Yersinia and Rickettsia

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Objectives

- Describe the general characteristics, epidemiology, pathogenesis, clinical presentation and management of *Y. pestis*
- Describe the general characteristics, epidemiology, classification, pathogenesis, clinical presentation and management of Rickettsia

Yersinia and plague

General Characteristics

- The most important species is *Y. pestis* which cause plague
- Gram-negative bacillus with a tendency toward pleomorphism
- Nonmotile
- Non-spore-forming
- It is a member of the Enterobacteriaceae family

Epidemiology

- The term plague is often used generically to describe any explosive pandemic disease with high mortality
- Medically, it refers only to infection caused by *Y. pestis*
- *Y. pestis* was the cause of the most virulent epidemic plague of recorded human history, the Black Death of the Middle Ages
- Plague is a disease of rodents transmitted by the bite of rat fleas (*Xenopsylla cheopis*)
- It exists in two interrelated epidemiologic cycles:

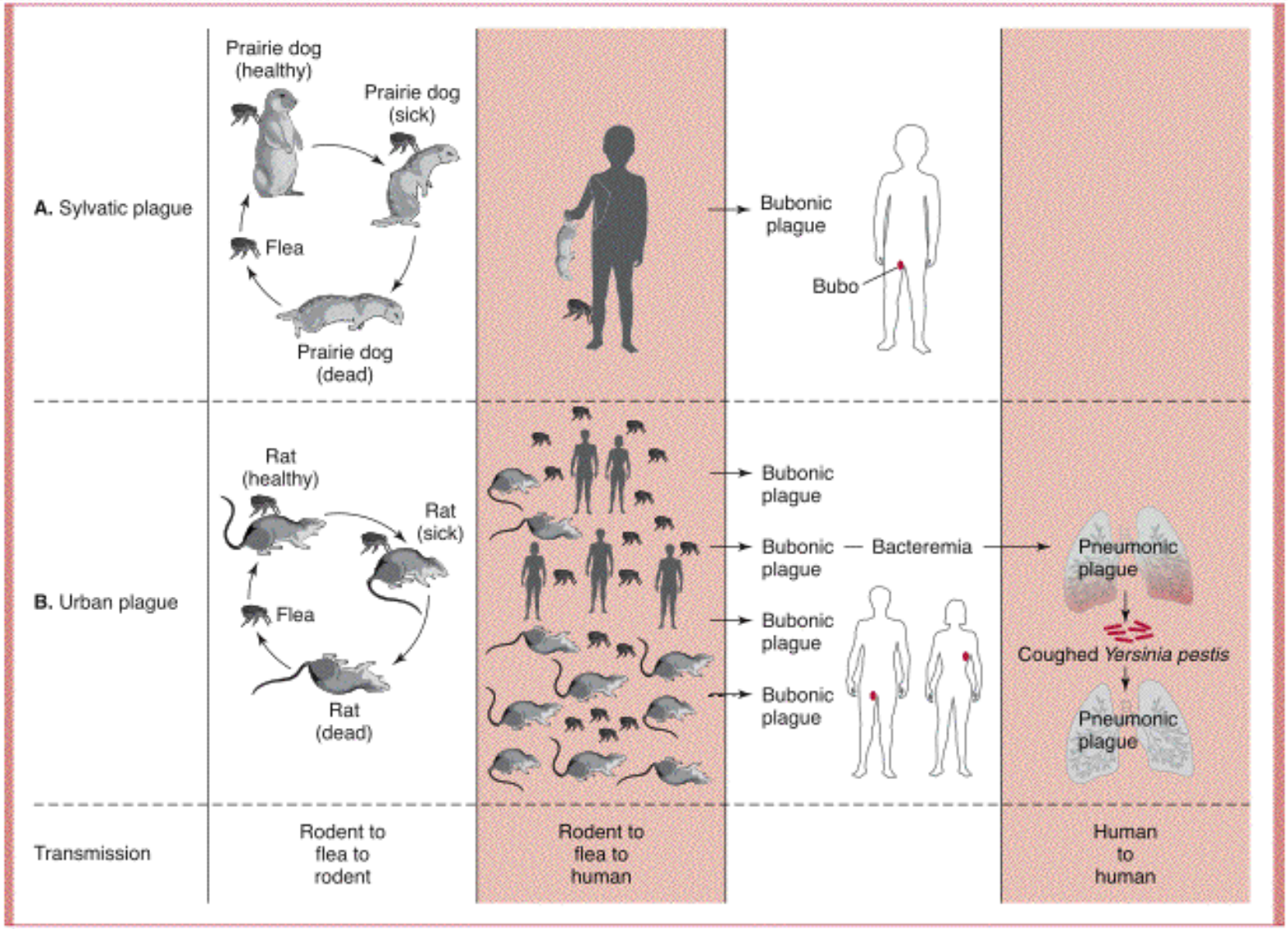
1. The sylvatic: endemic transmission among wild rodents
2. The urban: when infected rodents enter a city

- Humans can enter the cycle from the bite of the flea in either environment. However, chances are greater in the urban setting

- Transmission can be:

1. Flea to human infection: The bite of the flea is the first event in the development of a case of bubonic plague, which, even if serious enough to kill the patient, is not normally contagious to other humans
2. Human to human: Some patients with bubonic plague develop a secondary pneumonia by bacteremic spread to the lungs. This pneumonic plague is highly contagious person-to-person by the respiratory droplet route

The Epidemiology of Plague



Pathogenesis

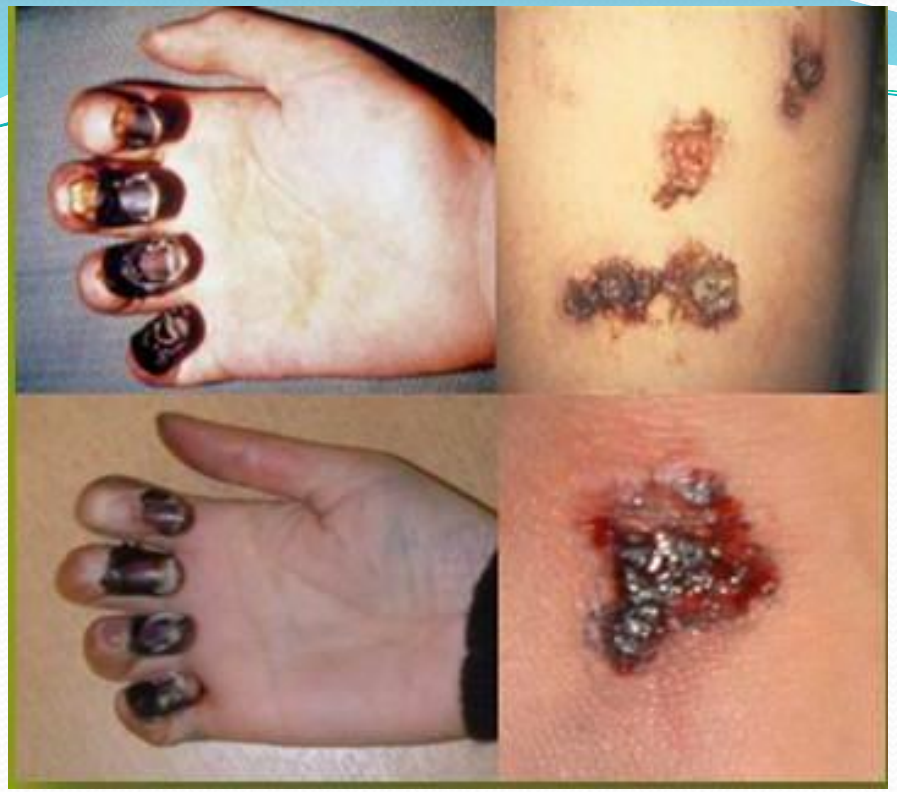
- The plague cycle begins when a rat flea feeds on a rodent infected with *Y. pestis*. Bacteria are taken with the blood meal and multiply in the infected flea. Some virulence factors such as the fibrinolysin and phospholipase are produced
- Once injected past the skin barrier by the flea, *Y. pestis* produces a new set of virulence factors as it senses the change from the temperature and ionic environment of the new host
- The organisms eventually reach the regional lymph nodes, where they multiply rapidly and produce a hemorrhagic suppurative lymphadenitis known clinically as the bubo
- Spread to the bloodstream quickly follows with toxicity due to lipopolysaccharide (LPS) endotoxin
- The bacteremia causes seeding of other organs, most notably the lungs, producing a necrotizing hemorrhagic pneumonia known as pneumonic plague

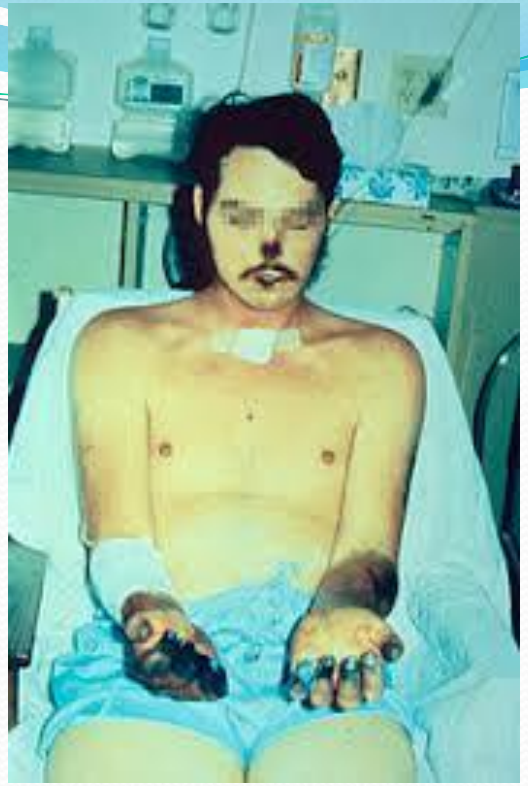
Clinical Manifestations

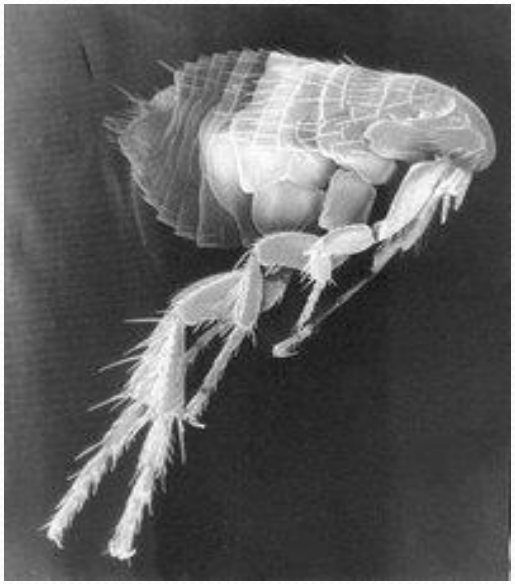
- The incubation period for bubonic plague is 2 to 7 days after the flea bite
- Onset is marked by fever and the painful bubo, usually in the groin or, less often, in the axilla
- Without treatment, 50 to 75% of patients progress to bacteremia and die in Gram-negative septic shock within hours or days of development of the bubo
- About 5% of victims develop pneumonic plague with mucoid, then bloody sputum

Primary Pneumonic Plague

- Has a shorter incubation period (2 to 3 days)
- Begins with only fever, malaise, and a feeling of tightness in the chest
- Cough, production of sputum, dyspnea, and cyanosis develop later in the course
- Death on the second or third day of illness is common, and there are no survivors without specific therapy
- A terminal cyanosis seen with pneumonic plague is responsible for the term Black Death
- Even today, plague pneumonia is almost always fatal if appropriate treatment is delayed more than a day from the onset







Diagnosis

- The appropriate specimens are bubo aspirate, blood, and sputum
- Aspirates from the bubo typically reveal Gram-negative bacilli
- An immunofluorescence technique is available in public health laboratories for immediate identification of smears or cultures
- *Y. pestis* is readily isolated on the media used for other members of the Enterobacteriaceae (blood agar, MacConkey agar), although growth may require more than 24 hours of incubation

Treatment

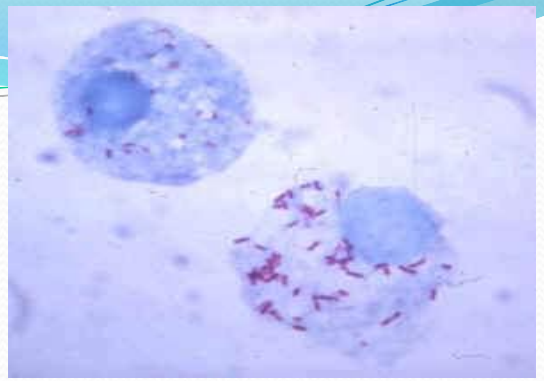
- Streptomycin is the treatment of choice for both bubonic and pneumonic plague. Tetracycline, chloramphenicol, and trimethoprim-sulfamethoxazole are alternatives
- Timely treatment reduces the mortality of bubonic plague below 10%. Of the 31 human cases of plague reported in the United States in 1984, 6 (19%) died

Prevention

- Urban plague has been prevented by rat control and general public health measures such as use of insecticides
- Sylvatic plague is virtually impossible to eliminate because of the size and dispersion of the multiple rodent reservoirs. Disease can be prevented by avoidance of sick or dead rodents and rabbits
- Eradication of fleas on domestic pets, which have been known to transport infected fleas from wild rodents to humans, is recommended in endemic areas
- The continued presence of fully virulent plague in its sylvatic cycle poses a risk of extension to the urban cycle and epidemic disease in the event of major disaster or social breakdown
- Chemoprophylaxis with tetracycline is recommended for those who have had close contact with pneumonic plague

Rickettsia

General Characteristics



- Gram-negative, stain poorly
- Small, pleomorphic coccobacilli
- Stain better with Giemsa stain
- Cultivation is costly and hazardous because aerosol transmission can easily occur
- Have cell wall, bigger than virus but smaller than bacteria
- Have DNA and RNA
- Have an ATP transport system that allows them to use host ATP
- Most rickettsiae have animal reservoirs and spread by insect vectors, which are prominent components of their life cycles
- Arthropod reservoirs and vectors include ticks, mites, lice or fleas

Tick

Flea

Lice

Mite

Classification

1. Rickettsia
2. Bartonella
3. Coxiella (does NOT cause skin rash)
4. Ehrlichia
5. Orientia
6. Anaplasma

Pathogenesis

Bites or faeces of arthropod

↓

Infects endothelial cells in small blood vessels

↓ (1st bacteremia)

Enter phagocytes and then induce lysis followed by replication and release

↓ (2nd bacteremia)

Endothelial cells, micro blood vessels in whole body

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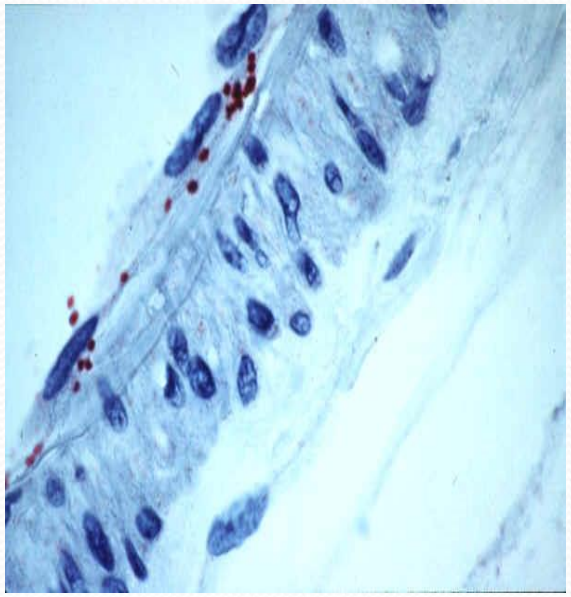
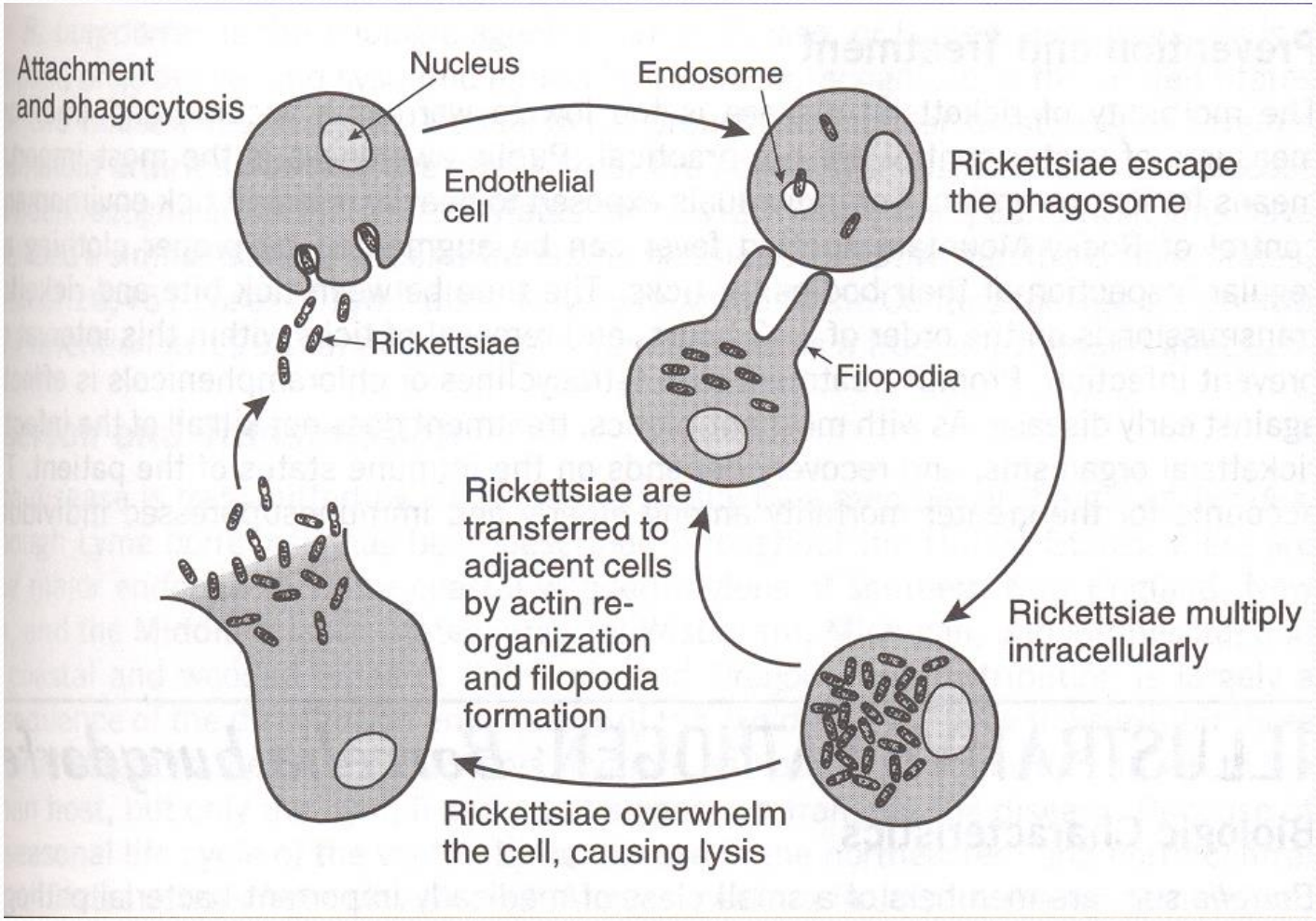
Fever, rash, headache, etc

Arthropod



Vasculitise

Rickettsia cell-to-cell spread



Clinical Presentations

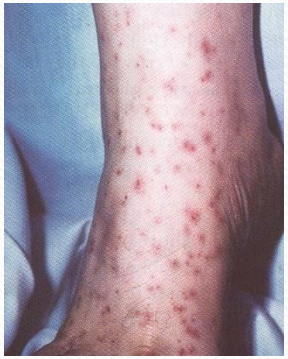
The diseases caused by Rickettsia are all characterized by fever, headache, myalgias, and usually a rash

1. Typhus fevers

- Incubation is 5-18 days
- Symptoms include a severe headache, chills, fever, and after a fourth day, a maculopapular rash caused by subcutaneous hemorrhaging as Rickettsia invade the blood vessels
- The rash begins on the upper trunk and spread to involve the whole body except the face, palms of the hands, and the soles of the feet
- The disease lasts about 2 weeks and the patient may have a prolonged convalescence

2. Rocky mountain spotted fever

- Caused by *R. rickettsii* and transmitted by ticks that must remain attached for hours in order to transmit the disease
- An incubation of 2-6 days is followed by a severe headache, chills, fever, aching, and nausea
- After 2-6 days a maculopapular rash develops, first on the extremities, including palms and soles, and spreading to the chest and abdomen
- If left untreated, the rash will become petechial with hemorrhages in the skin and mucous membranes due to vascular damage
- Death may occur during the end of the second week due to kidney or heart failure



3. Q fever

- Caused by *Coxiella burnetii*
- The infection is acquired by inhalation of infectious material
- After an incubation of 14-26 days there is a sudden onset of fever, chills, and headache, but no rash
- The disease is characteristically an atypical pneumonia lasting 5-14 days with a low mortality rate

4. Trench fever

- Caused by *Rochalimaea quintana* and transmitted by body lice
- After an incubation of 6-22 days, the patient experiences a headache, exhaustion, leg pains, and a high, relapsing fever
- A roseolar rash occurs and the patient usually recovers

Laboratory Diagnosis

- Direct detection of Rickettsia in tissues (Giemsa stain or direct fluorescent antibody test)
- Weil-Felix reaction – in certain rickettsial infections (typhus group) antibodies are formed that will agglutinate OX strains of Proteus vulgaris
- This is used as a presumptive evidence of typhus group infection, however, the test is not very sensitive or specific and many false positives occur
- Agglutination or complement fixation tests using specific Rickettsial antigens are better serological diagnostic tests

Treatment and Prevention

- Chloramphenicol or tetracycline
- Wear protective clothing and use insect repellents
- Avoidance or reduction of tick contact