Chapter 24

Chlamydiae

-- ***Chlamydiae*** are **obligate intracellular** bacteria which cause some **sexually transmitted** diseases (**urethritis** and **cervicitis**).

-- They also cause other infections such as **pneumonia**, **psittacosis**, **trachoma**, and **lymphogranuloma venereum**.

-- ***C. trachomatis*** causes **eye**, **respiratory** and **genital tract** infections.

-- It is the most common cause of sexually transmitted diseases in US.

-- The infection is associated with **Reiter's syndrome**, an autoimmune disease.

-- ***C. pneumoniae*** and ***C. psittaci*** cause **pneumonia** and **psittacosis** respectively.

-- These are sufficiently different at molecular level to be reclassified as a new genus called ***Chlamydophila***.

Important Properties

-- They are **obligate intracellular** bacteria.

-- They **lack the ability to produce sufficient energy** to grow independently and therefore can grow only inside host cell.

-- They have a rigid cell wall but **do not have a typical peptidoglycan** layer.

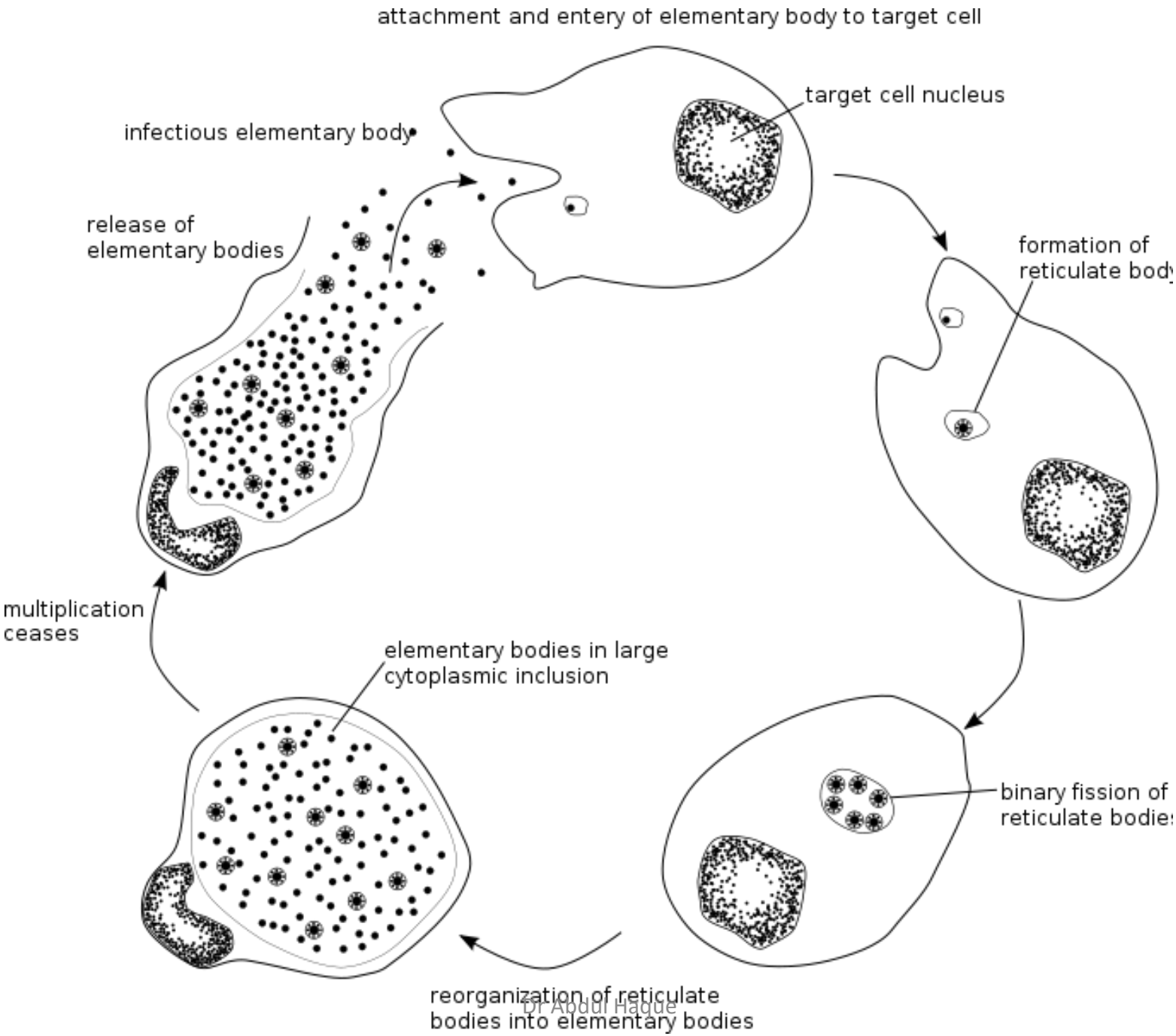
-- Their cell wall resembles those of **Gram negative** bacteria but **lack muramic acid**.

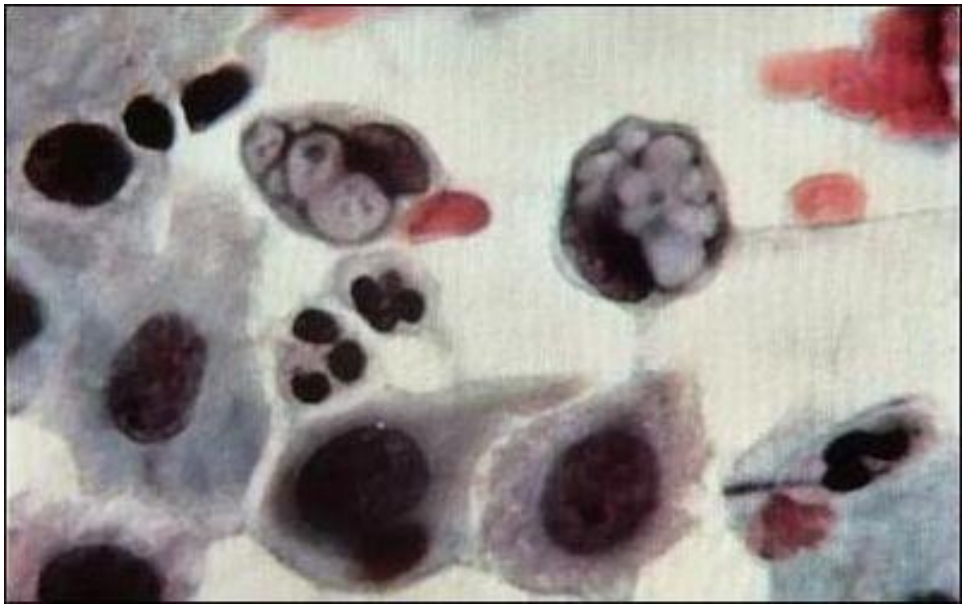
Unique life cycle

-- It begins when extracellular, metabolically inert, “spore like” **elementary body** enters the cell and reorganizes into a larger, metabolically active **reticulate body**.

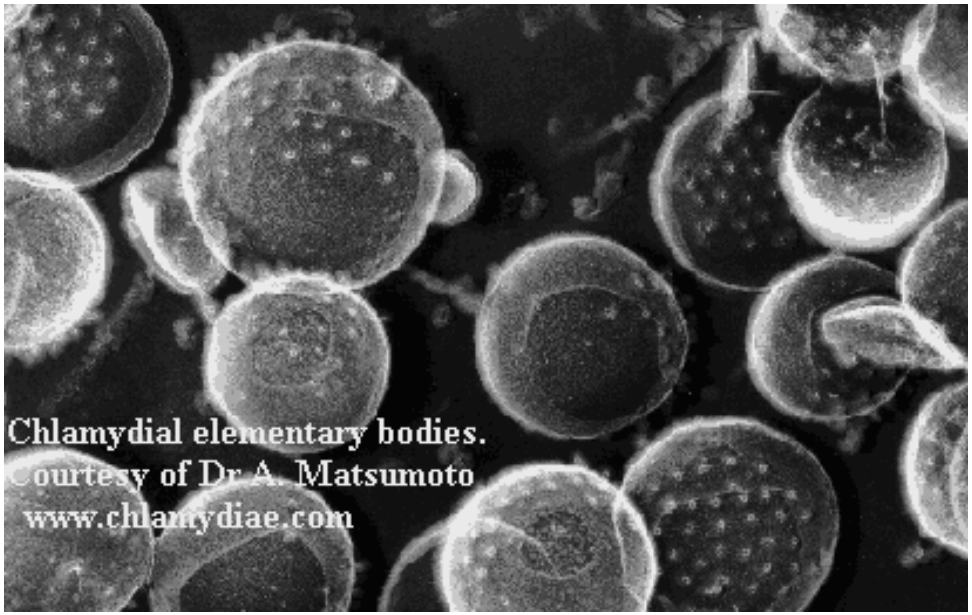
-- They undergo **repeated cycles of binary fission** to form **daughter reticulate bodies** which then **develop into elementary bodies** which are **released from cell**.

-- Within cells, the site of replication appears as an **inclusion body** which can be stained and visualized microscopically and help in laboratory diagnosis.


attachment and entery of elementary body to target cell
target cell nucleus
infectious elementary body
release of
elementary bodies
formation of
reticulate body
multiplication
ceases
elementary bodies in large
cytoplasmic inclusion
binary fission of
reticulate bodies
reorganization of reticulate
bodies into elementary bodies



Inclusion bodies



-- All ***Chlamydiae*** share a **group specific LPS antigen** which is detected by **CFT** (complement fixation test).

-- They also possess **species-specific** and **immunotype specific** antigens which are detected by **immunofluorescence**.

-- ***C. trachomatis*** has at least **15** and ***C. pneumoniae*** and ***C. psittaci*** **one** immunotype.

Transmission and Epidemiology

-- ***C. trachomatis*** infects **only humans** and is usually transmitted by **close personal contact** (e.g., sexually or by passage through the birth canal).

-- Individuals with **asymptomatic infection** are **major reservoirs**. In trachoma, transmission is by finger-to-eye or fomite-to-eye contact.

-- Sexually transmitted disease has world-wide distribution and in 10-30% cases ***N. gonorrhea*** is **co-infector**.

-- **Trachoma** is found in **dry, hot regions** such as northern Africa where it is **leading cause of blindness.**

-- ***C. pneumoniae*** infects **only humans and** is transmitted through **aerosol**.

-- ***C. psittaci*** infects **birds** and **humans** are infected by **inhalation** of organisms in dry bird feces.

Pathogenesis and Clinical findings

-- ***Chlamydiae*** infect primarily **epithelial cells** of the **mucus membranes** of the **lungs**.

-- They **rarely** cause invasive, disseminated infections.

-- ***C. psittaci*** infects the **lungs** primarily.

-- The infection may be **asymptomatic** or may produce high fever and pneumonia.

-- It is generally **not communicable**.

-- ***C. pneumoniae*** causes **upper and lower respiratory tract infections**, esp. bronchitis and anemia in young adults.

-- **Types A, B and C** of ***C. trachomatis*** cause **trachoma** which may cause **blindness** but there is no systemic disease.

-- **Types D-K** cause **genital tract infections**.

-- In **men**, it is a common cause of **nongonococcal urethritis** which is characterized by a urethral discharge.

-- The infection may progress to **epididymitis, prostatitis**, or **proctitis**.

-- In **women**, **cervititis** develops and may progress to **salpingitis** and **pelvic inflammatory disease** (PID) which may result in **infertility** or **ectopic pregnancy**.

-- **Infants** of infected mothers often develop **mucopurulent conjunctivitis** 7-12 days after delivery and some develop **chlamydial pneumonitis** 2-12 weeks after birth.

-- The patients with genital infections have high incidence of **Reiter's syndrome**, an autoimmune disease, characterized by **urethritis**, **arthritis,** and **uveitis**.

-- Infection by ***C. trachomatis*** leads to formation of antibodies and cell-mediated reactions but not to resistance to reinfection or elimination of organisms.

Laboratory Diagnosis

-- ***Chlamydiae*** form **cytoplasmic inclusions**, which can be seen with special stains (e.g., **Giemsa stain**) or by **immunofluorescence.**

-- The **Gram stain is not useful**.

-- In exudates, the organism can be identified within epithelial cells by **fluorescent antibody staining** or **hybridization with a DNA probe**.

-- Chlamydal antigens can also be detected in exudates or urine by **ELISA**.

-- A **PCR based test** using the patient's urine can also be used for diagnosis.

-- ***Chlamydiae*** **can be grown in cell cultures** treated with **cycloheximide,** which inhibits host cell but not chlamydial protein synthesis, thereby enhancing chlamydial replication.

-- Only ***C. trachomatis*** **inclusions contain glycogen** so they can be identified by **iodine staining**. Exudates give positive culture in nearly half of the cases.

-- Serological tests can be used for ***C. pneumoniae*** and ***C. psittaci***, but not for ***C. trachomatis*** because of high false positivity.

Treatment

-- All ***Chlamydiae*** are **susceptible to tetracyclines**, such as doxycycline and macrolides.

-- Drug of choice for ***C. trachomatis*** is **azithromycin**.

-- For **neonatal conjunctivitis** and **pneumonia**, **oral erythromycin** is preferred.

-- For other ***Chlamydiae***, **doxycycline** is preferred.

Prevention

-- There is **no vaccine**.

-- **Prompt treatment** of patient and associated people within 60 days should be done.

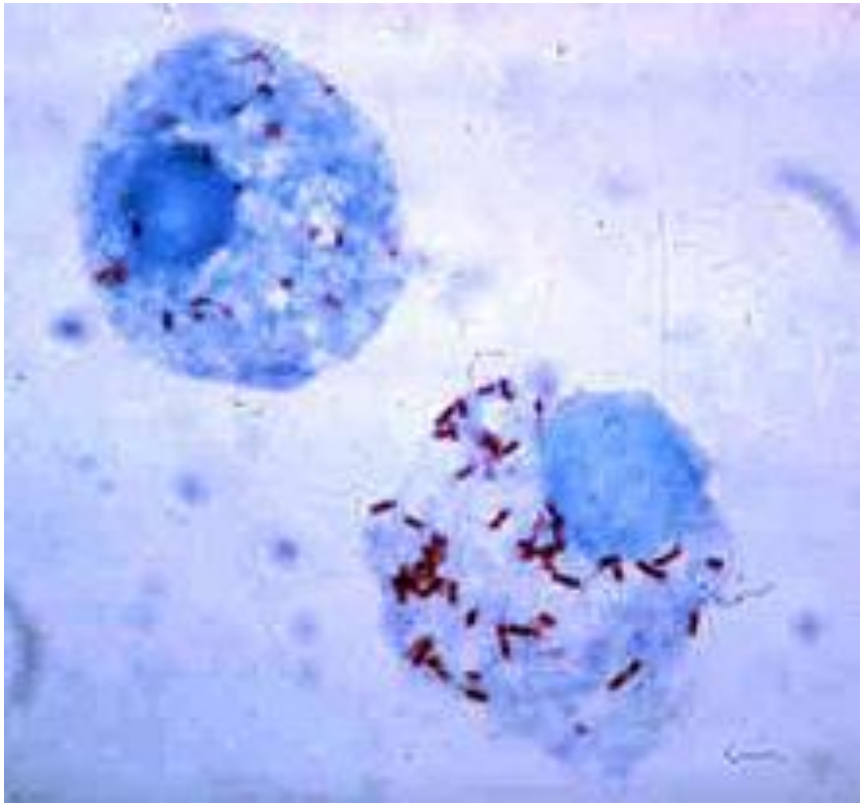
-- **Oral erythromycin** given to **newborns of infected mother** can prevent **inclusion conjunctivitis** and **pneumonitis**.

-- **Ointment is not so effective**.

-- **Psittacosis** in humans is controlled by restricting the importation of **psittacine birds**, destroying sick birds and adding **tetracycline** to bird feed.

Rickettsiae

Rickettsiae are **obligate intracellular bacteria** which cause **typhus, Rocky Mountain spotted fever** and other spotted fevers, and **Q fever**.



Important Properties

Rickettsiae are **very short rods** that are **barely visible** in the light microscope.

Structurally, their **cell wall resembles that of Gram negative rods**, but they **stain poorly** with standard **Gram stain**.

-- ***Rickettsiae*** are **obligate intracellular parasites** because they are **unable to produce sufficient energy** to replicate extracellularly.

-- They must be grown in **cell culture**, **embryonated eggs**, or **experimental animals**.

-- They **divide by binary fission** within the host cell, **unlike chlamydiae** which have a distinct intracellular cycle.

-- Several ***Rickettsiae*** (***R. prowazekii, R. tsutsugamushi***, and ***R. rickettsii***) possess antigens that **cross-react** with antigens of the OX trains of ***Proteus vulgaris***.

-- The **Weil-Felix test** is based on this cross reactivity.

-- ***Coxiellla burnetti*** has a **spore like stage** that is highly resistant to drying which makes it more infective.

-- It also has a **very low ID50**, estimated to be app. **one organism**.

-- **Phase 1** organisms isolated from patients are **virulent** and synthesize certain surface antigens.

-- **Phase 2** antigens are produced by **repeated passage in culture**, are **non virulent** and have lost the ability to synthesize certain surface antigens.

-- The clinical importance of phase variation is that patients with chronic Q fever have a **much higher antibody titer** to Phase 1 than those with acute Q fever.

Transmission

-- ***Rickettsiae*** are maintained in nature in certain **arthropods** such as **ticks, lice, fleas**, and **mites**.

-- They are generally transmitted to humans by **bite of the arthropod**.

-- They circulate widely in the blood stream infecting primarily the **endothelium of the blood vessel walls**.

-- ***Coxiellla burnetti*** is transmitted by **aerosols** and inhaled into lungs.

-- Virtually all rickettsial diseases are **zoonoses** with exception of epidemic typhus.

-- **Epidemic typhus occurs only in humans** because the causative agent ***R. prowazekii*** is transmitted by the **human body louse**.

Pathogenesis

The **typical lesion** caused by ***Rickettsiae*** is a **vasculitis**, particularly in the endothelial lining of the vessel wall where the organism is found.

Damage to the blood vessels of the skin results in **characteristic rash**, and edema and hemorrhage, which is caused by **increased capillary permeability**.

-- The basis for pathogenesis by these organisms is **unclear**.

-- There is some evidence that **an endotoxin may be involved** but its role is not confirmed.

-- **No exotoxins** and **cytolytic enzymes** have been found.

Clinical findings and epidemiology

Rocky Mountain Spotted Fever

-- There is **acute onset** of non-specific symptoms such as fever, headache, myalgias, and prostration.

-- The **typical rash** appears after 2-6 days as **macules** which frequently progress to **petechiae**.

-- The rashes **begin from hand and foot**, and moves inward towards trunk.

-- Beside headache, **delirium** and **coma** can occur.

-- **Disseminated intravascular coagulation**, **edema**, and **circulatory collapse** may ensue in **severe cases**.

-- The **diagnosis must be made on clinical grounds** and treatment started.

-- **Lab diagnosis** depends on detection of **rise in antibody titer** and it takes many days.

-- ***R. rickettsii*** are passed by the **transovarian route** from tick to tick.

-- **Dogs** and **rodents** may also be reservoirs.

-- Humans are **accidental hosts**.

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

-- Most cases occur in **children** during spring and early summer.

-- **It can be fatal if untreated.**

-- If diagnosed, recovery by treatment is **prompt.**

Q fever

-- **Unlike** other rickettsial diseases, the main organ involved is **lungs**.

-- It begins suddenly with fever, severe headache, cough, and other influenza like symptoms.

-- In nearly 50% cases, disease progresses to **pneumonia**.

-- **Hepatitis** is also common.

-- **Combination of pneumonia and hepatitis is suggestive of Q fever.**

-- Unlike other rickettsial diseases, a **rash is rare**.

-- It is an **acute disease** and recovery is expected even in **absence of antibiotic treatment.**

-- Rarely chronic Q fever characterized by **life-threatening endocarditis** occurs.

-- **It is the only rickettsial disease not transmitted to humans by the bite of an arthropod.**

-- The important reservoirs are **cattle, sheep**, and **goats**.

-- ***C. burnetii*** causes an **inapparent** infection in these reservoirs and is found in high conc. in urine, feces, placental tissue, and amniotic fluid of the animals.

-- **Transmission to humans is by aerosols.**

-- It has **worldwide distribution**.

-- **Cow's milk** may cause subclinical infection.

Typhus

-- There are several forms: **louse borne epidemic typhus** caused by ***R. prowazekii***, **flea borne endemic typhus** caused by ***R. typhi***, **chigger-borne scrub typhus** caused by ***R. tsutsugumashi***, and several other rare forms.

-- **Epidemic typhus** begins with the sudden onset of chills, fever, headache, and other **influenza like symptoms** app 1-3 weeks after louse bite occurs.

-- After 5-9 days, a **maculopapular rash** begins on the **trunk and spreads over whole body** except face, palms, and soles.

-- Signs of **severe meningoencephalitis** including delirium and coma begin with the rash and continue into 2nd and 3rd weeks.

-- In untreated cases, **death occurs from peripheral vascular collapse or from bacterial pneumonia.**

-- It is transmitted from person to person by the **human body louse**, *Pediculus*.

-- When a **bacterimic patient** is bitten, the organism is ingested by the louse and multiplies in the gut epithelium.

-- It is **excreted in the feces of the louse** during the act of biting the next person and **autoinoculated** by the person when scratching the bite.

-- **Louse dies after a few weeks** so there is **no louse to louse** transmission.

-- So, human infection is an **obligatory** stage in the cycle.

-- A recurrent form is called **Brill-Zinsser disease** with similar but less severe symptoms.

Laboratory Diagnosis

-- **It is based on serological analysis.**

-- **Indirect immunofluorescence** and **ELISA** are the most common tests.

-- Weil-Felix reaction is **now not used** because of poor specificity and sensitivity.

-- A **four-fold or greater increase** in titer between acute and convalescent serum samples is most common way for diagnosis.

-- If clinical picture is **typical**, a single acute phase titer of **1:128 or greater** is accepted as presumptive evidence.

Treatment

-- The treatment of choice for all rickettsial diseases is **tetracycline** with **chloramphenicol** as second choice.

Prevention

-- It is based on **reducing exposure to arthropods** by wearing protective clothing and using insect repellents.

-- There are **no vaccines** for Rocky Mountain Spotted fever.

-- Prevention of typhus is based on **personal hygiene and delousing**.

-- A **vaccine is available for Q fever** and may be used by those at risk.


Thank You!