

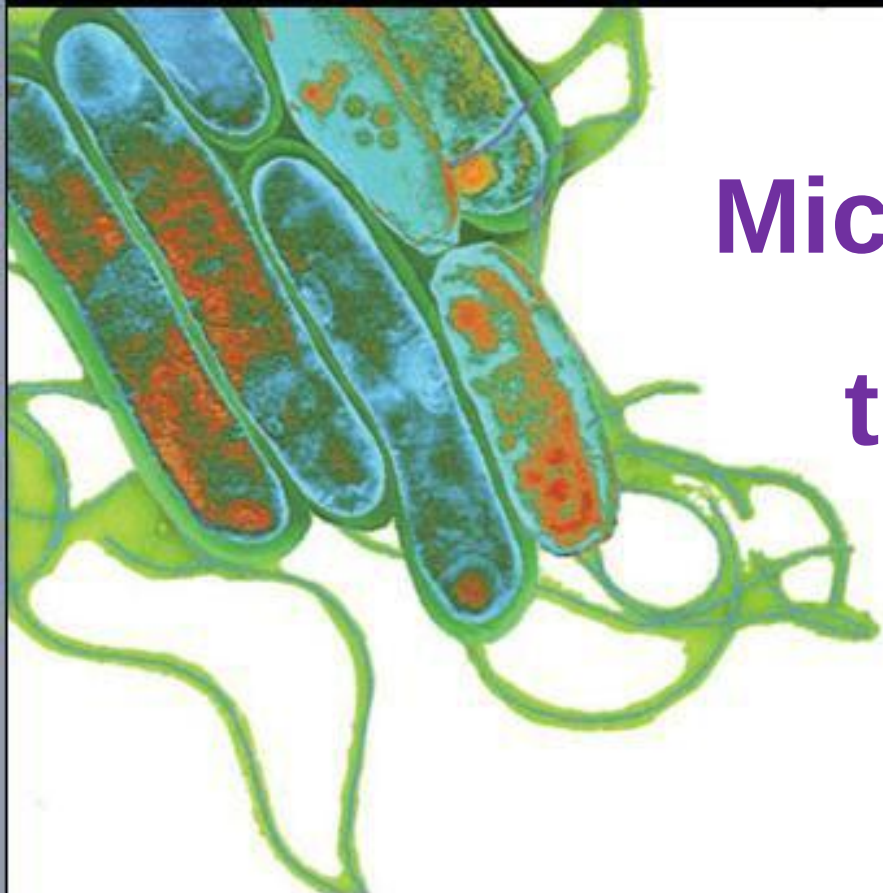


ninth edition

TORTORA | FUNKE | CASE

MICROBIOLOGY

an introduction



Microbial Diseases of the Cardiovascular and Lymphatic Systems (I)

LEARNING OBJECTIVES

- List the signs and symptoms of septicemia
- Differentiate gram-negative sepsis, gram-positive sepsis, and puerperal sepsis.
- Describe bacterial endocarditis and rheumatic fever.
- Discuss the epidemiology of tularemia, brucellosis, anthrax, gas gangrene.
- Describe pathogens that are transmitted by animal bites and scratches.
- Compare and contrast the causative agents, vectors, reservoirs, symptoms, treatments, and preventive measures for plague, Lyme disease, and Rocky Mountain Spotted Fever.
- Describe infectious mononucleosis.
- Compare and contrast the causative agents, vectors, reservoirs, and symptoms for yellow fever.
- Compare and contrast the causative agents, modes of transmission, reservoirs, and symptoms for Ebola hemorrhagic fever and *Hantavirus* pulmonary syndrome. Also, for Chagas' disease, toxoplasmosis, malaria, and babesiosis.
- Describe Swimmer's Itch.

The Cardiovascular System

Both the cardiovascular system and the lymphatic system are susceptible to diseases caused by microorganisms.

- Two common cardiovascular diseases caused by infection with microorganisms are endocarditis and myocarditis.
- Endocarditis is inflammation of the inner tissue of the heart such as its valves caused by infectious agents.
- Myocarditis is inflammation of heart muscle and it is most often due to infection by common viruses.
- Bacteremia is the presence of bacteria in the blood.
- Vasculitis is inflammation of the vessel wall due to an infection or autoimmune disease.
- Lymphadenopathy is a disease of the lymph nodes due to infection, auto-immune disease, or malignancy.

Sepsis and Septic Shock

Septic shock occurs when a body's response to an infection (sepsis) leads to life-threatening low blood pressure.

- **Sepsis** results from certain bacterial infections, often acquired in a hospital. Having certain conditions, such as a weakened immune system, certain chronic disorders, an artificial joint, or heart valve increases the risk.
- **Symptoms of sepsis** include either fever or low body temperature, rapid breathing, chills and shaking, rapid heartbeat, decreased urine output, and confusion or delirium.
- **Severe sepsis** often causes extremely low blood pressure, which limits blood flow to the body and can result in organ failure and death. This is known as **septic shock**.
- **Sepsis is treated** with antibiotics, fluids, and medicines to support blood pressure and prevent organ damage.

Sepsis and Septic Shock

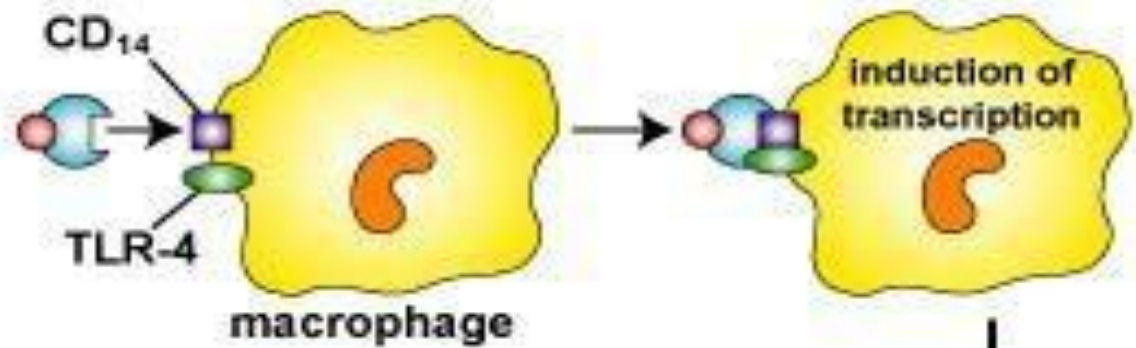
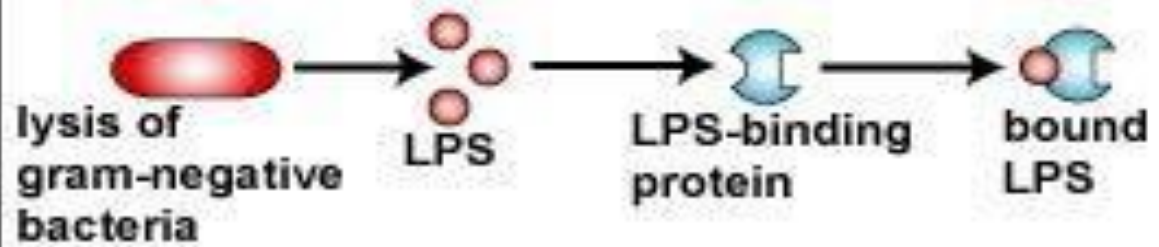
Sepsis: systemic inflammatory response syndrome (**SIRS**) caused by spread of bacteria or their toxin from a focus of infection.

Septicemia: Sepsis involving proliferation of pathogens in the blood.

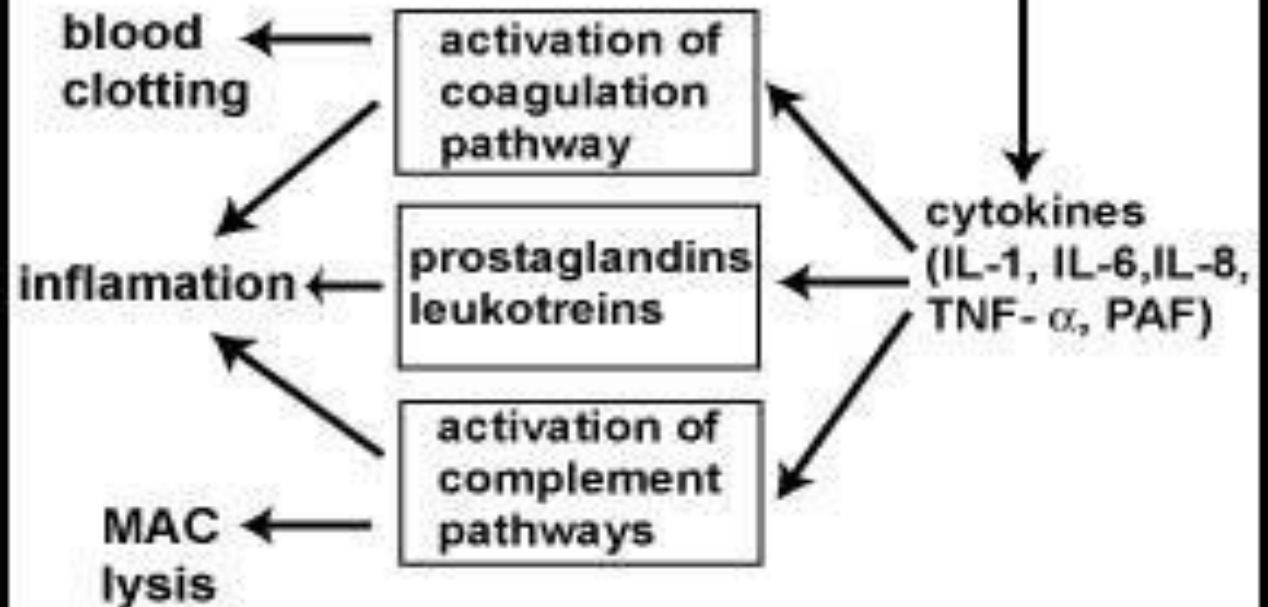
Gram-negative sepsis can lead to **septic shock**

Antibiotic-resistant enterococci (**VRE**) and group B streptococci cause **gram-positive sepsis**.

Puerperal sepsis (*S. pyogenes*): due to uterus infection following childbirth or abortion; can progress to peritonitis or septicemia.



DIC



A. Bacterial Infections of the Cardiovascular and Lymphatic Systems

- **Subacute Bacterial Endocarditis**
- **Rheumatic Fever**
- **Tularemia**
- **Brucellosis**
- **Anthrax**
- **Gas Gangrene**
- **Bite Wounds**

Subacute Bacterial Endocarditis:

- **Endocarditis** occurs when bacteria grow on the edges of a heart defect or on the surface of an abnormal valve after the bacteria enter the blood stream, **most commonly from dental procedures** but also from **procedures involving the gastrointestinal or urinary tract**.
- **The most important diagnostic test for endocarditis** involves a positive **blood culture**. A blood culture is a small sample of blood drawn from the vein which is grown in a special solution so that bacteria can be detected.
- **Symptoms and signs of endocarditis** vary but include prolonged fever, poor appetite, feeling weak or tired, joint pains, skin rashes, and changes in the nature of a previously present heart murmur.
- **Treatment** of bacterial endocarditis consists of a period of intravenous doses of appropriate antibiotics determined from blood tests under the supervision of an infectious disease specialist and cardiologist.

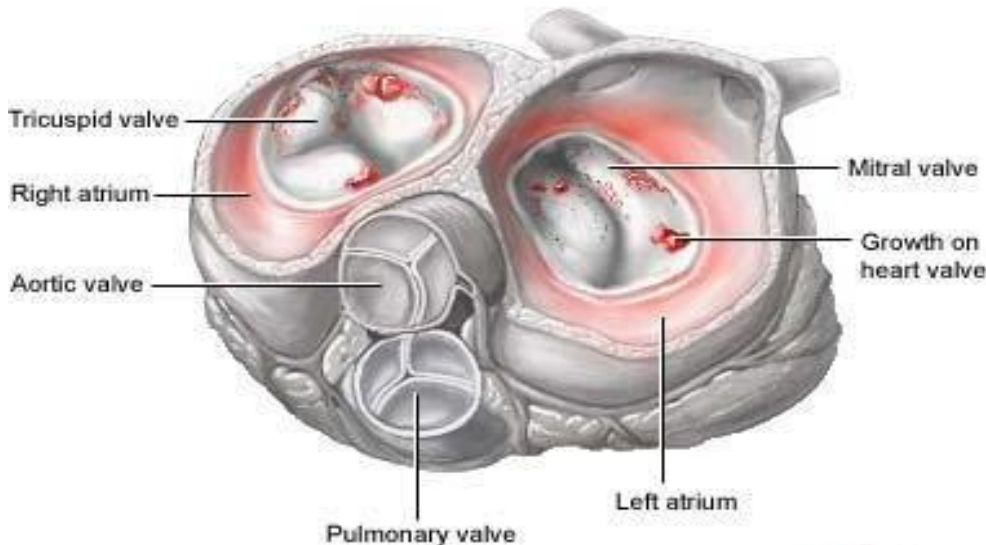
Subacute Bacterial Endocarditis:

Usually caused by alpha-hemolytic streptococci from mouth (dentist!)

Preexisting heart abnormalities are predisposing factors.

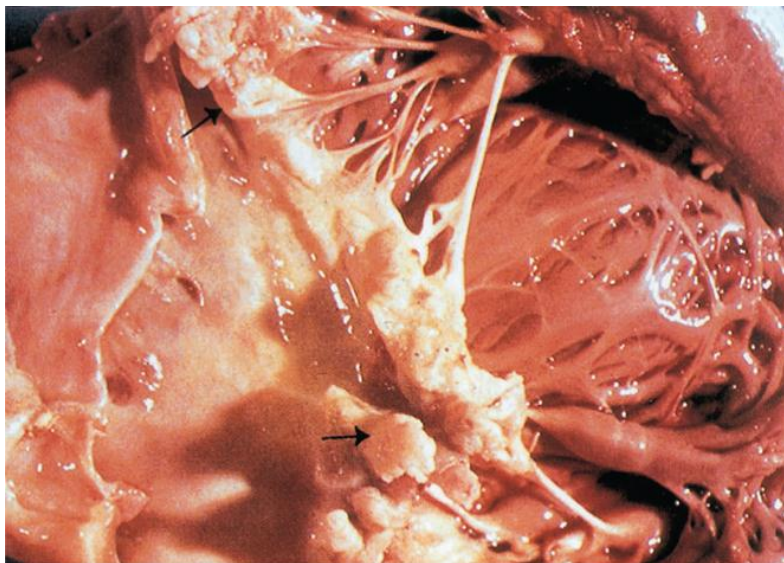
Signs include fever, anemia, and heart murmur.

Infective endocarditis is an infection of the heart chambers or valves



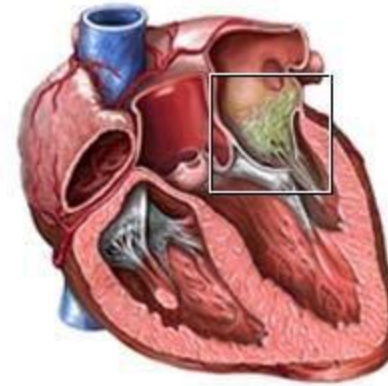
Acute bacterial endocarditis: usually caused by *S. aureus* → rapid destruction of heart valves.

Pericarditis: Streptococci

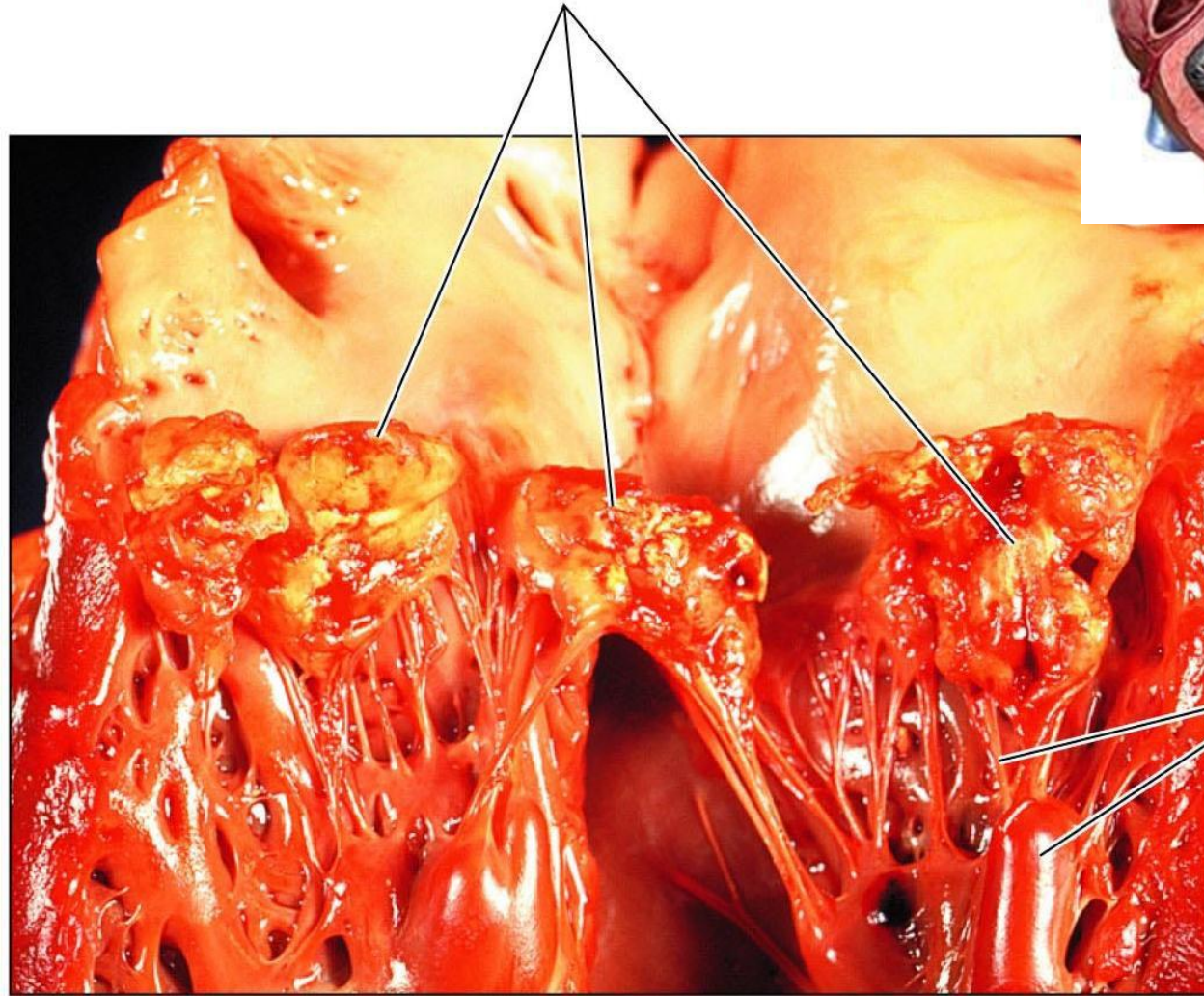


Endocarditis:

Endocarditis



Fibrin-platelet vegetations



Normal
appearance



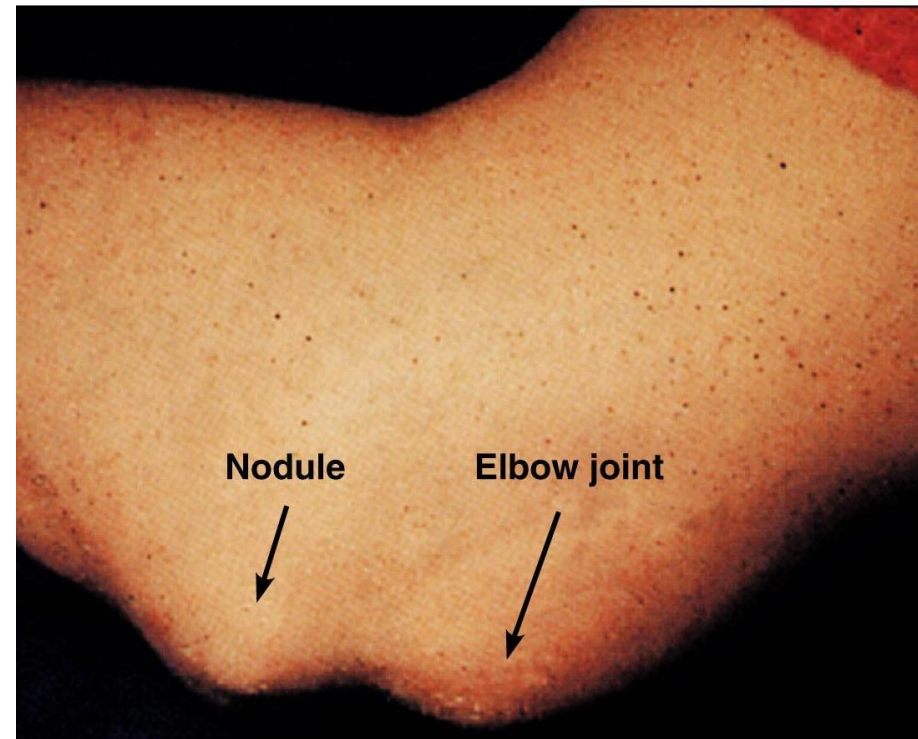
Rheumatic Fever:

Autoimmune complication of *S. pyogenes* infections. Expressed as arthritis or heart inflammation. Can result in permanent heart damage.

Antibodies against group A β -hemolytic streptococci react with streptococcal antigens deposited in joints or heart valves or cross-react with heart tissue.

Rheumatic fever can follow **strep throat**. Bacteria might not be present at time of rheumatic fever.

Prompt treatment of streptococcal infections can reduce the incidence of rheumatic fever.





Tularemia:

“Rabbit fever” caused by
Francisella tularensis

Bacteria reproduce in
phagocytes

Transmitted by bites and scratches of infected animals, carcass handling, tick bites (~ 200 cases/year)

Ulcer at the site of entry and enlargement of the regional lymph nodes → **Ulceroglandular** form (most common, plaguelike)

Aerosol infection → **pneumonic form** (bio weapon!)



Ulceroglandular Tularemia



Girl with ulcerating lymphadenitis colli due to tularemia, Kosovo, April 2000.

Pneumonic tularemia

- May follow ulcero-glandular tularemia
- Can be acquired directly by respiratory route
- Very few organisms can cause the disease (ID_{50} : 1-10 organisms)

High mortality

(30% untreated; <10% when treated)

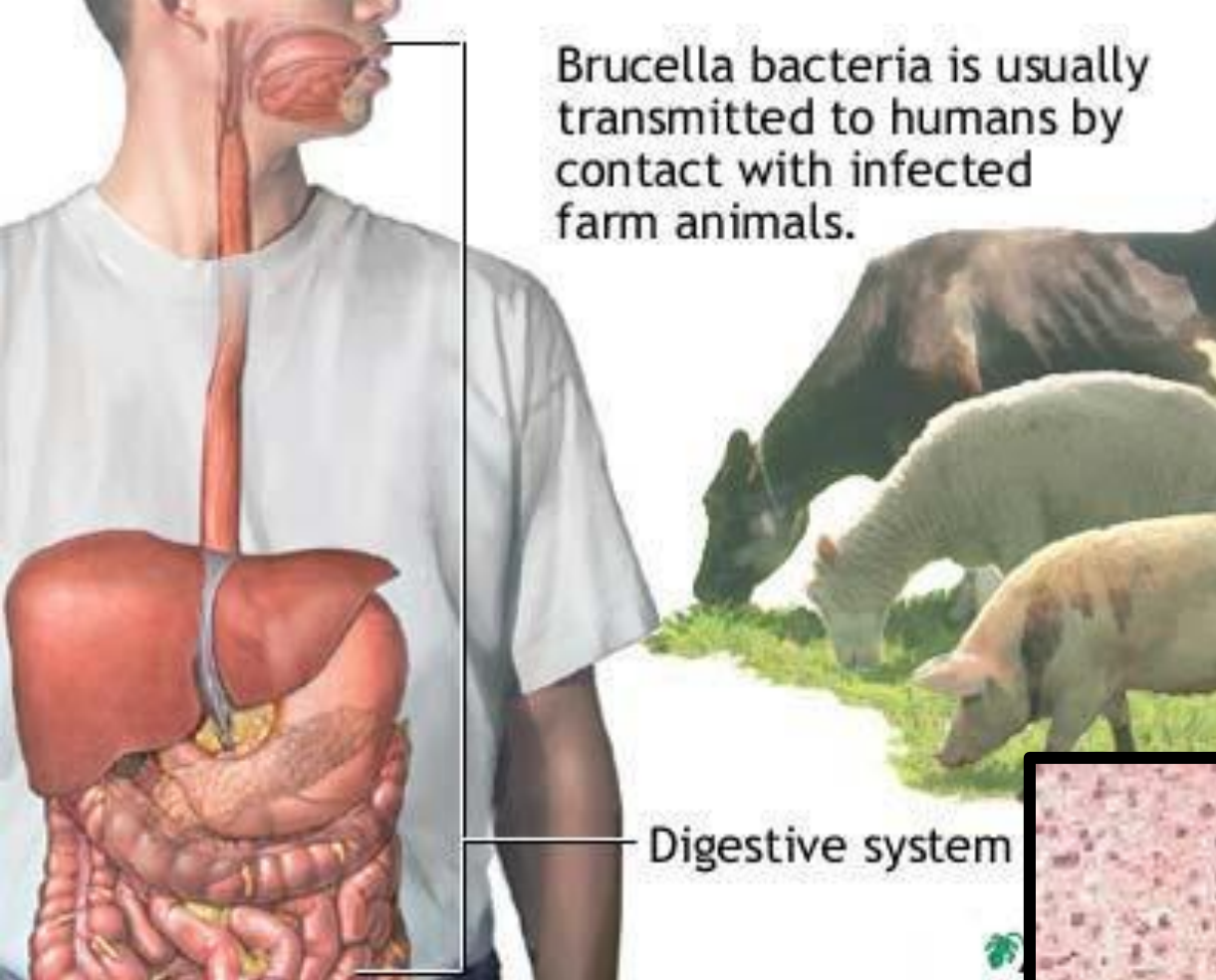


US Armed Forces Institute of Pathology

Brucellosis (Undulant Fever):

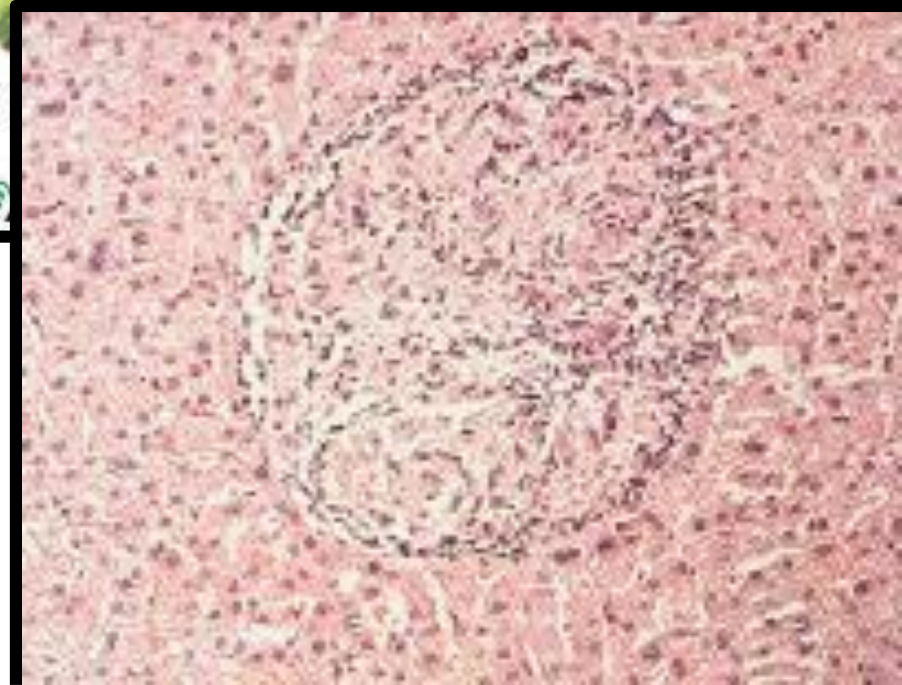
- *B. abortus* (cattle, **elk, bison**), *B. suis* (swine), *B. melitensis* (goats, sheep, camels)
- *Brucella*, gram-negative rods, grow in phagocytes
- Undulating fever spikes to 40°C each evening
- The bacteria enter through minute breaks in the mucosa or skin, reproduce in macrophages, and spread via lymphatics to liver, spleen, or bone marrow.
- Contact with infected animals (slaughterhouse workers, veterinarians, farmers, dairy workers) – also via ingestion of milk or milk products.
100-200 cases/y; worldwide incidence ~ 500,000.
- Mortality rate ~ 2 % (**endocarditis**)

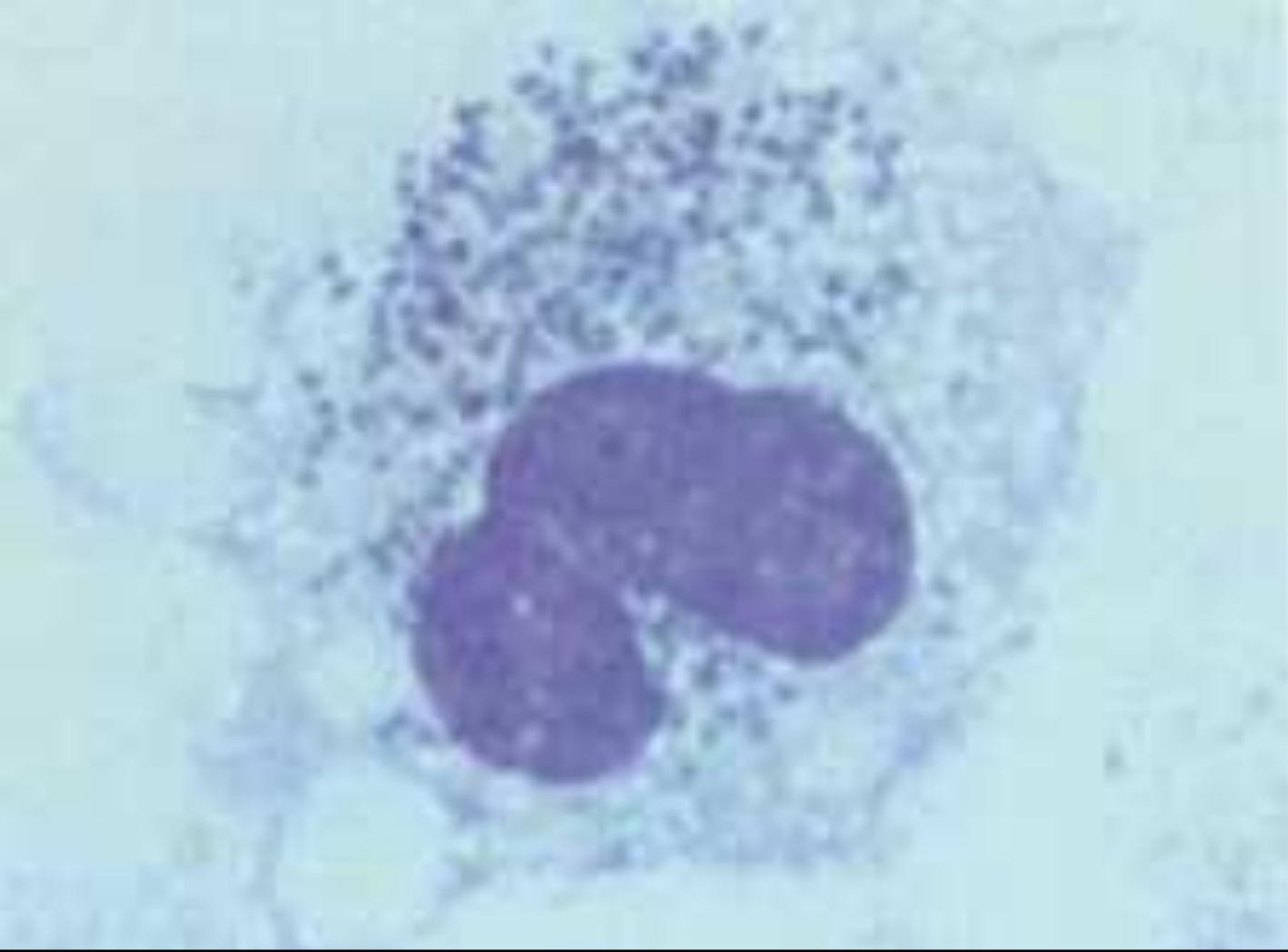
Brucella bacteria is usually transmitted to humans by contact with infected farm animals.



Digestive system

Well-formed hepatic granuloma from a patient with brucellosis





Methylene blue stain: Cultured human macrophage infected with *Brucella melitensis*. coccobacillary bacteria replicate in phagolysosomes (original magnification x 1,000). Photograph: Courtesy of Robert Crawford, Ph.D., Senior Scientist, American Registry of Pathology, Washington, DC.



Anthrax:

Bacillus anthracis G+ rod, ES, aerobic,
virulence factors: capsule, 3 exotoxins

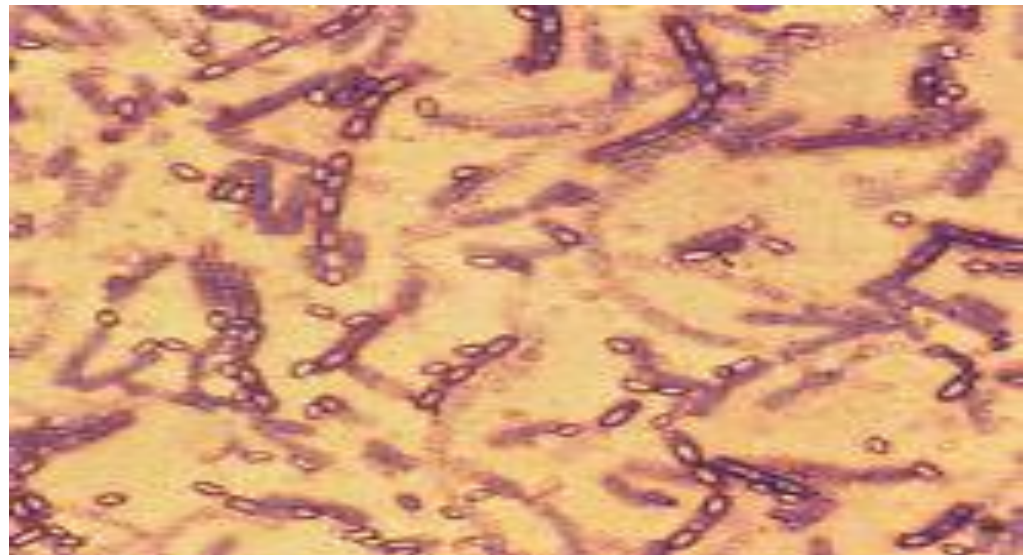
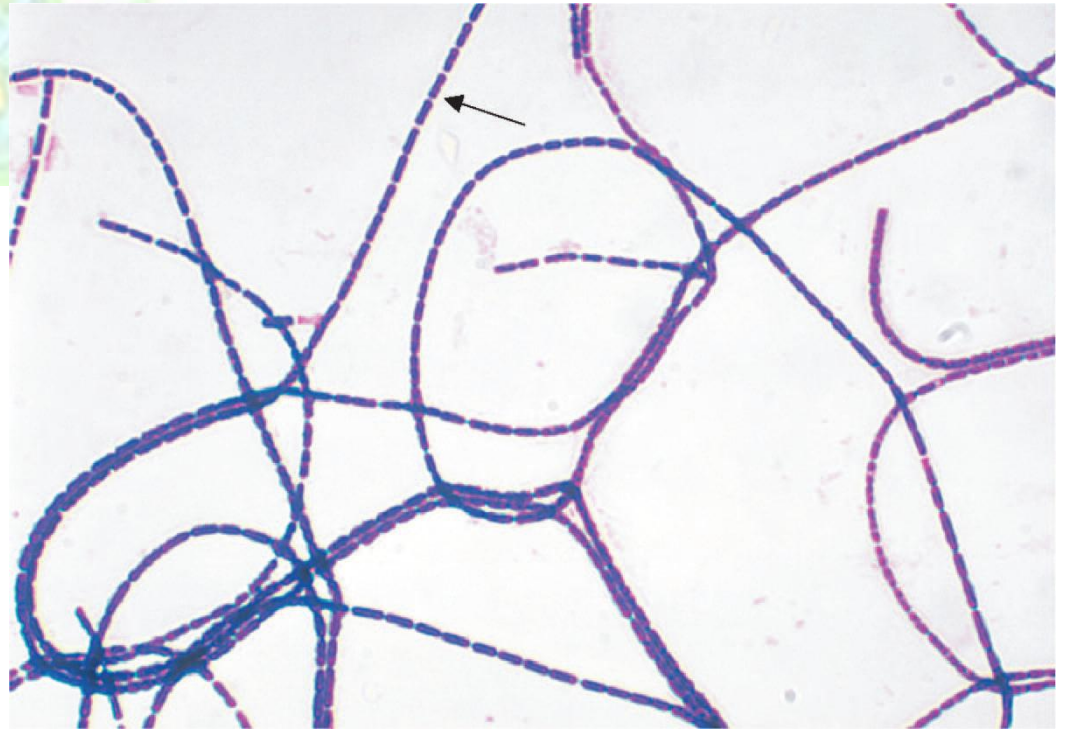
Zoonosis; found in soil

Cattle routinely vaccinated

In human:

- **Pulmonary anthrax** (wool sorter's disease),
Inhalation of endospores; 100% mortality
- **Cutaneous anthrax**, most common, endospores
enter through minor cut; 20% mortality
- **Gastrointestinal anthrax**: Ingestion of
undercooked contaminated food; 50% mortality

Treated with ciprofloxacin or doxycycline



Bacillus anthracis



Bacillus anthracis infects mostly farm animals and is usually spread to humans through a break in the skin

Cutaneous anthrax



Vesicular Papule at the site of infection



Blue black edema



Cutaneous anthrax



Rupture of papule
will reveal a black
eschar (malignant
pustule)



Cutaneous anthrax



(Malignant pustule)

Inhalation Anthrax



Spore inhalation and phagocytosis



Germination, replicate and infection of hilar lymph nodes

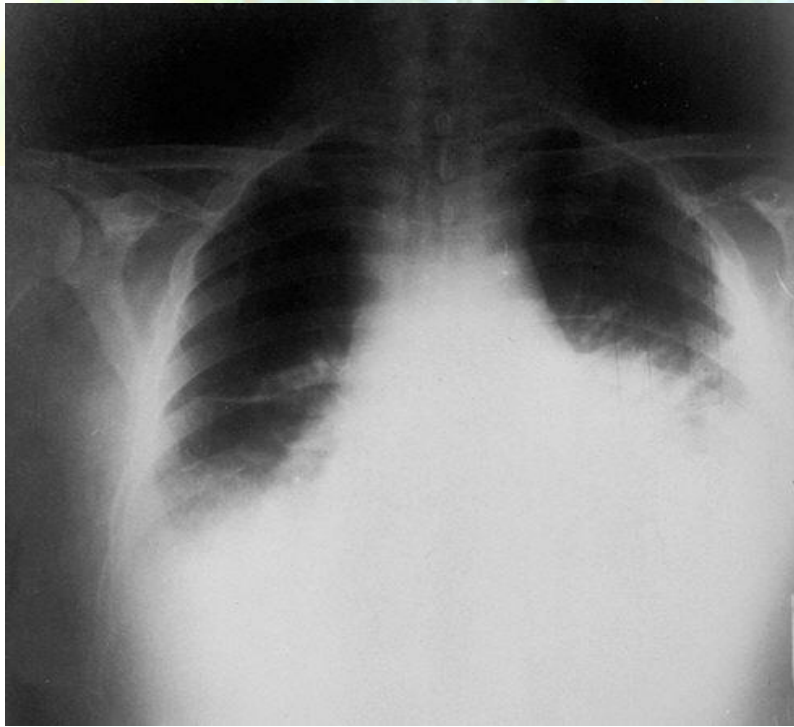


Hemorrhagic necrosis of lymph nodes

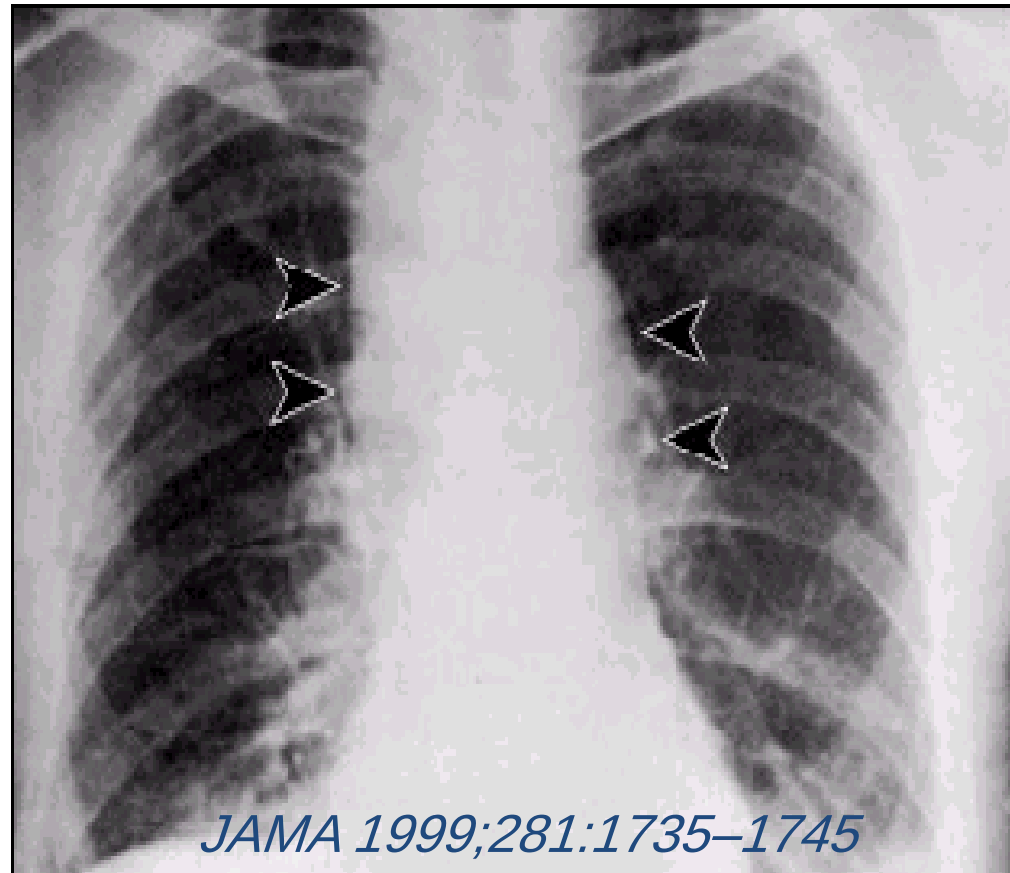


Fever, malaise, myalgia, and non-productive cough

Abrupt onset respiratory failure (1-2 d later)



**- Inhalation anthrax
demonstrating enlarged
mediastinal lymph nodes**



Gastrointestinal Anthrax



Ingestion of infected meat



Proliferation within the GI tract



Fever, acute abdomen, vomiting, bloody diarrhea



Intestinal eschar (similar to cutaneous lesion)

Spreads to mesenteric lymph nodes,
septicemia, shock and death

Gas Gangrene (Clostridial Myonecrosis):

Gangrene: Soft tissue death from ischemia $\Rightarrow$ especially susceptible to growth of anaerobic bacteria such as:

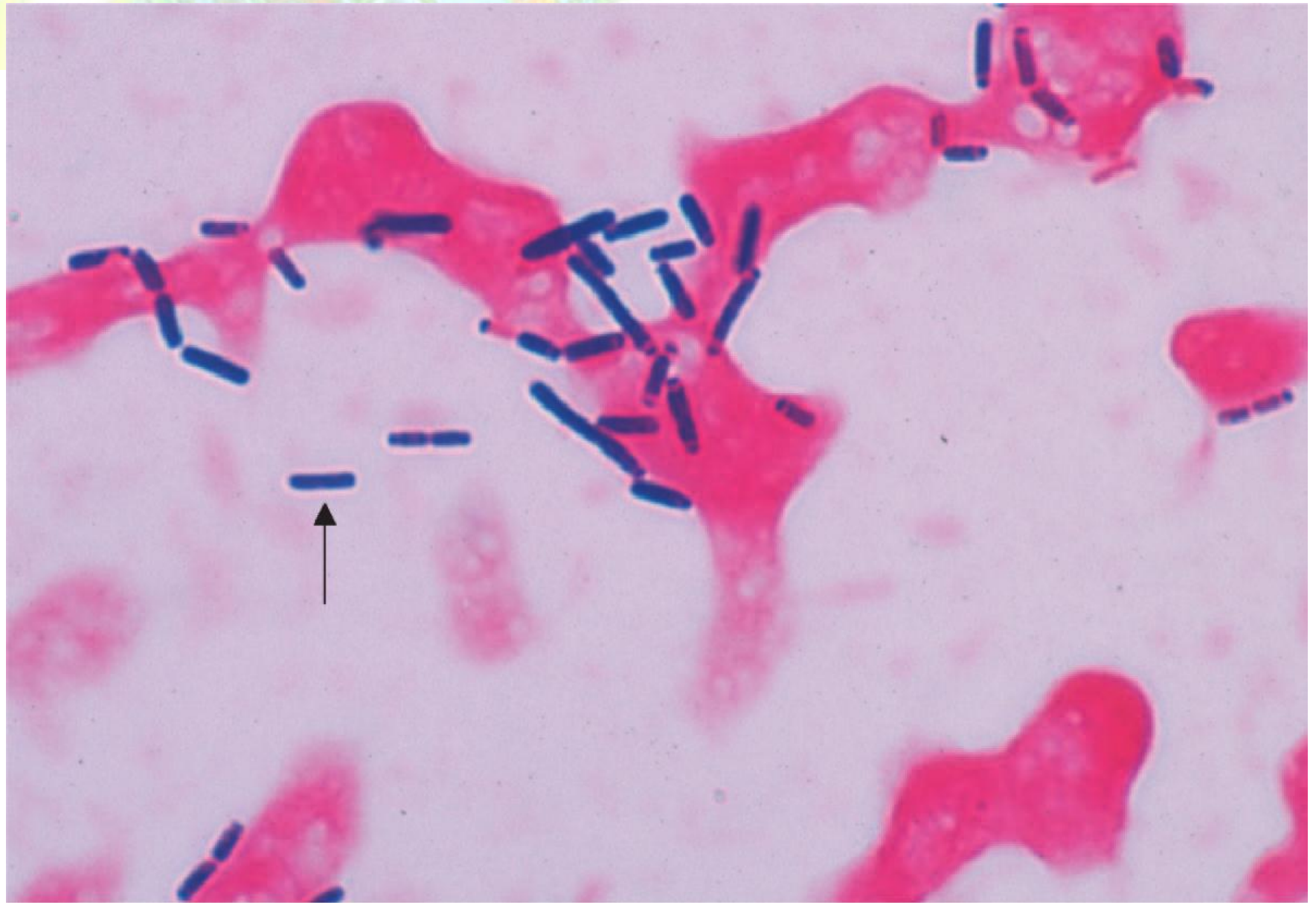
C. perfringens, G+ rod, ES, anaerobic, release of α toxin (cytotoxic), H_2 and CO_2

Ubiquitous in soil and dust – “war disease”

C. perfringens can invade the wall of the uterus during improperly performed abortions

Death due to toxemia

Treatment: debridement and amputation – hyperbaric chamber; antibiotics and antitoxin of limited value.

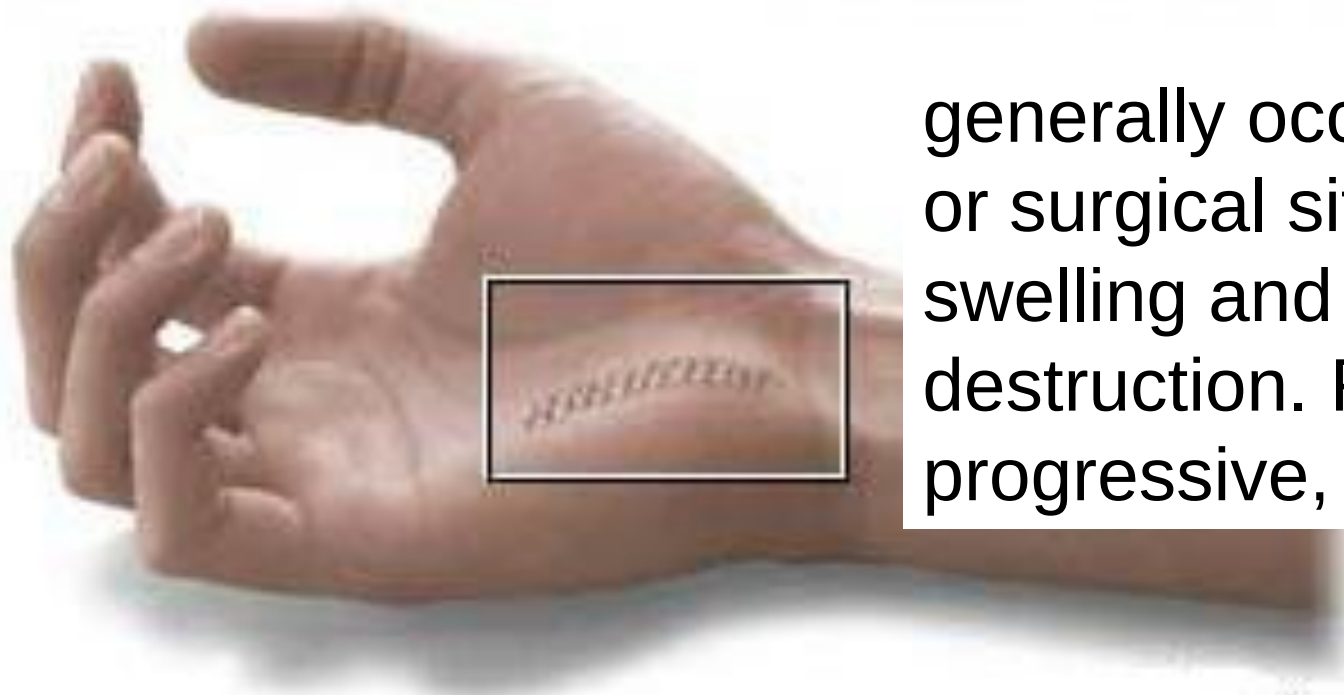




Clean wound



Gangrenous wound



generally occurs at wound or surgical site → painful swelling and tissue destruction. Rapidly progressive, often fatal.

Clinical Findings

- Pain, edema, and cellulitis
- Hemolysis and jaundice
- Shock and death may occur





Animal Bites and Scratches:

Anaerobic bacteria infect deep animal bites

Pasteurella multocida – normal flora of oral and nasopharyngeal cavity of **dogs** and **cats**; may cause septicemia

Bartonella henselae – (rickettsia) **Cat scratch disease**. Relatively common (~20,000 cases in US) – mostly in young – occasionally serious

Human bites – (not in book) normal mouth flora (incl. *S. aureus*, α hemolytic *S. viridans*, *H. influenzae* and various anaerobes)



Pasteurella multocida

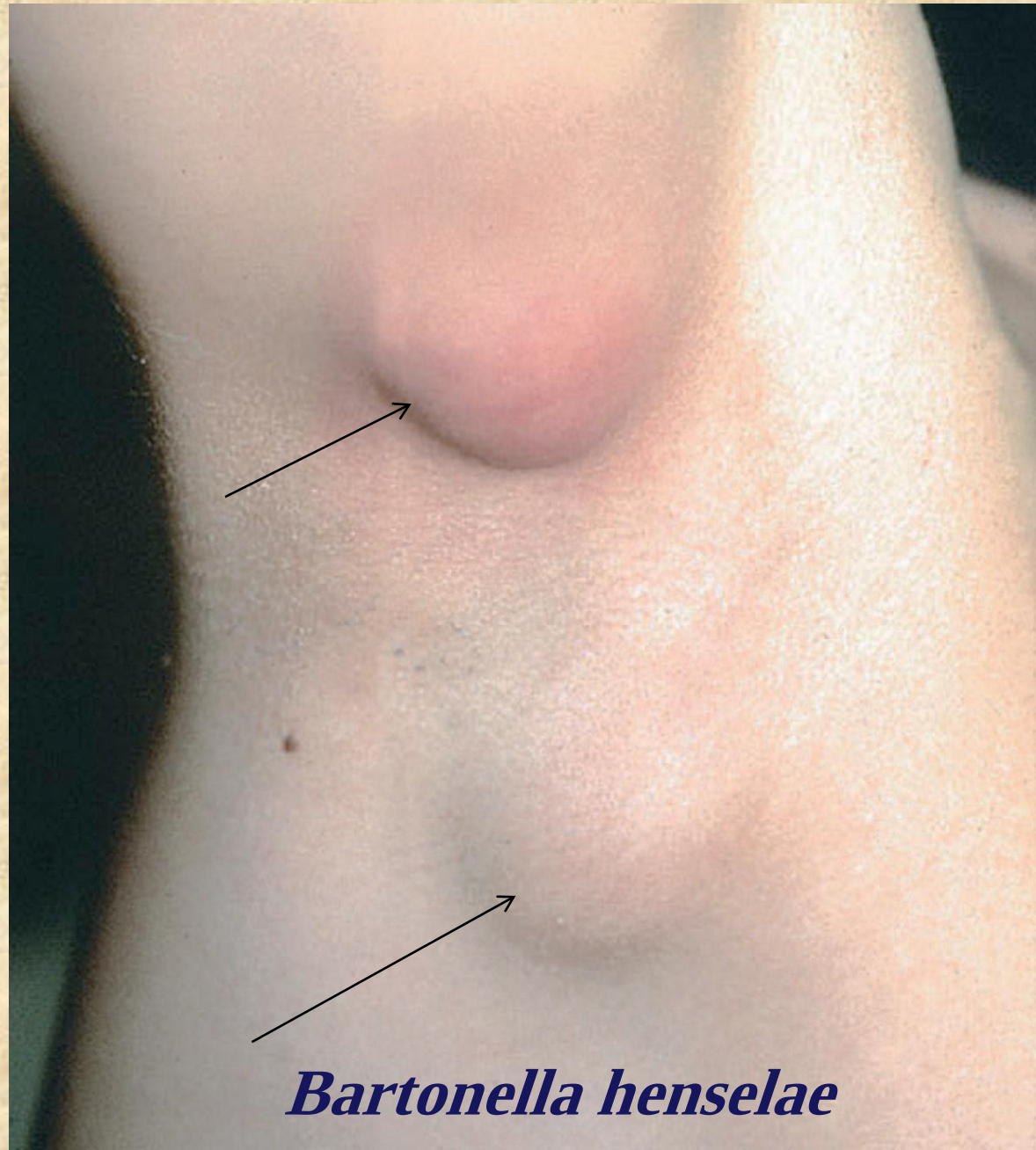
- Causes wound infections (cellulitis) associated with cat and dog bites
- Short, nonmotile, encapsulated, Gr-ve rod, with bipolar staining
- Normal flora in mouth of domestic animals
- Infections are polymicrobial
- Pathogenesis? Capsule & Endotoxin

BARTONELLA

- *Bartonella henselae* is the cause of cat-scratch disease
- Small, pleomorphic gram-negative rod, fastidious organism
- Transmitted by cat scratches or bites (kittens)
- Fever and tender, enlarged lymph nodes
- Systemic disease, as endocarditis or encephalitis is rare
- Diagnosis: Serology
- **No antibiotic** therapy is typically recommended and there is
no vaccine

Cat-scratch disease.

Note the two
enlarged, inflamed
axillary lymph
nodes



Bartonella henselae

B. *Vector-Transmitted Diseases*

- **Plague**
- Relapsing Fever
- **Lyme Disease**
- Ehrlichiosis
- Typhus
- Epidemic Typhus
- **Spotted Fevers**

Plague

“Black death”: *Yersinia pestis*,
G- rod, bipolar staining

Endemic in Southwest → sylvatic
plague

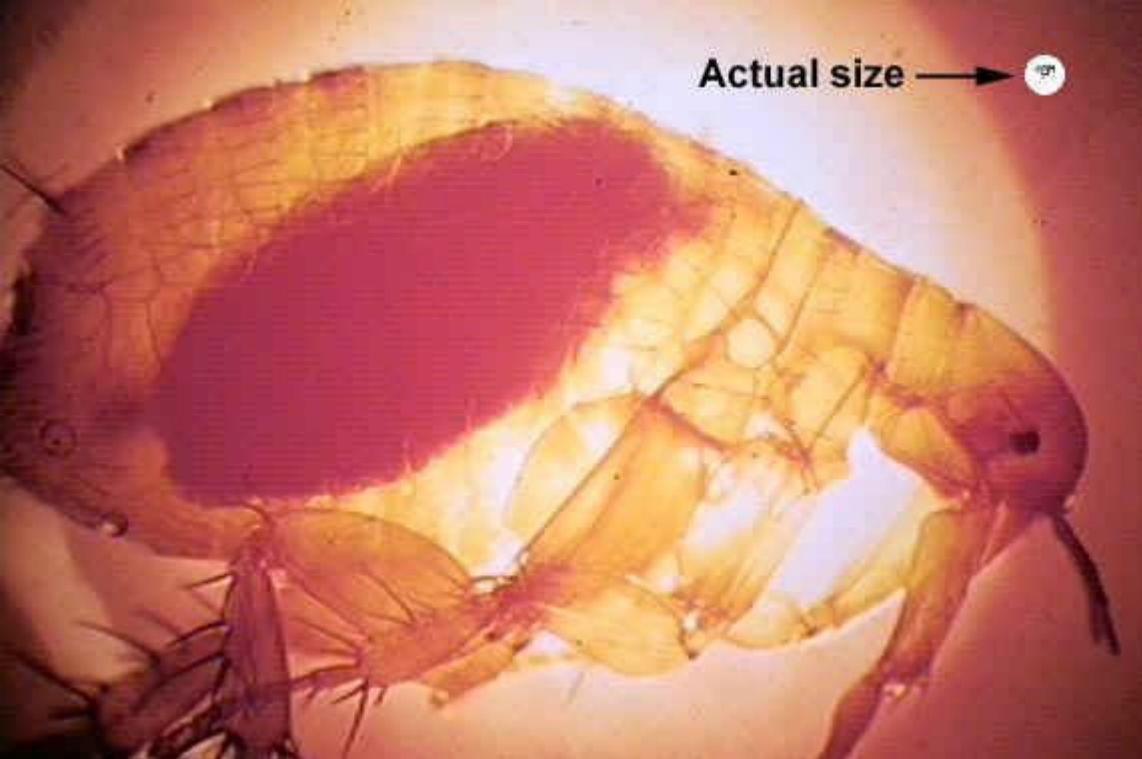
Reservoir: Rats, ground
squirrels, and prairie dogs

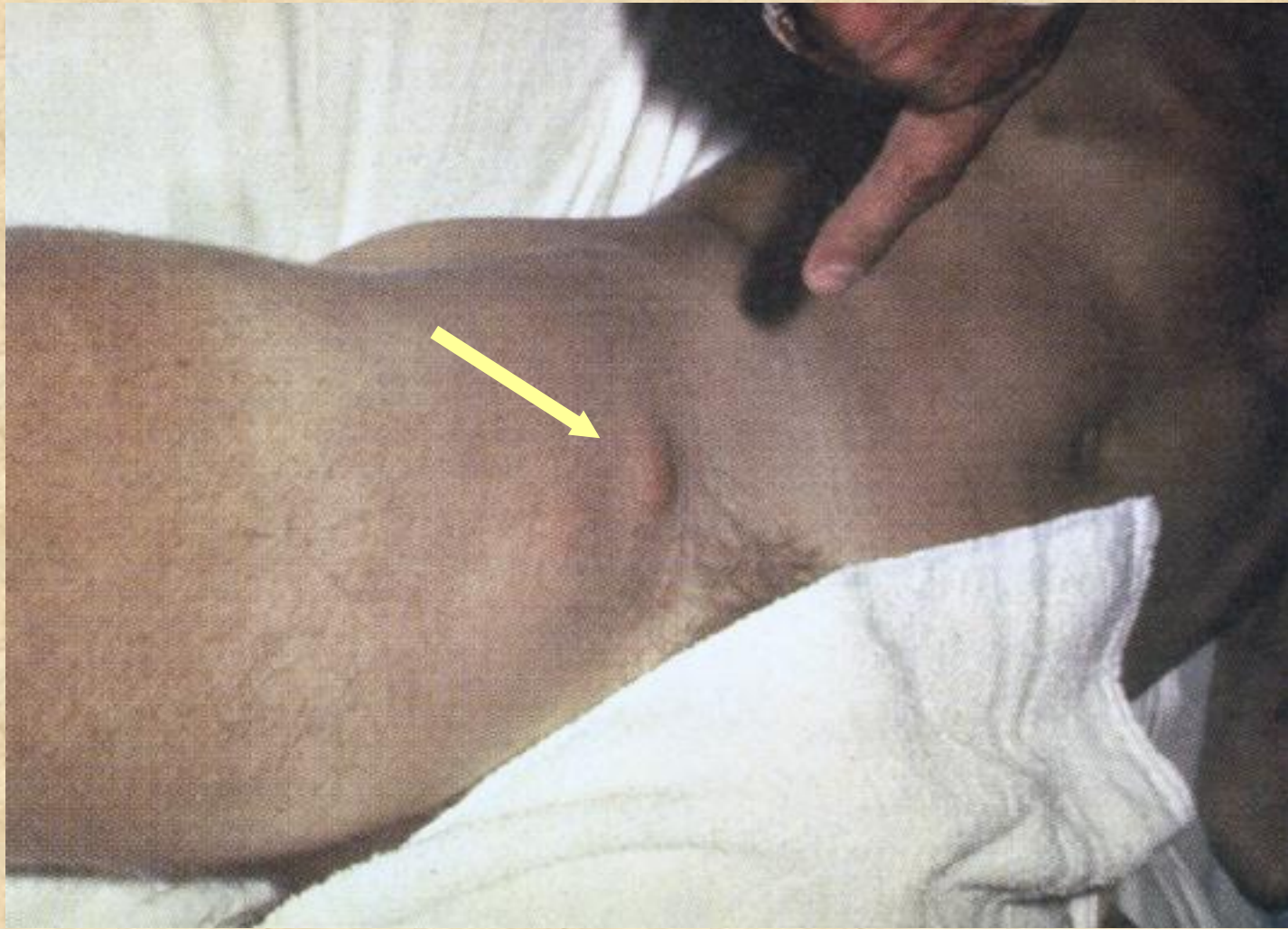
Vector: infected fleas

- **Bubonic plague:**
Bacterial growth in blood
and lymph
- **Septicemia plague:**
Septic shock
- **Pneumonic plague:**
Bacteria in the lungs



15th Century Plague
Physician

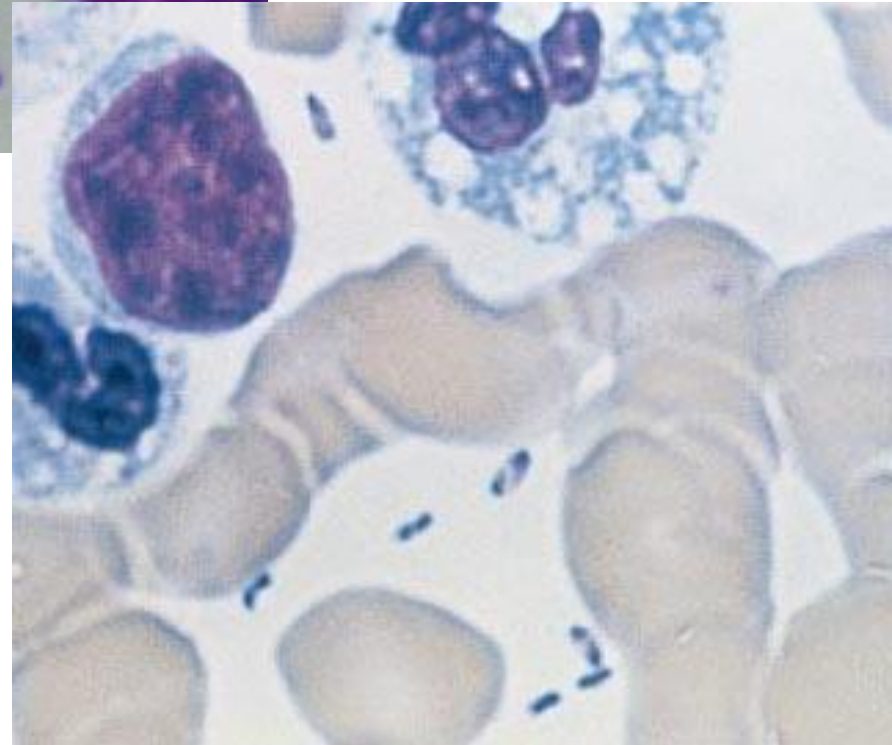




Swollen lymph glands (buboes) caused by plague bacteria in bubonic plague



Bipolar staining:
Dark stained **bipolar** ends in
Wright's stain (blood from
plague victim)



(CDC Public Health Image Library)

The different forms of plague



Sylvatic

-  In animals (rodents, rabbits, carnivores) only “wild animals”
-  Or urban cycle among urban rats



Bubonic

-  Flea (bite) to humans



Pneumonic

-  Human (aerosol) to human

Lyme Disease:

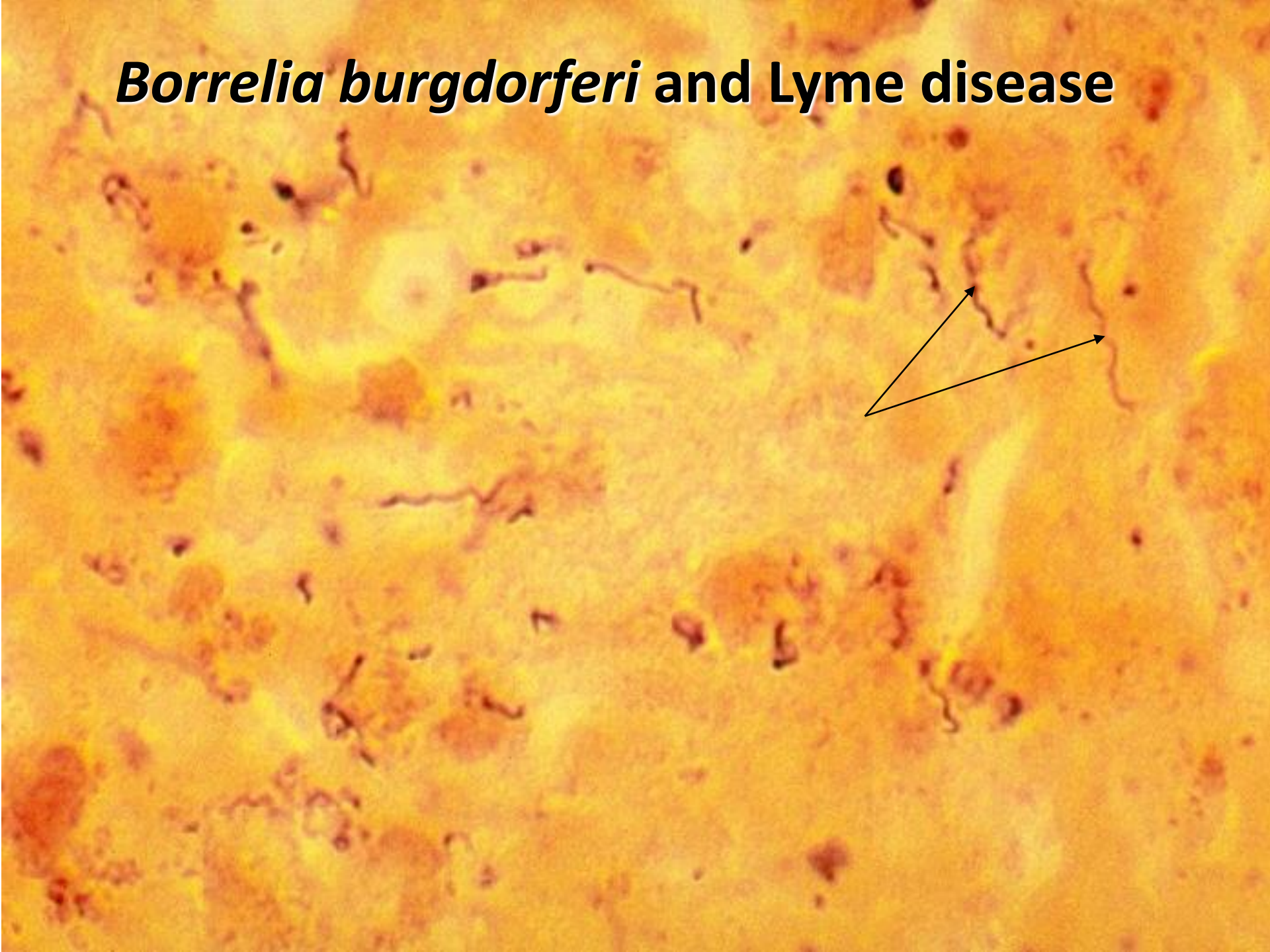
Zoonosis caused by *Borrelia burgdorferi*

Reservoir: mice, deer; Vector: *Ixodes* ticks

3 stages with various symptoms

1. **Early localized stage:** Bull's eye rash = erythema (chronicum) migrans ECM; flu-like symptoms
2. **Early disseminated stage:** Heart and Nervous system symptoms; also skin and joints affected
3. **Late stage:** Chronic arthritis

***Borrelia burgdorferi* and Lyme disease**



Ixodes scapularis / pacificus

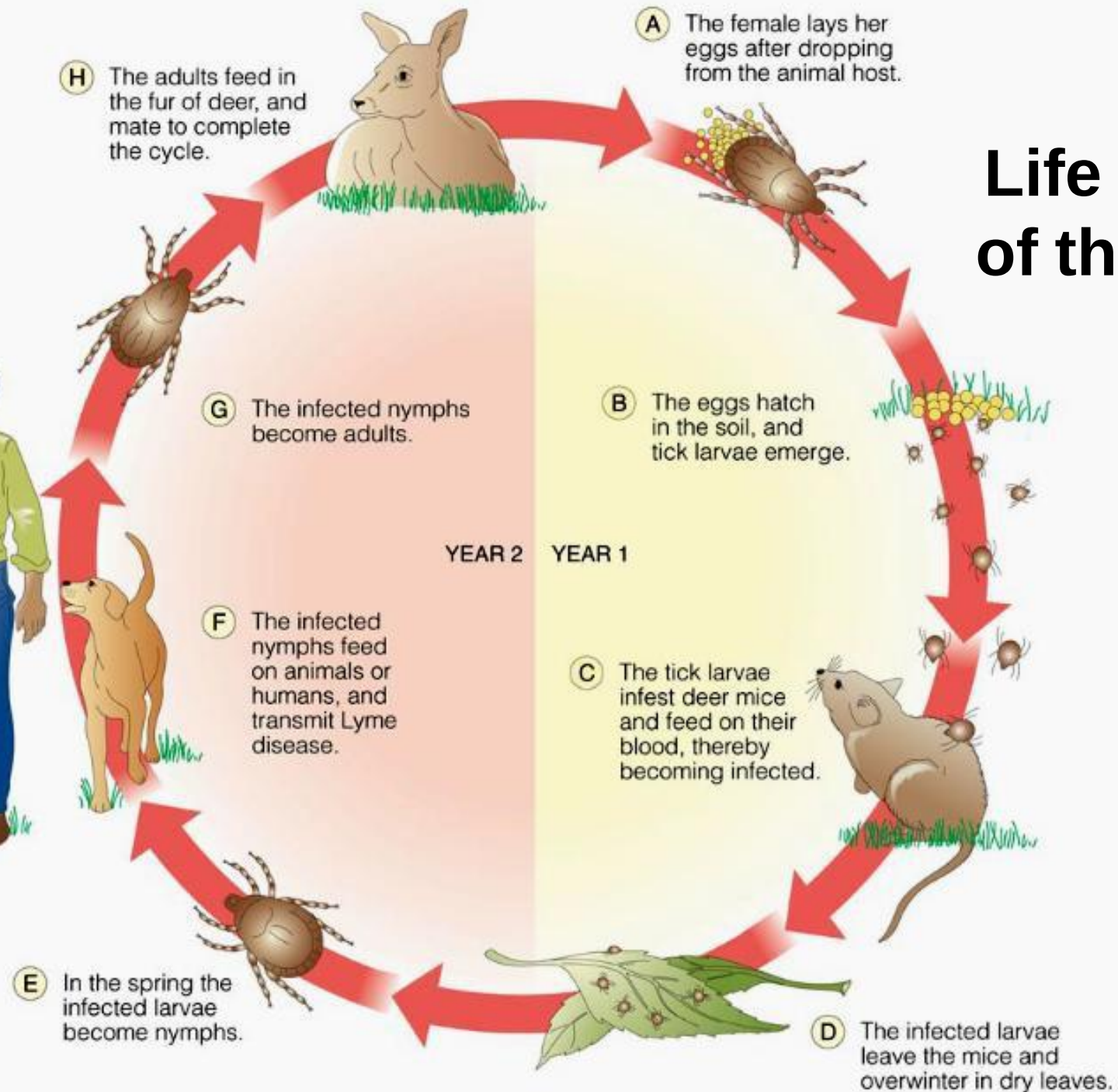


Lyme Disease



**Erythema
chronicum migrans**

Life Cycle of the Tick





Diagnosis:

- **Symptoms alone:** often misdiagnosis
- In most cases not possible to isolate and culture *B. burgdorferi* → **indirect serological tests** (tolb nretseW dna ASILE)
- **PCR**

Prevention

Treatment in early stages! (Doxycycline)

Borrelia recurrentis & *B. burgdorferi*

- Relapsing fever transmitted by human lice (endemic areas)
- *B. burgdorferi* – Lyme Disease
Ixodes tick vector
- Large spirochetes (~ 3x larger)
- Giemsa or Wright's blood stains
- Blood, CSF, skin lesion samples



Borrelia recurrentis

- Antigenic variation during a single infection results in repeated fevers
- Incubation 3-10 days
- Afebrile periods 4-10 days
- Recovery after 3-10 relapses due to persistent protective Ab to multiple antigenic variants
- Fatalities assoc. with liver/spleen localization



Ehrlichiosis:

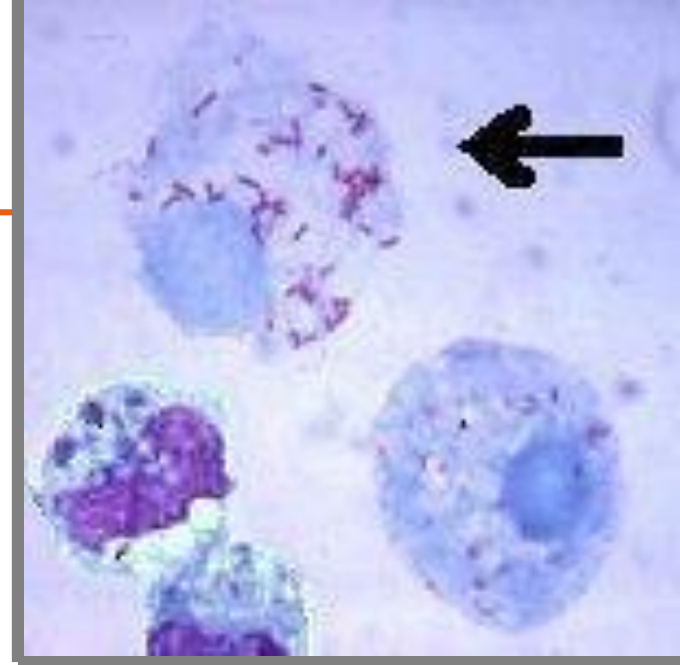
First described in 1986

Caused by *Ehrlichia* species and transmitted by *Ixodes* ticks – diseases of animals and humans

Obligately intracellular (in white blood cells)

- **Monocytic Ehrlichiosis (HME)**
- **granulocytic Ehrlichiosis (HGE)**

Nonspecific symptoms (similar to other diseases)



Lyme Disease, Ehrlichiosis and Anaplasmosis

Female tick



Male tick



Avoid tick
bites by wearing
proper clothing

Ehrlichiosis is a tick-borne bacterial infection, caused by bacteria of the family Anaplasmataceae, genera Ehrlichia and Anaplasma. These obligate intracellular bacteria infect and kill white blood cells

Rocky Mountain Spotted Fever (RMSF):

- *Rickettsia rickettsii*
- Zoonosis –
- Reservoir: mammals
- Vector: ticks
- Characteristic hemorrhagic rash – maculopapular – starts on palms and soles (unlike measles!)
- Can damage vital organs



Rocky Mountain Spotted Fever:

- Acute onset of non-specific symptoms as fever, severe headache
- Typical rash
- In severe cases, DIC & edema
- Caused by *R. rickettsii* (dog tick)
- It can be fatal if untreated



Spotted Fevers (*Rocky Mountain spotted fever*)

Rickettsia rickettsii

Measles-like rash except
that the rash appears on
palms and **soles** too



Rocky Mountain Wood Tick (*Dermacentor andersoni*)



Typhus:

- Louse-borne epidemic typhus (*R. prowazekii*)
- Flea-borne endemic typhus (*R. typhi*)
- Scrub typhus (*R. tsutsugamushi*)
- Sudden onset of chills, fever, headache (like influenza)
- Maculopapular rash (start on trunk)
- Severe meningoencephalitis may occurs
- Death in untreated cases (vascular collapse)
- Transmitted by human body louse (*Pediculus*)
- No louse-to-lice transmission



Treatment

- Prompt treatment is necessary since morbidity and mortality increases if treatment is delayed
- DOC is tetracycline
- 2nd DOC is chloramphenicol

Prevention

- Reducing exposure to the arthropod vector
- Personal hygiene and „delousing“ with DDT.
(*dichlorodiphenyltrichloroethane*)
- Typhus vaccine is available (*military*)
- Q fever vaccine (*high risk group*)