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۱. باکتری های داخل سلولی (ریکتزیا، کلامیدیا)

۲. مایکوپلاسما



Genus Rickettsia

Spotted fever group

- ✓ At least 17 species associated with human disease
- ✓ *R. rickettsii* (Rocky Mountain spotted fever)
- ✓ *R. akari* (rickettsialpox)

Typhus group

- ✓ *R. prowazekii* : Epidemic typhus
- ✓ *R. typhi* : Endemic (murine) typhus

Genus Orientia

- ✓ A single species
- ✓ *O. tsutsugamushi* : Scrub typhus

Rickettsiaceae



- ✓ Similar to Gram negative bacilli
- ✓ Stain poorly with the Gram
- ✓ Not have flagella, Surrounded by slime layer
- ✓ Seen best with Giemsa or Gimenez stains
- ✓ **Orientia** lacks both the peptidoglycan layer & LPS
- ✓ Obligate intracellular parasites
- ✓ Reservoirs: animal & arthropod
- ✓ Arthropod vectors (ticks, mites, lice, fleas)
- ✓ Humans are accidental hosts



Transmission

Organism	Disease	Arthropod Vector	Reservoir
<i>R. rickettsii</i>	Rocky Mountain spotted fever	Ticks	Dogs, rodents
<i>R. akari</i>	Rickettsialpox	Mites	Mice
<i>R. prowazekii</i>	Epidemic Typhus	Lice	Humans
<i>R. typhi</i>	Endemic Typhus	Fleas	Rodents
<i>O. tsutsugamushi</i>	Scrub Typhus	Mites	Rodents
<i>C. burnetii</i>	Q fever	None	Cattle, sheep, goats

Arthropod Vector



Tick



Mite



louse



Flea

Clinical Findings



Disease	Incubation (Days)	Clinical Presentation	Rash	Eschar	Mortality (%)
Rocky Mountain spotted fever	7	Abrupt onset: fever, headache, malaise,	>90 %: macular	No	10-25
Rickettsialpox	9-14	Abrupt onset; fever, headache, chills, myalgias, photophobia	100%; papulo-vesicular	Yes	Low
Epidemic Typhus	8	Abrupt onset; fever, headache, chills, myalgias, arthralgia	20-80% macular	No	20
Endemic Typhus	7-14	Gradual onset; fever, headache, myalgias, cough	50 %; papulo-vesicular	No	Low
Scrub Typhus	10-12	Abrupt onset; fever, headache. myalgias	<50% maculo-papular	No	1-15

Laboratory Diagnosis



Based on serologic analysis

ELISA

The Weil-Felix test

- ✓ **Cross-reaction of an antigen in many rickettsiae**
- ✓ **The O antigen found in *P. vulgaris* OX-2, OX-19, & OX-K**
- ✓ **Agglutination of patient's serum by *P. vulgaris***

Rickettsiae can be grown in cell culture or embryonated eggs



Tetracycline

Prevention: reducing exposure to the arthropod

Chlamydiaceae



Two genera clinically important

Chlamydia

Chlamydia trachomatis

Eye, respiratory, & genital tract infections

Chlamydophila

Chlamydophila psittaci

Psittacosis

***Chlamydophila pneumoniae* (TWAR strain)**

Atypical pneumonia

Chlamydiaceae

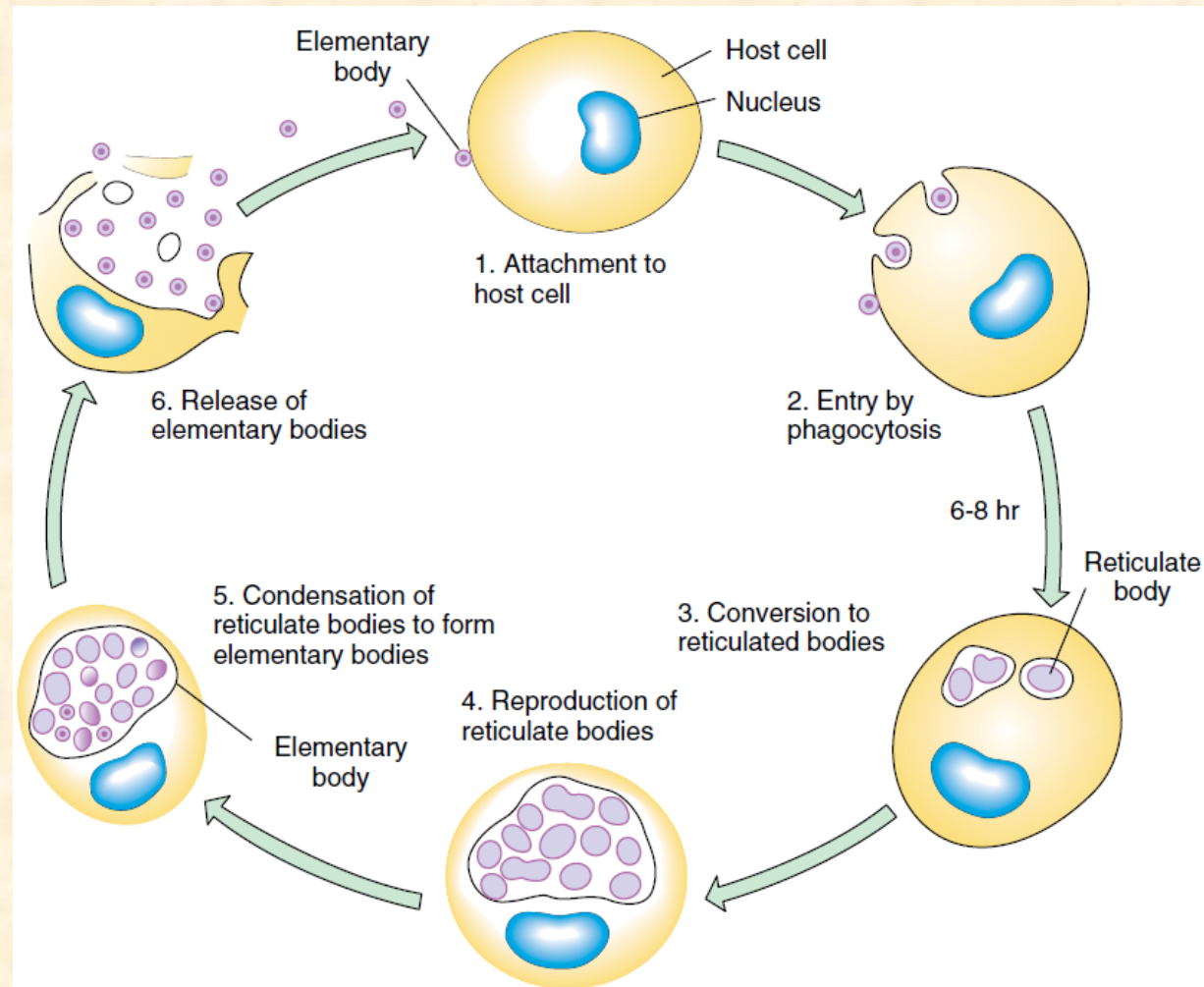


- ✓ **Small obligate intracellular parasites**
- ✓ **Contain DNA, RNA and ribosomes**
- ✓ **Inner & outer membrane**
- ✓ **LPS but no peptidoglycan**
- ✓ **Cell wall not well characterized**
- ✓ **Prokaryotic ribosomes**
- ✓ **Energy parasites**
- ✓ **Can't make ATP**

Chlamydiaceae



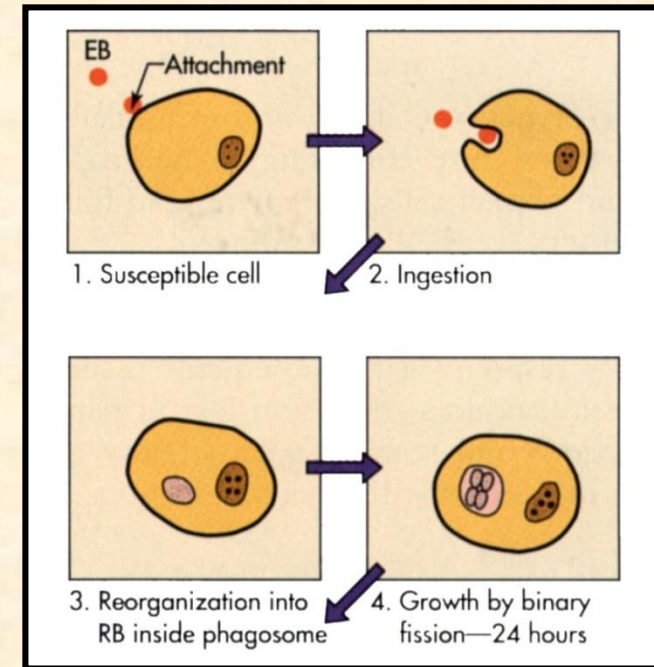
- ✓ **Unique growth cycle**
- ✓ **Elementary body (EB)**
- ✓ **Reticulate body (RB)**



Elementary body (EB)



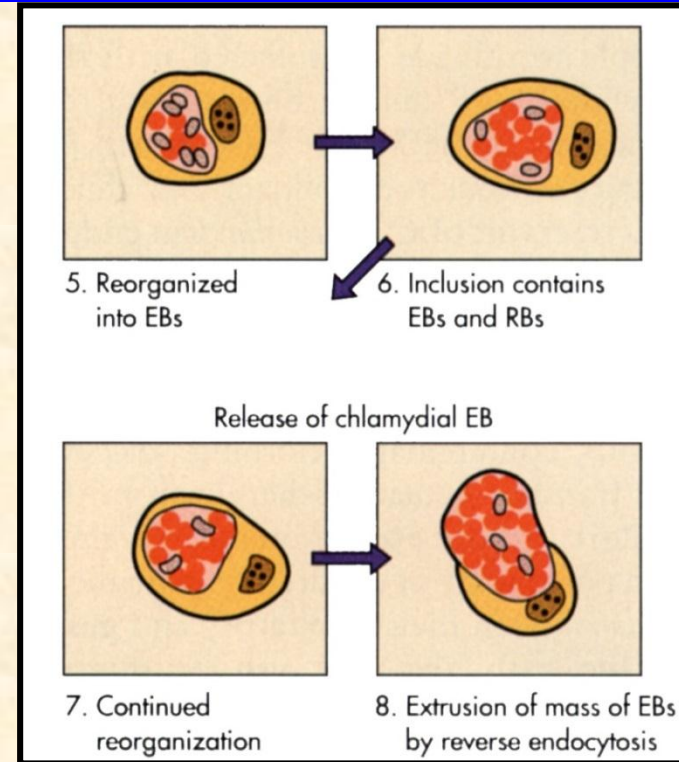
- ✓ **Metabolically inactive**
- ✓ **Infectious forms**
- ✓ **300- to 400-nm**
- ✓ **Do not replicate**
- ✓ **Attached to susceptible cells**
- ✓ **Inhibited fusion of lysosomes phagosome**
- ✓ **Much like a spore, resistant to many harsh environmental factors**



Reticulate body (RB)



- ✓ 6 to 8 hours after entering the cell
- ✓ EB reorganize into 800 to 1000 nm
- ✓ Metabolically active
- ✓ Synthesize their own DNA, RNA & protein
- ✓ Noninfectious
- ✓ Replicating chlamydial form



Chlamydia trachomatis



- ✓ **Infects only humans**
- ✓ **More than 15 immunotypes (A–L)**
- ✓ **Usually transmitted by close personal contact**
(Sexually or by birth canal)
- ✓ **Important reservoir**
Individuals with asymptomatic genital tract infections

Trachoma

- ✓ **Transmitted by finger-to-eye or fomite-to-eye contact**
- ✓ **A leading cause of blindness in developing countries**

Sexually transmitted disease

- ✓ **Occurs worldwide**
- ✓ **Urogenital infections**
- ✓ **Lymphogranuloma venerium**

Pathogenesis & Clinical Findings



- ✓ Infect primarily epithelial cells of the mucous membranes or the lungs
- ✓ Rarely cause invasive, disseminated infections

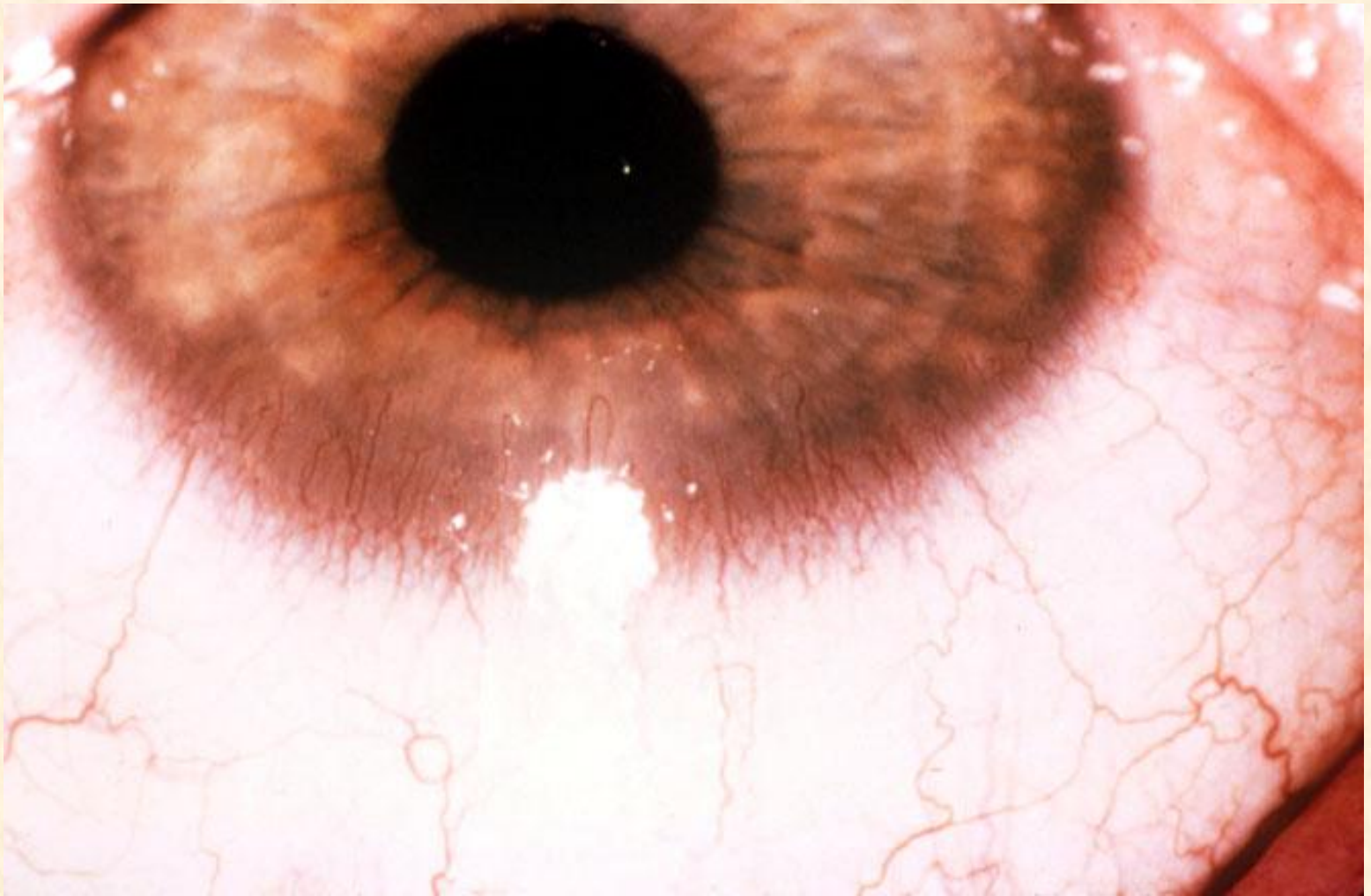
Types A, B, & C cause trachoma

- ✓ May recur over many years & may lead to blindness
- ✓ No systemic illness

Types D–K cause genital tract infections

- ✓ Occasionally transmitted to the eyes or the respiratory tract
- ✓ In men, common cause of nongonococcal urethritis (NGU)
- ✓ In women cause cervicitis & may progress to salpingitis & PID

Neovascularization in Trachoma



Trachoma Scarring



Pathogenesis & Clinical Findings

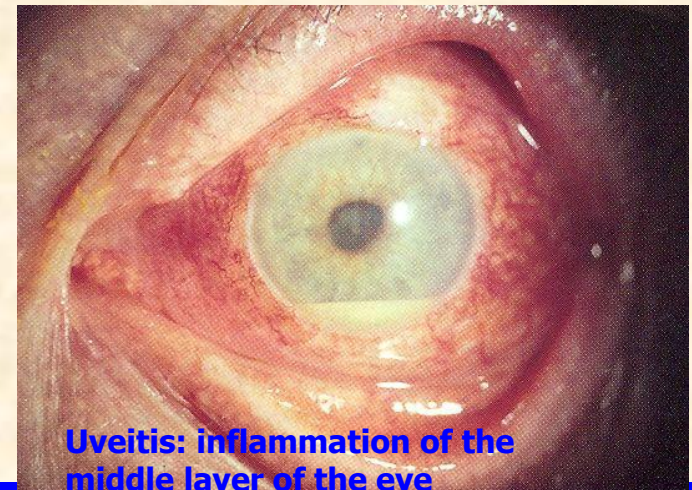


Infants born to infected mothers

- ✓ Often neonatal inclusion conjunctivitis 7–12 days after delivery
- ✓ Some develop chlamydial pneumonitis 2–12 weeks after birth

Patients with genital tract infections

- ✓ May incidence of **Reiter's syndrome**
- ✓ An autoimmune disease; cross-reacting antibodies
- ✓ Characterized by urethritis, arthritis, & uveitis



Uveitis: inflammation of the middle layer of the eye

Pathogenesis & Clinical Findings



Types L1–L3: lymphogranuloma venereum (LGV)

A sexually transmitted disease

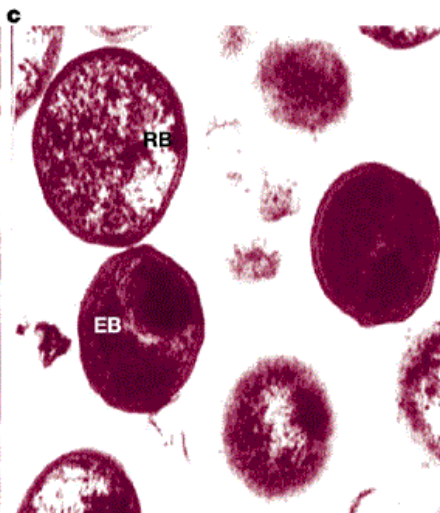
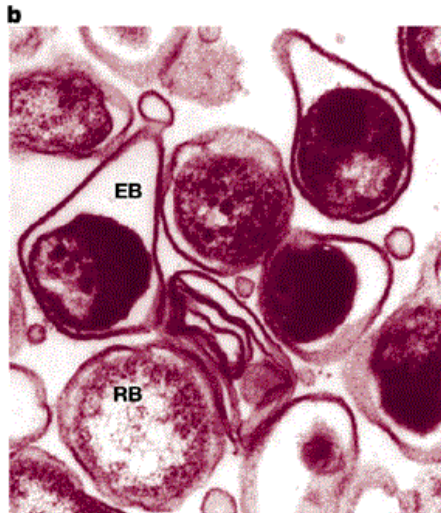
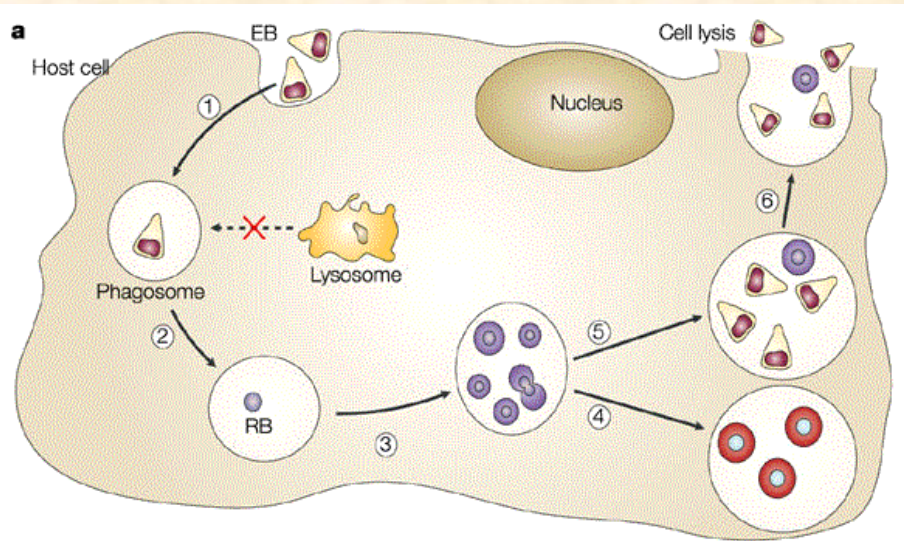
Lesions on genitalia & in lymph nodes

Chlamydophila pneumoniae



- ✓ **Most recognized species of Chlamydia**
- ✓ **Infects only humans**
- ✓ **Transmitted from person to person by aerosol**
- ✓ **Atypical pneumonia**
- ✓ **Risk factor for Guillain-Barre' syndrome**
- ✓ **TWAR agent**
- ✓ **Atherosclerosis ?**

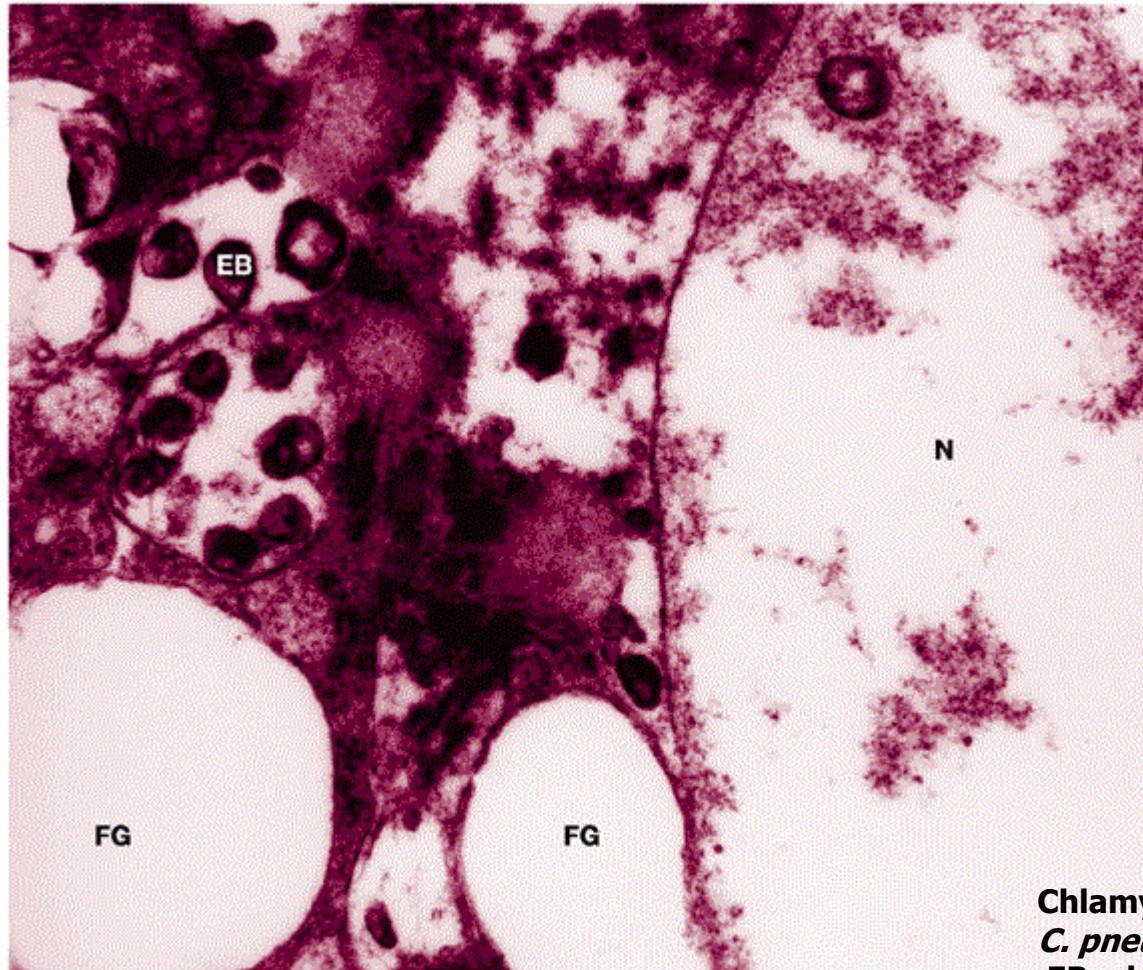
Lifecycle of *C. pneumoniae*



Nature Reviews Microbiology.
2004; 2, 23-32

Nature Reviews | Microbiology

Lifecycle of *C. pneumoniae*



Chlamydial inclusions containing pear-shaped *C. pneumoniae* elementary bodies.
EB, elementary body; FG, fatty globules; N, nucleus

Nature Reviews | Microbiology

Chlamydophila psittaci



- ✓ **Psittacosis (Parrot fever)**
- ✓ **Infects birds & many mammals**
- ✓ **Humans are infected by inhaling organisms in dry bird feces**
- ✓ **Hematogenous spread may organs**
- ✓ **Spleen & liver**
- ✓ **Local necrosis of tissue**



Laboratory Diagnosis



- ✓ Chlamydiae form cytoplasmic inclusions
- ✓ Can be seen with special stains (Giemsa stain)
- ✓ Or by immunofluorescence
- ✓ The Gram stain is not useful

Antigen detection

ELISA ; In exudates or urine

PCR based test

Using the patient's urine

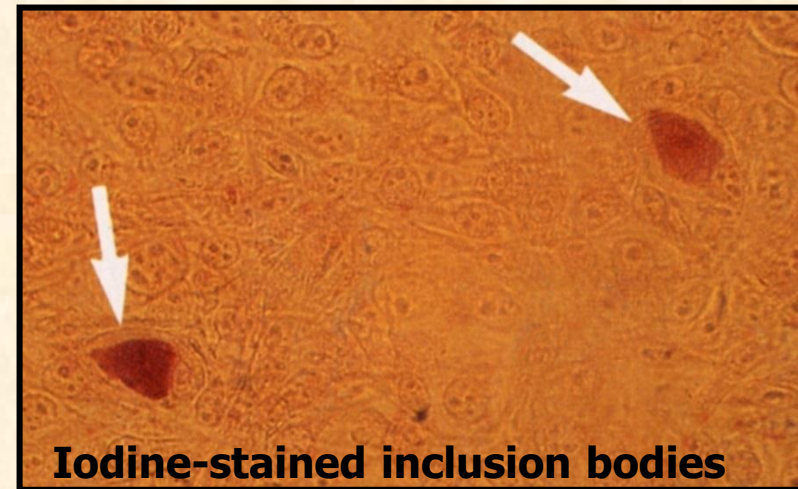
Cultures

Can be grown in cell cultures treated with cycloheximid

Forms inclusions containing glycogen

Serologic tests

Used to diagnose infections by *C. psittaci* & *C. pneumoniae*



Treatment & Prevention



- ✓ **Tetracyclines, such as doxycycline**
- ✓ **Neonatal inclusion conjunctivitis by erythromycin**
- ✓ ***C. trachomatis* sexually transmitted diseases by azithromycin**
(Because of coinfection with gonococci)
- ✓ **No Vaccines**

Mycoplasma



- ✓ The smallest free-living organisms
- ✓ Many are $< 0.3 \mu\text{m}$ in diameter
- ✓ Stain poorly with Gram stain
- ✓ Contains cholesterol
- ✓ Grow on artificial media
- ✓ Have complex nutritional requirements (several lipids)
- ✓ Grow slowly & require at least 1 week to form a visible colony
- ✓ The colony has a "fried-egg" shape
- ✓ Three human pathogens

Mycoplasma pneumoniae; Eaton's agent - respiratory

Mycoplasma hominis - urogenital

Ureaplasma urealyticum - urogenital

Pathogenesis of *M. pneumoniae*



- ✓ **Pathogen only for humans**
- ✓ **Transmitted by respiratory droplets**
- ✓ **In the lungs: is rod-shaped with a tapered tip**
- ✓ **Specific proteins: attachment to the respiratory epithelium**
- ✓ **The mechanism of inflammation is uncertain**
- ✓ **Has only one serotype**
- ✓ **Immunity: incomplete & second episodes of disease can occur**
- ✓ **Autoantibodies produced against red cells (**cold agglutinins**), brain, lung, & liver cells**
- ✓ **The most frequent cause of pneumonia in young adults**



Clinical Findings

- ✓ **The most common type of atypical pneumonia**
(formerly ; primary atypical pneumonia)
- ✓ **Other atypical pneumonias: legionnaires' disease, Q fever, psittacosis, & viral pneumonias such as influenza**
- ✓ **Atypical**
 - 1- A causative bacterium cannot be isolated on routine media
 - 2- The disease does not resemble pneumococcal pneumonia
- ✓ **The onset of *Mycoplasma* pneumonia is gradual**
- ✓ **Usually include a nonproductive cough, sore throat, or earache**

Clinical Findings



- ✓ Constitutional symptoms of fever, headache, malaise, & myalgias
- ✓ *M. pneumoniae* also causes bronchitis
- ✓ The extra-pulmonary manifestations include
 - Stevens-Johnson syndrome
 - Cardiac arrhythmias
 - Arthralgias
 - Neurologic manifestations (Guillan-Barre syndrome)

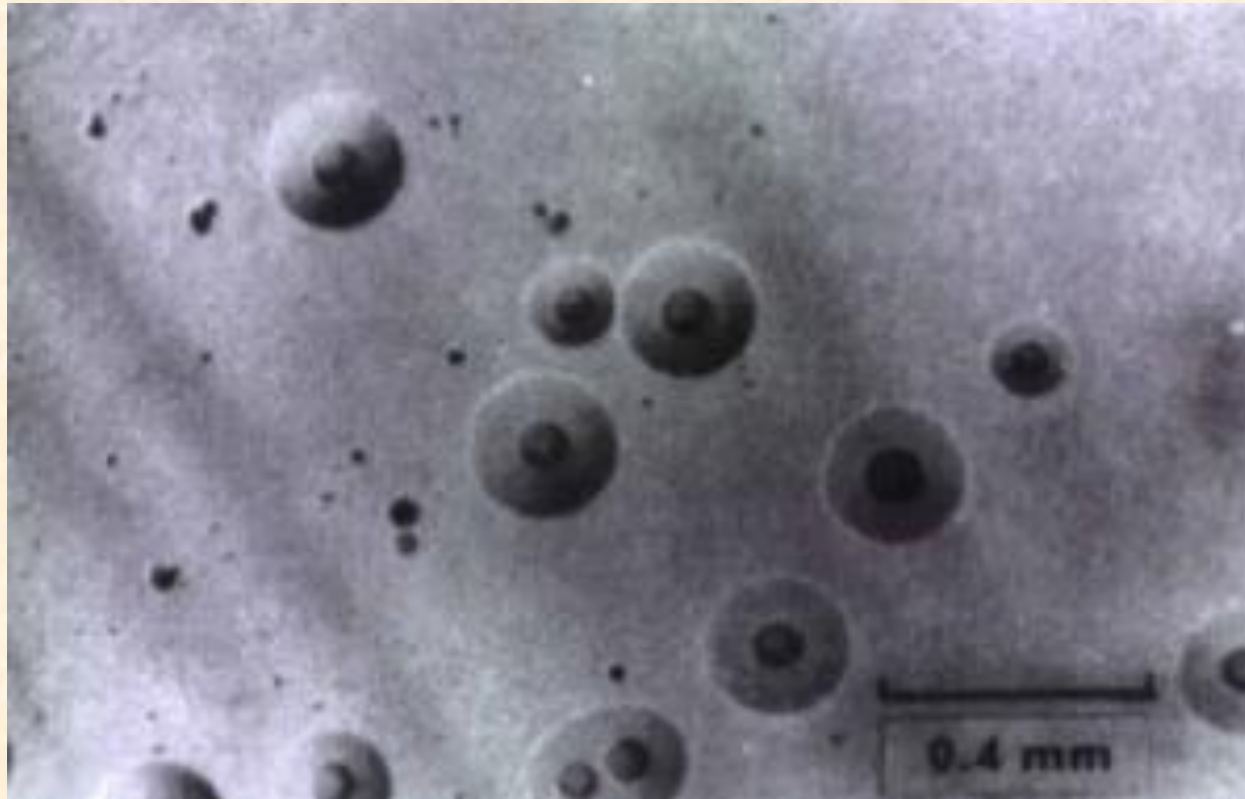


- ✓ **Cultures must be delivered immediately to the lab**
- ✓ **Should be placed in transport media**
- ✓ **If not plated immediately, should be frozen at -70°C**
- ✓ **Most infections detected via serologic evaluation**
- ✓ **A cold-agglutinin titer of 1:128 or higher is indicative of recent infection**

The test is nonspecific

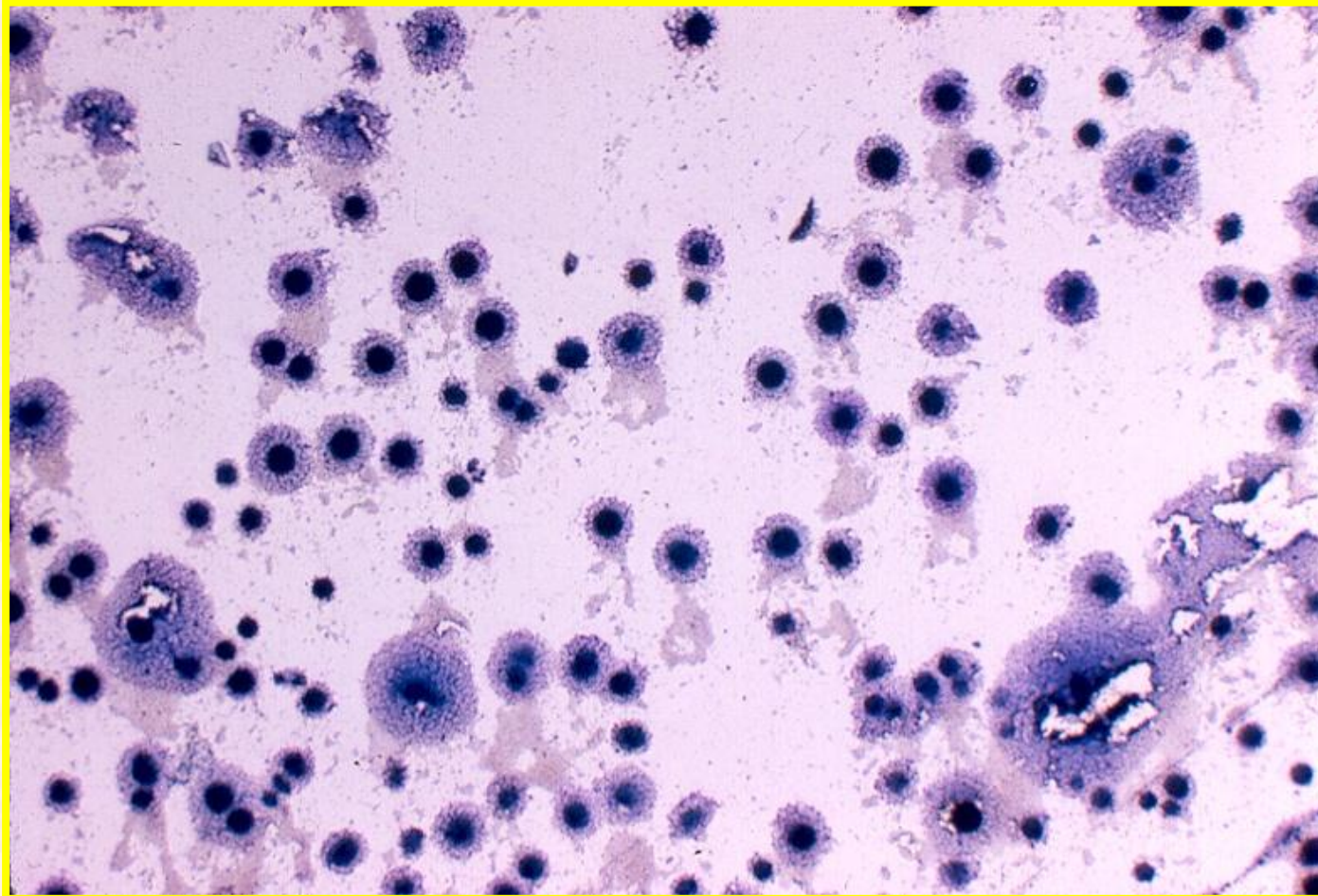
False-positive: in influenza virus & adenovirus infections

Laboratory Diagnosis



Fried-egg appearance of colonies of mycoplasmas. All mycoplasmas except *Mycoplasma pneumoniae* typically show this morphology. *M. pneumoniae* has a strict aerobic atmosphere requirement. It is one of the slowest growing mycoplasmas, and it appears as homogeneous granular colonies after incubation for 1 week or longer. The other mycoplasmas generally grow within 1 to 4 days. (From Razin S, Oliver O: Morphogenesis of *Mycoplasma* and bacterial L-form colonies, *J Gen Microbiol* 24:225-237, 1961.)

Dienes Stain





Treatment

**Choice : macrolide (erythromycin or azithromycin)
or a tetracycline (doxycycline)**

There is no vaccine