Mycoplasmas

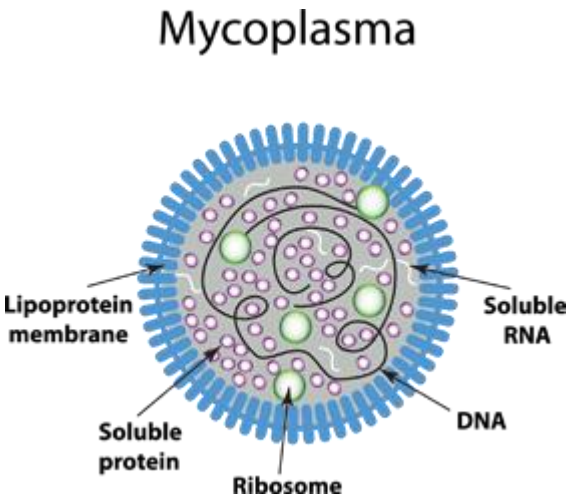
Lack cell wall (no peptidoglycan). Instead, they are enclosed in a **single plasma membrane** (composed of lipid bilayer). They are, therefore, plastic and pleomorphic and thus cannot be classified as either cocci or rods.

Mycoplasmas are also the **smallest of known free-living**, self-replicating prokaryotic cells.

Lacking cell walls, mycoplasmas are **insensitive to antibiotics** that inhibit cell division by preventing cell wall synthesis (such as penicillin). However, they are susceptible to other inhibitors of prokaryotic metabolism.

Because of their extremely small size, mycoplasmas frequently **pass through bacteriologic filters**.

Mycoplasma species are widely distributed in nature and include several **commensals commonly found in the mouth and genitourinary (GU)** tracts of humans and other mammals.



Three Mycoplasma species are definitively associated with human disease, namely **Mycoplasma pneumoniae**, which is the cause of a **atypical pneumonia**, and **Mycoplasma hominis** and **Ureaplasma urealyticum**, which are associated with a variety of GU diseases, such as urethritis, pelvic inflammatory disease (PID), and intrapartum infections.

Mycoplasma genitalium is a recently recognized sexually transmitted pathogen that causes nongonococcal urethritis (NGU).

Mycoplasmas have **limited biosynthetic capabilities** and require a variety of small, organic molecules for growth. Unlike other prokaryotes, mycoplasmas **contain sterols** in their cell membranes. Because most mycoplasma species cannot synthesize the sterol ring, they require an **external source of cholesterol** from serum or a similar medium supplement. Given appropriate supplementation, they **can be grown in cell-free media**. However, because of their fastidious growth requirements, these organisms are rarely cultured in the laboratory.

Mycoplasmas produce minute colonies on specialized agar after several days of incubation. The central portion of the colony penetrates the agar (Mycoplasma agar), whereas the periphery spreads over the adjacent surface, in some cases giving the colony a characteristic "**fried egg" appearance.**

M. pneumonia

is transmitted by **respiratory droplets** and causes a lower respiratory tract infection (**atypical pneumonia**, so named because the signs and symptoms are unlike typical lobar pneumonia). Also known as **walking pneumonia** (Patients often remain ambulatory throughout the illness). The organism accounts for approximately 20 percent of pneumonia cases as well as causing milder infections such as bronchitis, pharyngitis, and nonpurulent otitis media.

It spreads quickly in crowded areas, such as schools, college campuses, and nursing homes. The highest incidence of clinical disease is seen in older children and young adults (ages 6 to 20 years).

Pathogenesis

possesses a **membrane-associated protein**, P1, which functions as a cyto-adhesin. It is concentrated in a specialized organelle visible under electron microscopy, which binds sialic acid rich glycolipids found on certain host cell membranes. Among susceptible cell types are ciliated bronchial epithelial cells. The organisms grow closely **attached to the host cell luminal surface and inhibit ciliary action**. Eventually, patches of affected mucosa **desquamate**, and an i**nflammatory** response develops in

bronchial and adjacent tissues involving lymphocytes and other mononuclear cells. *M. pneumoniae* produces an exotoxin that is similar to **pertussis toxin**. The toxin is an adenosine diphosphate–ribosylase and results in extensive vacuolization and death of host cells. In infected individuals, organisms are shed in saliva for several days before onset of clinical illness.

Immunity

Infection with *M. pneumonia* **elicits both local and systemic** immune responses. Serum antibody to the P1 adhesin can be demonstrated, with antibody peaking 2 to 4 weeks after infection and gradually disappearing over the following year. An **immunoglobulin M** antibody, **the cold agglutinin**, is produced by approximately 60 percent of infected patients. [Note: This antibody's name derives from the fact that it reacts with the human erythrocyte antigen I, reversibly agglutinating I^+ red blood cells at temperatures of 0^oC to 4^oC but not at 37^oC.] Some patients develop very high titers of cold agglutinins. With exposure to cold temperatures this may result in ischemia and even necrosis of distal extremities [hands and feet] because of in vivo clumping of red blood cells.

Laboratory identification

Direct microscopic examination of clinical material for M. pneumoniae is of limited value. Sputum is **scanty and nonpurulent**, and the pathogen stains poorly or not at all using standard bacteriologic stains. Sputum samples or throat swabs can be cultured on special media, but, because isolation of the organism usually requires 8 to 15 days, **they cannot aid in early treatment decisions**. *M. pneumoniae* grows under both aerobic and anaerobic conditions and can be isolated on specialized media supplemented with serum. However, the organism is fastidious, and isolation is not commonly performed in clinical laboratories. **Serologic tests** are the most widely used procedures for establishing a diagnosis of atypical pneumonia due to *M. pneumoniae*. Specific antibody can be detected by **complement fixation**, using an extract of mycoplasmal glycolipids. A diagnosis is established by a fourfold rise in titer between acute and convalescent samples. Because symptoms of illness develop slowly, the initial serum sample may be positive. Molecular diagnostics,

including polymerase chain reaction (PCR) amplification, are replacing serological tests.

GENITAL MYCOPLASMAS

Three Mycoplasma species, *M. hominis* , *U. urealyticum* , *and M. genitalium*,

are human urogenital pathogens. They are often associated with sexually transmitted infections, such as NGU or puerperal infections (that is, infections connected with, or occurring during childbirth or the period immediately following childbirth).

M. hominis , *U. urealyticum* are common inhabitants of the GU tract, particularly in sexually active adults.

Both agents can be cultured. They grow more rapidly than *M. pneumoniae* and can be distinguished by their carbon utilization patterns: *M. hominis* degrades arginine, whereas U. urealyticum hydrolyses urea. [Note: Ureaplasma is sometimes referred to as a "T strain" of mycoplasma because it produces tiny colonies not visible to the naked eye.]

The major clinical condition associated with *M. hominis* is postpartum or post-abortal fever. The organism has been isolated from blood cultures in up to 10 percent of women so affected. In women, the organism has been isolated from the endometrium of patients with endometritis and from vaginal secretions of women who undergo premature labor or deliver low-birth-weight babies.

Mycoplasma genitalium

has been recognized as a sexually transmitted pathogen, resulting in a series of syndromes similar to those caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. The organisms appear to be resistant to doxycycline, which is the treatment of choice for NGU caused by C. trachomatis. Therefore, recommendations for testing for *M. genitalium* include cases in which the patient fails to respond to doxycycline treatment.

Chlamydia

The family Chlamydiaceae consists of small bacteria that are **obligate intracellular parasites**, depending on the host cell for energy in the forms of adenosine triphosphate (ATP) and nicotinamide adenine dinucleotide (NAD+). They grow in cytoplasmic vacuoles in a limited number of host cell types.

The family has **three important human pathogens**: ***Chlamydia trachomatis, Chlamydophila psittaci,* and *Chlamydophila pneumoniae***. **Complete genome sequence** analyses suggest separation of these bacteria into two genera is inconsistent with their evolutionary history (*Chlamydia* and *Chlamydophila*).

C. trachomatis infections cause diseases of the genitourinary (GU) tract and the eye, including many cases of nongonococcal urethritis (NGU) and ocular infections such as trachoma.

C. psittaci and C. pneumoniae infect the respiratory tract.

C. psittaci causes psittacosis and is spread to the respiratory tract of humans via inhalation of infected bird feces or respiratory secretions.

C. pneumoniae causes atypical pneumonia and is spread person to person via respiratory droplets.

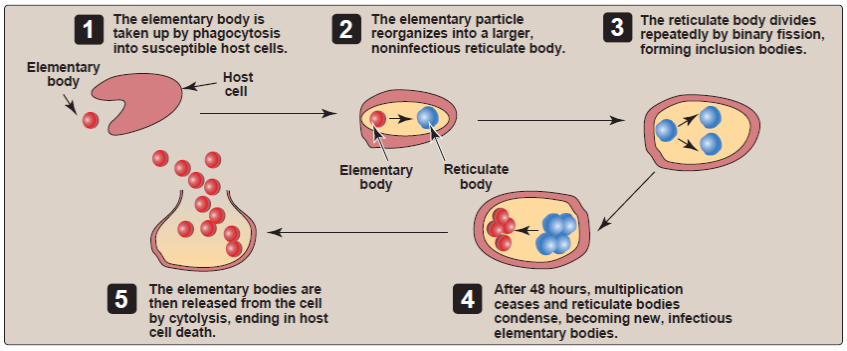
Chlamydiae are small, round-to-ovoid organisms that vary in size during the different stages of their replicative cycle. **The chlamydial cell envelope consists of two lipid bilayers resembling a gram-negative envelope. Although the presence of peptidoglycan has never been directly demonstrated in isolated organisms, genes for the biosynthesis**

of peptidoglycan are universally present in the genomes of the family. Cell wall active antimicrobials have negative impacts on the life cycle of the chlamydiae, inducing a persistent state that may contribute to the chronicity of infection.

Chlamydiae possess ribosomes and synthesize their own proteins and, therefore, are sensitive to antibiotics that inhibit this process, such as tetracyclines and macrolides.

Pathogenesis

Chlamydiae have a unique life cycle, with morphologically distinct **infectious and reproductive** forms. **The extracellular infectious form, the elementary body**, is a tiny, condensed, apparently inert structure that can survive extracellular cell-to-cell passage and initiate an infection. The elementary body is taken up by phagocytosis into susceptible host cells, a process facilitated by proteins in the chlamydial cell envelope that function as adhesins, directing attachment to glycolipid or glycopolysaccharide receptors on the host cell membrane. Once inside the cell, the elementary body prevents fusion of the phagosome and lysosome, protecting itself from enzymatic destruction. The particle reorganizes over the next 8 hours into a larger, noninfectious **reticulate body**, which becomes metabolically active and divides repeatedly by binary fission within an inclusion in the cytoplasm of the host cell. As the reticulate body divides, it fills the endosome with its progeny, forming an inclusion body. After 48 hours, multiplication ceases, and reticulate bodies condense to become new infectious elementary bodies. The elementary bodies are then released from the cell by cytolysis, ending in host cell death.



C. trachomatis is divided into a number of serotypes, which correlate with the clinical syndrome they cause.

Serotype A, B, C cause Trachoma: chronic keratoconjunctivitis that often results in blindness Trachoma is transmitted by personal contact, for example, from eye to eye via droplets, by contaminated surfaces touched by hands and conveyed to the eye, or by flies. Because of persistent or repeated infection over several years, the inflammatory response with attendant scarring leads to permanent opacities of the cornea and distortion of eyelids.

NGU is caused by serotypes D–K of C. trachomatis but also cause eye infections, for example, in infants born to genitally infected women.

serotypes L1, L2, and L3 cause lymphogranuloma venereum (LGV), a more invasive sexually transmitted disease. LGV is characterized by transient papules on the external genitalia, followed in 1 to 2 months by painful swelling of inguinal and perirectal lymph nodes.

Laboratory identification

Samples, particularly from the urethra and cervix in GU infection and conjunctivae in ocular disease, should be obtained by cleaning away overlying exudate and gently scraping to collect infected epithelial cells.
1. Direct tests: Microscopic examination using direct fluorescent antibody staining reveals characteristic cellular cytoplasmic inclusions.
C. trachomatis infections can be detected with high sensitivity and specificity using DNA amplification performed on urine specimens.
2. Culturing methods: C. trachomatis can be cultivated by tissue culture in several human cell lines.
3. Detection of serotypes: Serotypes of C. trachomatis can be determined by immunofluorescence staining with monoclonal antibodies.