence supports his claim (14).

There remain two problems in understanding the confusing epidemiology of malaria in California, and, perhaps, the rest of the United States. Anthropogenic

changes in the local ecology – damming and channeling rivers, introduction of the rice culture, destruction of riparian habitat, and so forth – have dramatically altered the landscape over the past 100 years. Thus, the mosquito species responsible for transmission may have changed over time. Second, the eastern U.S. malaria vector, *Anopheles quadrimaculatus,* is actually a complex of several sibling species. Researchers at the USDA-ARS lab in Gainesville, FL, helped determine that *An. quadrimaculatus* (a vector in the eastern United States) is a complex of at least five identical-looking species. This may be the case with *An. freeborni* in the West. The late Ralph Barr and coworkers determined that what appeared to be *An. freeborni* collected in several sites of malarial transmission in southern California were, in fact, a new species that they named in honor of W. B. herms (*Anopheles hermsi*). Therefore, it may be that earlier workers who suspected *An. freeborni* were correct to the extent that their technology (i.e., morphologic identifications) was capable of identifying the insects involved. Without access to mosquitoes collected in the past, especially those from early studies in which mosquitoes were still lumped as *Anopheles maculipennis*, it will be very difficult to determine what species were actually being studied. (As an aside, it would be very interesting to study extant laboratory colonies of "*An. freeborni*" and determine exactly which species are really being maintained and studied.)

We can draw two conclusions. First, the epidemiology/ecology of malaria is dynamic and may have changed over time, but the most likely vectors in the western United States at the present time are *An. hermsi, An. freeborni*, or *An. punctipennis*, with other species involved if conditions are appropriate. Second, to incriminate a specific vector, we must carefully consider the ecology of malarious foci and weigh all the factors that make an arthropod a good vector, not just focusing in on one or two.

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