



# HLS - Microbiology

Sheet #4

Lecture #4: Rickettsial Disease

Lecture Date: 19/03/2019

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*{ this sheet includes everything in the slides }*  
*Everything that's highlighted **blue** is a sheet note.*  
*Sheet correction link: [bit.ly/hlsmicro](https://bit.ly/hlsmicro)*



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## Lecture four Rickettsia and Q-fever

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- Rickettsia are intermediate in their characteristics between bacteria and viri; viri-like: small sized & require tissue-culture for growth  
bacteria-like: affected by antibiotics
- Rickettsia can be grouped by:
  - 1) the vector involved in transmission
  - 2) the disease they cause
  - 3) sometimes may be classified according to where they survive (in the nucleus or cytoplasm or both) (eg. C. Burnetti -> cytoplasm)

- Human pathogens in the family *Rickettsiaceae* are small bacteria of the genera *Rickettsia* and *Orientia*.
- Rickettsial diseases are a group of infections caused by the obligate intracellular bacteria *Rickettsia*.
- *Rickettsia* is a Gram-negative, small, cocco-bacilli that can present as cocci or bacilli, non-motile, non-spore forming, highly pleomorphic bacteria. They are group of microorganisms that phylogenetically occupy a position between bacteria and viruses.
- **These organisms are transmitted to humans by arthropods.** Many rickettsiae are transmitted transovarially in the arthropods (passage of parasites or infective agents from the maternal body to eggs within the ovaries). **(ie in pregnancy of the arthropod; therefore even the larvae stage can be infective)**
- Arthropods serves as both **vector** and **reservoir**.
- Rickettsial infections, typically are characterized by fever, rashes, and vasculitis.

Organism	Disease	Arthropod vector	Vertebrate reservoir	Clinical severity	Geographic distribution
<b>Spotted fevers<sup>c</sup></b>					
<i>R. rickettsii</i>	Rocky Mountain spotted fever	Tick <sup>a</sup>	Dogs, rodents	+	Rocky Mountain states, eastern USA
<i>R. akari</i>	Rickettsial pox	Mite <sup>a</sup>	Mice	-	Asia, Far East, Africa, USA
<i>R. conorii</i>	Mediterranean spotted fever	Tick	Dogs	+	Mediterranean
<b>Typhus</b>					
<i>R. prowazekii</i>	Epidemic typhus	Louse	Human <sup>b</sup>	++	Africa, South America
<i>R. typhi</i>	Endemic typhus	Flea	Rodents	-	worldwide
<i>Orientia tsutsugamushi</i>	Scrub typhus	Mite <sup>a</sup>	Rodents	++	Far East
<b>Others</b>					
<i>Coxiella burnetii</i>	Q fever	None	Sheep, goats, cattle	+	worldwide
<i>Bartonella quintana</i>	Trench fever	Louse	Human	+	Asia, Africa, Central and South America <sup>d</sup>
<i>Ehrlichia chaffeensis</i> <sup>e</sup>	Fever (ehrlichiosis)	Tick	?		USA, Japan ( <i>E. sennetsu</i> )

<sup>a</sup>Vertically transmitted in arthropod.

<sup>b</sup>Non-human vertebrates are possibly also involved.

<sup>c</sup>Other rickettsiae cause similar tick-borne fevers in Africa, India, Australia.

<sup>d</sup>Multiply extracellularly; 1 million soldiers infected in the First World War.

<sup>e</sup>Isolated at Fort Chaffee, Arkansas; parasitizes lymphocytes, monocytes, neutrophils.

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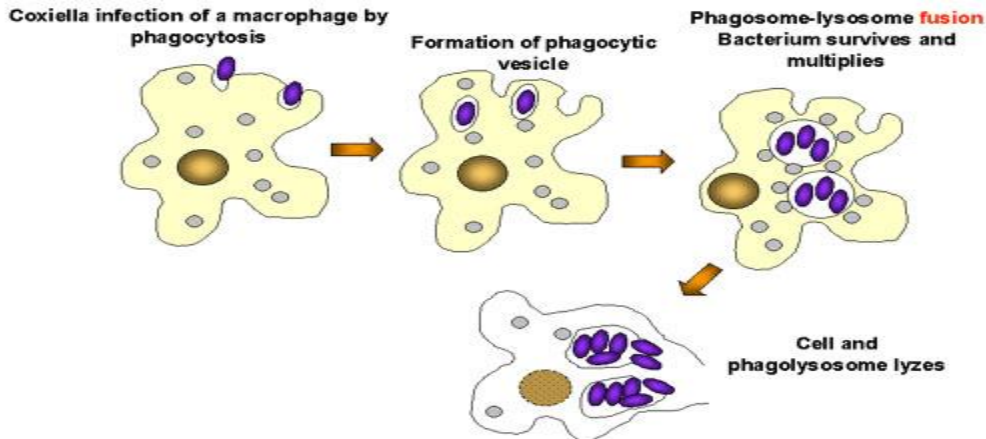
- The third group's diseases cause a mixture of symptoms (rash + fever + others)
- **In humans:** **Coxiella Burnetii** can be transmitted through the ingestion of unpasteurised milk (rarely), but mainly through respiratory secretion/droplets. (secretions of animals, especially at pregnancy/abortions -contaminate the environment through dry secretions that survive for a long period of time-, most commonly acquired by Veterinarians & farmers -direct contact with animals-). **In animals:** via arthropods.
- **Q fever** stands for Query fever – the cause of the disease was long a question mark.
- **Bartonella Quintana** caused Trench Fever (حمى الخندق) during WW1 transmitted by Lice: Hair or body lice
- { you are not required to know the geographic distribution }

## Coxiella burnetii

- Is a small obligate intracellular organism that has a membrane similar to gram-negative bacteria. *C. burnetii*, which causes Q fever, is resistant to drying, survive pasteurization at 60°C for 30 minutes, survive for months in dried feces or milk. This is due to the formation of endospore-like structures .
- Coxiellae grow only in cytoplasmic vacuoles.

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- Coxiella can survive classical pasteurisation (60 c x 30 mins) however can be killed by Flash pasteurisation (HTST) (72 c x 15 sec)



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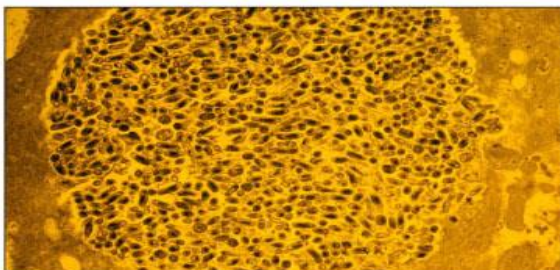
- Able to survive the low pH/high acidity in the phagolysosome
- After phagosome lysis-> goes to infect other cells.

- Can survive 7 to 10 days on wool at room temperature
- 1 month on fresh meat in cold storage
- 120 days in dust and more than 40 months in skim milk.

*Coxiella burnetii* has two antigenic phases:

1. During acute infection IgM and IgG antibodies against phase II antigens predominate (phase II antigens = 4 x phase I)
2. A persisting high titer of IgG antibodies against phase I is suspect for chronic infection (phase I antigens = 4 x phase II)

During the course of the infection, the outer membrane of the organism undergoes changes in its lipopolysaccharide structure (endotoxin-like activity), called phase variation. Differences in phase I and phase II antigen presentation can help determine if the infection is acute or chronic.



(a) *Coxiella burnetii* growing in placental cell.



(b) This cell has just divided; notice the endospore-like body (E), which is probably responsible for the relative resistance of the organism.

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- \*causes abortion in animals
- \*you can see the pleomorphism here

## Epidemiology

- *C. burnetii* is found in ticks, which transmit the agent to sheep, goats, and cattle, but transmission by ticks to humans is uncommon.
- Workers in slaughterhouses (عمال المسالخ) have contracted the disease as a result of handling infected animal tissues. #or from animal secretion
- *C. burnetii* is transmitted by the **Respiratory pathway** rather than through the skin. #Infection occur in labs by accident when they're doing culture or diagnosis.  
lab workers don't prefer the culture because it is dangerous and highly infectious .
- Rickettsiae are excreted in animals urine, feces, milk and **Rarely transmitted to humans by ingestion of unpasteurized milk.** #In past , they thought that it's only transmitted by unpasteurized milk because other cases weren't discovered Now it's Rarely transmitted through GIT and Mainly through RS.
- The placentas of infected cows, sheep, goats, and cats contain the organism, and parturition (مخاض الولادة) creates infectious aerosols.
- Shedding of *C. burnetii* into the environment occurs mainly during parturition; over  $10^9$  bacteria/ gram of placenta are released at the time of delivery. Aerosol or direct transmission can occur when infected animals are processed as meat, or while assisting deliveries.
- Due to persistence of the organism in the environment, dried infective material can contaminate water, dust, and soil; (#they're source of infection) *C. burnetii* has been isolated downwind up to ½ mile or more from a known source. Fomites (i.e., newborn animals, wool, bedding, clothing) can also be contaminated and serve as a source of infection. (#because it resists environmental condition , so it stays long time )
- *C. burnetii* has been naturally and experimentally isolated from a variety of arthropods, (mainly ticks but also cockroaches, fleas, lice, mites). (#arthropod transmit it only to animals Not humans) Feces of infected arthropods can serve as a source of *C. burnetii* infection and can remain infective for at least 19 months. #It's a long time and that because of endospore like structure; normal spores stay about 100,000 year.

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Why can't arthropods transmit disease to humans ?

- Maybe arthropod species that transmit the disease don't feed on humans blood , their target is animal tissue only .

### Other ways for transmission are

1. Person-to-person transmission (extremely rare).
2. Transplacental transmission may occur, resulting in congenital infection.
3. Transmission from blood transfusions, bone marrow transplants, and intradermal inoculations have also been reported.  
#They do normal tests for those who want to donate blood like AIDS , Hepatitis B and sexual disease . Rickettsia won't appear because it's obligate intracellular.  
Rickettsia tests aren't include .  
قد تظهر بعض الاعراض على الشخص المصاب مثل الحراره وهذا يمنع تبرعه بالدم
4. Transmission via sexual intercourse has been hypothesized for a rare number of human cases.

### Epidemiology

- Q fever is a zoonosis with worldwide distribution.
- The animal reservoir is large and include many wild and domestic **mammals, birds, and arthropods**. However, the primary reservoirs are considered to be **cattle, sheep, goats, and ticks**. #mostly in goat it was called goat fever .

### Human disease

- Incubation: 2 to 5 weeks
- Very low numbers of organism may cause disease (#even one single cell can cause disease , so it's highly infectious and dangerous).
- Humans are dead-end hosts (#because they either die or heal , so one doesn't transmit it .)
- Disease:: (#depend on immune system)
  - Asymptomatic (50%)
  - Acute
  - Chronic
- *Coxiella* can cause **Endocarditis, Pneumonitis and Hepatitis**.  
#Endocarditis is very important in diagnosis especially in chronic disease.

### Acute infection

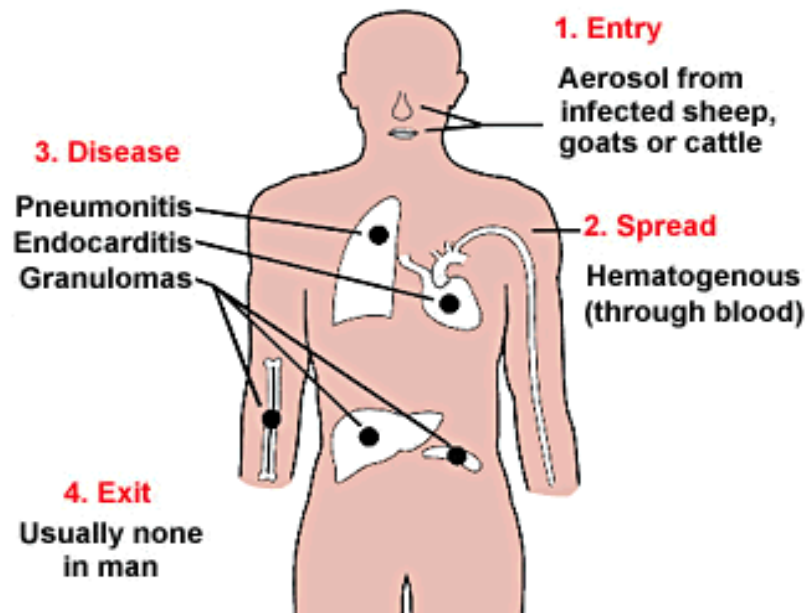
- Flu-like, self limiting
- Atypical pneumonia (30 to 50%)
- Hepatitis
- Skin rash (10%)
- Myocarditis, meningoencephalitis, pericarditis
- Death: 1 to 2%

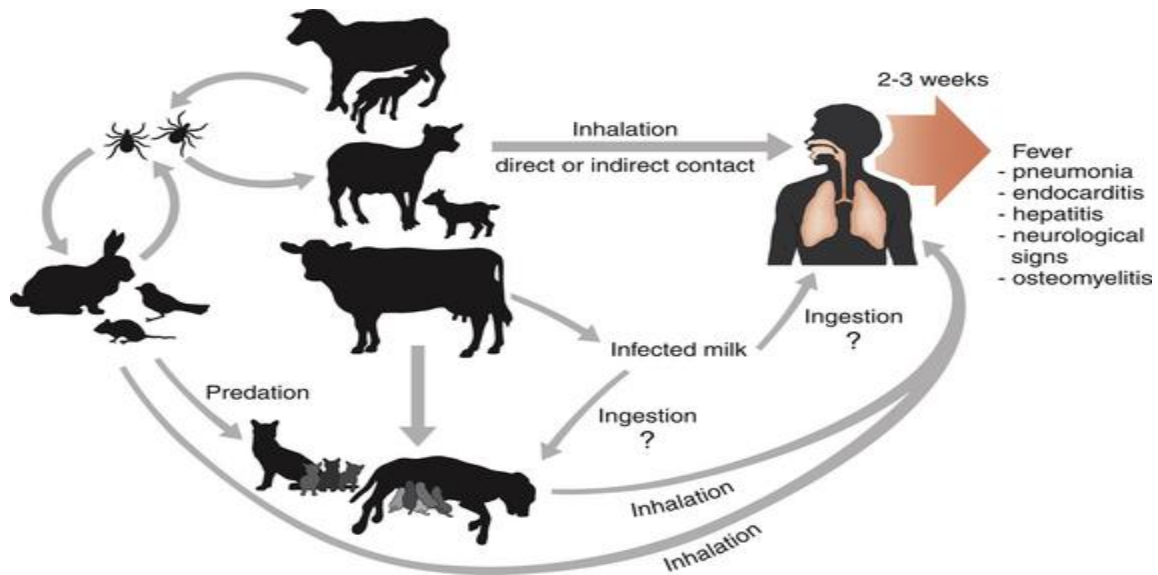
**Chronic disease:**

- 1 to 5% of those infected
- **Prior heart disease, pregnant women, immunocompromised, all are at risk**  
**(#these are risk factor that help to develop to chronic)**
- **Endocarditis**, hepatitis, Cirrhosis, Osteomyelitis

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- #the picture here is the pathway .
- Granulomas occur because it's obligate intracellular .
- Granulomas found in liver,spleen and bone .





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coxiella transmission :

1. by arthropods, but in humans not by arthropods but by direct or indirect contact without any necessity of intermediate vector .
2. Also From one animal to another by **predation** (الافتراس)
3. **Rarely** from animal to human or from one animal to another by ingestion the infected milk
4. From animal hosts to humans (farmers) through inhalation of contaminated aerosols , the aborted animals الحيوانات المجهضة contain large amounts of coxiella that may be transmitted to farmers because they are in contact with them
  - The incubation period ; **2-3 weeks**
  - No case was recorded that the bacteria had transmitted from one person to another
  - The infected patient either treated or dies so there is no way to transmit the bacteria to another healthy person .

### Clinical Findings

- **Chronic Q fever lasts more than 6 months. Infective endocarditis is the most common form of disease in this phase.**
- **Blood cultures for bacteria are negative??? ??##SN ; due to the bacteria is obligate intracellular** Antibody titer increase significantly.

### Laboratory Tests

#### 1. Culture & isolation

- Difficult & dangerous because of the highly infectious nature of rickettsiae



## 2. Serologic test

- **Weil-Felix test:** based on cross-reactivity between some strains of *Proteus* & *Rickettsia*

### <extra sheet note>


1. the test is cross reactions which occur between antibodies produced in acute rickettsial infection (patients serum) with antigens of certain proteus species , the cell wall antigens of certain proteus strains cross react with rickettsial antigens so are used in diagnosis of rickettsial infections by weil-felix test .

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2. We use proteus(need 20h to grow) because it doesn't need tissue culture like rickettsia which isn't cultivated in synthetic media and need more time to grow
3. THE first 3 tubes show precipitate and clear fluid that is mean the reaction occurred and the other tubes show turbidity عكورة دليل على عدم حصول التفاعل

**PROCEDURE OF WEIL -FELIX TEST**

- The Weil-Felix Test can be done as either a slide or a tube test. The antigens necessary (OX2, OX19, and OXK) can be obtained commercially.

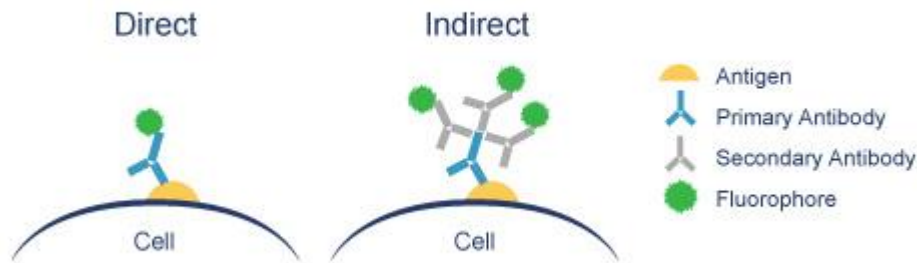


DR. T.V.RAO MD 10

- **Complement fixation:** not very sensitive & time consuming.
- **Indirect fluorescence (EIA):** more sensitive & specific; allows discrimination between IgM & IgG antibodies which helps in early diagnosis
- **Direct immunofluorescence:** the only serologic test that is useful for clinical diagnosis, 100% specific & 70% sensitive allowing diagnosis in 3-4 days into the illness
- **Rickettsial outer membrane LPS antigen** were used for detection of antibody.
- **PCR** has been useful in diagnosing culture-negative endocarditis caused by *C burnetii*.

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- direct immunofluorescence , tissue section on the slide and AG is fixed on the slide the fluorescence labeled antibodies are layered over the AG, then slide is washed to remove unattached antibodies finally examined under fluorescent microscope



## secondary antibody =anti- antibody (fluorescent-labeled antibody)

### Results interpretation;

**In acute Q fever**, the phase II antibody is usually higher than the phase I titer, often by 4-fold.

**In chronic Q fever**, Serum specimens drawn late in the illness demonstrate significantly higher phase I titers, sometimes much greater than 4-fold.

**##SN : in chronic infection mainly there is endocarditis**

### Prevention

- ✓ The presently recommended conditions of “high-temperature, short-time” pasteurization (HTST) at 71.5°C for 15 seconds are adequate to destroy viable *Coxiella* species.
- ✓ For *C burnetii*, an investigational vaccine made from infected egg yolk sacs is available.

