

Lecture-5

Characteristics of environmentally transmitted pathogens**by Arthropods :**

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Arthropods are largest of animal phyla. Many species of arthropod are medical and economic importance. They have also important role in transmission of pathogenic microorganisms because several arthropods serve either as intermediate host for parasite or as vectors for pathogenic microorganisms. It is later aspect (transmission) that concerns us in this section.

Two classes of arthropods make major contribution to disease transmission; six-legs such as insects and eight-legs such as tick and mite. Arthropods may serve either mechanical or biological vectors. Mechanical transmission refers to situation in which insect physically transports a pathogen from contaminated materials (such as food, water) to other objects. Cockroaches and flies are good examples. Biological transmission, a portion of life cycle of pathogen is carried out in the vector such as malaria in mosquito.

Insects carry pathogens passively on their mouth parts, on their bodies, or within their intestines. Transfer onto food or onto the host occurs directly because of the insect feeding, regurgitating, or defecating.

Example for Arthropod-borne pathogens:

House-fly : *Salmonella*, *Entameoba hitolytica*.

Black-fly: *Dirofilaria*, *Leucocytozoon*, Vesicular stomatitis virus.

Kissing bug: Chagas disease.

Mosquitos: Malaria, *Wuchereria*, yellow fever virus, encephalitis viruses.

Tse-tse fly(glossina): *Trypanosoma*.

Fleas: plague, *Rick.typhi*, Myxomaviruses, *Dipylidium caninum*.

Tick: *Rickettsia*, *Borrelia*, *Babesia*, Colorado tick fever virus.

Lice : *Borrelia*.

Rickettsia:**Important properties:**

1. Rickettsias are pleomorphic coccobacilli , they appearing either as small rods in pairs or may be seen as single cocci .
2. Rickettsia stained poorly with Gram stain. If stained, they are gram negative bacteria. But they are visible under light microscope when stained with Giemsa.

3. Rickettsias are obligate intracellular bacteria, because they are unable to produce sufficient energy to replicate extracellularly, they require coenzyme A, NAD, and energy from host cell. Therefore, it must be grown in cell culture or embryonated eggs.
4. Rickettsia does not multiply outside the cell, therefore it is unable to grow in cell free media.
5. Most rickettsia survives for short times outside the host or vectors, because they are quickly destroyed by drying, heating, or chemicals, except *Coxiella* resistant to drying and heat (60C/30min) due to formation of endospore-like structure.

Pathogenesis and clinical findings:

- **Pathogenesis** : Rickettsia have affinity for vascular endothelial cells located throughout the circulatory system. They enter the host cell by endocytosis into vacuole, a process similar to phagocytosis. By phospholipase A, the bacteria destroy the phagosome and begin to multiply in cytoplasm of the host endothelial cell (except causative agents of spotted fever, multiply in nucleus). The host cell eventually lyses and releases the rickettsia, spread via blood stream or lymphatics, and they are capable of infecting other cells. Rickettsia (except *Coxiella burnetii* multiplies in respiratory tract), when they multiply in endothelium cells lining of small blood vessels, they lead to cause **vasculitis**(vascular lesion) and damage to blood vessels. The cells become swollen and necrotic. Damage to vessels of skin results in characteristic rash and in edema and hemorrhage. Petechial rash develops in response to vascular damage.
- **Diseases** caused by rickettsia :
 - a. **Rocky mountain spotted fever(RMSF)** is derived from the region in which the disease was first found. RMSF is caused by *R.rickettsii*, *R.australis*, *R.conorii*, *R.sibirica*. The bacteria invade vascular cells and become widely disseminated. After 2-6 days from tick bite, the typical clinical feature is rash that appears on hands(palms), feet(soles) and spread rapidly on trunk. 10% of cases is spotless. Non-specific symptoms e.g Fever, severe headache, myalgia. Central nervous system changes such as mental confusion (delirium) and coma. DIC, thrombosis and blockage of small blood vessels may occur in severe cases. Eschar lesion (thick crust) is exhibited at site of bite in all etiologic agents of spotted fever, except *R.rickettsii*.

Rickettsialpox is spotted disease which is caused by *R.akari*. The disease is transmitted from animal to animal and to human by mite. The reservoir of this organism is mouse. The disease is characterized by biphasic syndrome; initial phase at site of

inoculation ,a papulovesicular lesion develops into black eschar within 5 days. Second phase ,generalized papulovesicular rash appears throughout the body. Each lesion develops into black eschar.

- b. **Typhus fever** : there are in several forms ; epidemic typhus caused by *R.prowazekii*. Endemic typhus (murine typhus) is caused by *R.typhi* . Scrub typhus is caused by *Orientia tsutsugamushi*(formerly: *R.tsutsugamushi*, tsutsuga means dangerous , mushi means mite) . Typhus fever appears influenza-like symptoms after 1-2weeks of arthropod bite. A rash begins on trunk and spread over the entire body . Delirium and coma may occur. Necrotic eschar at site of mite bite may occur in 50-80% of scrub cases. Recurrent form of epidemic is called Brill-Zinsser disease.
- c. **Q-fever:** Q stands for query because the cause of the fever was unknown(question mark) for many years. The disease was first described in Australia in 1937. Q-fever is caused by *C.burnetii*. The bacteria contaminate the soil (by animal's feces and urine) and enter a sporogenic cycle. Therefore it can survive for long period outside the host cell. It is transmitted to human by inhalation of aerosols of animals materials (urine ,feces , milk) or dust contaminated with bacteria .Unlike the other rickettsial disease, the main organ involved is the lungs and exhibit influenza-like symptoms; fever, headache and cough, with pneumonia(atypical pneumonia).
- d. **Ehrlichiosis;** *Ehrlichia* grow in cytoplasmic vacuole of leucocytes and it cause disease. Two forms of ehrlichiosis; human monocytic ehrlichiosis (HME) caused by *E. chaffeensis* , which characterized by acute fever ,myalgia, leucocytopenia and thrombocytopenia. Human granulocytic anaplasmosis (HGA) caused by *Anaplasma phagocytophilum*, the disease is similar to HME but more severe.

Transmission and epidemiology:

2. All rickettsial diseases are zoonoses (i.e,they have animal reservoir such as cattle , sheep, dogs, rodents), except epidemic typhus which occurs only in human because causative organism, *R.prowazekii* is transmitted from person to person by human body louse.
3. Route of infection : Most rickettsia are maintained in nature in certain arthropods and they are transmitted to human after prolonged exposure to bite of arthropod (ticks, mites , lice and fleas , which serves as vectors and reservoir of the organism) , except *Coxiella burnetii* which transmitted by aerosol. *R.rickettsii*

,*R.australis*, *R.conorii*, *R.sibirica* are transmitted to human by tick .
R.akari and *R.tsutsugamushi* are transmitted by larvae of mite(chigger) . *R.prowazekii* is transmitted from person to person by human louse bite(*Pediculus*) when the lice excrete the organism in its feces and introduce the pathogen through bite wound of lice into human body. *R.typhi* , it is transmitted by rat flea. *E. chaffeensis* is transmitted by lone star tick, whereas *Anaplasma phagocytophilum* is transmitted by deer and dog tick.

4. Certain animals serve as mammalian reservoirs; the animal reservoirs for *R.rickettsii* are dogs and rodents, for *R.akari* is mice, for *R.typhi* and *R.tsutsugamushi* are rodents, for *R.prowazeki* is human, and for *C.burnetii* are cattle ,sheep and goats.
5. Spotted fever commonly occurs in South and North America, Mediterranean countries, Africa, Australia and in other. Most cases (60%) of spotted fever occur in children during Spring and early Summer(during warm months) when the ticks are active. RMSF is potential lethal, the fatality rate can approach 20-30% if untreated. In RMSF ,no person to person transmission, except *R.rickettsii*. Typhus disease is worldwide (especially in South Asia, South America , Africa) in area of high rat infestation, also mite and lice. The disease is associated with wars and poverty. The Q-fever occurs worldwide, chiefly in individuals whose occupations expose them to livestock animals such as shepherds, farm workers and abattoir employees .

Control:

a. Prophylaxis :

1. Control on vectors by using insect repellent or insecticide.
2. Reducing exposure to arthropod by wearing protective clothing .
3. Elimination of rodents from households and surroundings.
4. Vaccine effective is available for Q-fever and typhus fever, not for RMSF.

- b. Antibiotic treatment:** drug of choice for all rickettsial diseases is tetracycline(Doxycycline). Chloramphenicol can be used as second choice.

Spirochetes:

1. They are elongated, flexible and thin-wall (versus other bacteria which have rigid and thick wall), spiral rods (coiled), and gram negative.
2. The spirochetes replicates by transverse binary fission, and at time , the cells may remain joined to each other(elongated).
3. They contain varying number of fine fibrils between cell wall and cytoplasmic membrane. The spiral shape and serpentine motility (undulation) depends on the integrity of these filaments.
4. Treponema and leptospira are so thin that they are seen only by dark field microscope or immunofluorescence. Borrelia are large can be seen in light microscope.
5. Culturing these organisms is very difficult. Some species can not be cultured on ordinary media .
6. They can be aerobic(such as leptospira), anaerobic or facultative anaerobic(eg; Treponema and Borrelia).

Borrelia:

Two species are important *B.recurrentis* and *B.burgdorferi*.

(1) *B.recurrentis*:

1. *B.recurrentis* is a large, loosely, irregular spiral .
2. The organisms are highly flexible and motile by rotation and twisting. They contain varying number of fine fibrils between cell wall and cytoplasmic membrane. The spiral shape and serpentine motility (undulation) depends on the integrity of these filaments.
3. *B.recurrentis* can survive for several months at 4C in culture media or in blood.
4. The borreliae are genetically variable. The antigenic composition of this organism can undergo variation during infection course. The instability of antigenic structure has made classification of borreliae difficult.

Transmission and epidemiology :

B.recurrentis can be transmitted by arthropods:

a. Lice: *B.recurrentis* is transmitted from person to person by human body louse (*Pediculus*). Humans are only host. Louse-borne disease can be epidemic. The crowding living conditions, malnutrition, and cold climate can be predisposing factors.

b.Tick : *B.recurrentis* transmitted from animal to human (zoonotic)by soft tick(*Ornithodoros*). The bacteria are passed transovarially in ticks(from tick to tick) . They survive long period of time in these arthropods, a phenomenon that plays an important role in maintaining the organism in nature.

Endemic areas usually have large population of rats. Rodents are main reservoir, which serves as source of infection. Tick-borne disease is not epidemic.

Human disease (relapsing fever) is acquired either by bite or crushing of lice or tick. Relapsing fever is occurring worldwide. The mortality rate is low in endemic, but in epidemic, it may reach 30%.

Pathogenicity:

B.recurrentis and other species is etiological agent of **relapsing fever** in human after Borrelia has been transmitted via blood. The name of disease is derives from the fact that infection can be repeated 3-10 time due to antigenic variation (its ability to change its surface protein antigens).

- a. **Onset of illness** is sudden, with chills and a sharp rise in body temperature (fever) after exposure to infected arthropod , 3-10 days incubation period. Many borreliae are present in blood at this stage, and the fever persists for 3-5 days.
- b. **Second attack** can occur in 4-10 days, and chills, fever , and severe headache, malaise are typical symptoms. **Successive recurrences** follow the same pattern.
- c. **Tissues affected:** large numbers of this organisms can be found in many organs , in spleen and liver of person who have died of relapsing fever. Hemorrhagic lesions typically are found in gastrointestinal tract and kidney. Borreliae occasionally are found in CSF and brain of patients with meningitis.

Control:

- a. Prophylaxis:
 1. Avoidance of arthropod vectors by use of insecticide.
 2. No effective vaccine is available due to variation occur in antigenic structure.
- b. Antibiotic: The variability in disease makes it difficult to evaluate the efficacy of antibiotic. Tetracycline ,penicillin, erythromycin may be effective.

(2) *B.burgdorferi*:

The organism is large loosely spiral, flexible and highly motile.

Transmission and Epidemiology:

B.burgdorferi is etiologic agent of Lyme (zoonosis disease) . The bacteria are transmitted from animal to humans by hard ticks (*Ixodes*) .The nymphal stage of tick transmits the disease more than adult and larval stage.

The mice (white-footed mice) are main reservoir , upon which the nymph feed. While the deer(white-tailed deer) is obligatory host in

life cycle of tick , but is not important reservoir. Most exposure are in May through July (80% of cases occurring in June and July) , when the nymph is more active, however, larva (active in August and September) and adult (active in spring and fall) also feed on humans and can transmit *B.burgdorferi*. The disease occurs worldwide ,especially in USA, average at least 10,000 cases per year.

Pathogenicity:

Lyme disease occurs in three stages:

a.First stage(primary): the lesion usually being rash occur at site of bite about 7 days after the tick bite(*Ixodes*) , but the incubation period can range from 3-32 days .A papule appears on skin , which characterized by development of red, circular lesion (erythema chronicum migrans) in 80% of patients. This lesion is painless. The organism invading many organs. Joint stiffness, headache, stiff neck and flu-like symptoms often accompany the lesion.

b.Second stage: After several weeks, the disease is characterized by development of symptoms such as: multiple skin patches ,arthritis , central and peripheral nervous system disorders (polyneuropathy) eg: facial paralysis and meningitis .

c.Third stage : of disease typically occurs 3-4 weeks (or more) after the initial erythema migrans. Arthritis and neurologic symptoms become chronic. Cardiac defects (irregular heart beats) involvement may include bradycardia and tachycardia.

Control:

1. Prevention :
 - A. Avoidance of exposure to ticks by wearing protective cloths or using insect repellents or insecticide.
 - B. Vaccination: vaccine containing recombinant outer surface proteins (OspA vaccine) has efficacy of 66-76%
2. Antibiotic therapy: Tetracycline,Amoxicillin, Vancomycin , Ceftriaxone.

Yersinia:

- Yersiniae are Gram negative rods, showing bipolar staining.
- Catalase positive and oxidase negative.
- Some species (*Y. pseudotuberculosis*, and *Y. enterocolitica*) are motile at 25C but not at 37C and other species (*Y. pestis*) are non-motile.
- Some species (*Y. pestis*) are encapsulated and other species are non-encapsulated.
- Aerobic or facultative anaerobic.
- Grow at low temperature (room temperature), optimum temp. for growth is 27C. It takes 2-3 days for formation of single colony.
- They are capable of fermenting many sugars (non-lactose ferment) with production of acid and no gas.

Yersinia species cause a variety of diseases in mammals, birds, and fish. *Yersinia* is named for Alexandre Yersin, who first identified *Y. pestis* in 1894.

Transmission and Pathogenesis :

The medically important species of *Yersinia* include *Y. pestis*, *Y. pseudotuberculosis*, and *Y. enterocolitica*.

Yersinia enterocolitica and *Y. pseudotuberculosis* are enteric pathogens that infect a wide variety of mammals and birds. Transmission generally occurs after ingestion of food or water that has been exposed to contaminated fecal matter. Generally, they cause syndromes ranging from mild diarrhea disease to systemic infection such as septicemia. Enterocolitis is characterized by fever, abdominal pain and diarrhea. These symptoms commonly resolve in 1-3 weeks. Sequelae may include reactive polyarthrititis and erythema nodosum.

Y. pestis, the causative agent of plague and septicemia, is generally transmitted from animal to animal via the bite of an infected flea. The infectious cycle begins when a flea ingests a blood meal from an infected animal. The organism multiplies in the flea's foregut. When the flea next attempts to feed on a new animal, these bacteria transmit to this new animal.

Plague is a zoonotic disease, rats are common reservoirs in urban areas of some countries (urban plague). Plague is found in wild animals (prairie dogs, squirrels) as reservoirs (sylvatic plague).

Human is an accidental and dead-end host. Two types of plague;

Bubonic (septicemic) plague:

Infected flea on wild animal reservoirs (sylvatic plague) or on urban rats (urban plague) are major vectors of transmission of bubonic plague.

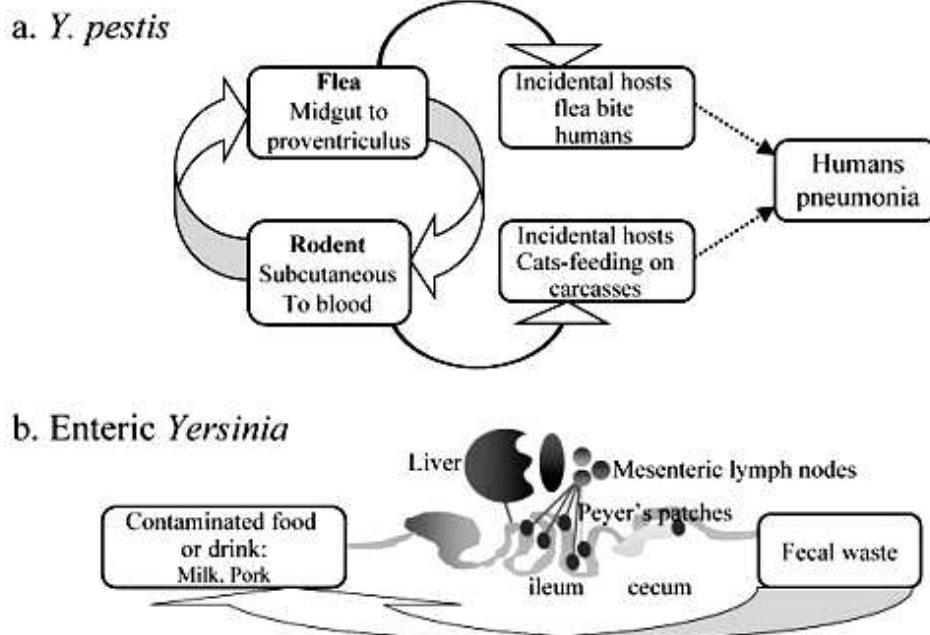


Figure 21.1. A comparison of transmission cycles of (A) *Y. pestis* and (B) the enteric *Yersinia* spp. *Y. pestis* life cycle involves transmission between fleas and rodents with the bacteria inoculated subcutaneously into rodents, eventually spreading to blood, followed by ingestion by a flea. *Y. enterocolitica* and *Y. pseudotuberculosis* are transmitted by ingestion of contaminated foods.

Bacteria spread from the site of inoculation to local and regional lymph nodes, where they are ingested by macrophage. It survive in macrophage (intracellular), replicate, and causes massive inflammatory swelling of lymph nodes (ie, bubo). Organism spread rapidly from buboes during blood stream to other organs, causing systemic endotoxin-related necrosis (hemorrhagic) of peripheral blood vessels, sepsis, shock due to hypotension, pharyngitis, meningitis and failure of heart and kidney. Plague disease cause high death rate so-called **black death**, medieval name for bubonic plague, which killed 50% of its victims. One feature of disease is bleeding beneath skin, causing dark blue or black bruises (black patches).

Bubonic (septicemic) plague is characterized by high fever, swelling, hemorrhagic, painful of lymph nodes of groin or axilla. The infection may progress to bacteremic phase with sudden onset of fever, chills, hemorrhagic lesion and sepsis. Mortality is high when left untreated.

Pneumonic plague results from inhalation of infectious aerosols or embolization of bacteremic organism to the lung. Infected humans with pneumonic plague transmit organism person to person through respiratory

aerosols. The disease may develop during epidemics. Development of disease is rapid and fatal during epidemics.

Treatment;

Streptomycin is the drug of choice for treatment of bubonic and pneumonic plague. The ciprofloxacin ,chloramphenicol, trimethoprim as alternatives.

Tetracycline and Garamicin are effective antibiotics against enterocolitis.

Prevention;

- Control on rats and flea.
- Sick and dead rodent should never be touched with bare hands.
- Public health measures & Isolation of patient.
- Vaccine is available for high risk of acquiring plague. It can provide short-time protection.

Table 7–6. Bacterial diseases transmitted by insects.

Bacterium	Insect	Reservoir	Disease
Gram-negative rods			
<i>Yersinia pestis</i>	Rat fleas	Rodents, eg, rats, prairie dogs	Plague
<i>Francisella tularensis</i>	Ticks (<i>Dermacentor</i>)	Many animals, eg, rabbits	Tularemia
Spirochetes			
<i>Borrelia burgdorferi</i>	Ticks (<i>Ixodes</i>)	Mice	Lyme disease
<i>Borrelia recurrentis</i>	Lice	Humans	Relapsing fever
Rickettsias			
<i>Rickettsia rickettsii</i>	Ticks (<i>Dermacentor</i>)	Dogs, rodents, and ticks (<i>Dermacentor</i>)	Rocky Mountain spotted fever
<i>Rickettsia prowazekii</i>	Lice	Humans	Epidemic typhus
<i>Ehrlichia chafeensis</i>	Ticks (<i>Dermacentor</i>)	Dogs	Ehrlichiosis