



# MICROBIOLOGY

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Subject

Chlamydia trachomatis, Ureaplasma and Gardnerella

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# Genito-Urinary System

## *Chlamydia trachomatis, Ureaplasma and Gardnerella*

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# *Chlamydia trachomatis*

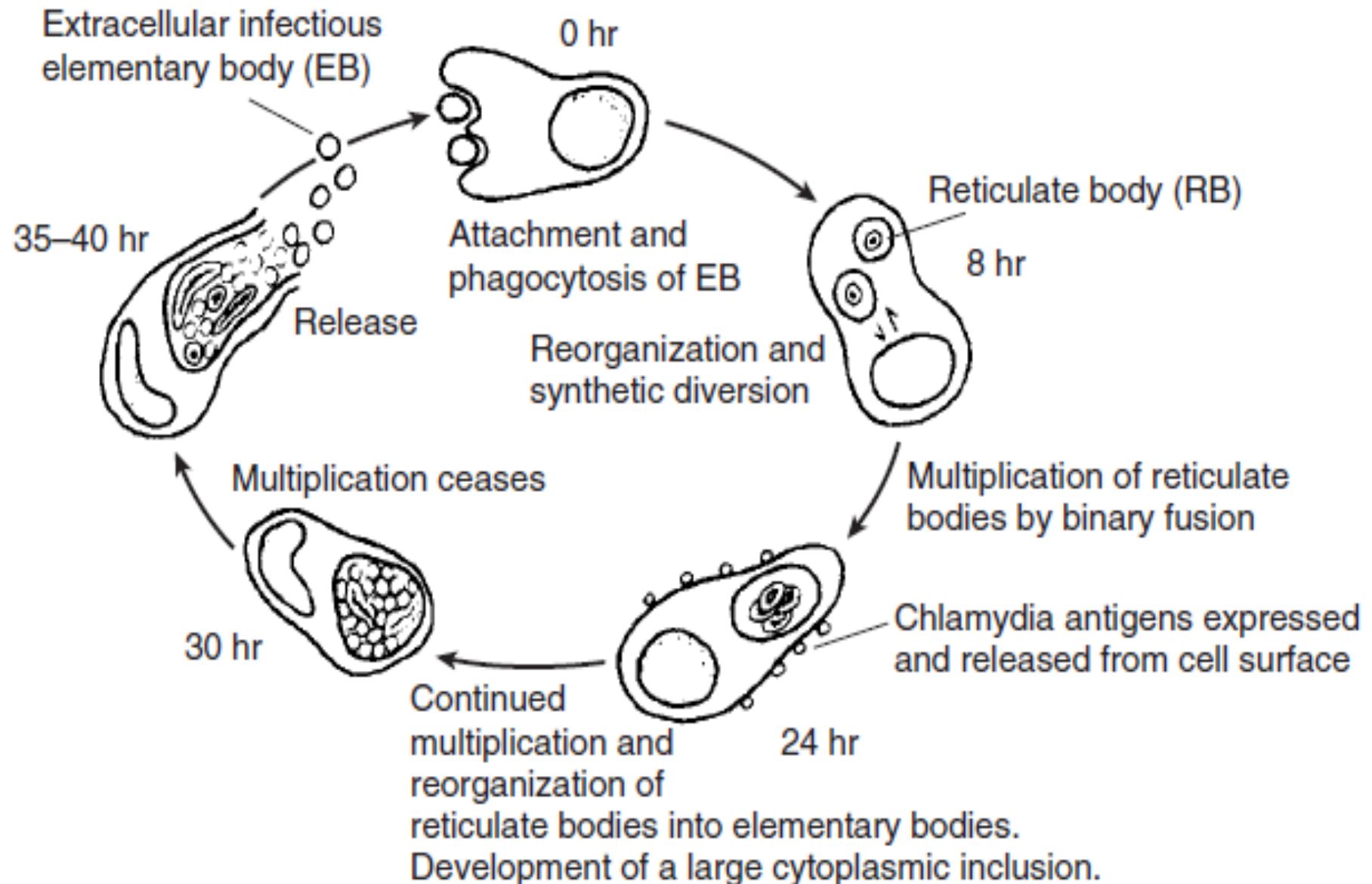
- *C. trachomatis* are round cells between 0.3 and 1  $\mu\text{m}$  in diameter depending on the replicative stage. The envelope surrounding the cells includes a trilaminar outer membrane that contains lipopolysaccharide and proteins similar to those of Gram negative bacteria. A major difference is that chlamydiae lack the peptidoglycan layer between the two membranes.
- They are obligate intracellular parasites and have not been grown outside eukaryotic cells.

## REPLICATIVE CYCLE

- The replicative cycle involves two forms of the organism: a small, hardy infectious form termed the **elementary body** (EB), and a larger fragile intracellular replicative form termed the **reticulate body** (RB).
- The EB is a metabolically inert form. The cycle begins when the EB attaches to unknown receptors on the plasma membrane (usually columnar or transitional epithelial cells). It then enters the cell in an endocytotic vacuole and begins the process of converting to the replicative RB.

- As the RBs increase in number, the endosomal membrane expands by fusing with lipids of the Golgi apparatus eventually forming a **large inclusion body**. After 24 to 72 hours, the process reverses and the RBs reorganize and condense to yield multiple EBs. The endosomal membrane then either disintegrates or fuses with the host cell membrane, releasing the EBs to infect adjacent cells.
- *C. trachomatis* also inhibits apoptosis of epithelial cells, thus enabling completion of its replicative cycle.

# Reproduction cycle of *Chlamydia*



# *Chlamydia trachomatis* Diseases

## EPIDEMIOLOGY

- *C. trachomatis* causes disease in several sites, including the conjunctiva and genital tract. It is spread by secretions and is the most common sexually transmitted disease.
- Humans are the sole reservoir. Neonatal conjunctivitis contracted from maternal genital infection (2 to 6% of newborn infants).

- The prevalence of chlamydial urethral infection in US men and women ranges from 5% in the general population to 20% in those attending sexually transmitted disease clinics.
- The proportion of men with mild to absent symptoms is higher than in gonorrhea.
- Non-gonococcal urethritis is most commonly caused by *C. trachomatis* and less frequently by *Ureaplasma urealyticum*.
- Reinfection is common.



# PATHOGENESIS

- Chlamydiae have a tropism for epithelial cells of the endocervix and upper genital tract of women, and the urethra, rectum and conjunct. of both sexes. The LGV biovar enter through breaks in the skin or mucosa.
- Early - Once infection is established, there is a release of proinflammatory cytokines such as interleukin-8 by infected epithelial cells.
- Later - If the infection progresses further, aggregates of lymphocytes and macrophages may form in the submucosa; can progress to necrosis, fibrosis and scarring.

# IMMUNITY

- *C. trachomatis* infections do not reliably result in protection against reinfection (secretory IgA may confer some partial immunity) against genital tract reinfection. Any strain-specific protection that may result is short-lived.
- Local production of antibody, along with CD4+ lymphocytes that traffic to the genital mucosa may play a role in mitigating most acute infections. This would at least partially explain why most untreated chlamydial genital tract infections are persistent, but often subclinical.

## CLINICAL ASPECTS

### Genital Infections

- The clinical spectrum of sexually transmitted infections with *C. trachomatis* is similar to that of *Neisseria gonorrhoeae*. *C. trachomatis* can cause urethritis and epididymitis in men and cervicitis, salpingitis, and a urethral syndrome in women. In addition, three strains of *C. trachomatis* cause **LGV**, another sexually transmitted disease.

- *C. trachomatis* urethritis is manifested by dysuria and a thin urethral discharge. Infections of the uterine cervix may produce vaginal discharge, usually asymptomatic.
- Ascending infection in the form of salpingitis and pelvic inflammatory disease occurs in an estimated 5 to 30% of infected women.
- The scarring produced by chronic or repeated infection is an important cause of sterility and ectopic pregnancy.

■ More than 50% of all infants born to mothers excreting *C. trachomatis* during labor show evidence of infection during the first year of life. Most develop inclusion conjunctivitis, but 5 -10% develop infant pneumonia syndrome.

■ LGV is a sexually transmitted infection caused by *C. trachomatis* strains L1, L2, or L3. It is characterized by transient genital lesions followed by multilocular suppurative involvement of the inguinal lymph nodes. The primary genital lesion is usually a small painless ulcer or papule, which heals in a few days. Abscesses, strictures, fistulas if chronic.

## DIAGNOSIS

- Epithelial cells from the site of infection are required for detection. For genital infections, **cervical specimens** are preferred in females and **urethral scrapings** in males.
- Isolation of *C. trachomatis* has been the “gold standard” for diagnosis. It is achieved in cell culture using idoxuridine- or cycloheximide-treated **McCoy cells**.
- Isolation requires special treatment of cell lines, the cells are stained with fluorescein-labeled monoclonal antibodies to detect intracytoplasmic chlamydiae.

- Ligase chain reaction (LCR) or polymerase chain reaction (PCR) are the most sensitive methods of diagnosis.
- Serodiagnostic methods have little use in diagnosis of chlamydial genital infection because of the difficulty of distinguishing current from previous infection. Detection of IgM antibodies against *C. trachomatis* is helpful in cases of infant pneumonitis.
- *Chlamydial* serology is also useful in the diagnosis of LGV, but most satisfactory method is isolation of an LGV strain from aspirated bubos or tissue biopsies.



## TREATMENT

- Strains of *C. trachomatis* are sensitive to tetracyclines, macrolides and some fluoroquinolones. Azithromycin is given as a single oral dose for non-LGV *C. trachomatis* infection.
- Erythromycin for pregnant women and infants.
- Doxycycline is an alternative for *C. trachomatis* and is the drug of choice for treating LGV.



## PREVENTION

- Prophylaxis for infants using **topical erythromycin** or **silver nitrate** on the conjunctiva has limited effectiveness for *Chlamydia*, because 15 to 25% of exposed infants still develop inclusion conjunctivitis.
- The primary approach to prevention of all forms of genital and infant *C. trachomatis* infection comprises detection of this infection in sexually active individuals and appropriate treatment, including infected women late in pregnancy.
- No vaccine is available or under development.

# *Ureaplasma urealyticum*

- Ureaplasma is a unique microbe in that it lacks a cell wall. It is ubiquitous in nature as the smallest of free-living microorganism.
- *Ureaplasma urealyticum* and *Mycoplasma hominis* cause genitourinary tract infections.
- The organisms have diameters of about 0.2 to 0.3 mm, but they are highly plastic and pleomorphic, may appear as coccoid bodies, filaments, and large multinucleoid forms. They do not have a cell wall and are bounded only by a single triple layered membrane that, unlike other bacteria, contains sterols.

- The genus *Ureaplasma* contains a single species, *U. urealyticum*, of which some 14 serotypes have been described. *Ureaplasma* is distinguished from *Mycoplasma* by its production of urease. On special *Ureaplasma* agar media, colonies are small and circular and grow downward into the agar.

## EPIDEMIOLOGY

- The main reservoir of human strains is the genital tract of sexually active men and women; it is rarely found before puberty.

## MANIFESTATIONS

- Because of the high colonization rate, it has been difficult to associate specific illness with *Ureaplasma*; however, studies suggest that approximately one half of cases of nongonococcal, nonchlamydial urethritis in men may be caused by *U. urealyticum*.
- In women, *Ureaplasma* has been shown to cause chorioamnionitis and postpartum fever. The organism has been isolated from 10% of women with the latter syndrome.

## DIAGNOSIS AND TREATMENT

- Men with nongonococcal urethritis should be treated since *Ureaplasma infection* may be involved. **Tetracycline** is the treatment of choice because it is also active against *Chlamydia*, but tetracycline-resistant strains of *Ureaplasma* have been reported that have been associated with recurrences of nongonococcal urethritis in men.
- In such cases, **spectinomycin** treatment or **quinolone** antimicrobics is also effective.
- Women with postpartum fever due to *U. urealyticum* may respond to **tetracycline**.

## *Gardnerella vaginalis*

- *G. vaginalis* is a facultatively anaerobic gram-variable rod. It has been demonstrated to cause a wide variety of infections; however, it is most commonly recognized for its role as one of the organisms responsible for bacterial vaginosis.
- *G. vaginalis* grows as small, circular, convex, gray colonies on Chocolate agar;. A selective medium for *G. vaginalis* is colistin-oxolinic acid blood agar.

- While typically isolated in genital cultures, it may also be detected from other sources, such as blood, urine and pharynx. Although a chief cause of bacterial vaginosis, it may be isolated from women without any signs or symptoms of infection.
- It is associated microscopically with clue cells, which are epithelial cells covered in bacteria.
- Although BV is not considered a sexually transmitted disease, sexual activity has been linked to development of this infection.

## Epidemiology

- *Gardnerella vaginalis* has been reported to occur in up to 100% of women with signs and symptoms of bacterial vaginosis (BV) and in up to 70% of women with no signs or symptoms of BV.
- *G vaginalis* has been isolated in up to 80% of the urethras of male sexual partners of women with BV.
- The incidence of BV in patients attending obstetric clinics is 10-25% and may be as high as 30-65% in patients attending sexually transmitted disease clinics.

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# PATHOGENESIS

- Bacterial vaginosis (BV), formerly known as nonspecific vaginitis, was named because bacteria are the etiologic agent in this infection and an associated inflammatory response is lacking. BV is the most common cause of vaginitis.
- BV is known to be a synergistic polymicrobial infection. Some of the associated bacteria include *Lactobacillus* species and anaerobes.
- Vaginal flora becomes altered, causing an increase in the local pH. This may result from a reduction in the H<sub>2</sub>O<sub>2</sub> producing lactobacilli.

# CLINICAL ASPECTS

## MANIFESTATIONS

- Symptoms of infection typically include a gray, thin, and homogeneous vaginal discharge that is adherent to the vaginal mucosa, associated with a "musty" or "fishy" odor.
- The amount of discharge is quite variable, and there is little vulvar or vaginal irritation associated with this infection, but the pungent odor is usually the chief complaint.
- Evidence of cervicitis should prompt a workup for concomitant infection with *N. gonorrhoeae*, *C. trachomatis*, or Herpes simplex virus.

## DIAGNOSIS

- A wet mount preparation of physiologic saline mixed with vaginal secretions should be examined under low- and high-power objectives. There are few WBCs & lactobacilli.
- The characteristic "clue cells" are identified as numerous stippled or granulated epithelial cells.
- Cultures are seldom necessary to establish a diagnosis.

## TREATMENT

- The treatment of choice for *G. vaginalis* is oral metronidazole, 500 mg twice daily for 6 days. A single dose of 2 g proved effective in treatment of adolescent patients, but in general a 5- to 7-day course of treatment is more effective. The drug is contra-indicated during early pregnancy and lactation.
- Cephradine, 500 mg by mouth 4 times daily for 6 days, will eliminate *G. vaginalis* from the vagina and relieve symptoms but has little effect on the anaerobic flora of the vagina.