

# 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.

**The rickettsiae has six genera:**

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

# The Rickettsiae

- The clinical manifestations of all the acute presentations 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 occurrence 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.
- It can survive standard disinfectants
- **It replicates in host monocytes and macrophages. (Resistant to the phagolysosomal environment).**
- The organism is **killed by pasteurization.**

# Transmission

- This bacteria naturally infects some animals, such as goats, sheep, and cattle.
- *C. burnetii* bacteria are found in the birth products (i.e. placenta, amniotic fluid), urine, feces, and milk of infected animals.

# How do people become infected with *C. burnetii* bacteria?

- **Most** infections are contracted by **breathing** in **air contaminated** with the *C. burnetii* organism from animals aborting or birthing
- From **dried contaminated** materials
- Through **direct contact between infected materials** (tissues, fluids, wool, straw, manure, etc) and skin abrasions or mucous membranes.
- By **drinking unpasteurized milk**
- **Via tick bites**

# Transmission

- **Person-to-person** transmission is extremely **rare**.
- **Transplacental** transmission may **occur** resulting in **congenital infection**.
- Transmission from blood transfusions, bone marrow transplants, and intradermal inoculations have also been reported.
- Sexual transmission in a rare number of human cases.
- Persons at risk include
  - Farmers, livestock producers, veterinarians, abattoir workers
  - Laboratory personnel performing culture and diagnostics

# Disease in Human

- **Incubation period**

Varies from 2 to 40 days (mean around 20 days).

- **Infectious dose**

As few as one organism is capable of causing disease.

- **Clinical illness**

- 60% asymptomatic
- 40% show signs of clinical illness.

- **The clinical forms of the disease are:**

- A. Acute (less than 6 months duration)
- B. Chronic (greater than 6 months duration).

# 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. In more severe cases, a nonproductive cough with pneumonitis may develop.

# Disease in Human

## Acute Infection

- Many clinically ill patients will have abnormal liver enzymes, and some will develop hepatitis although jaundice is rare.
- Exanthema (rash) occurs in about 10% of cases.
- Rarely meningoencephalitis or pericarditis may occur with acute infection.
- Only 2% of acute infections require hospitalization and a similar percentage result in death.

# 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
- Endocarditis is the major clinical presentation and accounts for 60 to 70% of all chronic Q fever cases.
- Infection can also affect the liver causing granulomatous hepatitis or cirrhosis. Kupffer cells are considered to be target cells for *C. burnetii*.
- Involvement in bone has also been reported.

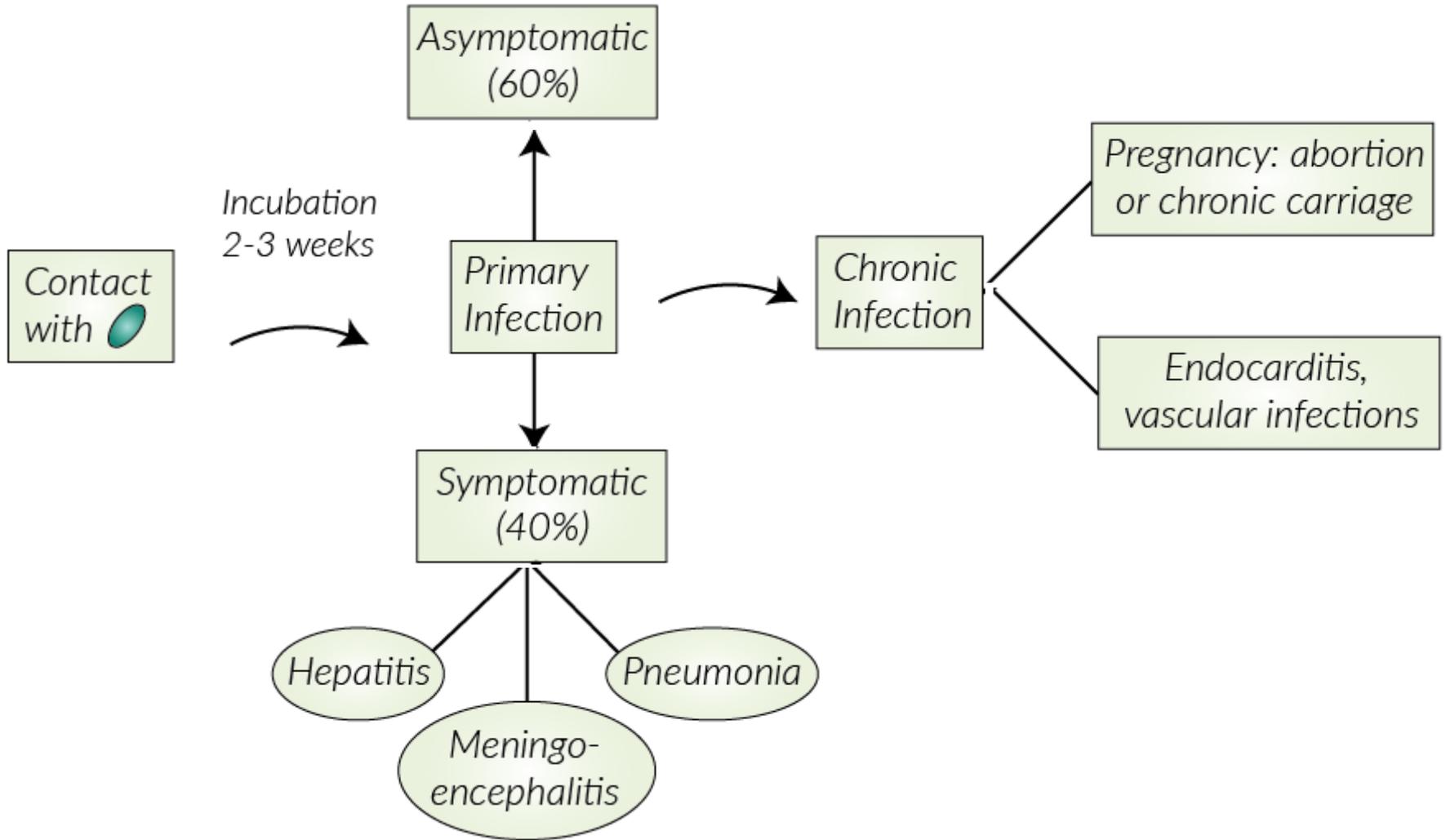
# Human Disease

## 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

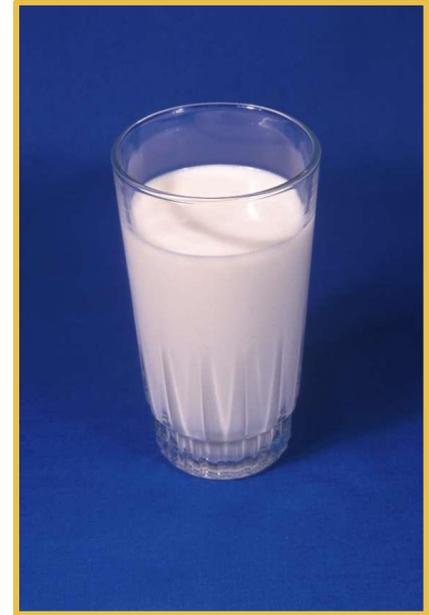


# Prognosis

- 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

# 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

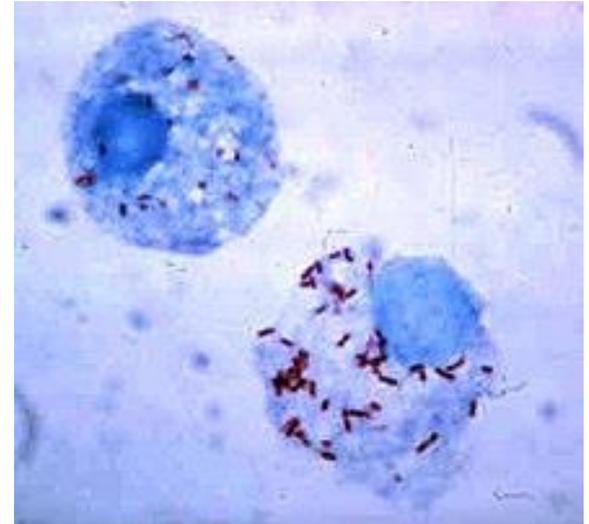


*Rickettsia prowazekii*

# *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***

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

# ***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

- The rickettsia harbouring louse bites a human to engage in human blood meal and causes a **pruritic** reaction on the host's skin.
- 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 with resultant multi-organ vasculitis.

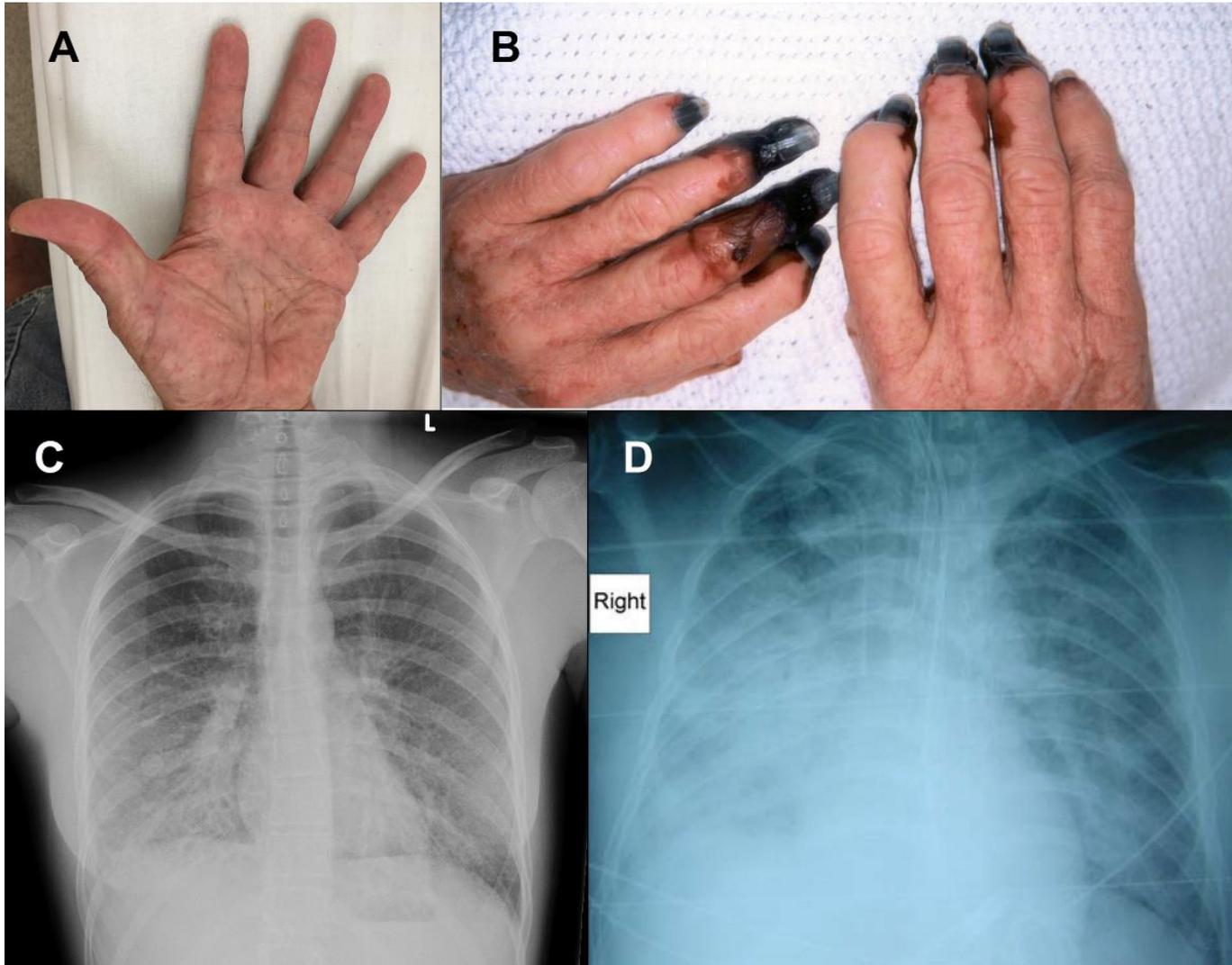
# Pathophysiology

- 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).
- Tachypnoea
- 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