Chapter 20

Zoonotic Gram negative rods

-- **Zoonoses** are human diseases caused by microorganisms that are **acquired from animals**.

-- Some zoonotic organisms are **acquired directly** from the animal reservoir.

-- Others are **transmitted by vectors** such as mosquitoes, fleas, or ticks.

Four Gram negative rods are medically important zoonotic pathogens:

Brucella spp

Francisella tularensis

Yersinia pestis

Pasteurella multocida

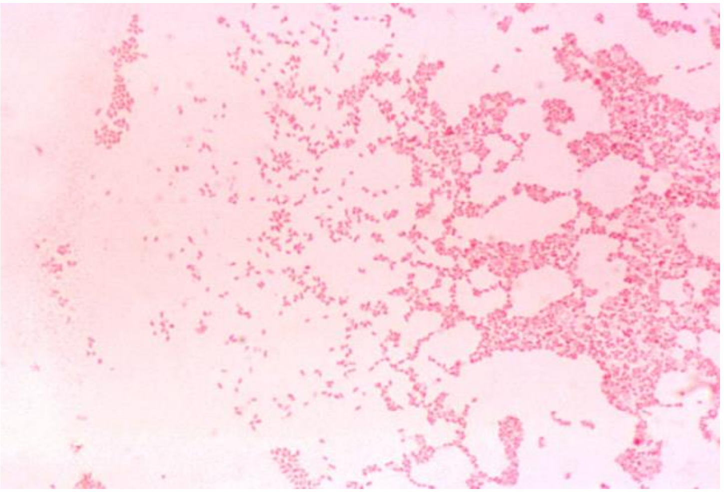
Brucella

Brucella spp cause **Brucellosis (undulant fever).**

Important properties

These are Gram negative rods **without a capsule**.

Three important species are ***B. melitensis*** (**goats and sheep**), ***B. abortus*** (**cattle**) and ***B. suis*** (**pigs**).



Pathogenesis and Epidemiology

-- The organisms enter the body either by **ingestion of contaminated milk products** or **through the skin by direct contact** in an occupational setting such as an **abattoir**.

-- They **localize in the reticuloendothelial system**, namely the lymph nodes, liver, spleen, and bone marrow.

-- Many organisms are killed by **macrophages,** but **some survive within these cells** and are thus **protected from antibody**.

-- The host response is **granulomatous** with lymphocytes and epitheloid giant cells which can progress to form focal abscesses.

-- The mechanism of pathogenesis is not well defined except that **endotoxin is involved**.

-- **No exotoxins** are produced.

-- The disease occurs **worldwide** due to **lack of pasteurization** procedures.

Clinical findings

-- After an incubation period of 1-3 weeks, **non specific symptoms** such as fever, chills, fatigue, malaise, anorexia and weight loss occur.

-- The onset can be acute or gradual. The **undulating** (rising and falling) fever pattern occurs in a **minority of cases**.

-- **Enlarged lymph nodes, liver, and spleen** are frequently found.

-- **Pancytopenia** (reduction in all three parameters) occurs.

-- *B. melitensis* infections tend to be **more severe and prolonged** whereas those by *B. abortus* are **more self-limited**.

-- **Osteomyelitis** is the most common complication.

-- Secondary spread from person to person is rare.

Laboratory Diagnosis

Enriched culture medium and incubation in 10% CO_2 is needed. **Blood culture** is done.

They form **small, convex, smooth translucent (yellowish and pearl-like)** colonies in 48 hours on **blood agar**.

-- **Presumptive identification** can be done by **slide agglutination** with ***Brucella*** antiserum.

-- If **organism is not isolated**, analysis of a serum sample from the patient to detect **rise in antibody** may be done.

-- In absence of an acute-phase serum specimen, a **titer of at least 1:160** in the **convalescent phase** serum sample is **diagnostic**.

Treatment

-- The treatment of choice is **tetracycline plus rifampin**.

-- There is **no significant resistance** to these drugs.

Prevention

-- It involves **pasteurization of milk, immunization of animals**, and **slaughtering of infected animals**.

-- There is **no human vaccine**.

Francisella

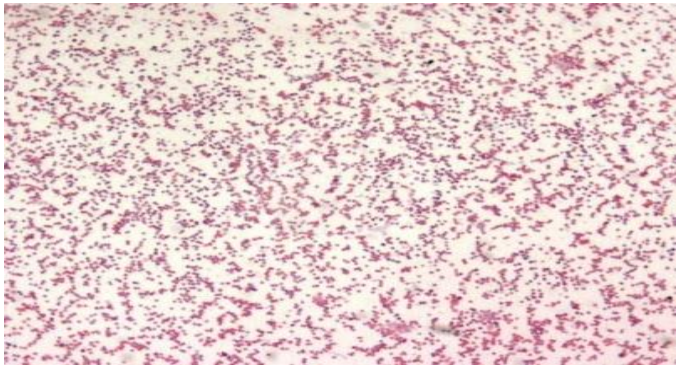
Francisella tularensis causes **tularemia**.

Important properties

F. tularensis is a **small, pleomorphic**, Gram negative rod.

It has a **single serotype** and **two biotypes, A and B** which are distinguished primarily on the basis of their virulence and epidemiology.

Type A is more virulent and primarily found in US. Type B is found in Europe.



Pathogenesis and Epidemiology

-- It has been isolated from more than **100 different species of wild animals** including rabbits, deer and many rodents.

-- Transmission among animals is via **ticks, mites, and lice**, esp. ***Dermacentor*** ticks that feed on blood of wild rabbits.

-- In tick, bacteria are passed to offspring by **transovarian** route.

-- **Humans are accidental "dead end" hosts** who acquire infection by biting of vector or skin contact while removing animal hides.

-- Rarely organism is **ingested** in infected meat causing **GIT tularemia**, or is **inhaled** causing **pneumonia**.

-- There is **no person to person spread.**

-- The organism enters the **skin**, forming an ulcer at the site in most cases.

-- It then localizes to the cells of reticuloendothelial system and **granulomas** are formed.

-- **Caseation necrosis** and **abscesses** can also form.

-- Symptoms are mainly caused by endotoxins.

-- **No exotoxin** is found.

Clinical findings

Presentation can vary from sudden onset of an influenza-like syndrome to prolonged onset of a low-grade fever and lymphadenopathy.

App. 75% of cases are **"ulceroglandular"** type, in which the site of entry ulcerates and the regional lymph nodes are swollen and painful.

Other, less frequent forms include **glandular**, **oculoglandular, typhoidal, gastrointestinal**, and **pulmonary**.

Disease usually confers **life long immunity**.

Laboratory Diagnosis

-- **Culture is usually not attempted because high risk of infection** by inhalation and requirement of special **cysteine-containing medium**.

-- The most commonly used diagnostic method is the **agglutination test** with acute- and convalescent –phase serum samples.

-- **Fluorescent-antibody staining** of infected tissue may also be used.

Treatment

-- **Streptomycin** is the drug of choice.

-- There is **no significant antibiotic resistance**.

Prevention

-- It involves **avoiding being bitten by ticks** and **careful handling of wild animals.**

-- There is a **live, attenuated vaccine** given only to persons whose profession brings them in close contact with animals.

It is experimental and not commercially available

Yersinia

-- ***Yersinia pestis*** is the cause of **plague**, also known as **black death**.

-- It **still exists** in many parts of world.

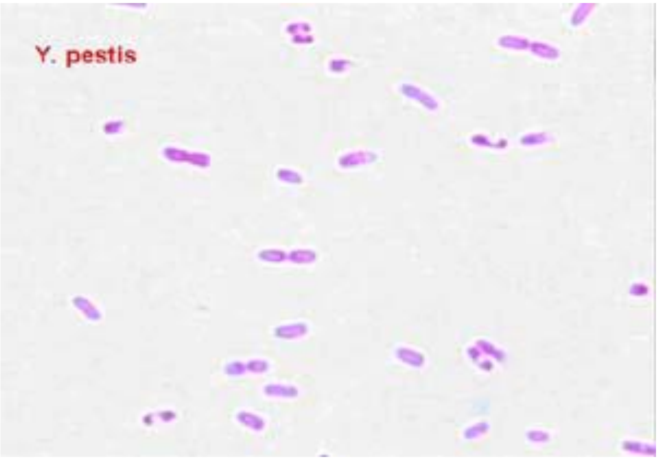
-- Two other species, ***Y. enterocolitica*** and ***Y. pseudotuberculosis*** are **human pathogens** as well.

Important properties

-- *Y. pestis* is a small Gram negative rod that exhibits **bipolar staining (resembles a safety pin).**

-- Freshly isolated organisms **possess a capsule** composed of a protein-polysaccharide complex which is responsible for virulence.

-- It is **one of the most virulent bacteria known** and has a strikingly low ID_{50} (**1-10 organisms are capable of causing disease**).



Pathogenesis and Epidemiology

-- The plague bacillus has been **endemic in wild rodents** for thousands of years.

-- The **enzootic (sylvatic)** cycle consists of transmission among wild rodents by fleas.

-- In the US, **prairie dogs** are the main reservoir.

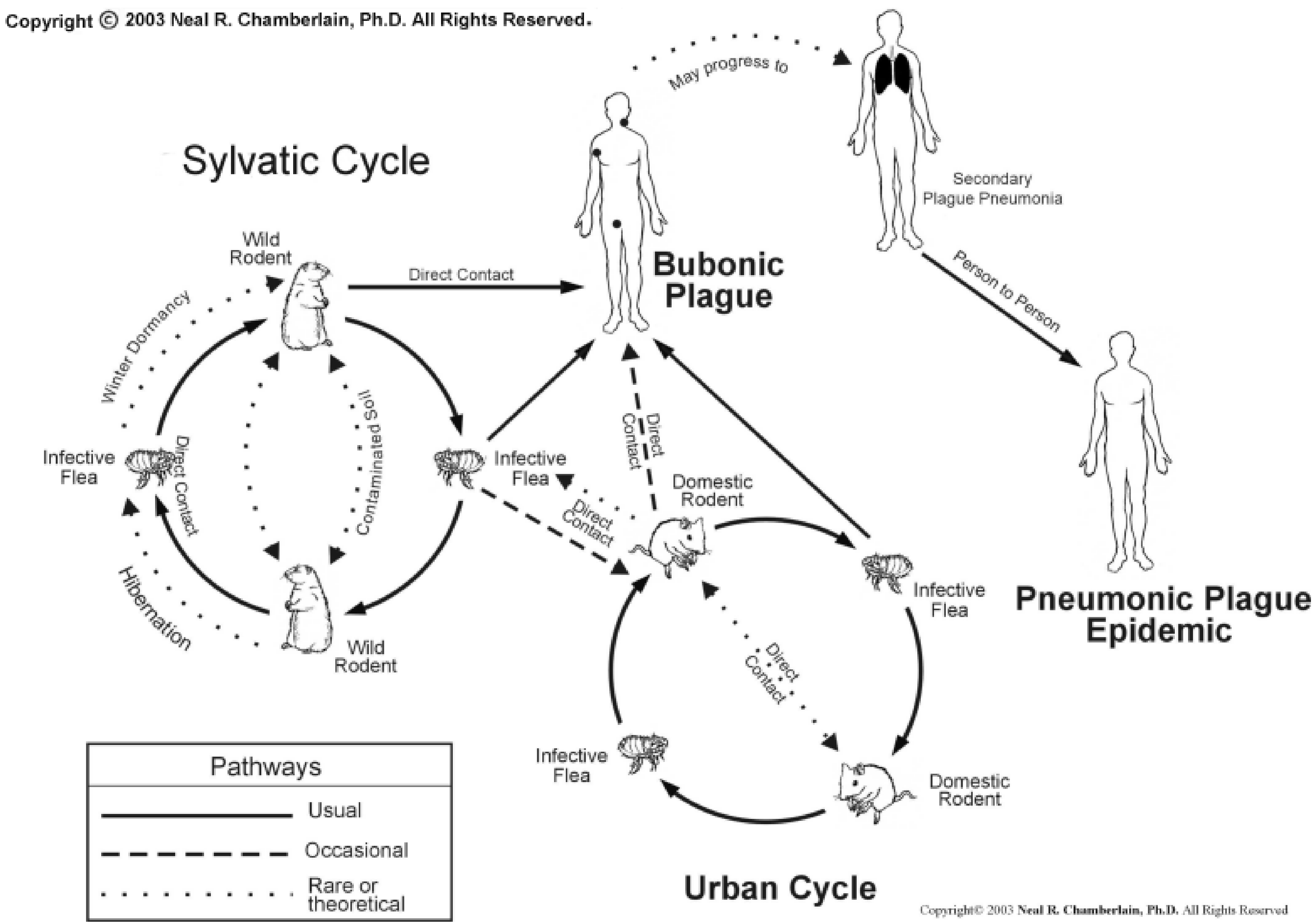
-- Rodents are relatively resistant and most are asymptomatic.

-- **Humans are accidental hosts**.

-- The urban cycle consists of transmission of bacteria among urban rats with **rat flea as vector**.

-- The flea ingests bacteria from rodents. **A thick biofilm forms in upper GIT** of flea that prevent ingestion of food.

-- The **“blocked flea”** then **regurgitates the organism** into the blood stream of the next animal or human it bites.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Sylvatic Cycle
May progress to
Secondary Plague Pneumonia
Bubonic Plague
Direct Contact
Person to Person
Wild Rodent
Winter Dormancy
Contaminated Soil
Infective Flea
Direct Contact
Infective Flea
Direct Contact
Domestic Rodent
Direct Contact
Hibernation
Wild Rodent
Infective Flea
Pneumonic Plague Epidemic
Direct Contact
Infective Flea
Domestic Rodent
Pathways
Usual
Occasional
Rare or theoretical
Urban Cycle
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-- The organism spreads to **lymph nodes** which become **swollen and tender.**

-- They are called **buboes** and thus the name **bubonic plague**.

-- The organisms can reach **high concentration in blood** and disseminate to form **abscesses** in many organs.

-- The **endotoxin related symptoms** including **disseminated intravascular coagulation** and **cutaneous hemorrhages** gave the name **black death**.

-- **Respiratory droplet transmission** of organisms from patients of **pneumonic plague** can occur.

There are several virulence factors:

1) the **capsular antigen F-1** which protects from phagocytosis

2) **endotoxin**

3) **exotoxin**

4) two proteins **V and W antigens** which allow the organism to survive and **grow intracellularly** – mode of action is not known.

-- Another set of factors which contribute to its extraordinary virulence are called **Yops (Yersinia outer proteins).**

-- They are injected into human cell via **type III secretion systems** and **inhibit phagocytosis** and **cytokine production** by macrophages and neutrophils.

Clinical findings

-- **Bubonic plague is the most frequent form.**

-- It begins with **pain and swelling of the lymph nodes** draining the **site of flea bite** and systemic symptoms such as high fever, myalgias, and prostration.

-- The **affected nodes enlarge** and become **very tender**.

-- These **bubos** are an early characteristic sign.

-- **Septic shock** and **pneumonia** are the main life-threatening subsequent events.

-- **Pneumonic plague** can arise either from **inhalation of an aerosol** or from **septic emboli** that reach the lungs.

-- Untreated **bubonic plague** is fatal in app. **half the cases**, and untreated **pneumonic plague** is **invariably fatal**.

Laboratory Diagnosis

Smear and culture of blood or pus from the **bubo** is the best diagnostic procedure.

Great care must be taken by the physician during aspiration and by laboratory workers doing cultures **not to create an aerosol** that might transmit the disease.

Chocolate agar is used for cultivation.

The colonies are **white, pearl like and sticky.**

-- **Giemsa stain** reveal the **safety pin** morphology better than Gram stain.

-- **Fluorescent antibody staining** can be used to identify the organisms in tissues.

-- A rise in antibody titer to the **capsular antigen** can be useful retrospectively.

Treatment

-- The treatment of choice is a **combination of streptomycin and tetracycline**, although streptomycin alone may also be used.

-- The **treatment should not wait for laboratory results** as disease progress very rapidly.

-- Incision and drainage of buboes are not usually necessary.

Prevention

-- It involves **controlling of rats** in urban areas and **avoiding flea bites** and contact with rodents.

-- A patient with plague must be placed in strict isolation (**quarantine**) for 72 hours after antibiotic therapy is started.

-- Only close contacts need prophylactic tetracycline, but all contacts should be observed for fever.

-- **A case of plague must be reported to authorities.**

-- A vaccine made of **formalin killed organisms** provides **partial protection to bubonic but not pneumonic plague.**

Pasteurella

-- ***P. multocida*** causes **wound infections** associated with **cat** and **dog bites.**

-- It is a short, **encapsulated** Gram negative rod that exhibits **bipolar** staining.

Pathogenesis and Epidemiology

-- It is part of **normal flora in the mouths of many animals**, particularly **domestic cats** and **dogs**, and is transmitted by **biting**.

-- About 25% bites become infected with **sutures** acting as a predisposing factor.

-- Most bite infections are **polymicrobial** with a variety of facultative anaerobes and anaerobic organisms present in addition to ***P. multocida***.

-- Only thing known about pathogenesis is that the **capsule** is a virulence factor and **endotoxin is present**.

-- There is **no exotoxin**.

Clinical findings

-- A **rapidly spreading cellulitis** at the site of an animal bite is indicative of ***P. multocida*** infection.

-- The incubation period is brief, usually **less than 24 hours**.

-- **Osteomyelitis** can complicate cat bites in particular because they bite deep.

Laboratory diagnosis

-- It is made by **cultivation of samples** from wound site.

Treatment

-- **Penicillin G** is the treatment of choice.

-- There is **no significant antibiotic resistance**.

Prevention

-- People **bitten by a cat** should be given **ampicillin** and bites **should not be sutured.**

Bartonella

-- ***B. henselae*** is the cause of **cat scratch disease** and **bacillary angiomatosis.**

-- ***B. henselae*** is a small **pleomorphic** Gram negative rod.

-- It is a fastidious organism and **does not grow on blood agar**.

Pathogenesis and Epidemiology

-- **Cat scratches or bites**, esp. from kittens, are the main mode of transmission.

-- It is a **part of oral flora of cat**. It may also be transmitted by **bite of cat fleas.**

-- Cat urine or feces are not a risk factor.

-- Person to person transmission is also not important.

-- Disease is **self limiting**.

Clinical findings

-- Cat scratch disease is characterized by **fever and tender, enlarged lymph nodes**, typically on the **same side as the scratch**.

-- A **papule** at the site of the scratch may precede the lymphadenopathy.

-- It has a long course but eventually resolves even without antibiotics.

-- A small number of patients develops systemic disease such as **endocarditis** or **encephalitis**.

-- In **immunocompromised persons**, especially AIDS patients, ***B. henselae*** causes **bacillary angiomatosis (BA)** characterized by **raised, cherry red vascular lesions** in the **skin** and **visceral organs.**

-- The lesions appear **papular** or **nodular**.

-- **Bacillary peliosis** (peliosis hepatis) is similar to bacillary angiomatosis except that the lesions occur **primarily in liver and spleen**.

Laboratory Diagnosis

-- The diagnosis of **CSD** is usually made **serologically**.

-- The diagnosis of **BA** is often made by finding **pleomorphic rods in biopsy tissue.**

Treatment

-- **No antibiotic therapy** is typically recommended for **CSD**.

-- In case of severe lymphadenitis, **azithromycin** is the drug of choice.

-- Treatment of **BA** with **doxycyline** or **erythromycin** is effective.

Prevention

-- Antibiotics are not recommended.

-- There is **no vaccine**.


Thank You!