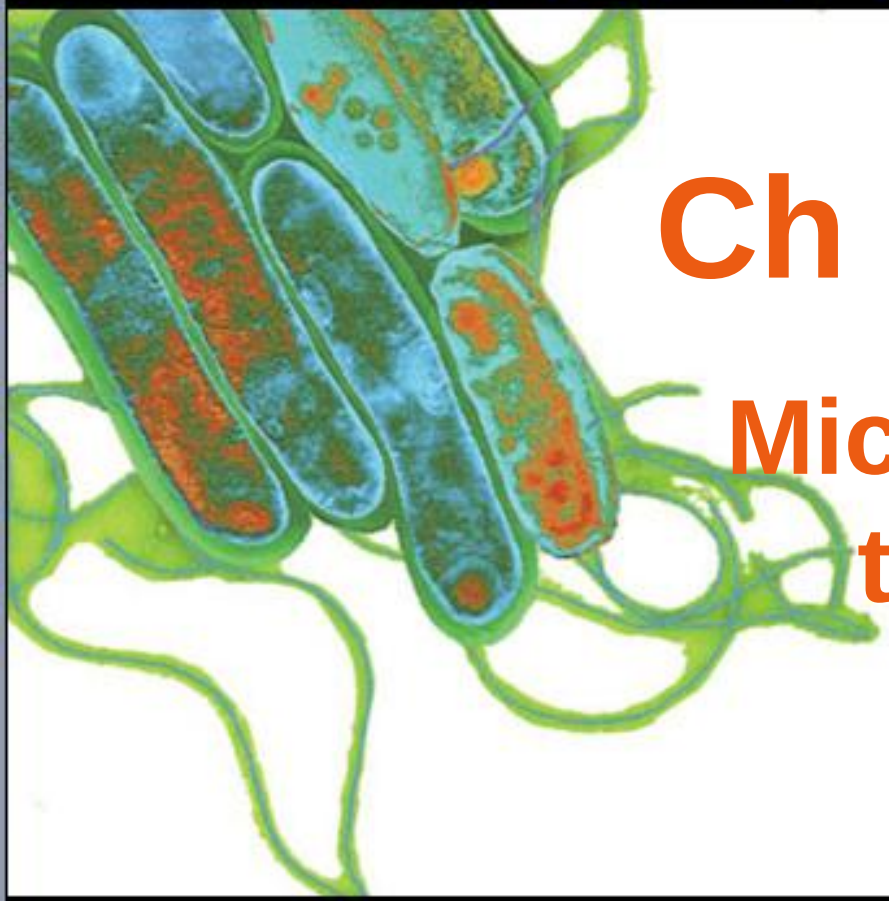
ninth edition

TORTORA | FUNKE | CASE

MICROBIOLOGY

an introduction



Ch 23

Microbial Diseases of the Cardiovascular and Lymphatic Systems

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.

Compare and contrast the causative agents, modes of transmission, reservoirs, symptoms, and treatments for Chagas' disease, toxoplasmosis, malaria, and babesiosis.

Describe Swimmer's Itch

Sepsis and Septic Shock

Sepsis: SIRS caused by spread of bacteria or their toxin from a focus of infection.

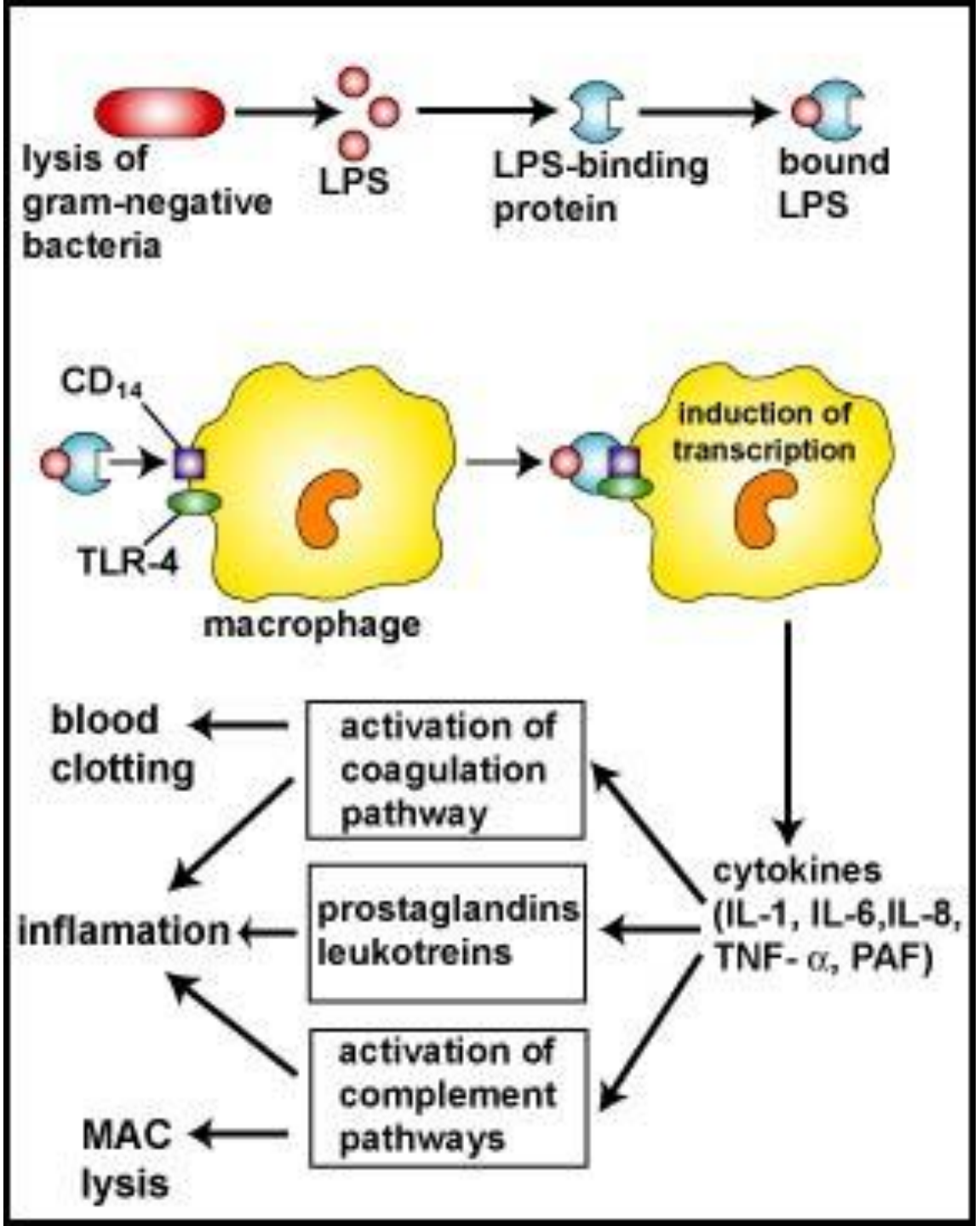
Septicemia: Sepsis involving proliferation of pathogens in the blood.

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

Antibiotic-resistant enterococci 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


lysis of gram-negative bacteria
LPS
LPS-binding protein
bound LPS
CD14
TLR-4
macrophage
induction of transcription
blood clotting
activation of coagulation pathway
inflamation
prostaglandins leukotreins
cytokines (IL-1, IL-6,IL-8, TNF- α, PAF)
activation of complement pathways
MAC lysis

Bacterial Infections of the Cardiovascular and Lymphatic Systems

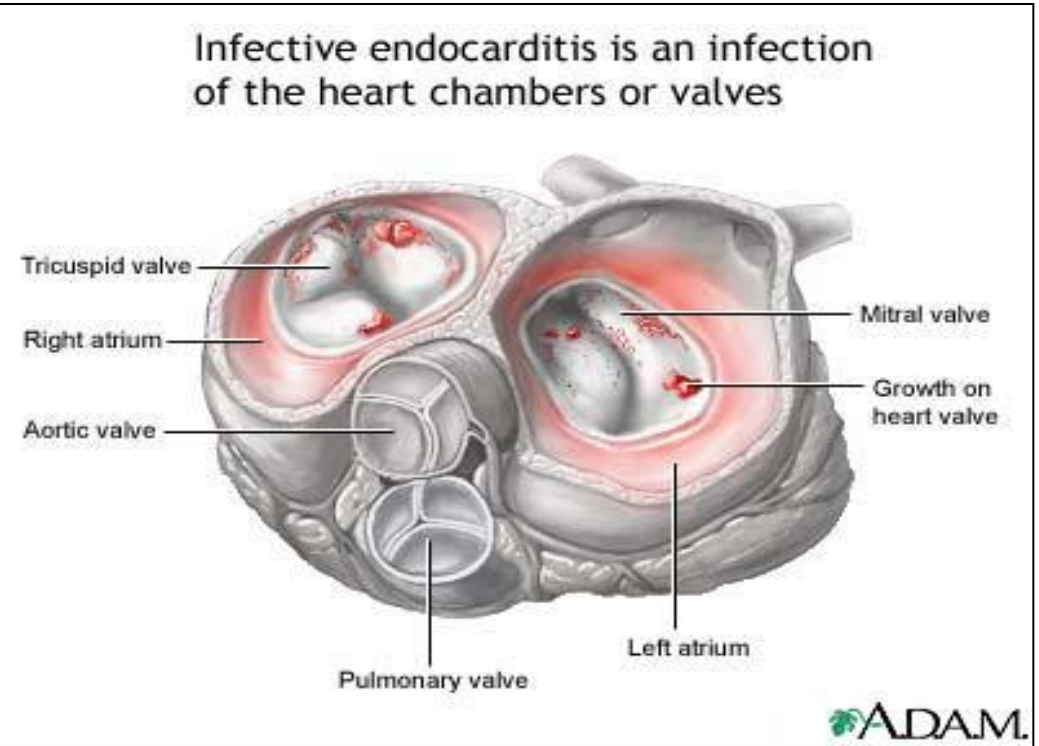
- Subacute Bacterial Endocarditis
- Rheumatic Fever
- Tularemia
- Brucellosis
- Anthrax
- Gas Gangrene
- Bite Wounds

Subacute Bacterial Endocarditis:

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

Preexisting heart abnormalities are predisposing factors.

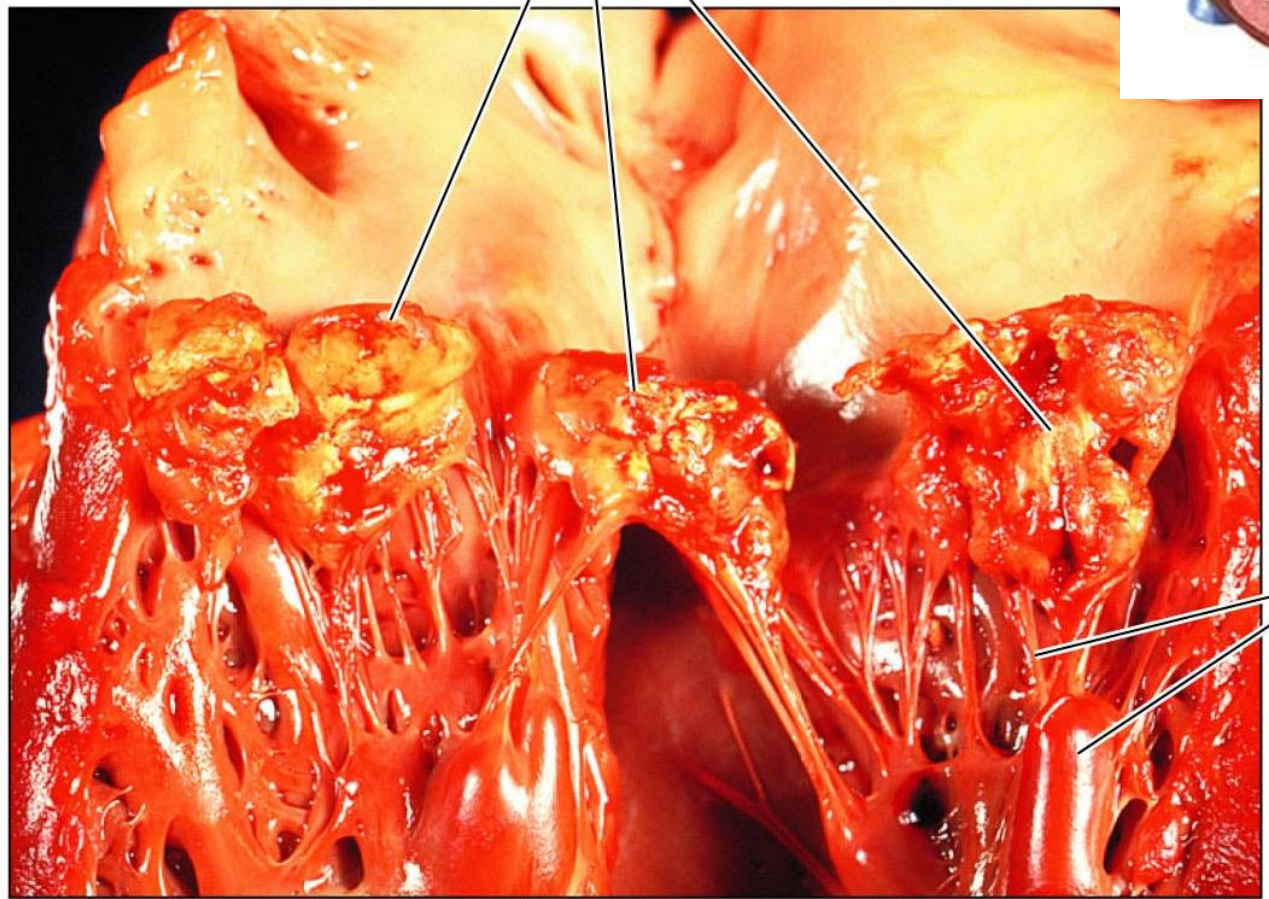
Signs include fever, anemia, and heart murmur.



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

Pericarditis: Streptococci

Endocarditis



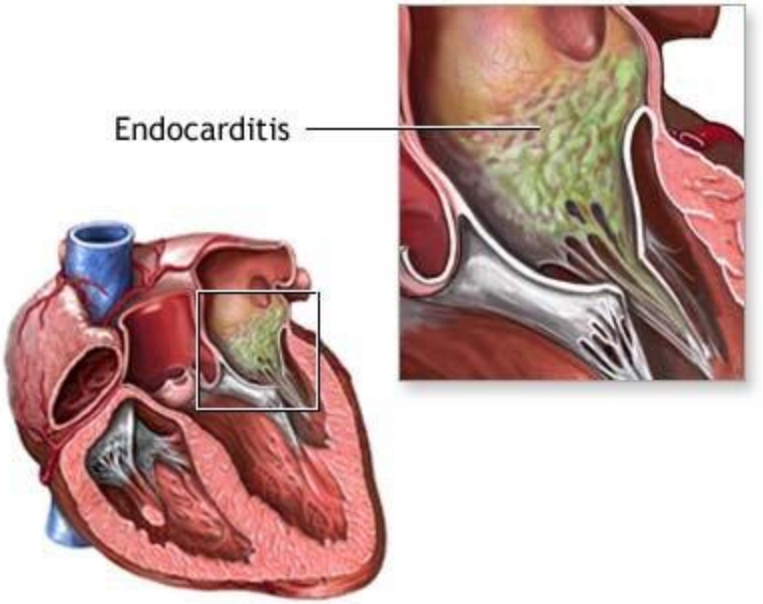


Fig 23.4

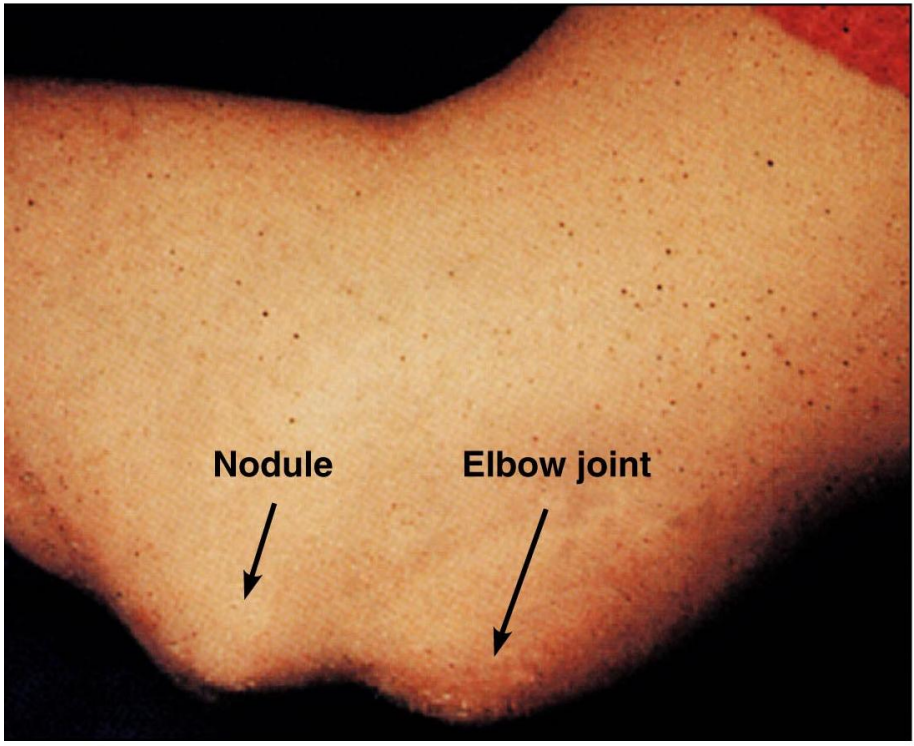
Rheumatic Fever

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

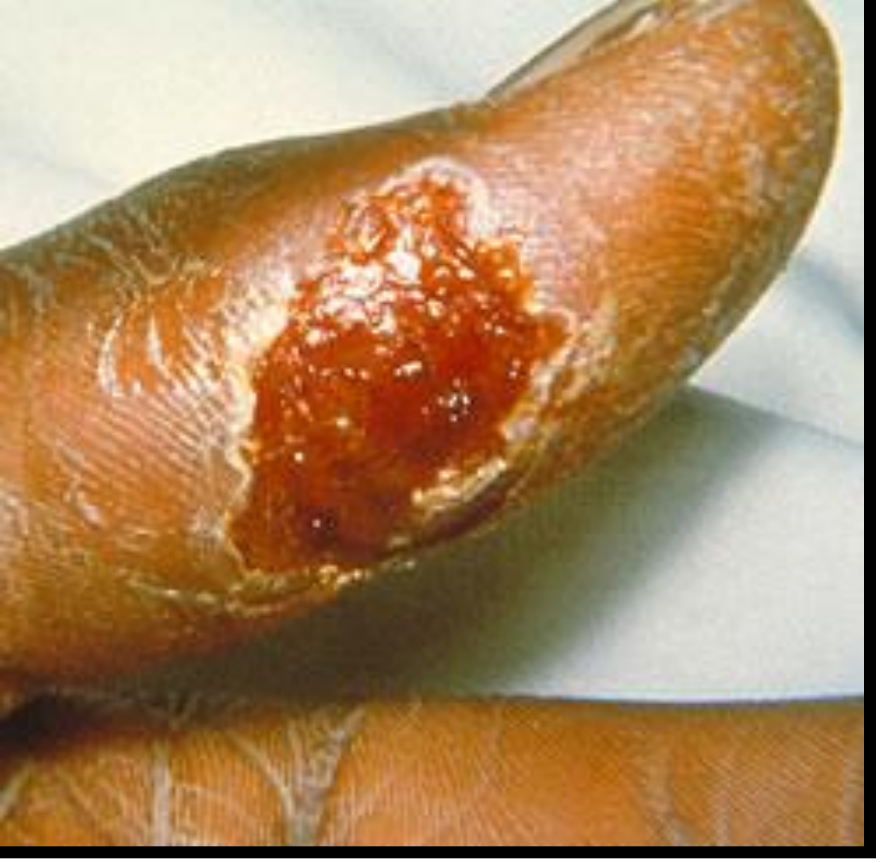
"Rabbit fever" caused by *Francisella tularensis*

Bacteria reproduce in phagocytes

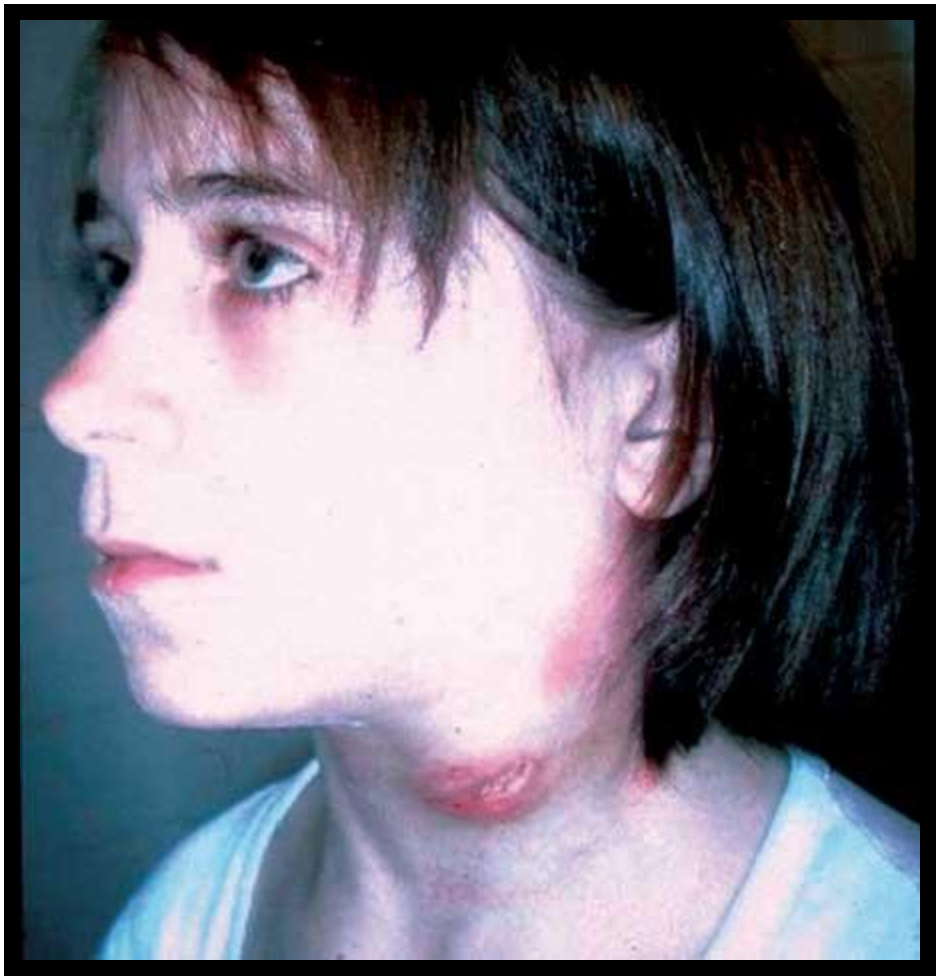
Transmitted by bites and scratches of infected animals, carcass handling, tick bites (~ 200 cases/year)

Ulcer at the site of entry and enlargement of the regional lymph nodes → Ulcero-glandular form (most common, plaguelike)

Aerosol infection → pneumonic form (bio weapon!)

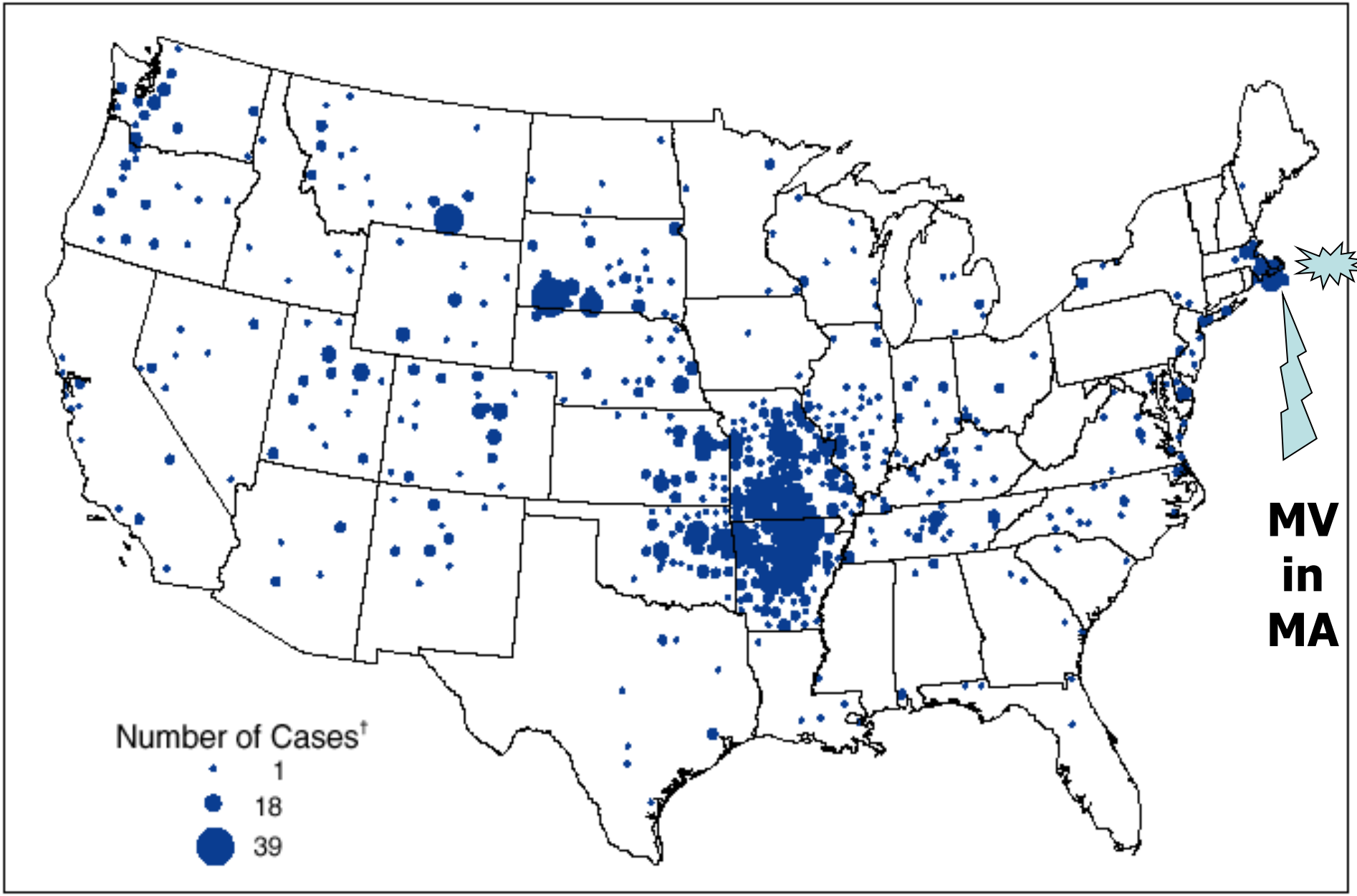


Ulceroglandular Tularemia



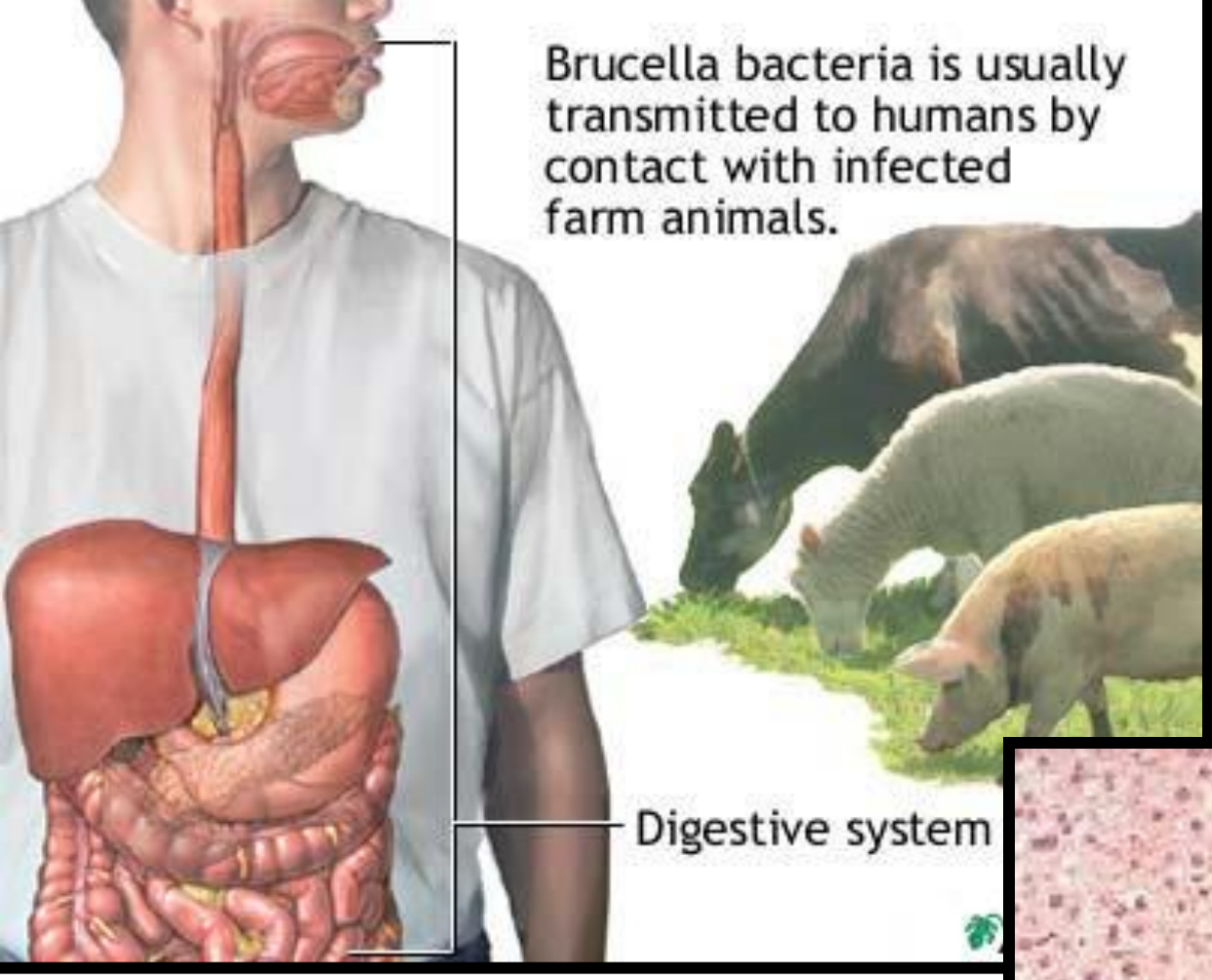
Girl with ulcerating lymphadenitis colli due to tularemia, Kosovo, April 2000.

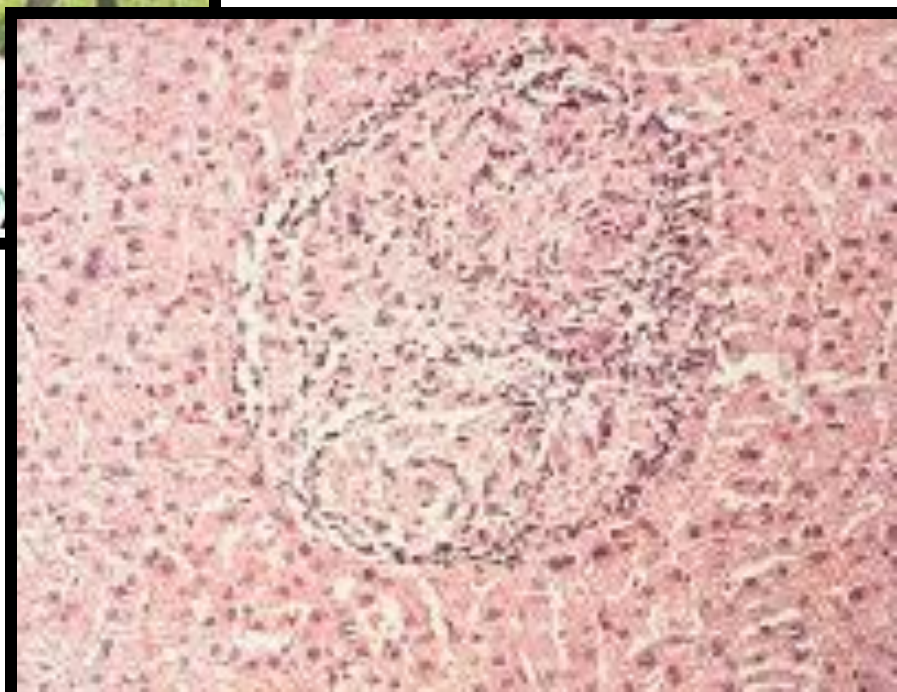
FIGURE 2. Reported cases* of tularemia — United States, 1990–2000



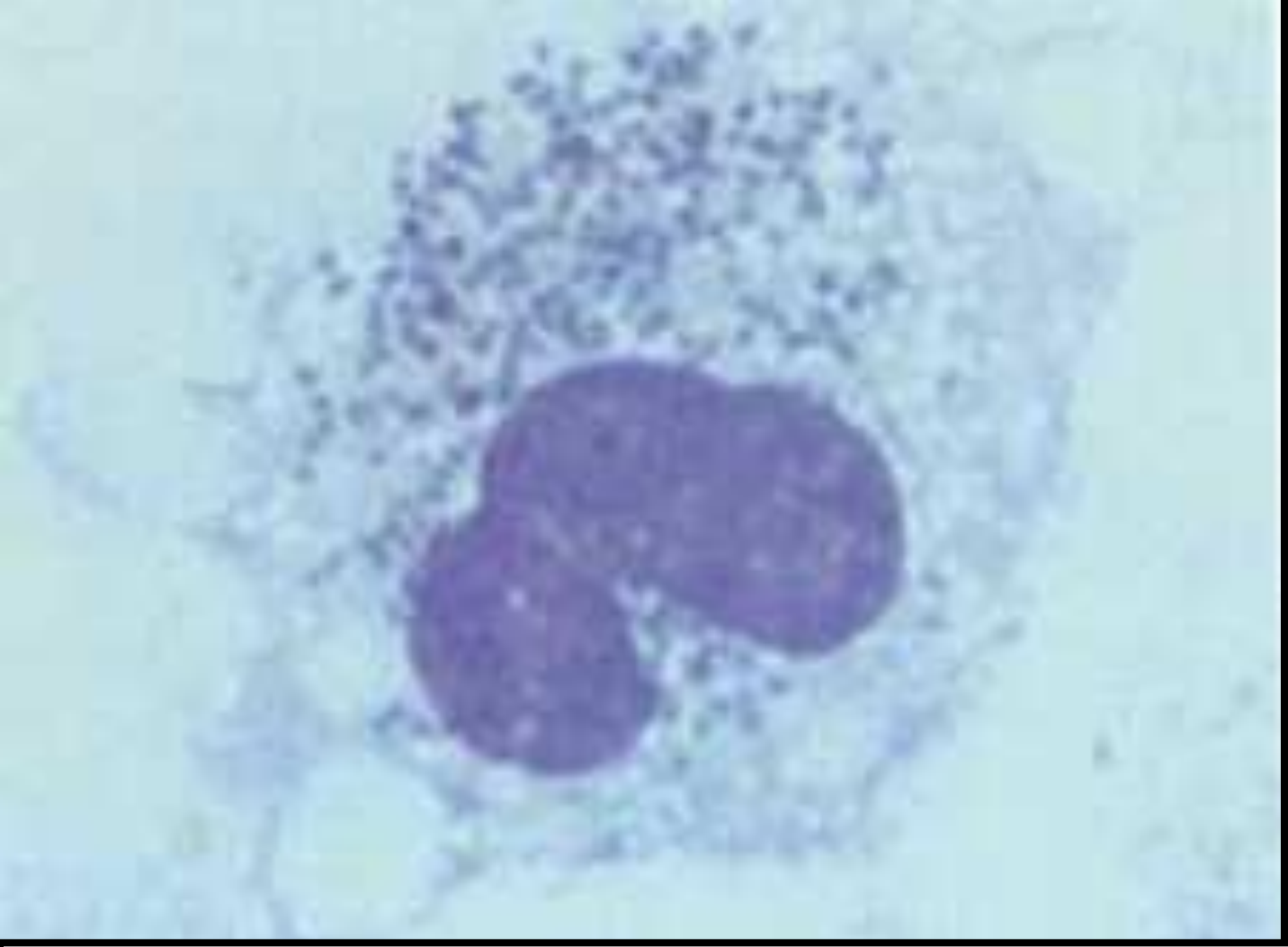
Brucellosis (Undulant Fever)

- ***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)



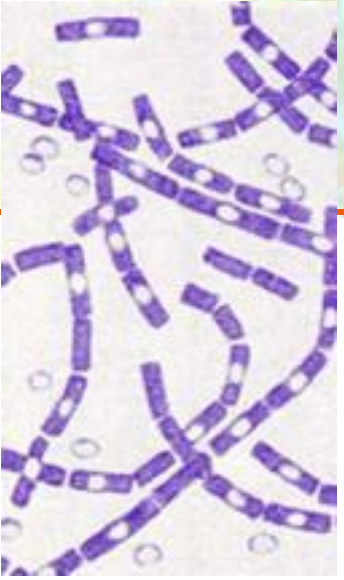


Well-formed hepatic granuloma from a patient with brucellosis



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** (woolsorter"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

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

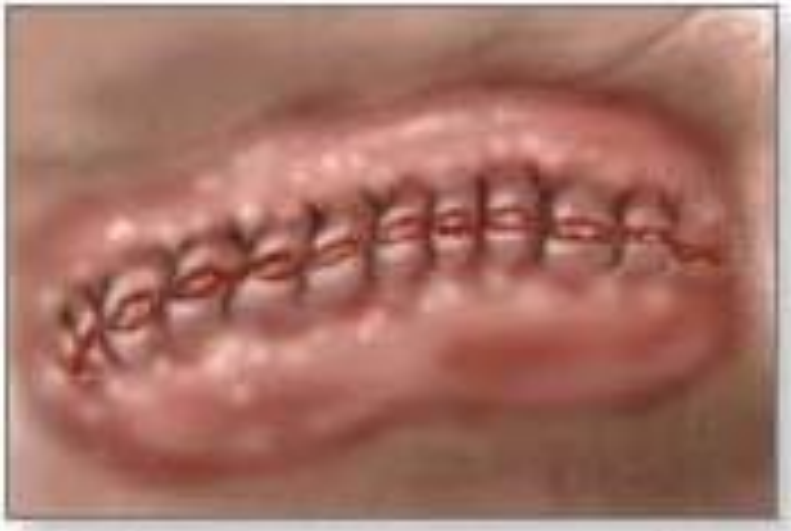
Ubiquitous in soil and dust – "war disease"

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

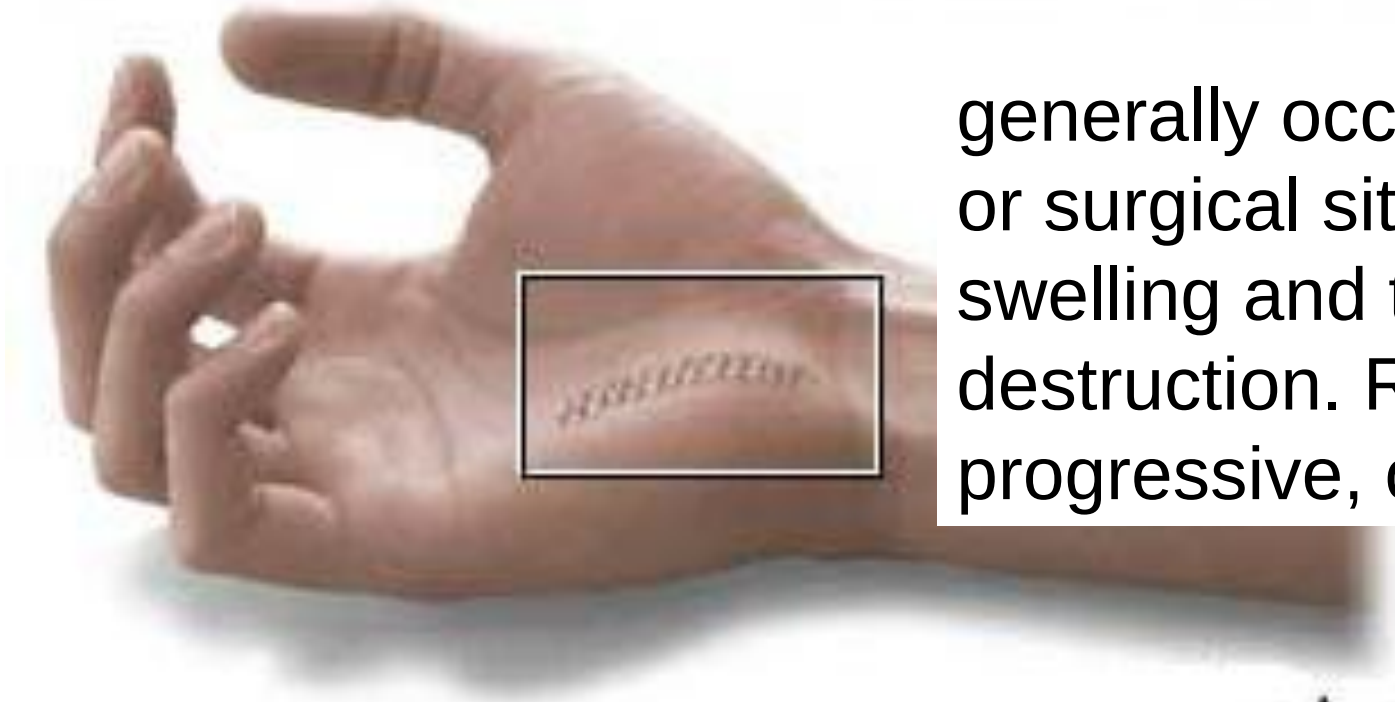
Death due to toxemia

Treatment: debridement and amputation – hyperbaric chamber; antibiotics and antitoxin of limited value (why?)

Clean wound



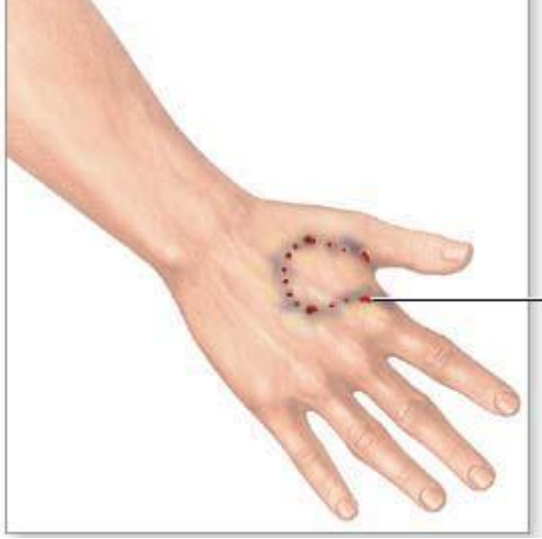
Gangrenous wound



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

A.D.A.M.

Animal Bites and Scratches



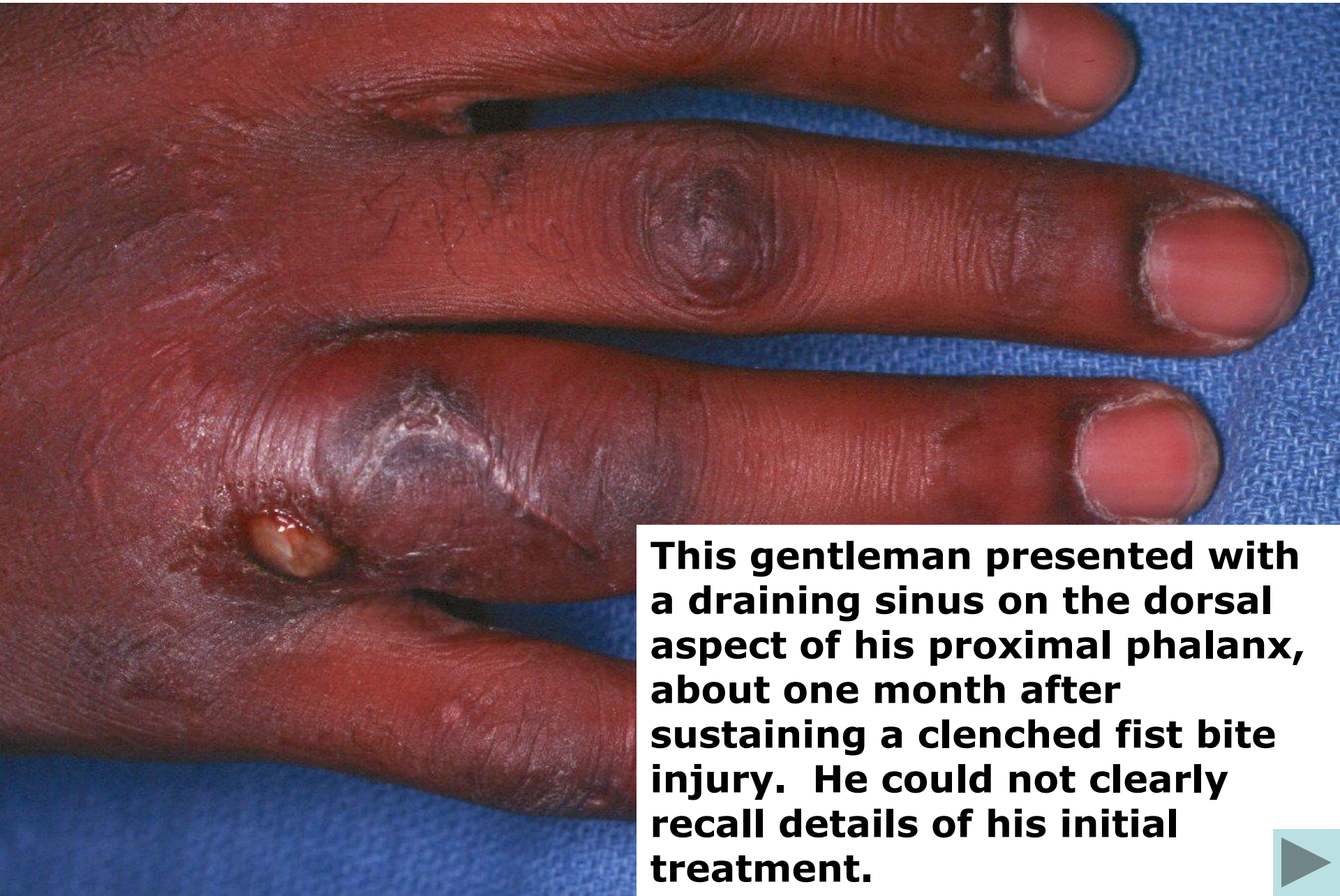
Anaerobic bacteria infect deep animal bites

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

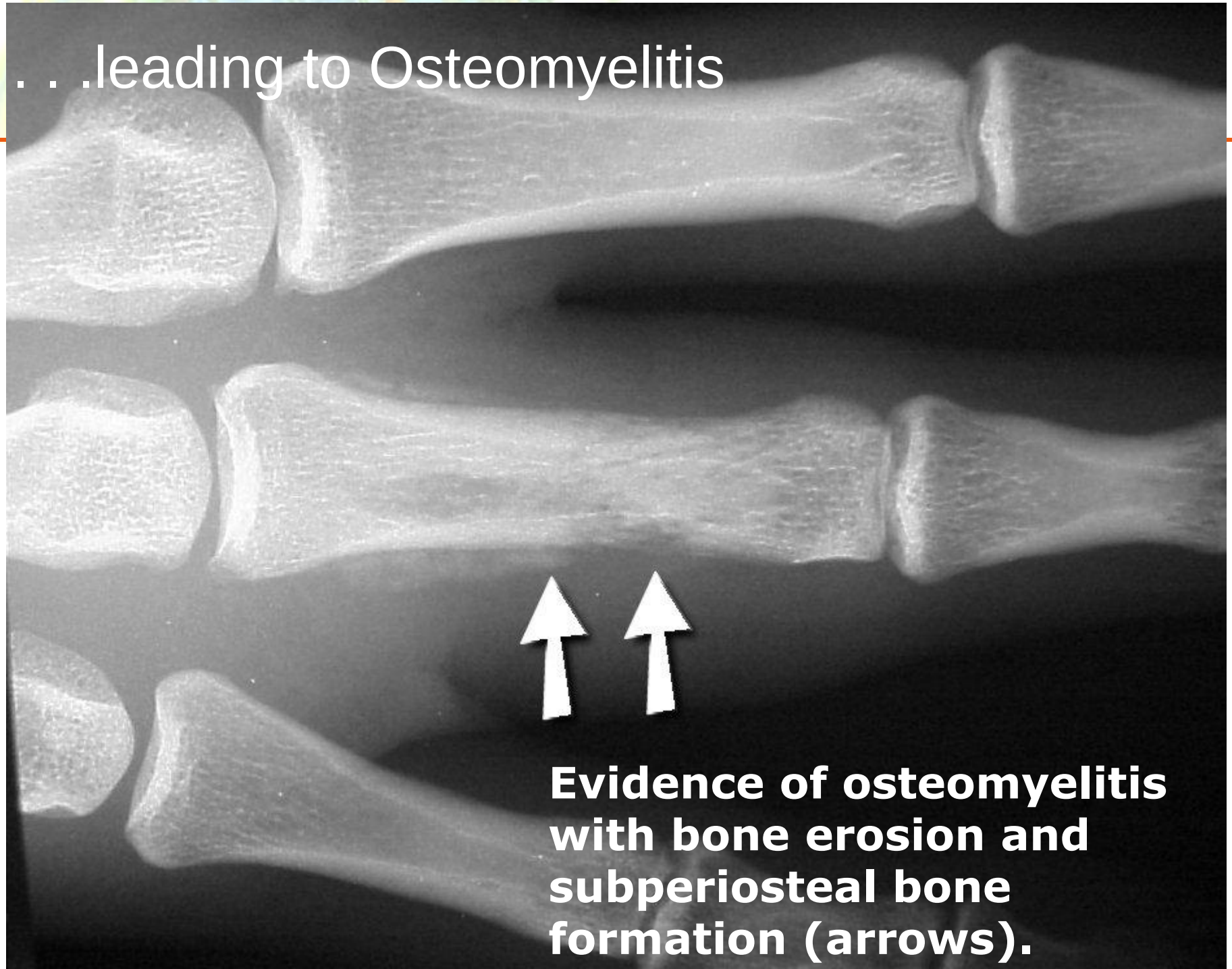
Human bites – (not in book) normal mouth flora (incl. *S. aureus*, α hemolytic *S. viridans*, *H. influenza* and various anaerobes)

Clenched Fist Bite Injury . . .



This gentleman presented with a draining sinus on the dorsal aspect of his proximal phalanx, about one month after sustaining a clenched fist bite injury. He could not clearly recall details of his initial treatment.

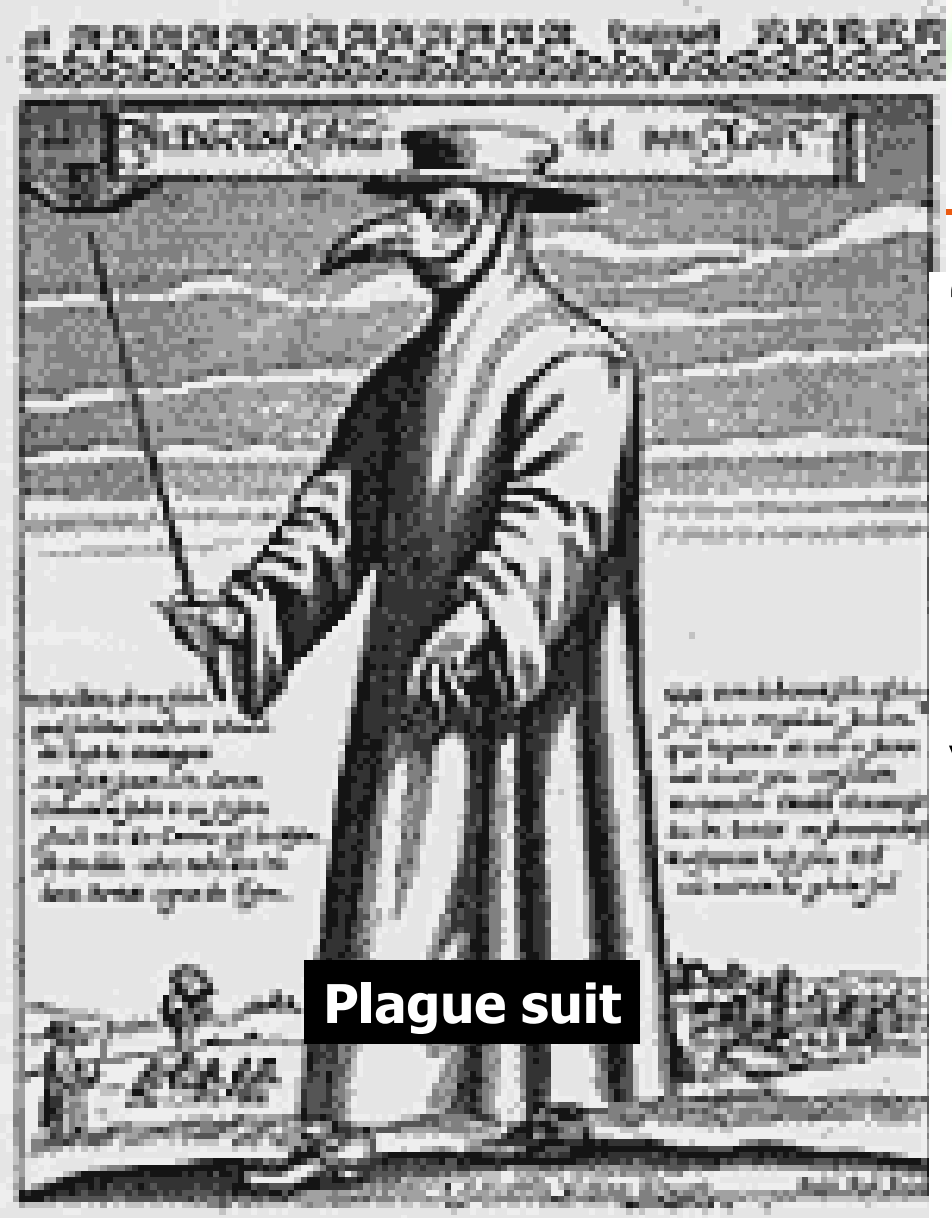
. . .leading to Osteomyelitis



Evidence of osteomyelitis with bone erosion and subperiosteal bone formation (arrows).

Vector-Transmitted Diseases

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



15th Century Plague Physician

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

The Black Death

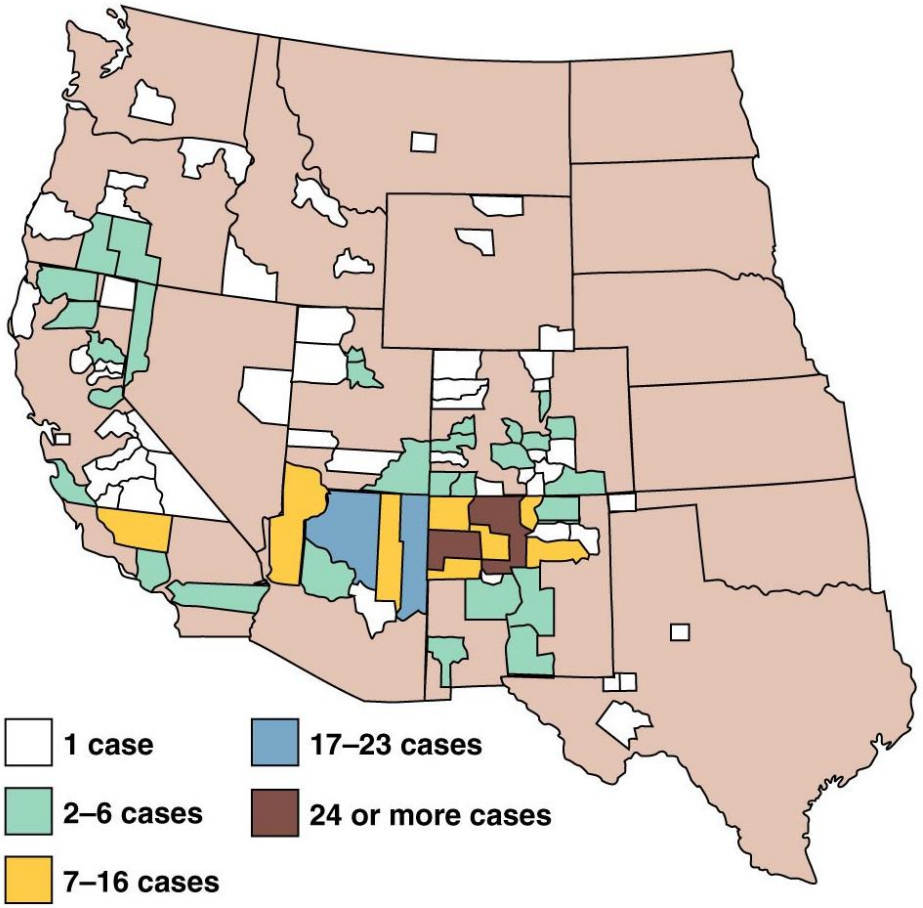
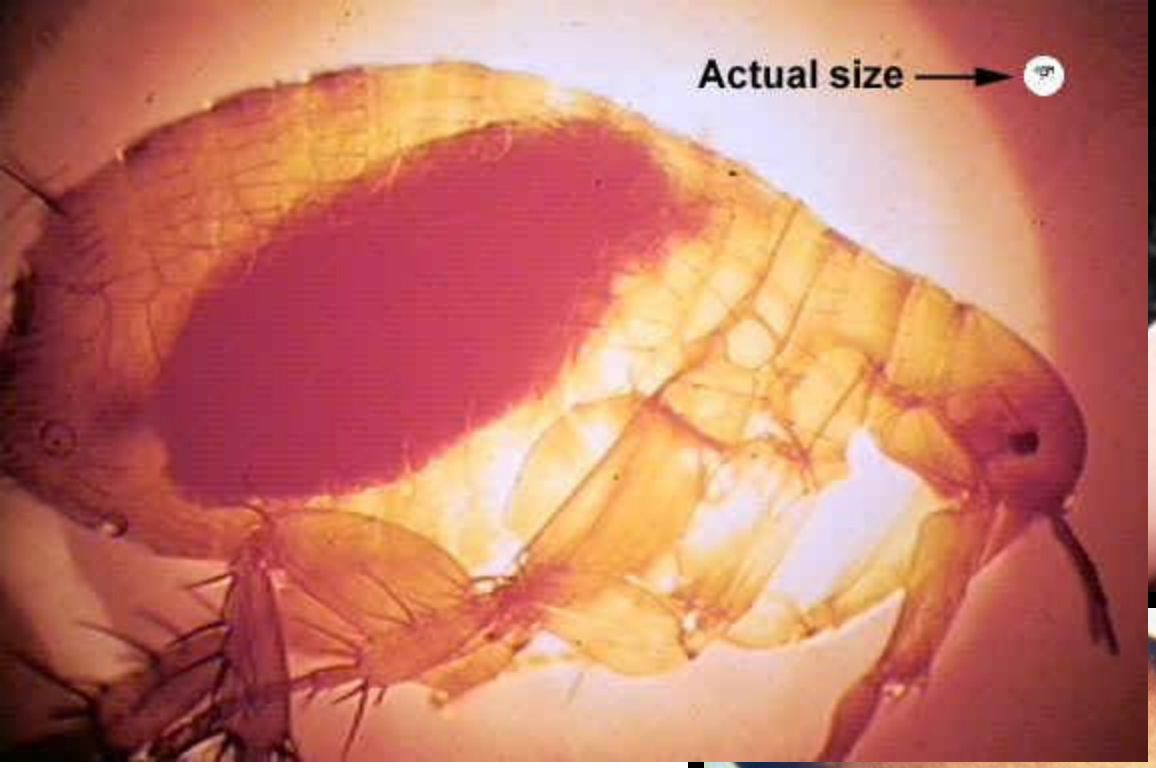
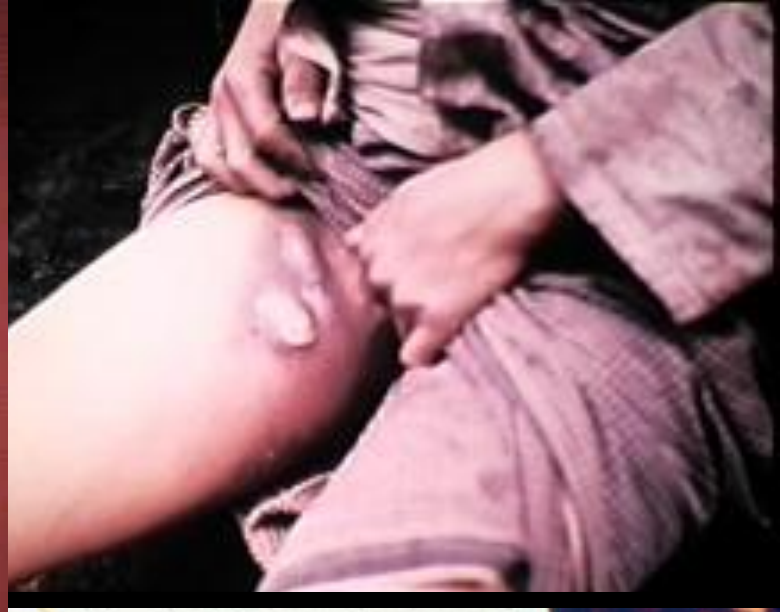
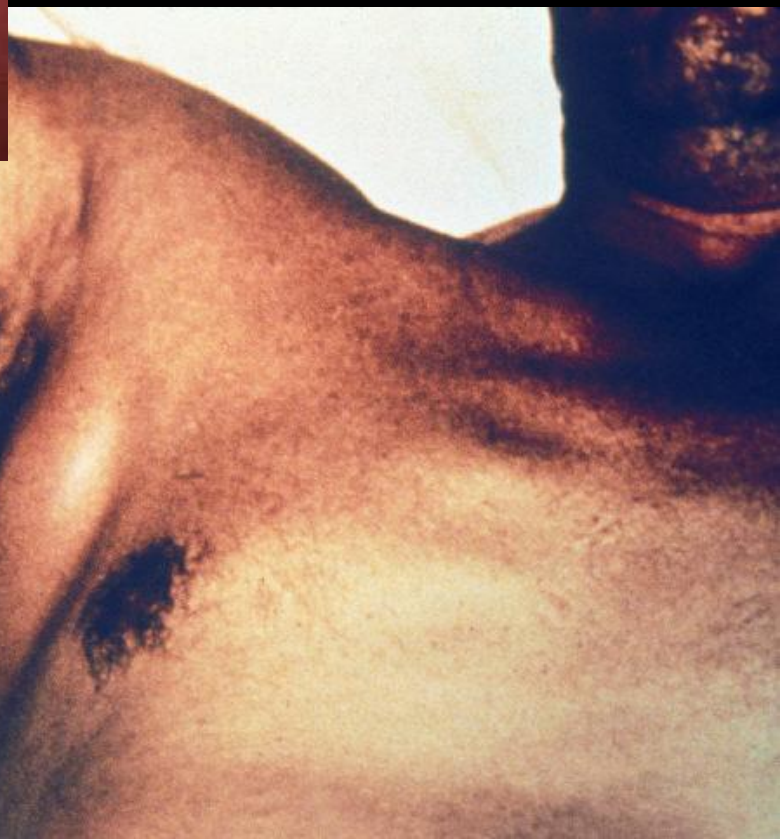
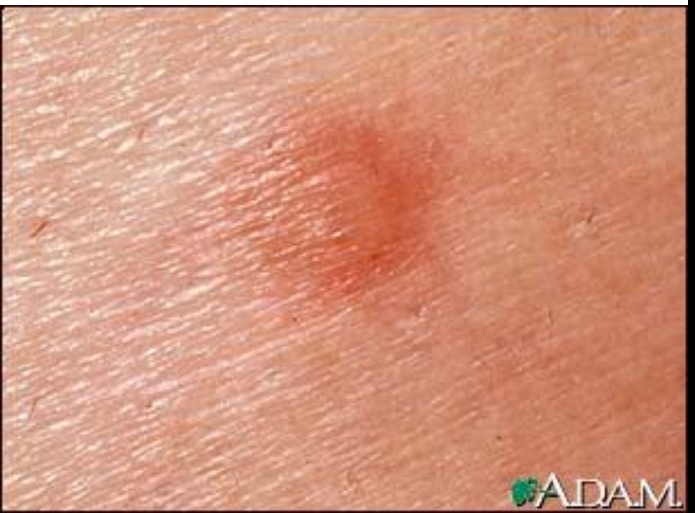


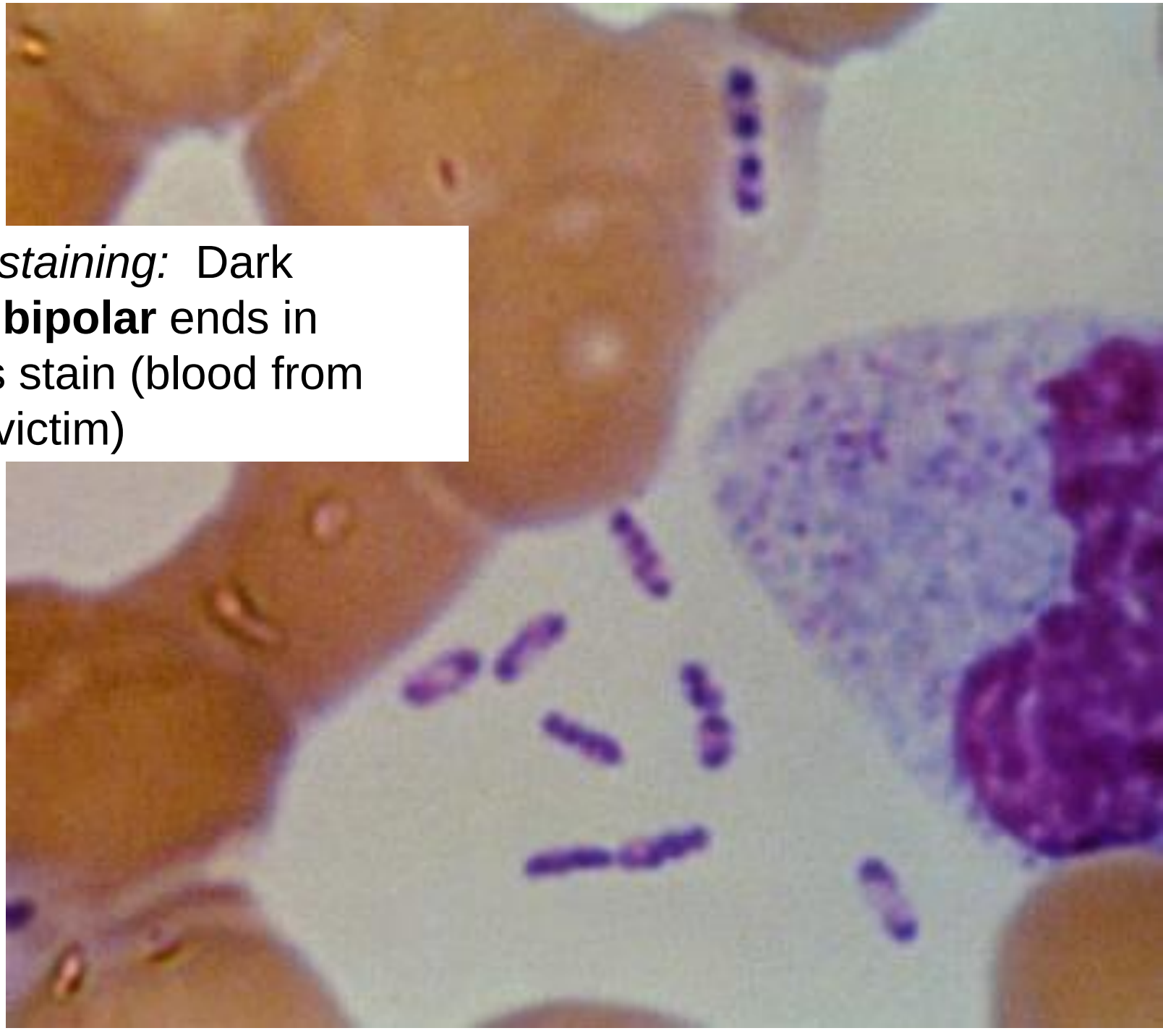
Fig 23.11


Actual size






A.D.A.M.



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

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

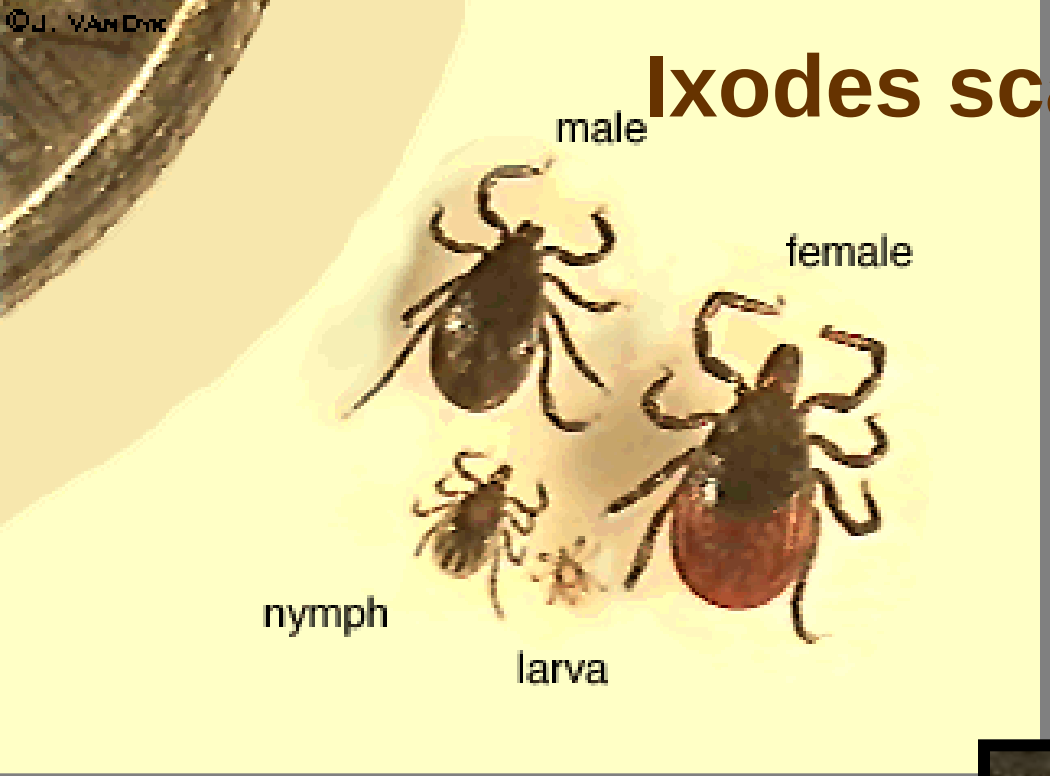
Diagnosis

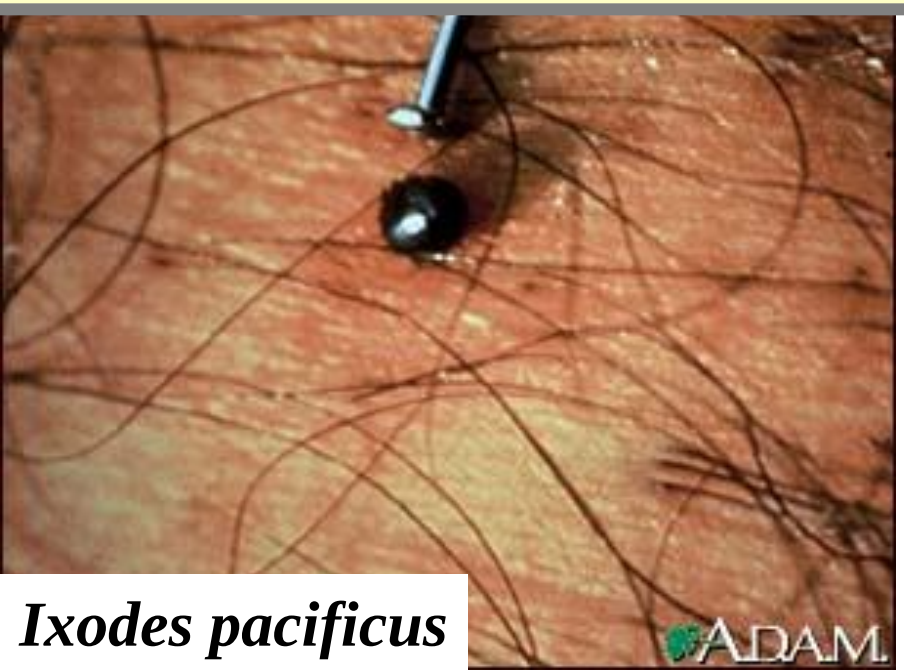
- Symptoms alone: often misdiagnosis
- In most cases not possible to isolate and culture *B. burgdorferi* $\rightarrow$ **indirect serological tests** (ELISA and Western blot)
- PCR

Prevention

Treatment in early stages!

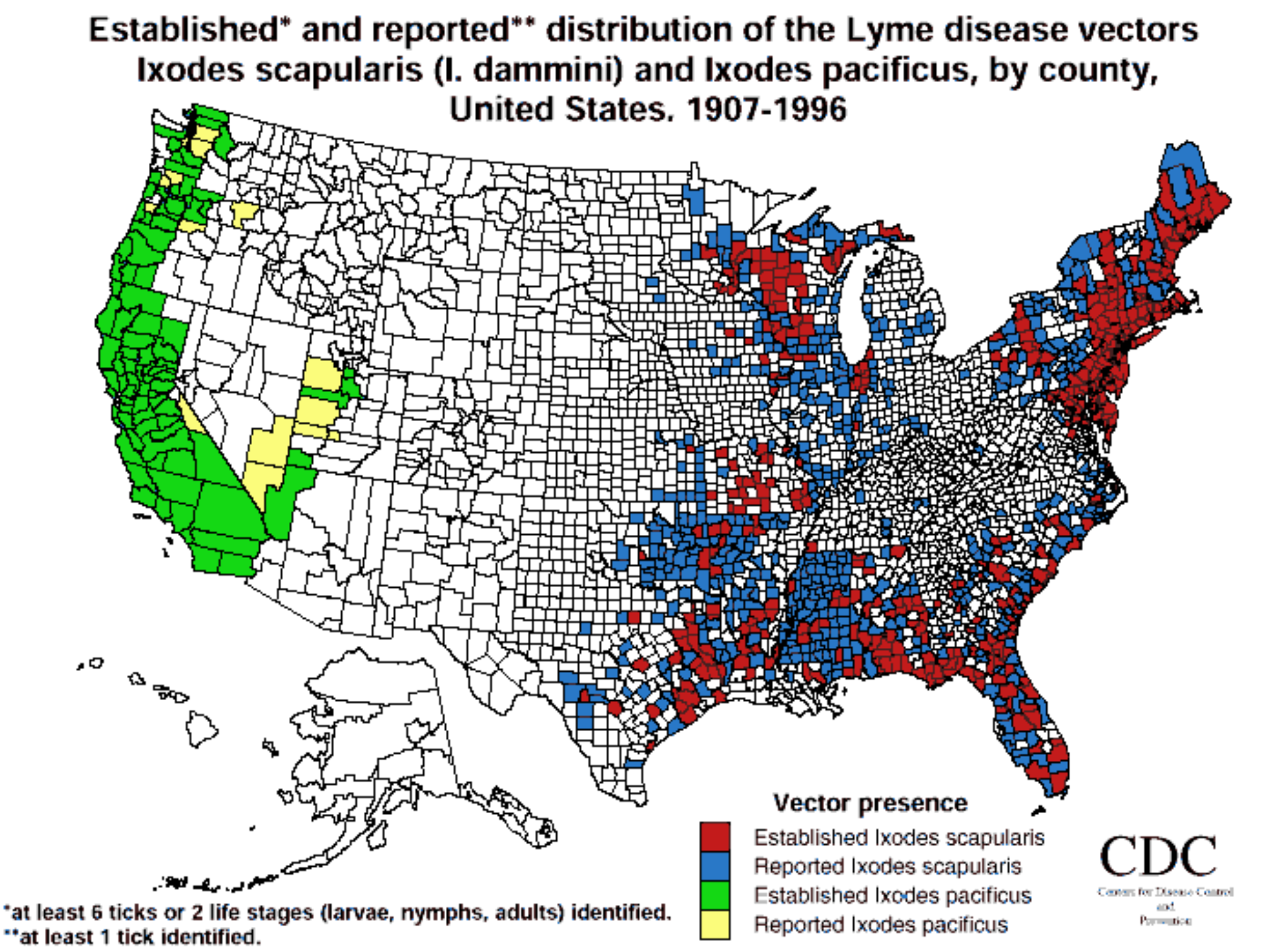
Ixodes scapularis / pacificus





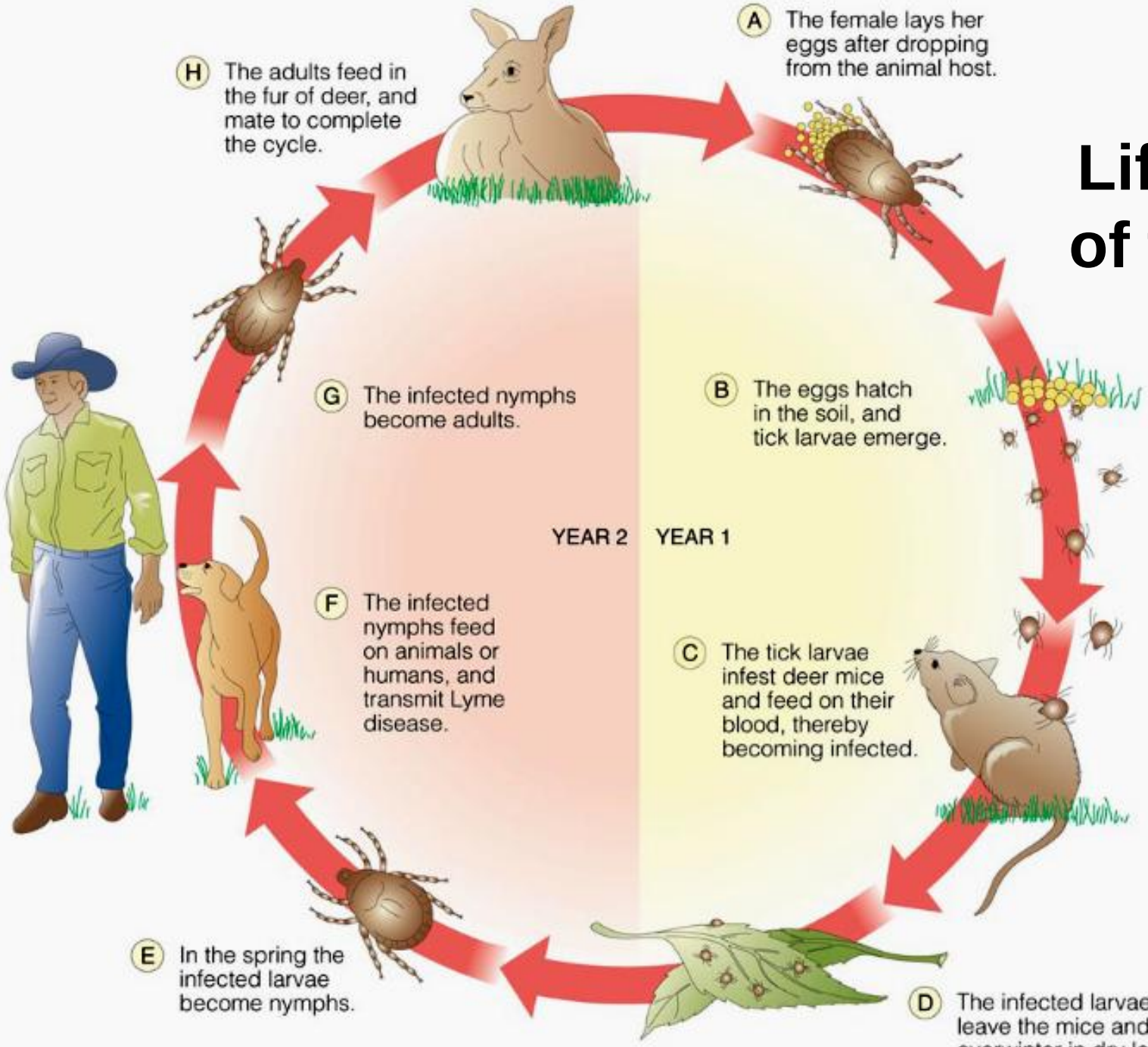
Ixodes pacificus

Established* and reported** distribution of the Lyme disease vectors Ixodes scapularis (I. dammini) and Ixodes pacificus, by county, United States. 1907-1996



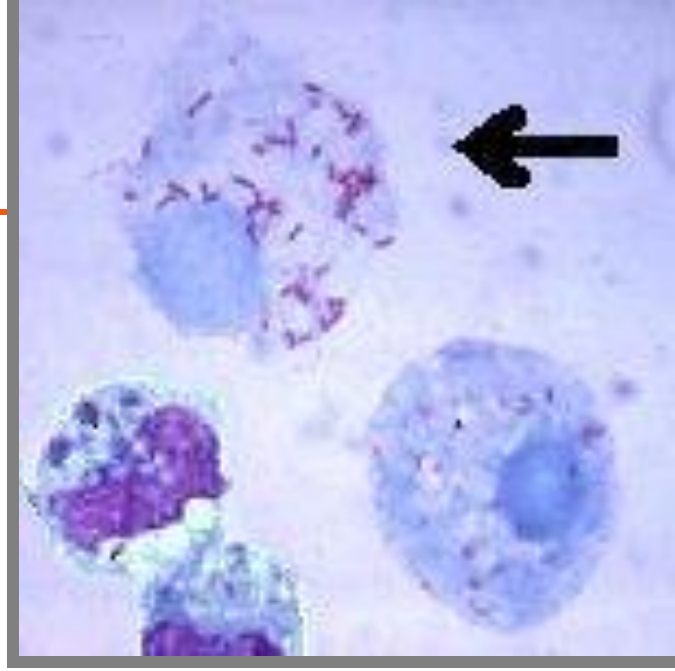
*at least 6 ticks or 2 life stages (larvae, nymphs, adults) identified.
**at least 1 tick identified.

Life Cycle of the Tick



Compare to Fig 23.13a

Ehrlichiosis



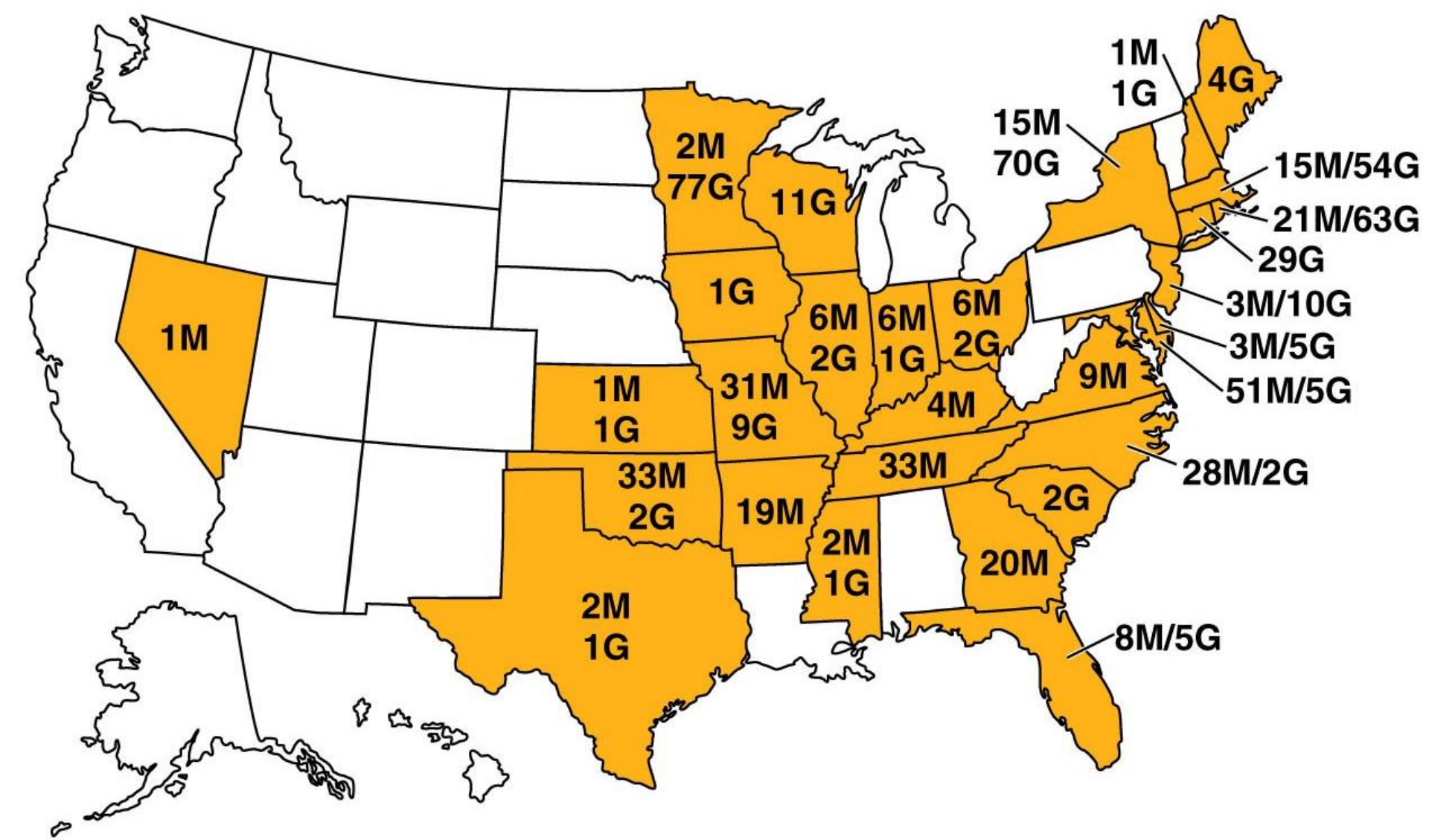
First described in 1986

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)


1M
2M
77G
11G
1M
1G
4G
15M
70G
15M/54G
21M/63G
29G
1G
6M
2G
6M
1G
6M
2G
3M/10G
3M/5G
51M/5G
9M
1M
1G
31M
9G
4M
33M
28M/2G
33M
2G
19M
2G
2M
1G
20M
2M
1G
8M/5G
Reported cases, granulocytic (G) and monocytic (M)
No reported cases

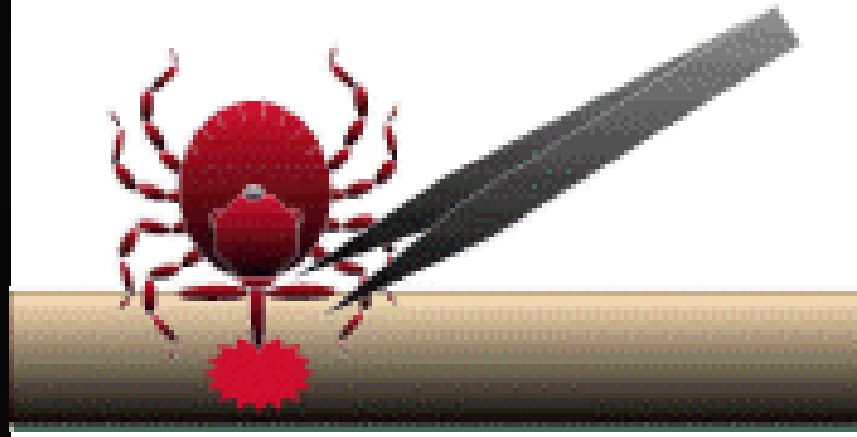
HME and HGE

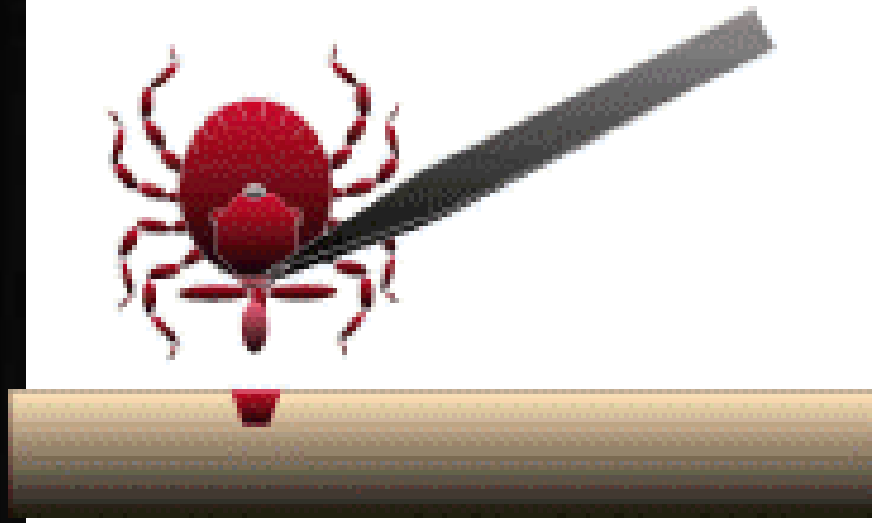
Lyme Disease and Ehrlichiosis

Female tick

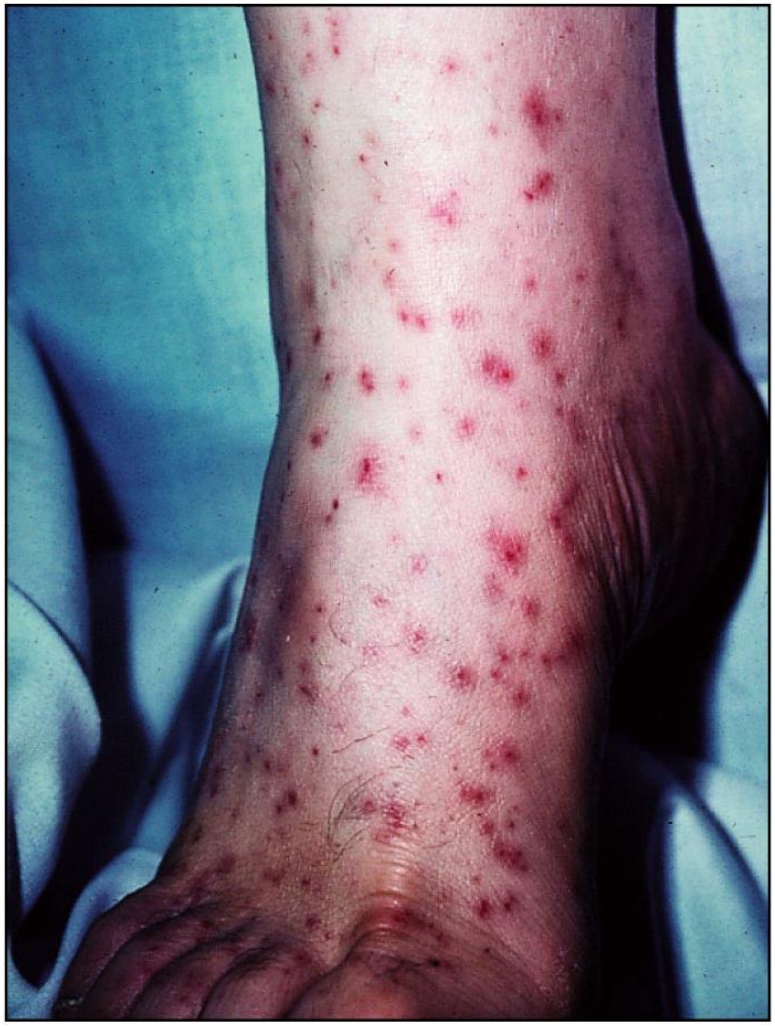
Male tick

Avoid tick bites by wearing proper clothing



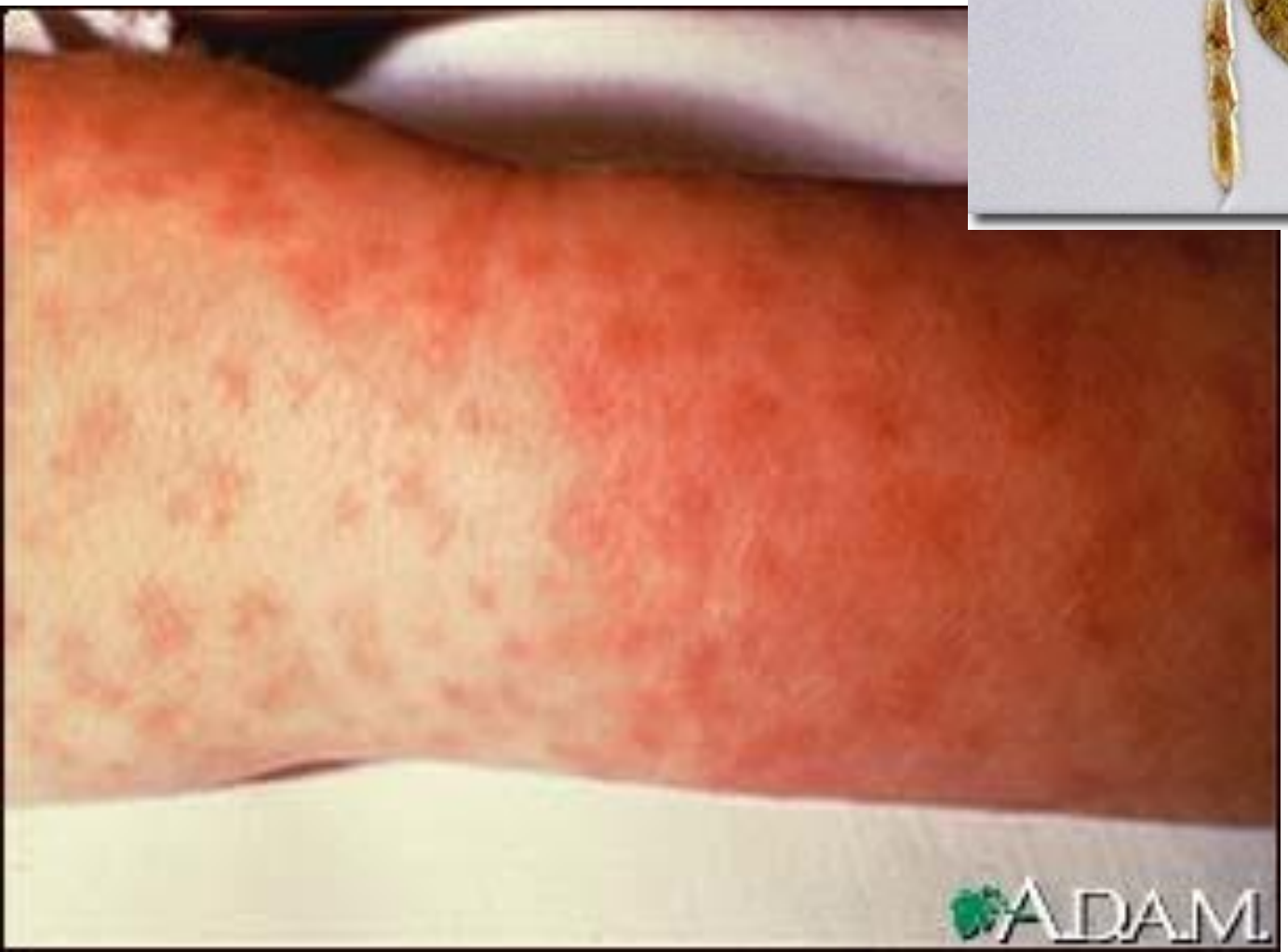


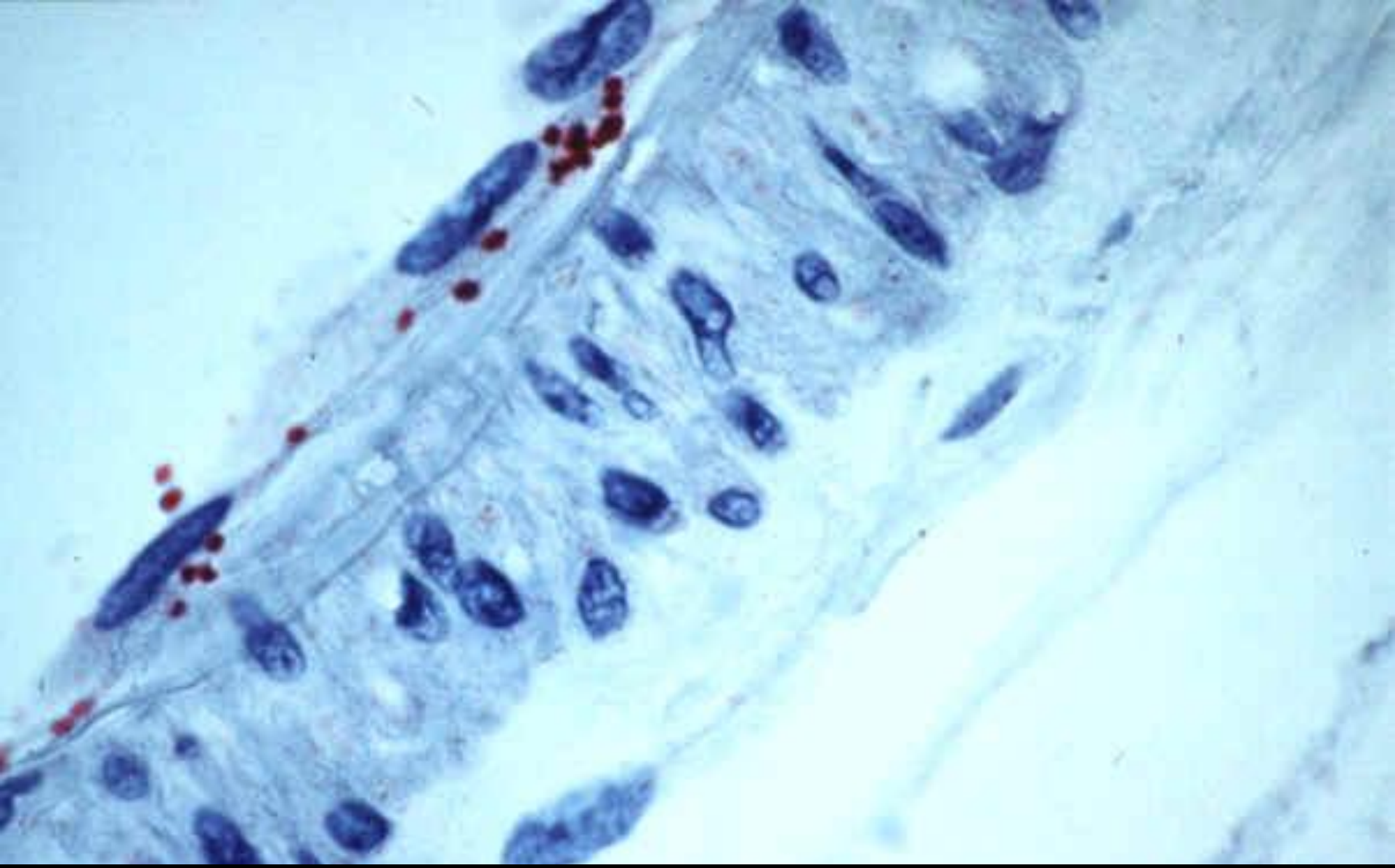
Rocky Mountain Spotted Fever (RMSF)



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

Rocky Mountain Wood Tick (*Dermacentor andersoni*)





Red structures indicate immunohistological staining of *Rickettsia rickettsii* in endothelial cells of a blood vessel from a patient with fatal RMSF

Spotted Fevers (Rocky Mountain Spotted Fever)

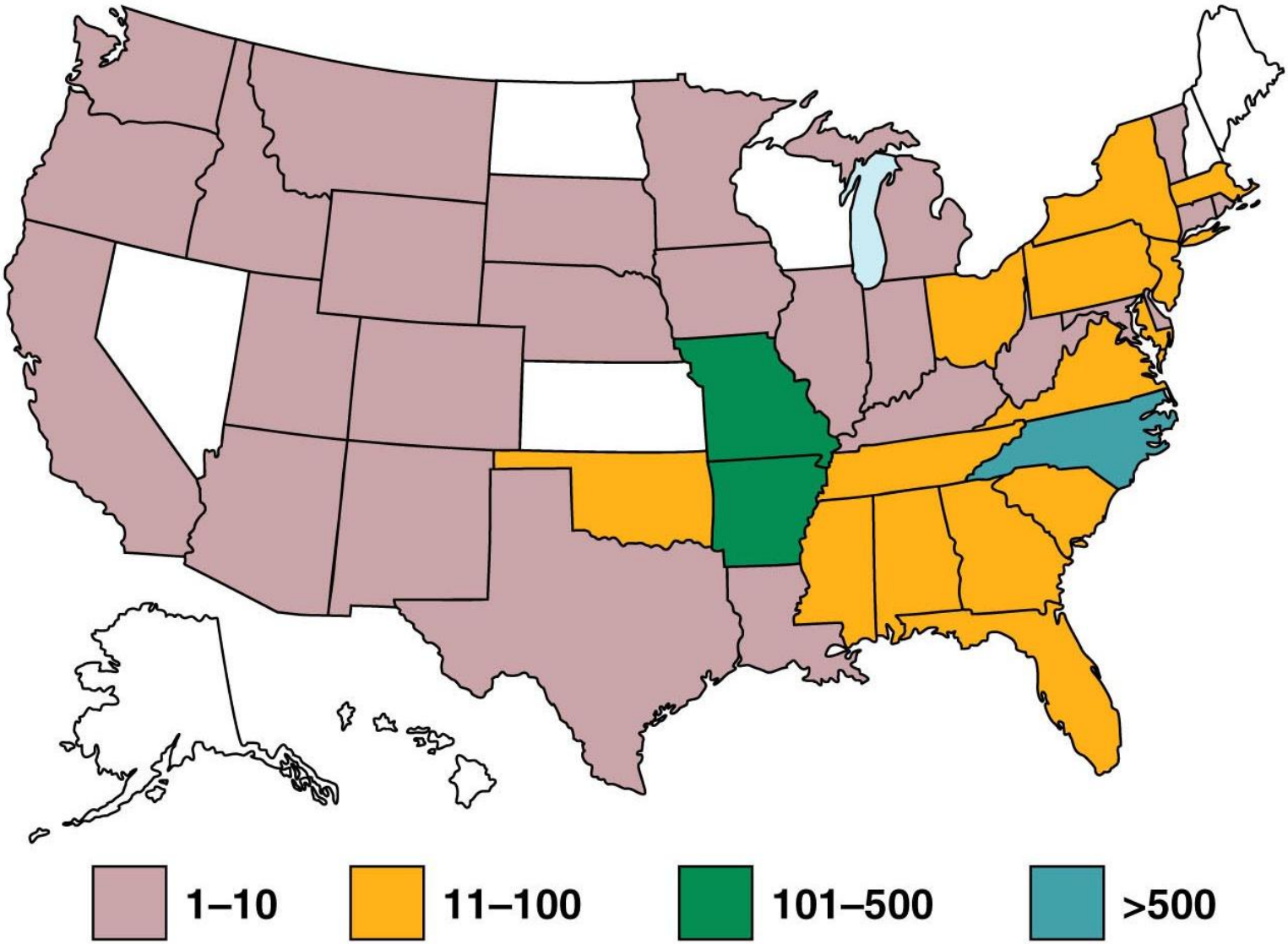


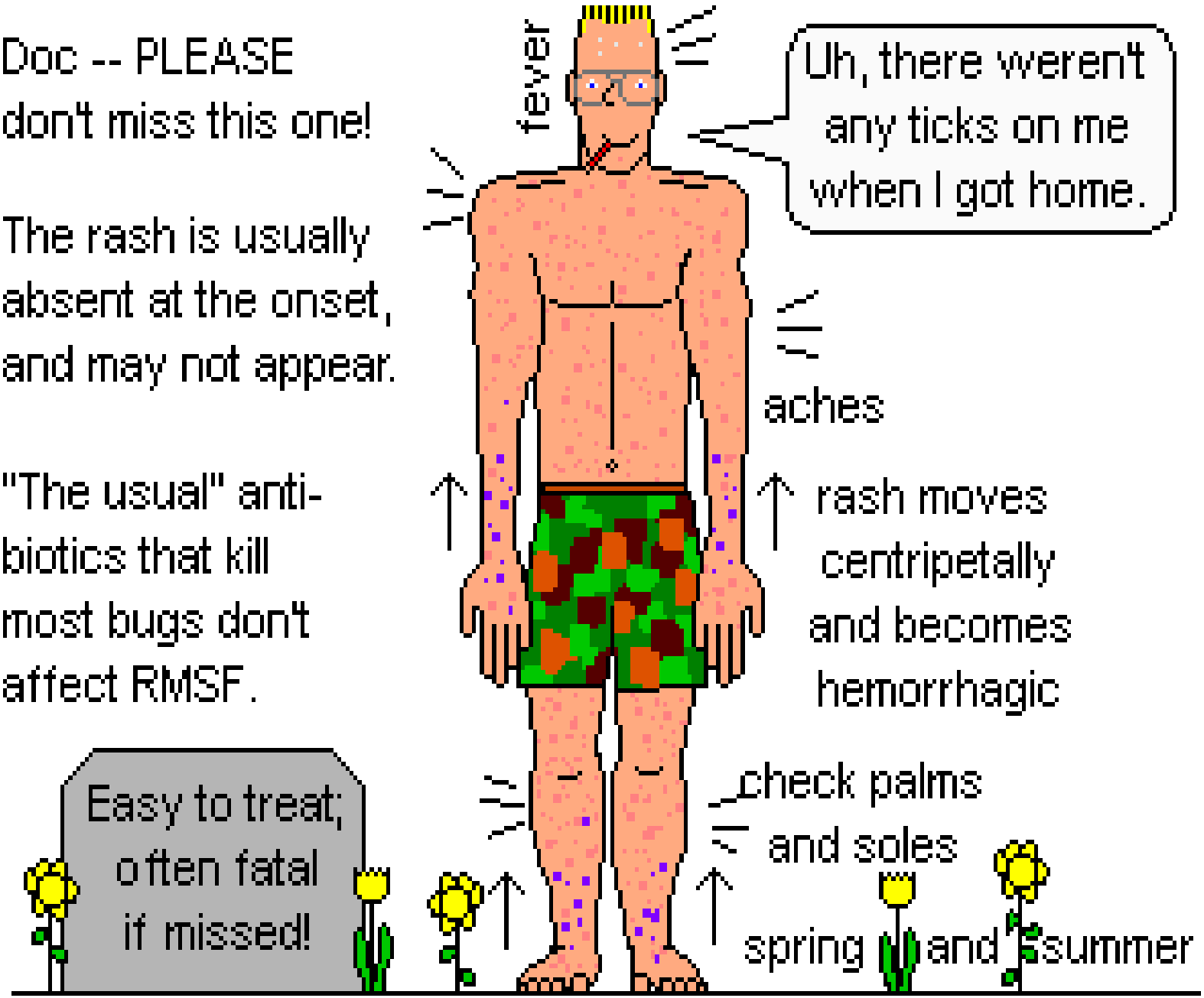
Figure 23.16

Rocky Mountain Spotted Fever

Doc -- PLEASE don't miss this one!

The rash is usually absent at the onset, and may not appear.

"The usual" anti-biotics that kill most bugs don't affect RMSF.



VIRAL DISEASES OF THE CARDIOVASCULAR AND LYMPHATIC SYSTEMS

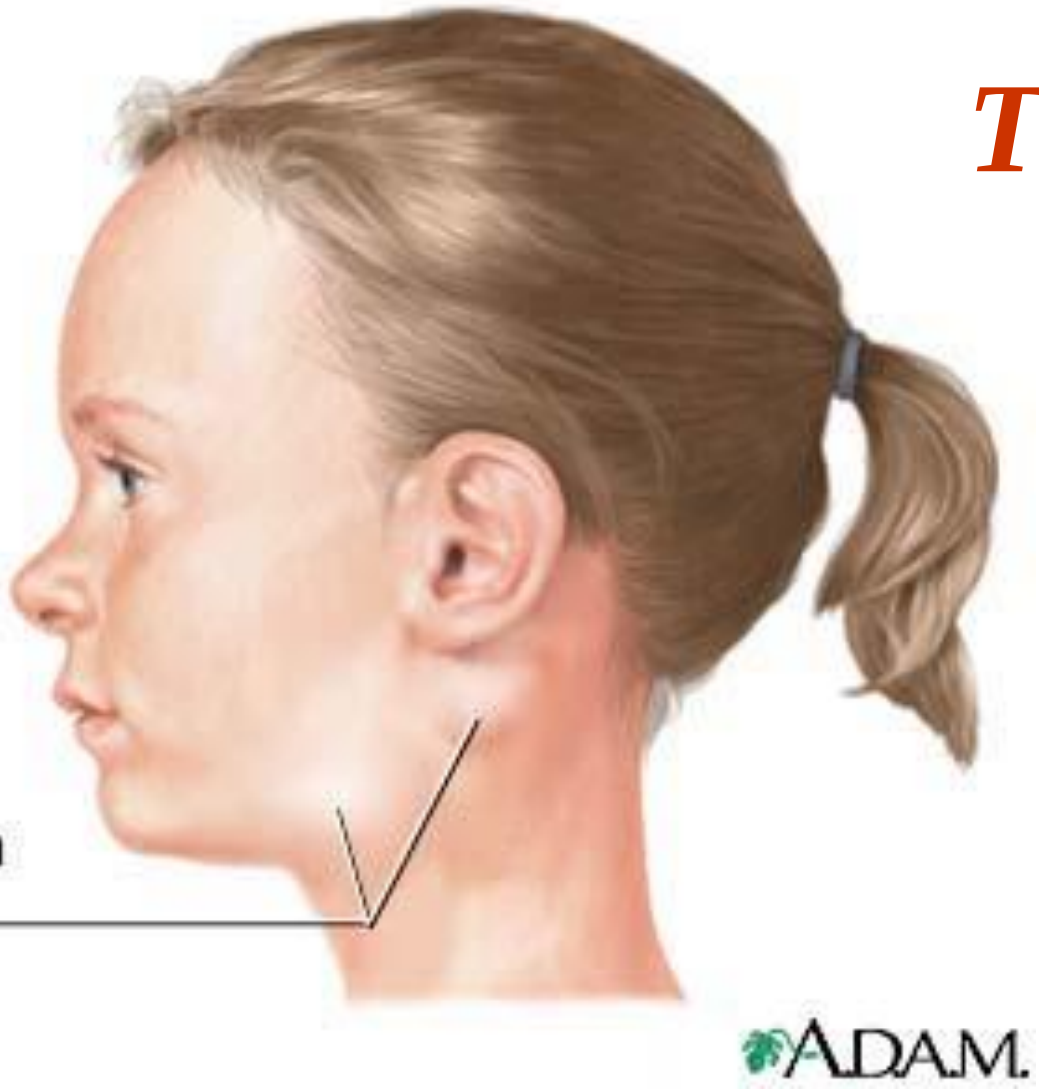
- Infectious Mononucleosis
- Viral Hemorrhagic Fevers

Infectious Mononucleosis

- "Kissing disease" – caused by **Epstein-Barr virus** (EBV) of *Herpesviridae*, also known as HHV-4
- Well-established relationship between ***HHV-4*** and oncogenesis (Burkitt's Lymphoma etc.)
- Virus multiplies in parotid glands and is present in saliva. It causes the proliferation of atypical lymphocytes (life-long infection) – Transmission via saliva
- Most people (~95%) infected. Childhood infection usually asymptomatic. Adolescent infection → Mononucleosis.
- Characteristic triad: fever, pharyngitis, and lymphadenopathy (+spleno- and hepatomegaly) lasting for 1 to 4 weeks.

Mononucleosis causes:

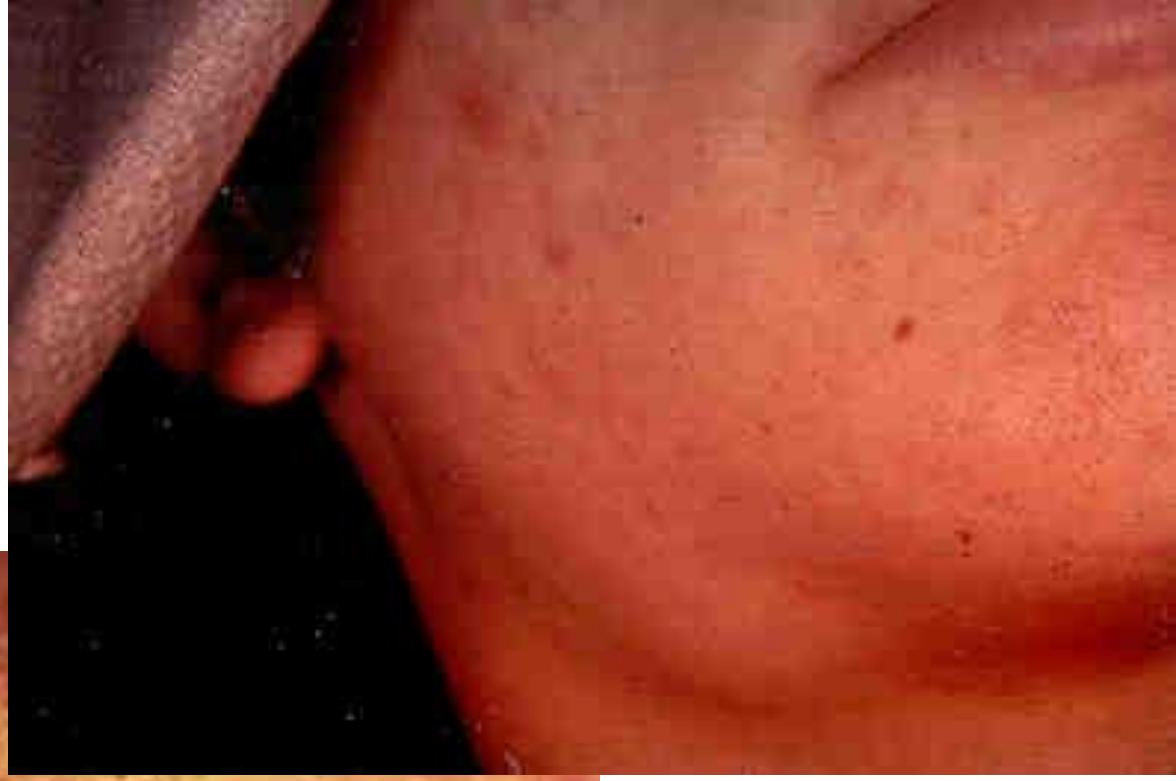
- Fever
- Fatigue
- Sore throat
- Swollen lymph glands

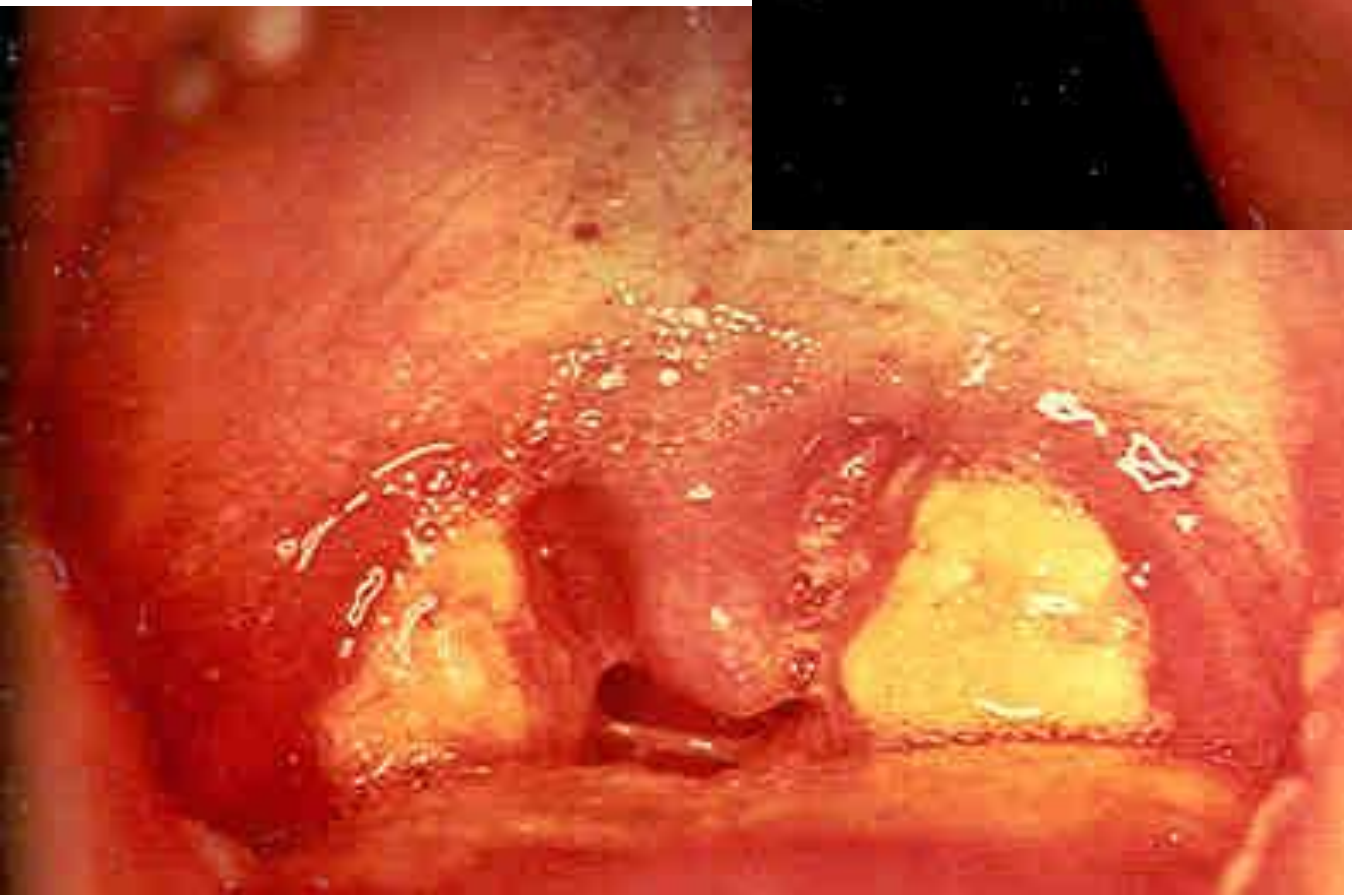


Triad

Swollen lymph nodes, sore throat, fatigue and headache are some of the symptoms of mononucleosis. It is generally self-limiting and most patients can recover in 4 to 6 weeks without medications.

Young adults present with fever, pharyngitis, lymphadenopathy, and tonsillitis.



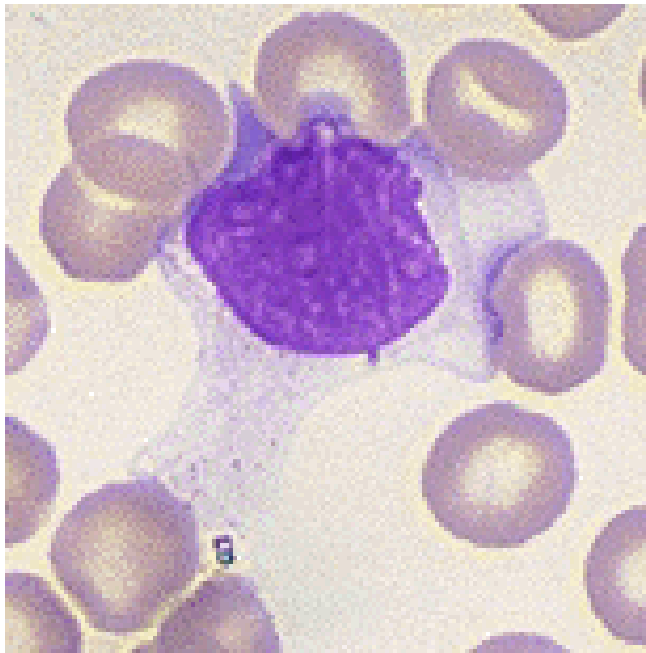


- Proliferation of infected B cells results in massive activation and proliferation of T_c cells (CD8 cells) $\rightarrow$ characteristic lymphoid hyperplasia.

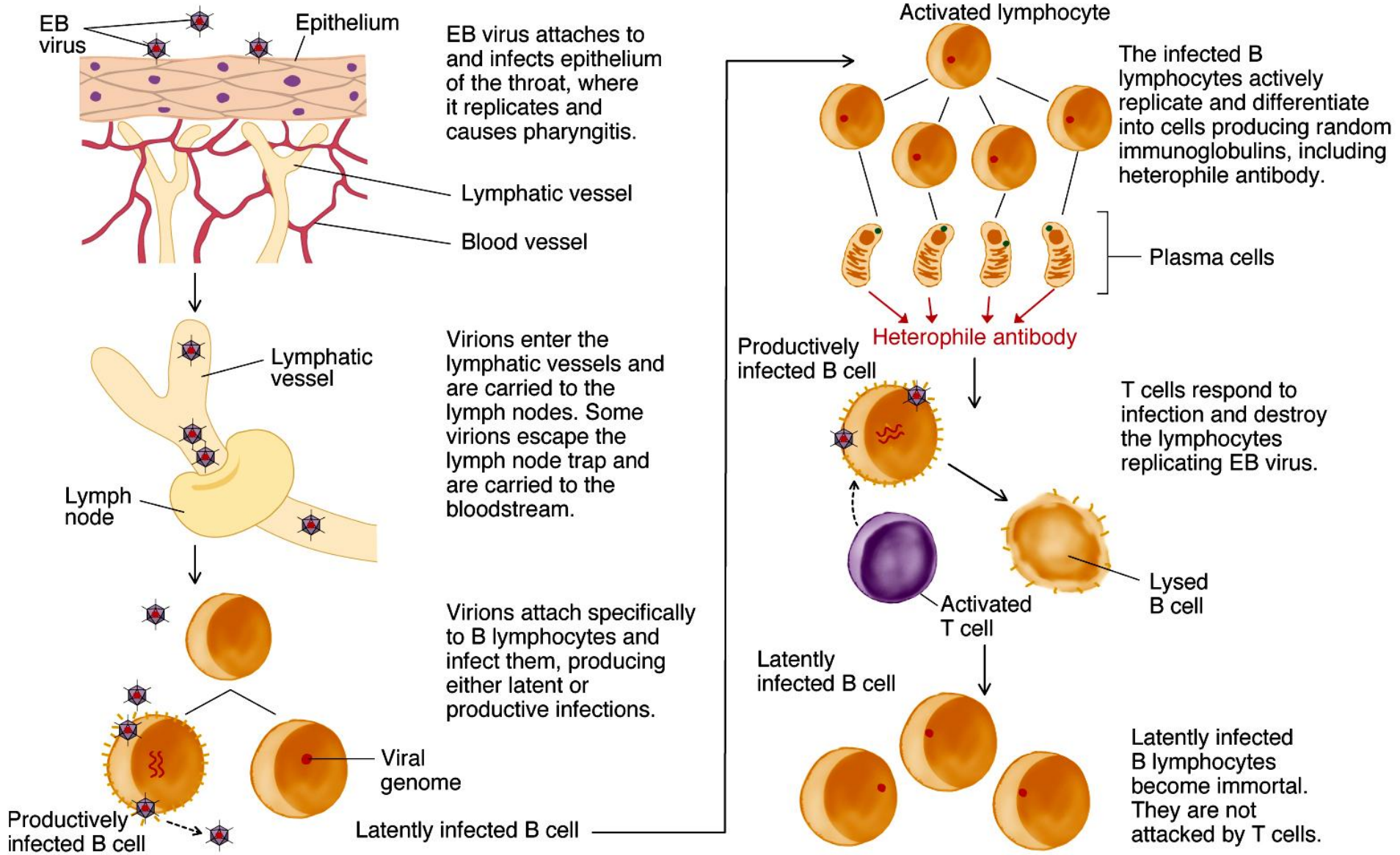
- Transformation of B cells to immortal plasmacytoid cells $\rightarrow$ secrete a wide variety of IgMs = heterophile antibodies (Monospot test)

- Commercially-available test kits are 70-92% sensitive and 96-100% specific

"Downy cell“: lymphocytes infected by EBV or CMV in infectious mononucleosis. Cytoplasmic rim is intensely blue and has tendency to "stream" around adjacent red cells.



Pathogenesis of infectious mononucleosis



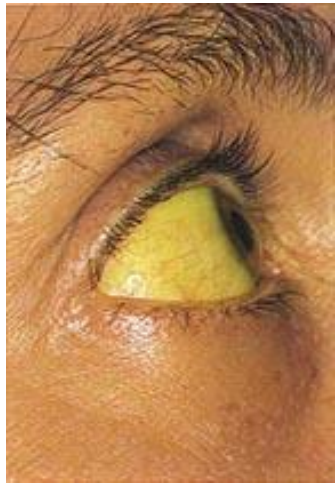
Viral Hemorrhagic Fevers

- Enveloped RNA viruses: Arenaviruses, filoviruses, bunyaviruses, and flaviviruses
- Viruses geographically restricted to where their host species live
- For some viruses, after accidental transmission from host, humans to human transmission
- Human cases or outbreaks sporadic and irregular. Not easily predictable

➢ **Marburg VHF**: 1967 outbreak in Marburg (D) – imported from Africa; Mortality rate 25%

➢ **Ebola HF**: 1995 major outbreaks in Zaire and Sudan; Mortality rate 50 – 90%

Classic Viral Hemorrhagic Fevers: Yellow Fever



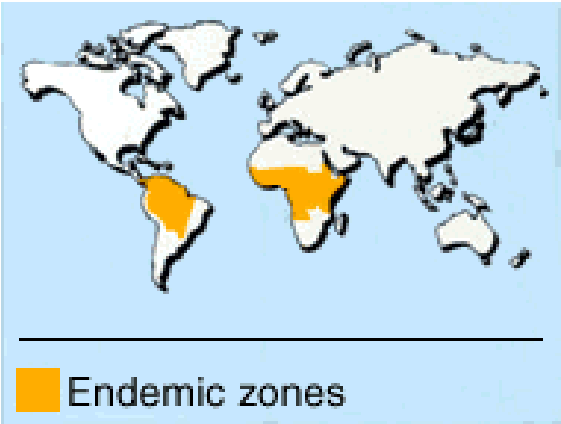
Caused by arbovirus (flaviviridae)
transmitted by mosquitoes

Direct damage to liver and heart → jaundice, hemorrhaging, weak heart → circulatory and kidney failure

African and American tropical jungles

Diagnosis: test for presence of virus-neutralizing antibodies

No treatment Highly effective attenuated vaccine



Hantavirus Pulmonary Syndrome (HPS)

Korean hemorrhagic fever caused by Hantaan virus of ***Bunyaviridae***

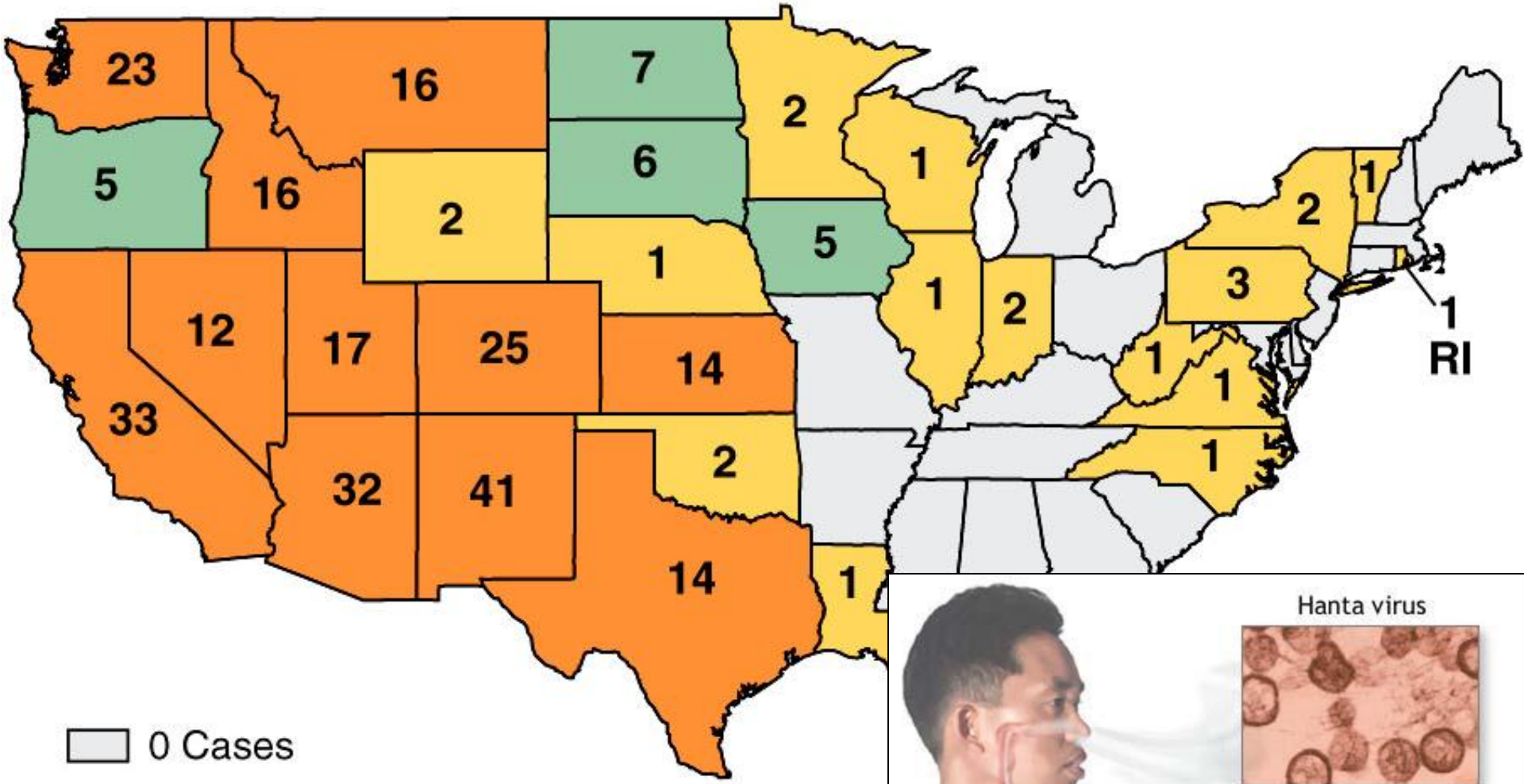
HPS first reported in US in spring of 1993.

Transmission through urine, droppings, or saliva of infected rodents → humans breathe in aerosolized virus. No person to person transmission in US

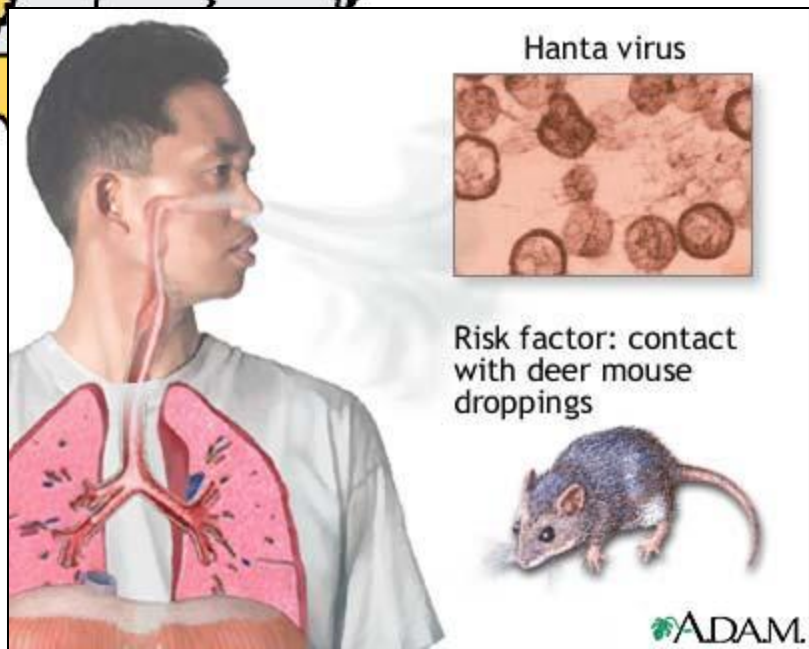
Sudden respiratory failure

Mortality rate > 35%

Total Cases (N = 289 in 31 States)



Hanta Virus Cases



PROTOZOAN DISEASES OF THE CARDIOVASCULAR AND LYMPHATIC SYSTEMS

- **American Trypanosomiasis (Chagas' Disease)**
- **Toxoplasmosis**
- **Malaria**
- **Babesiosis**

American Trypanosomiasis or Chagas Disease

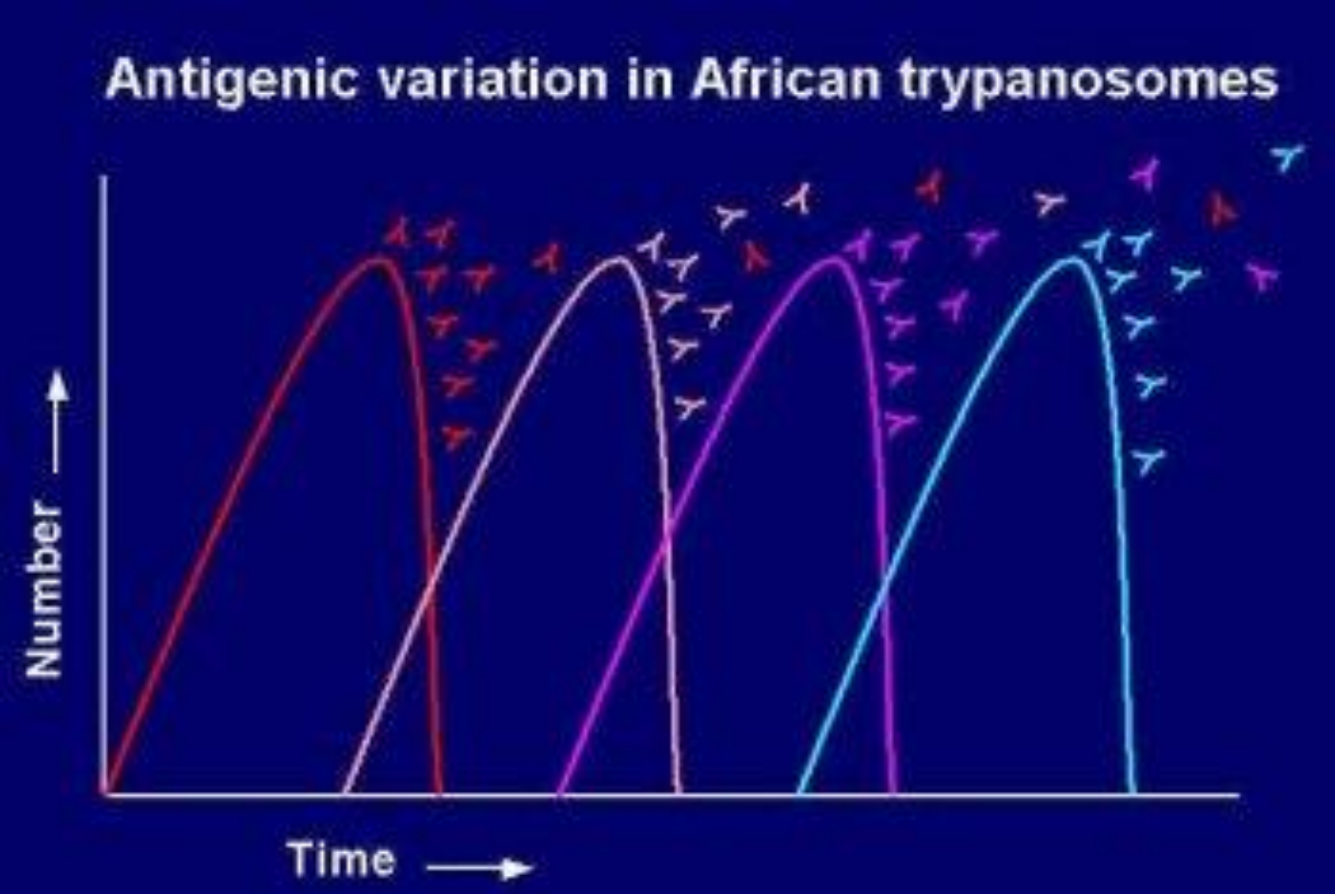
Trypanosoma cruzi

Reservoir: Rodents, opossums, armadillos

Vector: night feeding reduviid bugs (kissing bugs)

Symptoms in 1% of infected. Acute phase (fever etc.) to chronic phase (heart damage)

Antigenic variation ⇒ persistent evasion of immune system
⇒ Cyclic parasitemia (7-10 days)

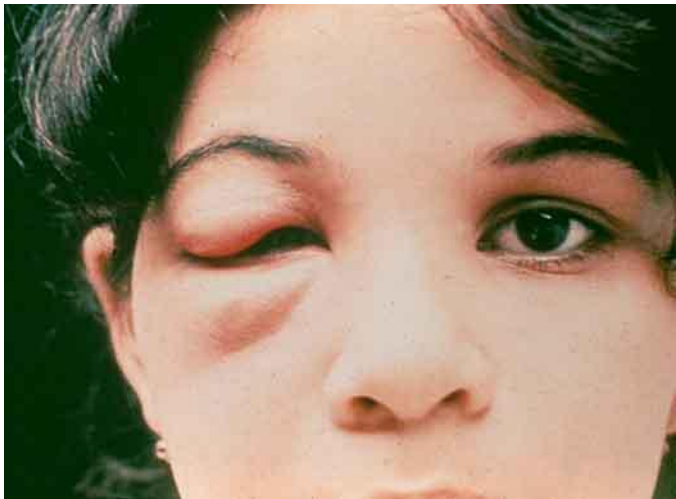


*Course of trypanosome infection: emergence of variant surface glycoproteins (**VSG**) - Host antibodies indicated with Y's.*

Millions in Latin America affected. No cure and little effective treatment

Romaña's sign: pathogonomic, early sign of Chagas disease.

→ Unilateral severe conjunctivitis, swelling of eyelid, inflammation of tear gland, swelling of regional lymph nodes.



Toxoplasmosis

Toxoplasma gondii

> 60 mio people infected in US (mostly asymptomatic)

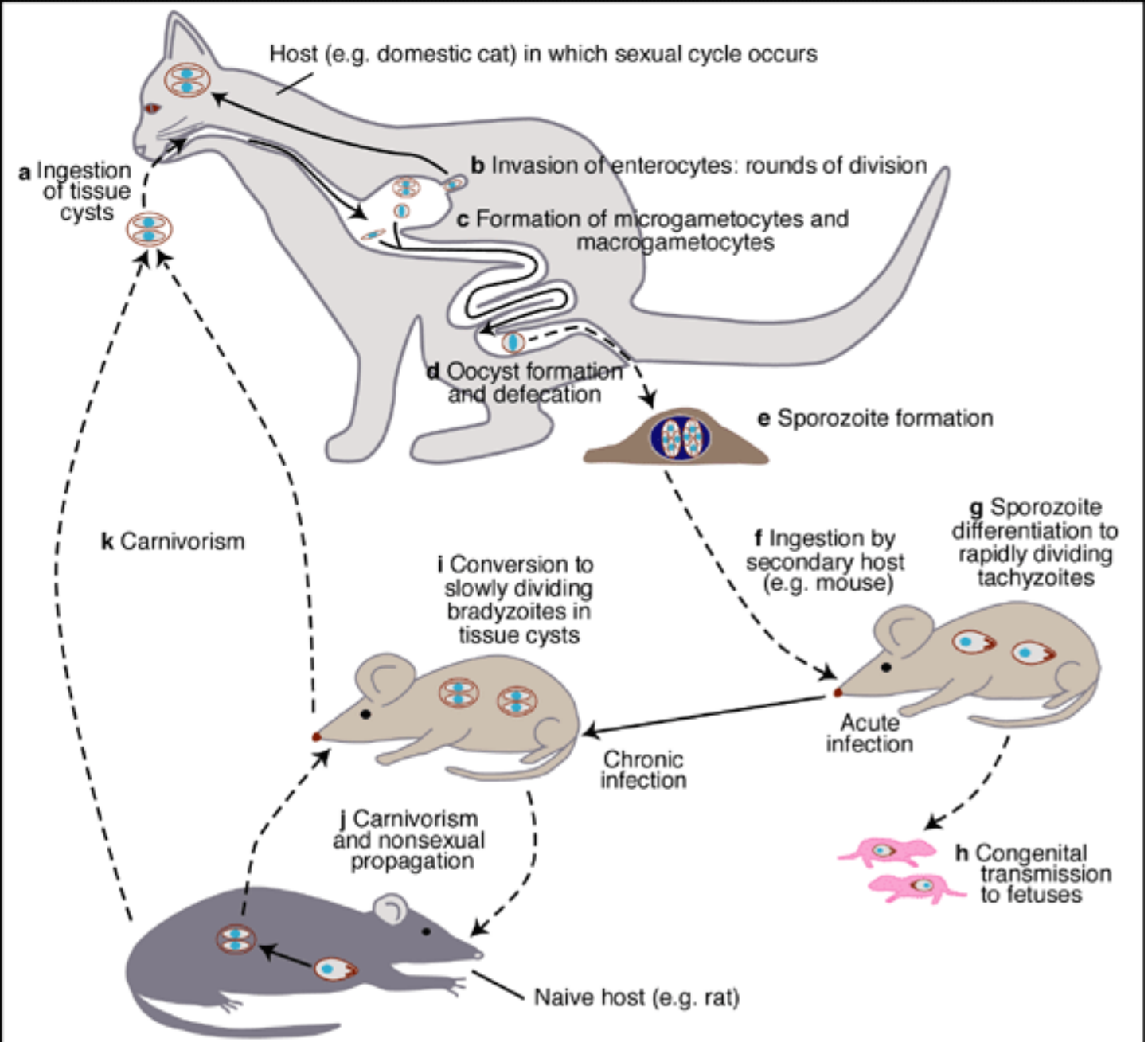
Zoonosis – Transmission via undercooked meat, cat feces, drinking water. Flu-like symptoms

Can cross placenta ⇒ Congenital risk (TORCH) → brain damage or vision problems

Risk of new infection or reactivation in the immunosuppressed

T. gondii undergoes sexual reproduction in the intestinal tract of domestic cats, and oocysts are eliminated in cat feces.

Toxoplasmosis can be identified by serological tests, but interpretation of the results is uncertain.



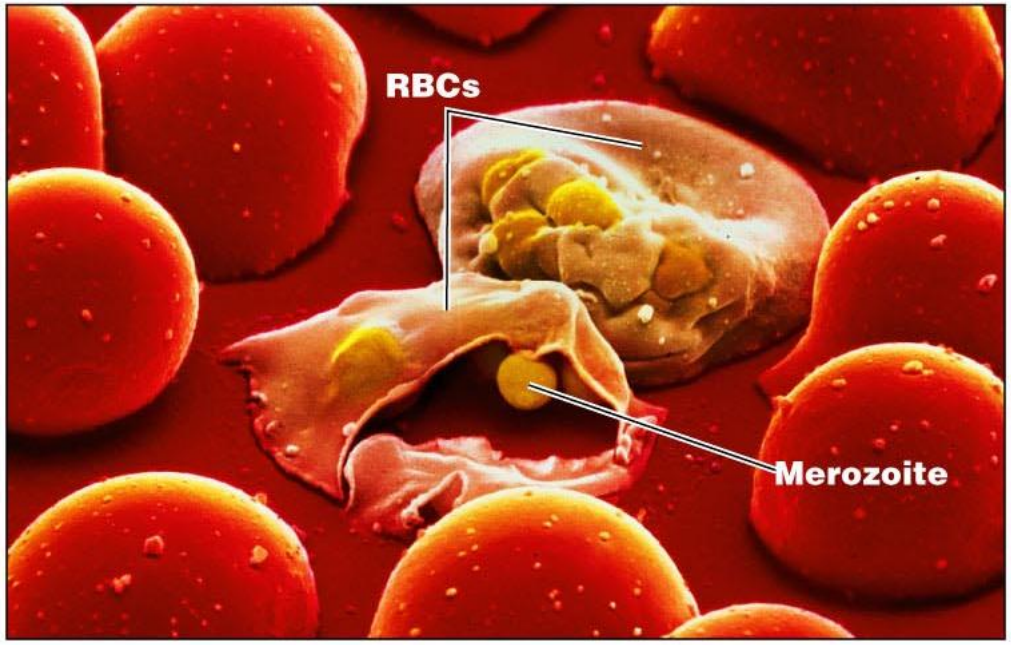
The *Toxoplasma gondii* life cycle

Compare to Fig. in book

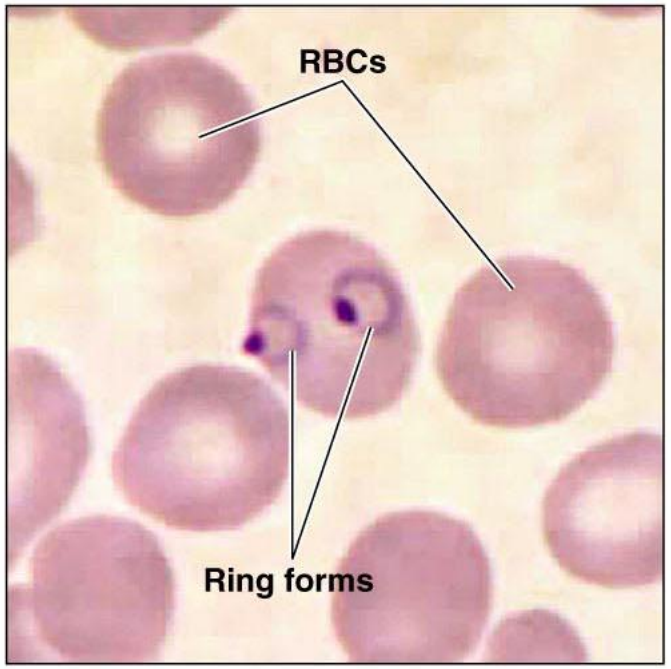
Malaria

- Four species of Plasmodium: ***P. falciparum*** (malignant)
- Vector: *Anopheles* mosquito
- Worldwide 300-500 million cases; ~ 1.5 – 3 million people die; ~ 1,200 cases in US
- *Plasmodium* infects red blood cells $\Rightarrow$ microscopic diagnosis
- Symptoms: chills, fever, vomiting, headache; at intervals of 2 to 3 days
- New drugs are being developed as the protozoa develop resistance to drugs such as chloroquine.

Microscopic Diagnosis



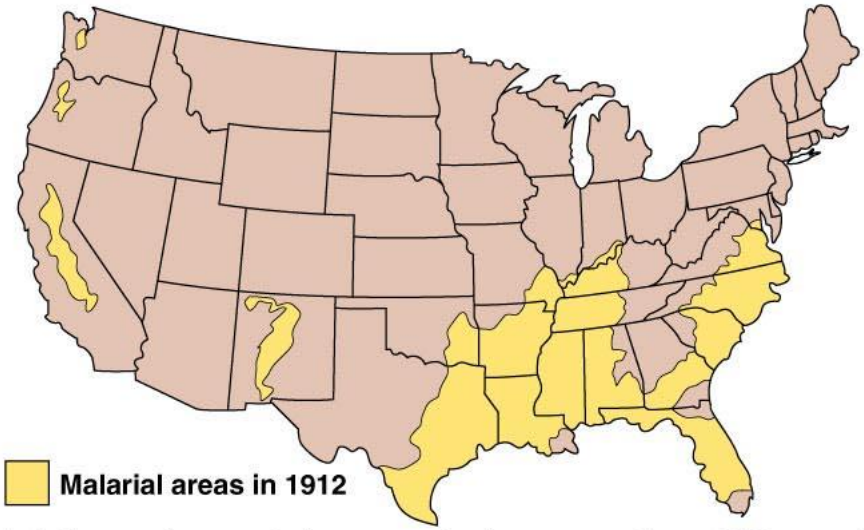
(a) Merozoites being released from lysed RBC. SEM 1 μm



(b) Malarial blood smear; note the ring forms. LM 5 μm

Figure 23.25

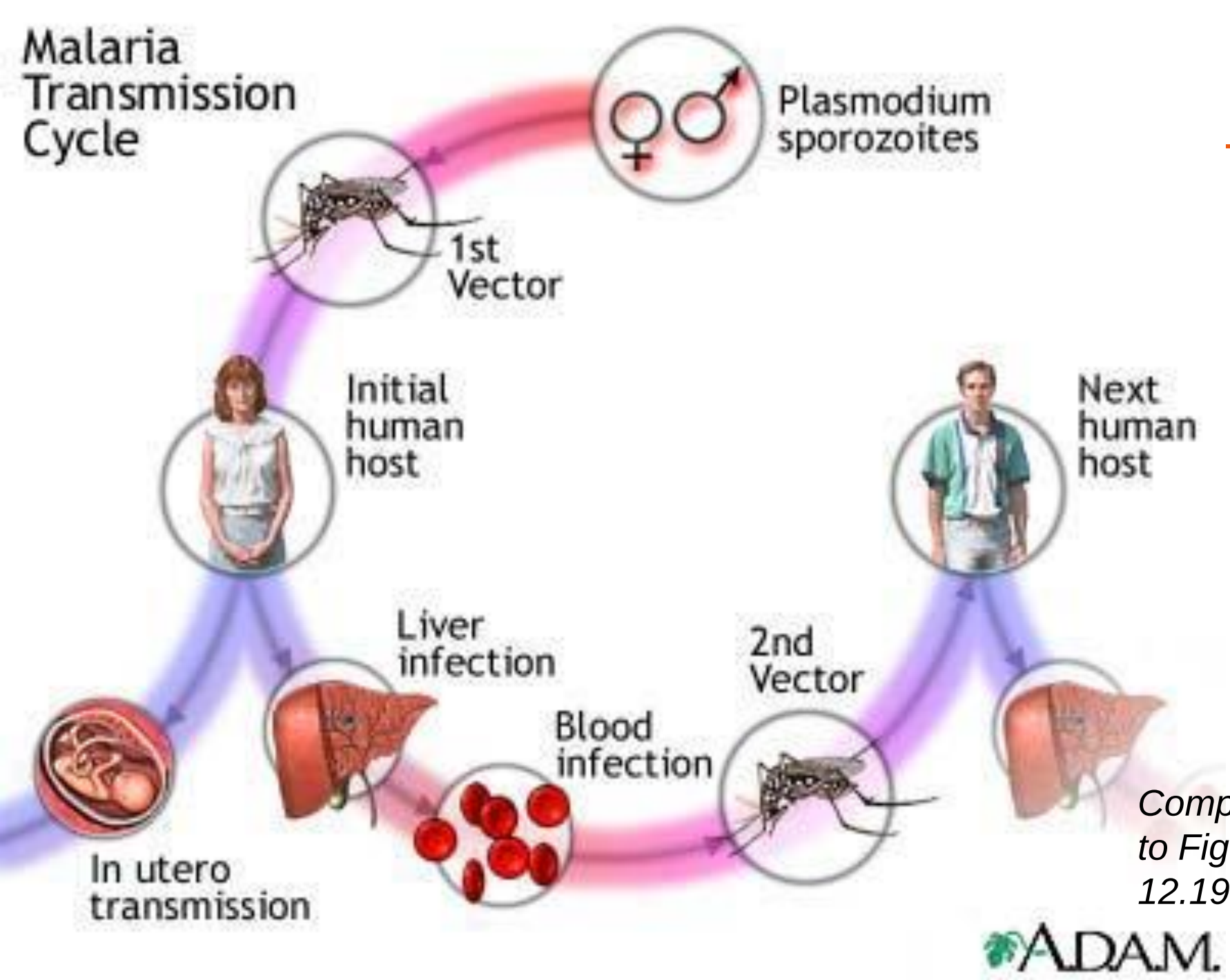
Malaria



(a) Areas where malaria was endemic as recently as 1912

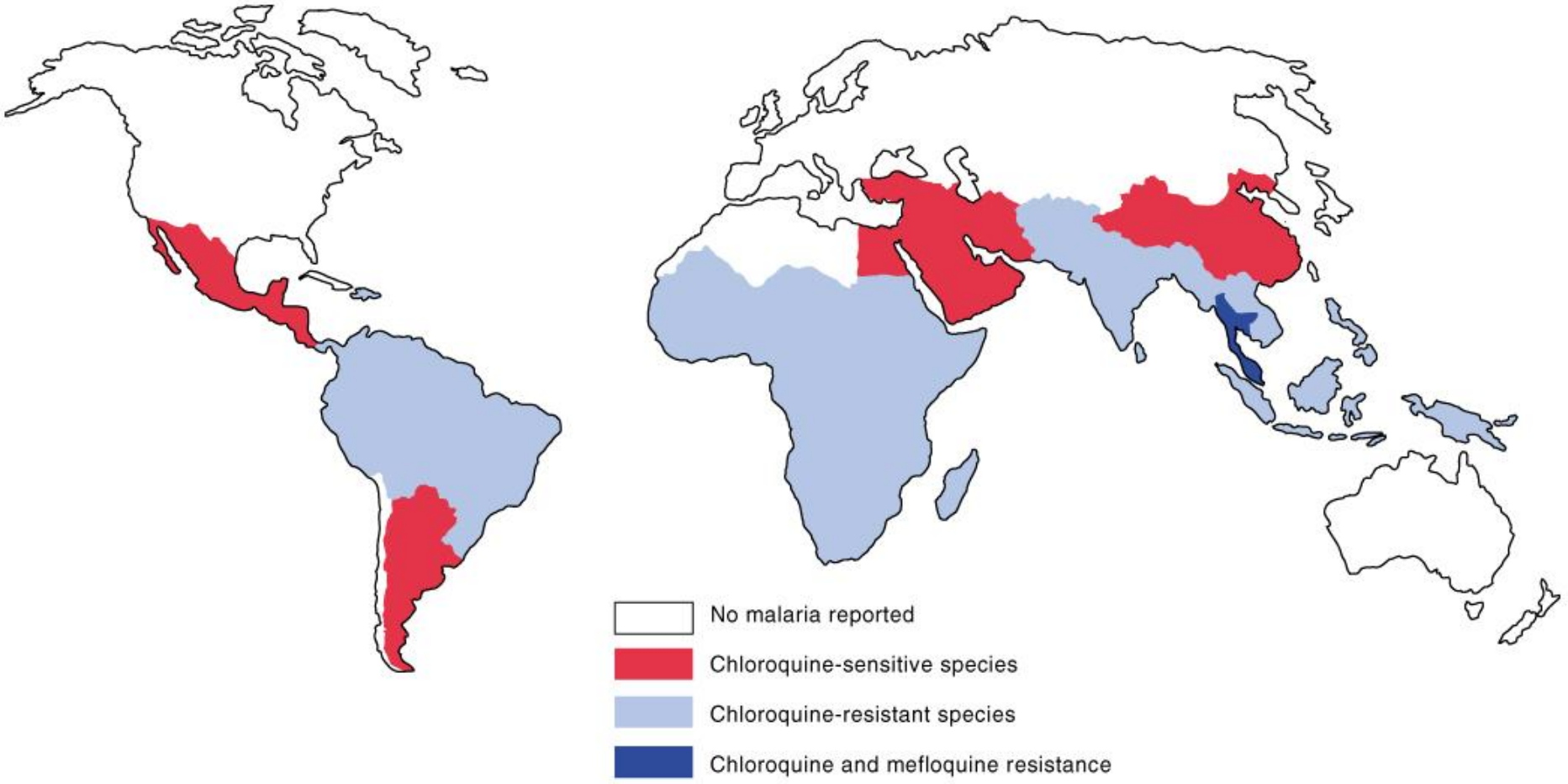
(b) Graph showing reported cases of malaria in the United States, 1967 to (*) the first 26 weeks of 2005

Figure 23.24



Compare to Fig 12.19

Distribution of Malaria



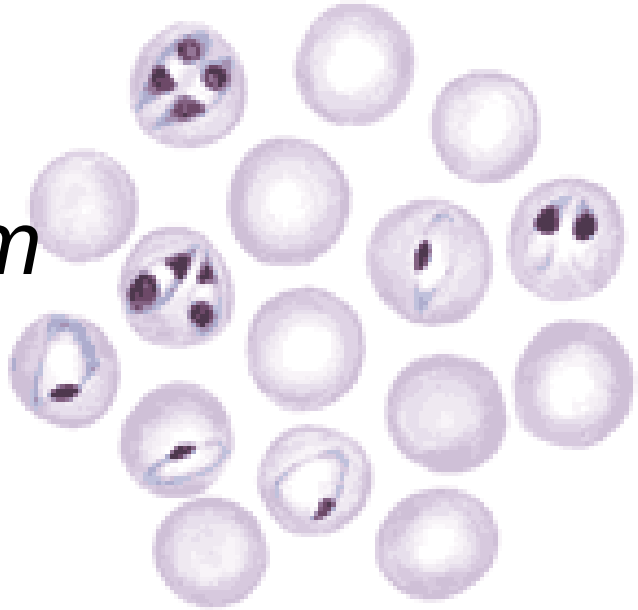
Babesiosis

Babesia microti

Vector *Ixodes* tick - Zoonosis

Hemoprotozoan → rupture of RBCs → hemolytic anemia

In malaria-endemic areas *misdiagnosis* as *Plasmodium*

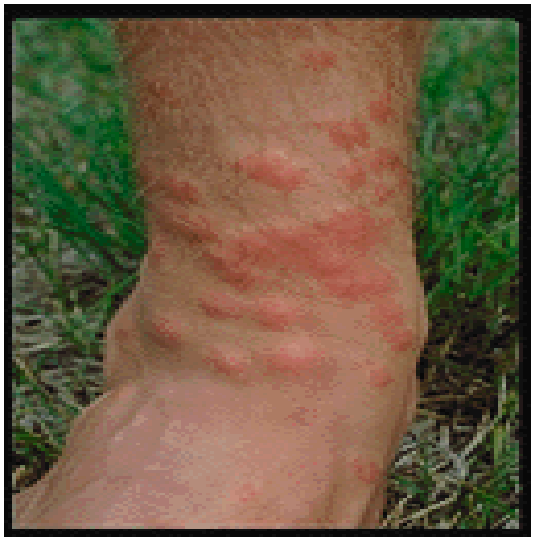


Schistosomiasis / Bilharzia(sis)

- *Schistosoma mansoni, S. haematobium*, and *S. japonicum*
- 250 million people infected worldwide
- Cercaria penetrates skin when exposed to contaminated water → worms grow inside blood vessels and produce eggs → eggs travel to liver (liver damage), intestine or bladder.
- Treatment available *(praziquantel)*

Fig 17.2

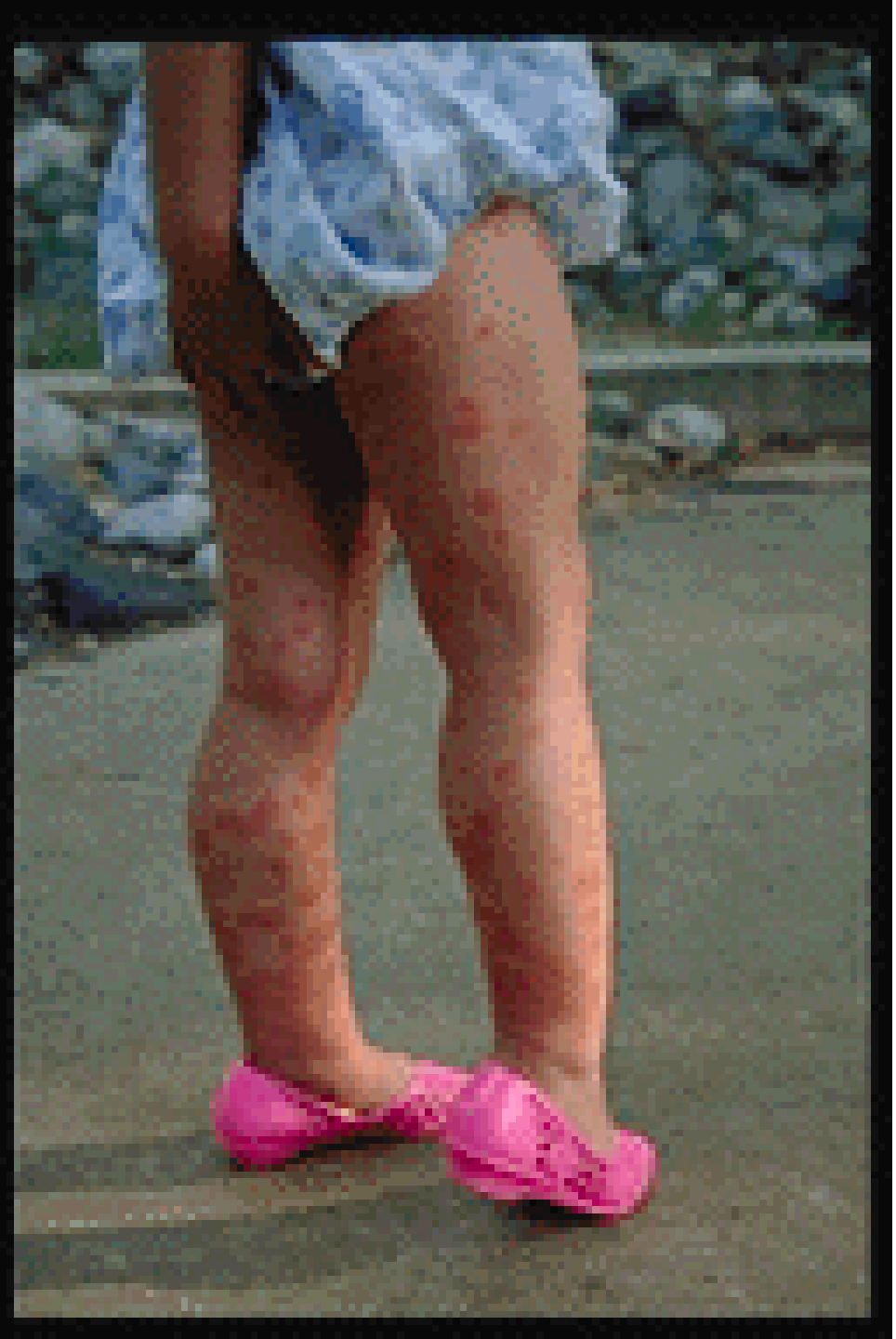
Other Schistosomes: **Swimmer's Itch** or Cercarial Dermatitis



Schistosome cercaria accidentally enters human skin (bird is definitive host for adult parasite)

Almost every state in US (Most predominant in the north). Also in more than 30 countries.

Disappears without treatment (~ 7 days) – no internal organs involved



Parasites die after entering → dermatitis in previously sensitized individuals. Sensitivity rarely disappears; usually gets worse in subsequent exposures.

Widely scattered from Michigan lakes to Alaska.