The Rickettsiae
HLS Module
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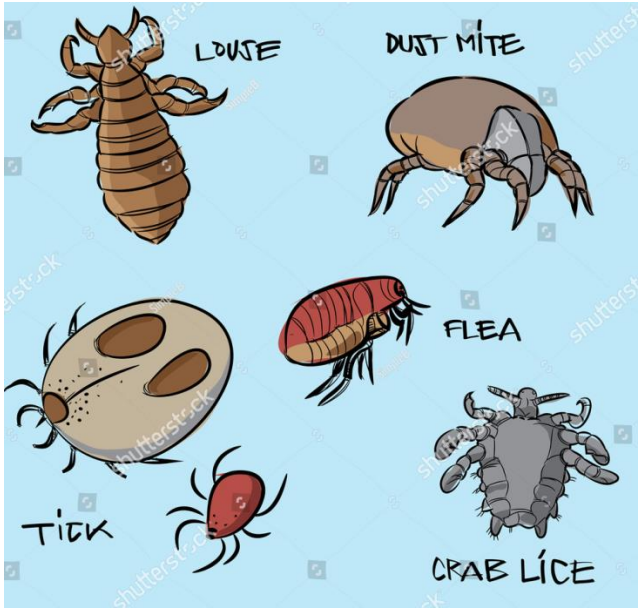
The Rickettsiae

- The rickettsiae are a heterogeneous group of small, obligately intracellular, gram-negative coccobacilli and short bacilli, most of which are transmitted by a tick, mite, flea, or louse vector.

القراد العث البراغيث القمل

The rickettsiae has six genera:

- ***Rickettsia***
- ***Coxiella***
- *Orientia*
- *Ehrlichia*
- *Anaplasma*
- *Neorickettsia*



The Rickettsiae

- The clinical manifestations of all are similar during the first 5 days: fever, headache, and myalgias with or without nausea, vomiting, and cough.

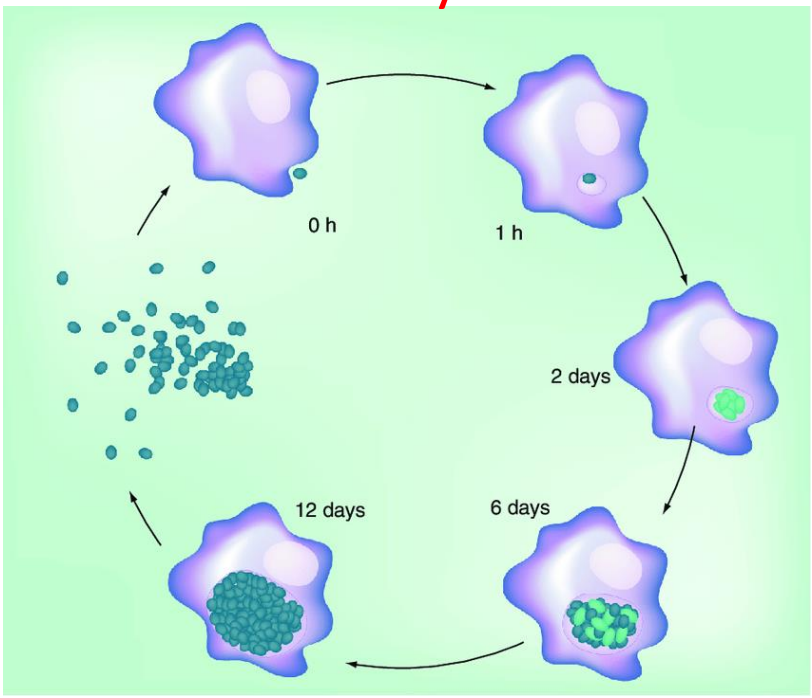
- As the course progresses, clinical manifestations—including ocurrence of a macular, maculopapular, or vesicular rash; pneumonitis; and meningoencephalitis— vary from one disease to another.

Coxiella burnetii

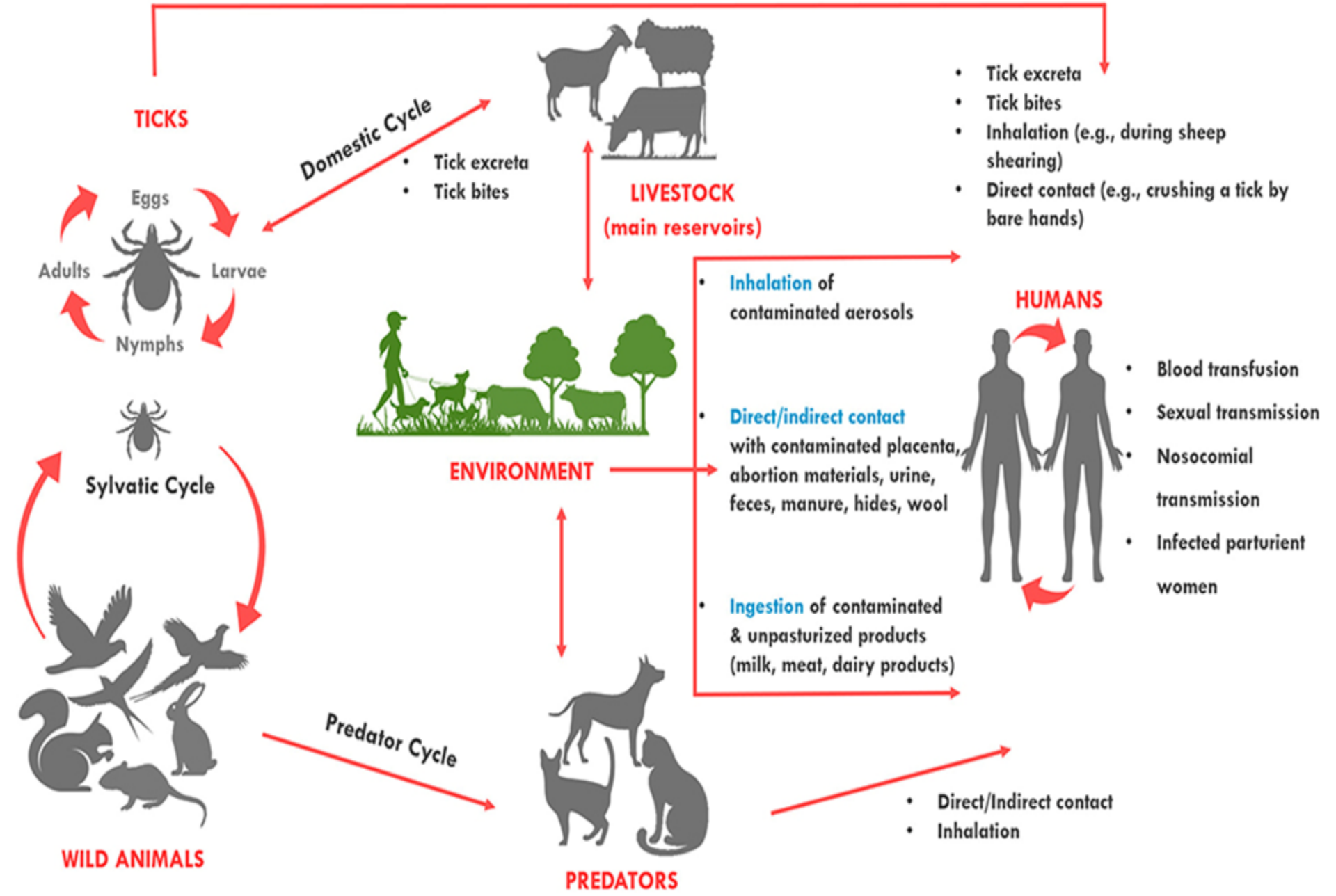
Coxiella burnetii

- The causative agent of Q fever.
- The "Q" comes from "**query**" fever, the name of the disease until its true cause was discovered in the 1930s
- Highly resistant to environmental stresses (spore-like structure).
- It can survive standard disinfectants.
- The organism is killed by pasteurization.
- It replicates in host monocytes and macrophages. (Resistant to the phagolysosomal environment).
- C. burnetii bacteria are found in the birth products (i.e. placenta, amniotic fluid), urine, feces, and milk of infected animals.

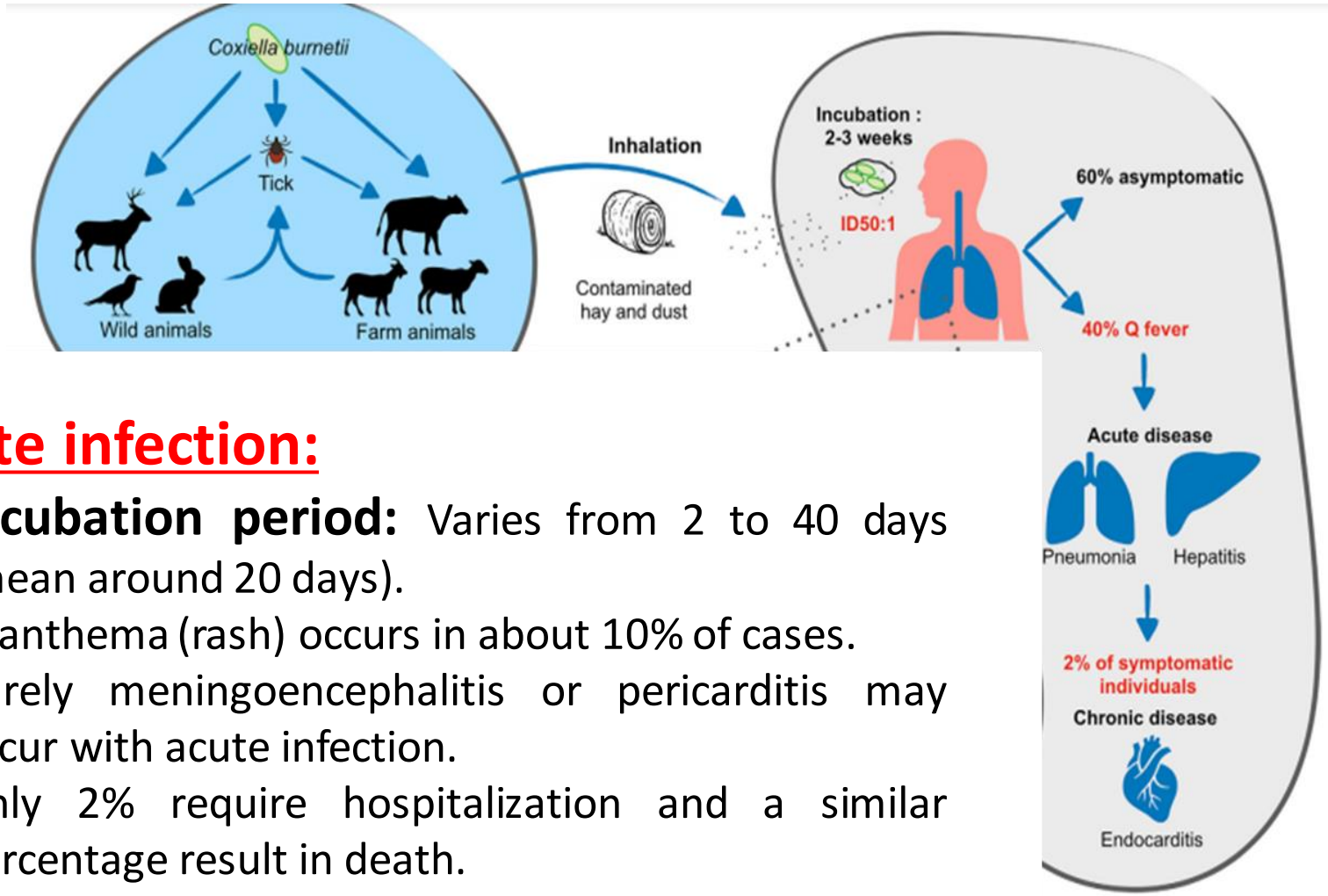
Life cycle



Transmission



Disease in Human



Acute infection:

- **Incubation period:** Varies from 2 to 40 days (mean around 20 days).
- Exanthema (rash) occurs in about 10% of cases.
- Rarely meningoencephalitis or pericarditis may occur with acute infection.
- Only 2% require hospitalization and a similar percentage result in death.

Disease in Human

Acute Infection

- **Symptoms** :

  Vary in severity and duration; a self-limited febrile or flu-like illness often occurs.

- **Signs include**

  Fever, chills, “sweats”, headache, fatigue, anorexia, malaise, myalgia, and chest pain.

- **Duration of illness:**

From 1-3 weeks.

- **Outcomes of acute infection:**

30 to 50% of patients with symptomatic illness will develop pneumonia.

Human Disease

Chronic Disease

- Occurs in 1 to 5% of cases.
- It is typically **develops** in persons with **pre-existing cardiac valvular disease**, **Immunocompromised** persons and **pregnant** women
- Complications includes:
  - Endocarditis is the major clinical presentation (60 to 70% of all chronic Q fever cases).
  - hepatitis or cirrhosis. Kupffer cells are considered to be target cells for *C. burnetii*.
- Involvement in bone has also been reported.

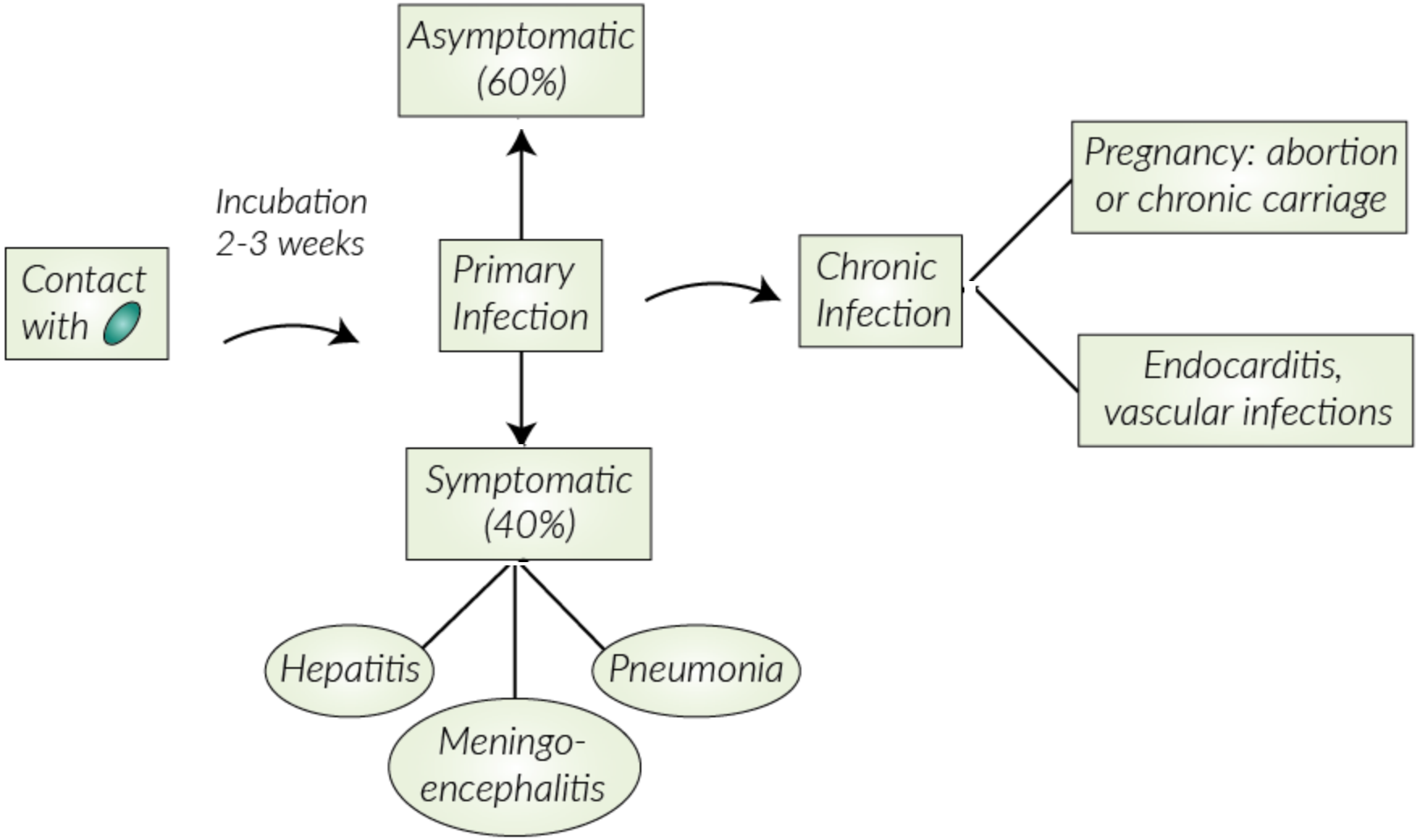
Human Disease

Risk to Pregnant Women

- Most asymptomatic
- Transplacental transmission
- Reported complications
  - In-utero death
  - Premature birth
  - Low birth weight
  - Placentitis
- Pregnants may pose a degree of risk to medical staff

Animal Disease

- Sheep, cattle, goats
  - May be asymptomatic
  - Reproductive failure
    - Abortions
    - Stillbirths
    - Infertility
    - Weak newborns
    - Low birth weights
  - Carrier state


Asymptomatic (60%)
Incubation 2-3 weeks
Contact with
Primary Infection
Chronic Infection
Pregnancy: abortion or chronic carriage
Endocarditis, vascular infections
Symptomatic (40%)
Hepatitis
Pneumonia
Meningo-encephalitis

Prognosis

- Self-limiting: resolve within 2-14 days.
- 50 to 60% of cases are asymptomatic, and complications from the acute form of disease are rare.
- 2% of persons infected develop severe disease and require hospitalization.
- The mortality rate is 1% or lower if treated.
- Active chronic disease is usually fatal if untreated.
- In patients with endocarditis, the fatality rate can range from 45 to 65%; additionally, 50 to 60% need valve replacement surgery.

Prevention and Control

- Pasteurization
- Disinfection (10% bleach)
- Eradication not practical
  - Too many reservoirs
  - Constant exposure
  - Stability of agent in environment

Q Fever as a Biological Weapon

- Low infectious dose
- Stable in the environment
- Aerosol transmission

Q Fever: Lab Findings and Diagnosis

Laboratory Findings:

- Elevated Liver Enzymes
- Elevated alkaline phosphatase
- Leukocytosis, Thrombocytopenia, Anemia of chronic disease
- Increased CPK and ESR
- Blood cultures are usually negative

Diagnosis:

- Serology and Indirect Immunofluorescence Assay (IFA)
- High Antibody titer
- Persistent/Chronic Infection
- Anti-mitochondrial antibody positive, anti-smooth muscle antibody positive, APLA positive without rheumatologic disorder
- Very high Antibody titer

Prevention and Control

- Tick prevention
- Disposal of birth products
- Separate new or sick animals

Treatment

- Treatment
  - Doxycycline
  - Chronic disease – long course
    - 2 to 3 years of medication
- Immunity
  - Long lasting (possibly lifelong)

Case

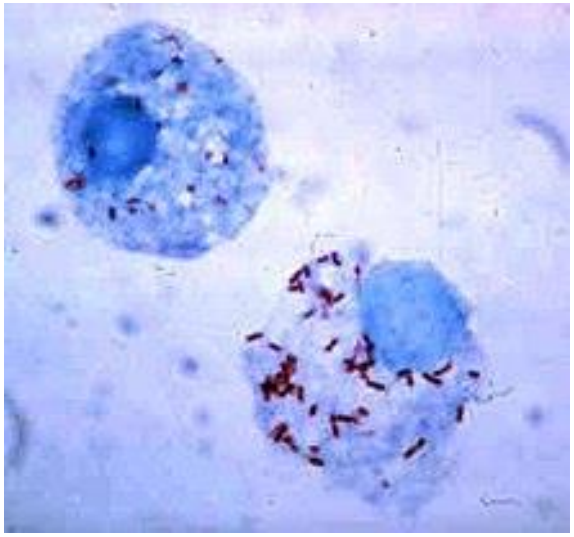
- Male dairy farmer
  - Age 46
  - Sudden onset of fever, chills, cough
  - Initially diagnosed as influenza
  - Symptoms persisted for 2 weeks
  - Presented to emergency room
  - Again diagnosed as influenza
- Referral to infectious disease specialist
  - Tested positive for Q fever
  - Antibiotics for 5 days
  - Resolved in 2 weeks

Rickettsia prowazekii

Rickettsia- Introduction

Rickettsia

- Nonmotile, intracellular gram-negative, nonspore-forming, highly pleomorphic bacteria.
- The term "rickettsia" has nothing to do with rickets (vitamin D deficiency); but it was named after its discovery by Howard Taylor Ricketts.



Diseases caused by Rickettsia

Species	Disease	Reservoir
R. prowazekii	Epidemic typhus, Brill-Zinsser disease	Human body louse
R. typhi	Endemic typhus	Rat flea
R. rickettsii	Rocky-Mountain spotted fever	Ticks
R. conori	Boutonneuse fever	Ticks
R. australis	Australian tick typhus	Ticks
R. siberica	Siberian tick typhus	Ticks
R. akari	Rickettsial pox	Mites

Disease caused by Rickettsia

- Typhus refers to a group of infectious diseases that are caused by rickettsial organisms and results in an acute febrile illness.
- **Epidemic typhus** (also called "camp fever", "jail fever", "hospital fever", "ship fever“, "petechial fever", "Epidemic louse-borne typhus,“ and "louse-borne typhus”
- The name typhus comes from the **Greek** meaning **hazy** or **smoky** and commonly used as a **word** for **delusion**, describing the **state of mind** of those infected.

Epidemic typhus

A. Cause: Rickettsia prowazekii.
B. Vector: Body lice.

- Pediculus corporis (common).
- Pediculus capitis.

Pathophysiology

- A p**ruritic** reaction on the host's skin after a louse bites rickettsia harboring .
- A louse defecates as it eats; when the host **scratches** the site, the **lice are crushed** and *Rickettsia* is inoculated into the bite wound.
- The rickettsia travel to the blood stream and rickettsaemia develop.
- Rickettsia **parasitizes** the **endothelial** cells of the blood vessels.
- The organisms proliferate and cause endothelial cellular enlargement, damage, with resultant multi-organ vasculitis.

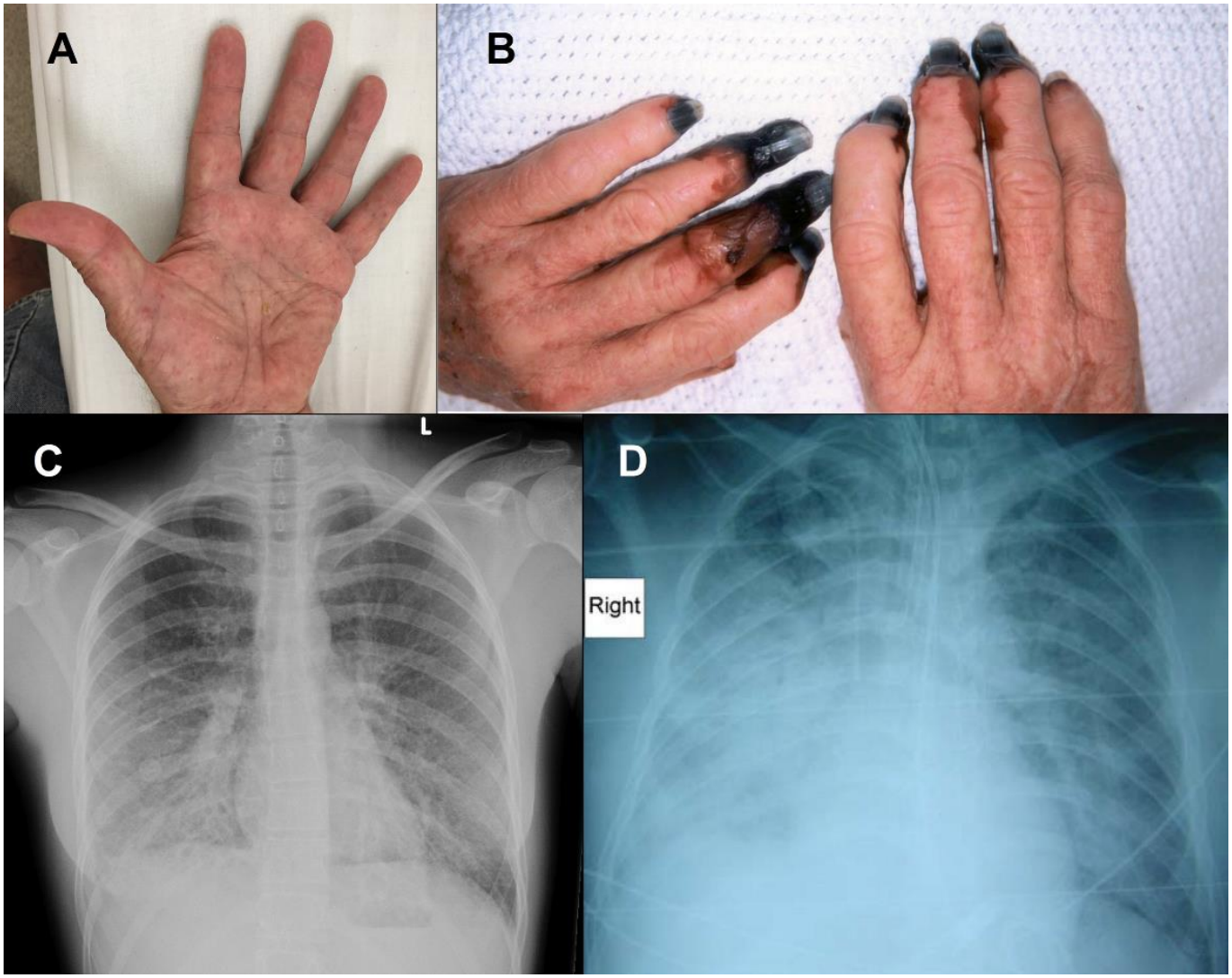
Pathophysiology

- Multi-organ **vasculitis** may cause thrombosis (deposit of leucocytes, macrophages and platelets).
- Gangrene of the distal portions of the extremities, nose, ear lobes and genitalia may occur as the result of thrombosis of supplying blood vessels
- Vasculitis may also result in loss of intravascular colloid with subsequent hypovolaemia and decrease tissue perfusion and possibly organ failure and loss of electrolytes.

Clinical findings

- The incubation period is approximately 12 days for the typhus group.
- Abrupt onset of fever.
- Headache occurs abruptly and continues constantly.
- Non-productive cough.
- Rigors, Myalgia, Malaise.
- Rash: appears after 4-5 days (is macular/papular/petechial).
- Tachypnoeia
- Digital gangrene.
- Mild hepatosplenomegaly
- Conjunctival congestion
- Relative bradycardia consistent with the rise of temperature.
- Lymphadenopathy (regional or generalized).

Clinical findings



Epidemic typhus

Diagnosis

- Renal function test
- Urinalysis.
- Liver functional tests.
- Full blood picture.
- Electrolytes.
- Indirect immunofluorescence (IFA) or enzyme immunoassay (EIA) testing.
- Polymerase chain reaction (PCR).
- Complement fixation (CF) tests.
- Histology of biopsied tissues sections.

Epidemic typhus

Treatment

- Doxycycline 200 mg PO or IV for 3 days, then maintenance dose 100 mg PO or IV Plus Chloramphenicol.
- Alternatives in doxycycline resistance:

  - Azithromycin.

  - Rifampicin