Urogenital Tract Module Chlaymdia, Gardenella and ureaplasma

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Gardnerella Vaginitis

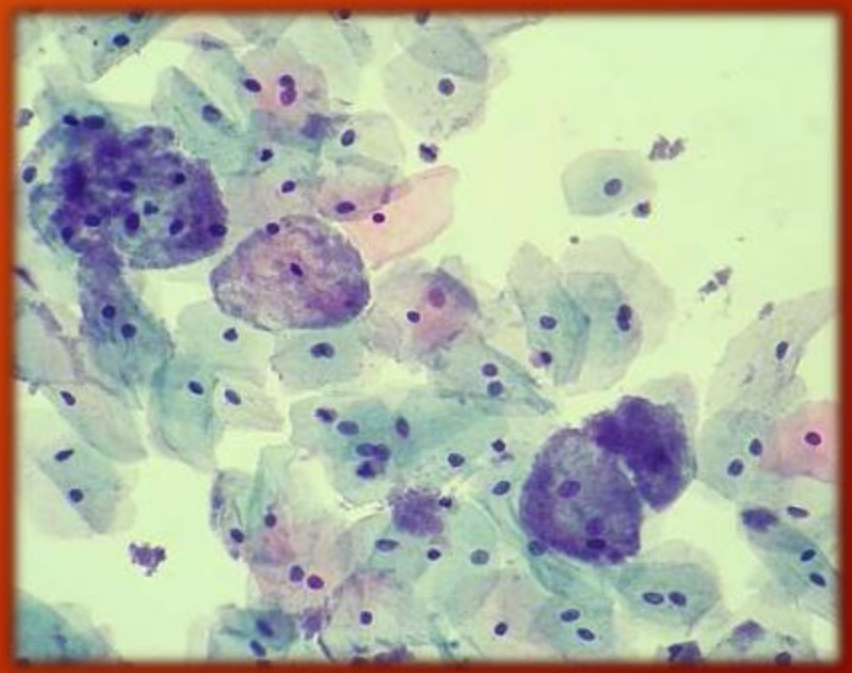
- Gram-variable-staining rod, facultative anaerobic bacteria (actually has a Gram-positive cell wall, but because the cell wall is so thin it can appear either Gram-positive or Gram-negative under the microscope).
- Small (1-1.5 µm diameter) non-spore forming, non-motile coccobacilli.
- Previously classified as Haemophilus vaginalis and afterwards as Corynebacterium vaginalis.

Gardnerella Vaginitis

- Growth: grows as small, circular, convex, gray colonies on chocolate agar; it also grows on HBT agar.
- Can cause bacterial vaginosis in some women as a result of a disruption in the normal vaginal micro flora.

Can be isolated from other Areas

- Typically isolated in genital cultures. May also be detected in other samples from blood, urine, and pharynx



What is Bacterial vaginosis

- Bacterial vaginosis is the most common cause of abnormal vaginal odour and discharge. It is caused by a change in the type of bacteria found in the vagina. Normally, bacteria belonging mostly to the Lactobacillus family live harmlessly in the vagina and produce chemicals that keep the vagina mildly acidic. In bacterial vaginosis, Lactobacillus bacteria are replaced by other types of bacteria that normally are present in smaller concentrations in the vagina.

Risk factors

- Risk factors that seem to increase the likelihood of bacterial vaginosis include a history of multiple sex partners, a sexual relationship with a new partner, cigarette smoking, vaginal douching and the use of the intrauterine contraceptive device (IUD). Although most of these risk factors are related to sexual activity, women who have never had vaginal intercourse can also develop bacterial vaginosis.

Culturing

- Grows on Blood and Chocolate Agar
- Hemolytic colonies on Human and Rabbit blood agar,
- Catalase -
- Oxidase -

Symptoms

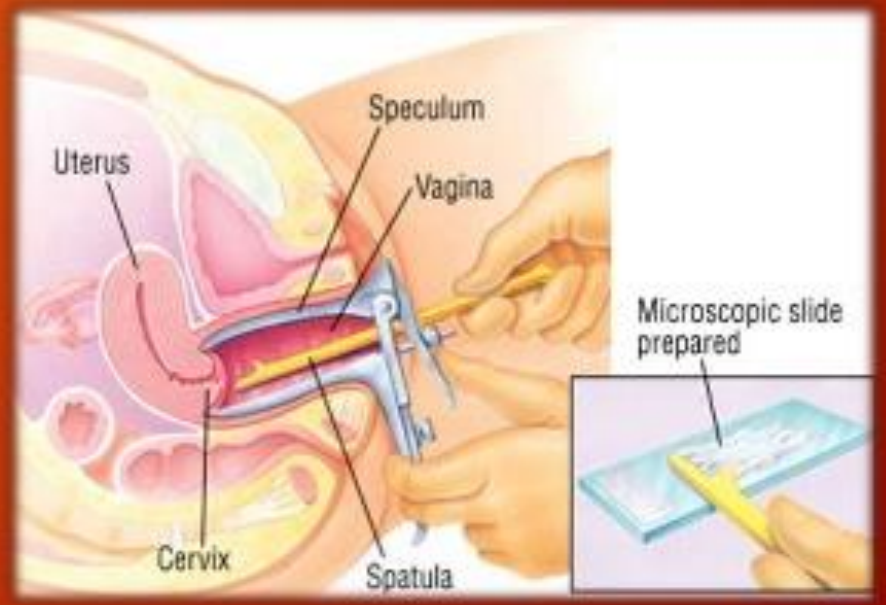
- Up to 50% of women diagnosed with bacterial vaginosis do not have symptoms. In others, it causes an unpleasant "fishy" vaginal odor and a yellow or white vaginal discharge. For some women, these symptoms are especially bothersome during or after intercourse.

Observation of Vaginal Discharge

- The discharge seen in bacterial vaginosis tends to be thinner than the "cheesy," thick discharge seen in vaginal yeast (Candida) infections. Bacterial vaginosis usually does not cause significant irritation of the vulva or pain during intercourse. If you have these symptoms, your doctor will check for other possible causes.

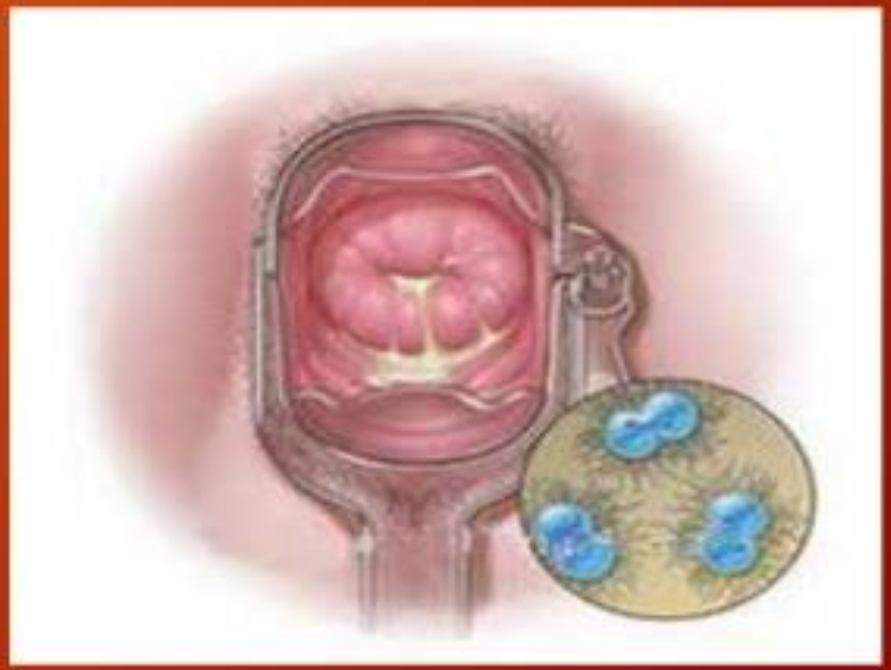
No perfect test

- There is no perfect test, but if you have three of the following four criteria, it is highly likely that you have bacterial vaginosis:
- 1 White, thin, coating on your vaginal walls during the pelvic exam



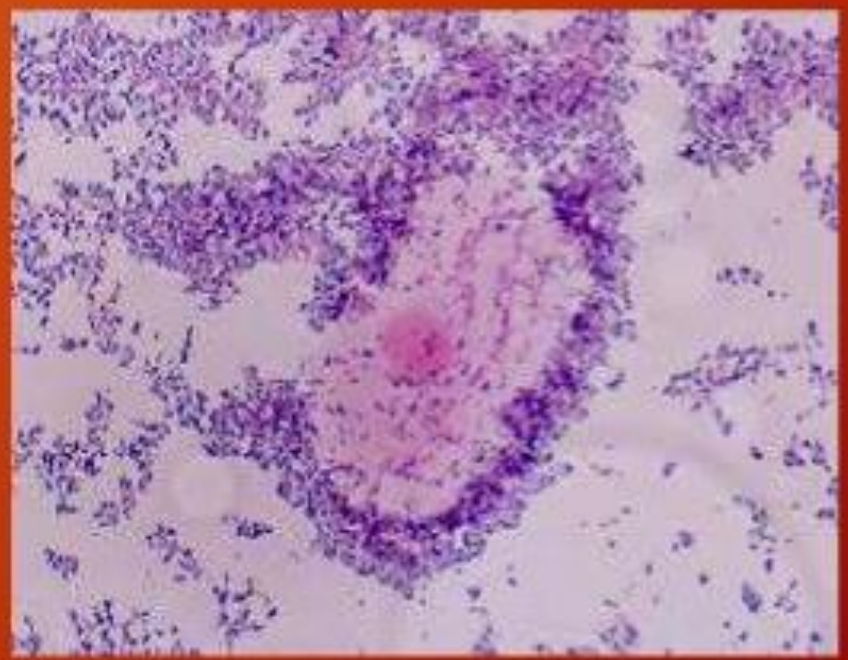
Diagnosis

- 2 pH test of vaginal discharge that shows low acidity (pH greater than 4.5)
- 3 Fishy odor when a sample of vaginal discharge is combined with a drop of potassium hydroxide on a glass slide (the "whiff test")

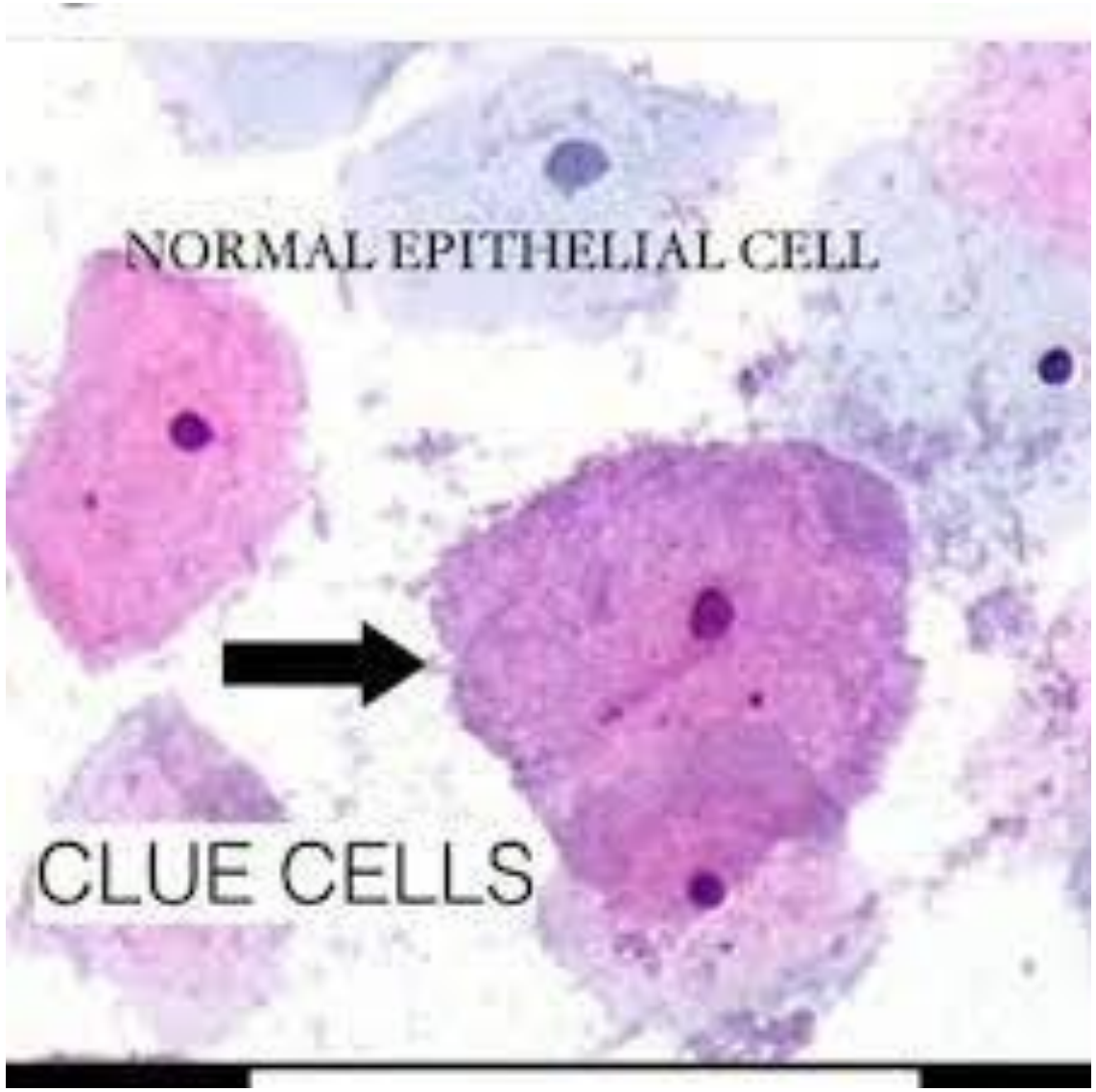


Clue cells

- 4 Clue cells (vaginal skin cells that are coated with bacteria) visible on microscopic exam of vaginal fluid



Clue cells



Newer methods in diagnosis of Genital Infections

- DNA probes have been developed to directly detect the presence of candida, trichomonas and Gardnerella, thus providing a more objective diagnosis. Since Gardnerella is a normal part of the vaginal flora, the DNA probe test is designed to be relatively insensitive, detecting only pathogenic levels of Gardnerella. The Affirm VP III Microbial Identification System (Becton Dickinson) is a commercially available DNA probe office-based test kit that simultaneously detects the presence of Gardnerella, trichomonas and candida.

Treatment

- Commonly treat bacterial vaginosis with metronidazole (Flagyl or MetroGel-Vaginal) or clindamycin (Cleocin). Either can be taken by mouth or applied as a vaginal cream or gel. However, the U.S. Centers for Disease Control and Prevention (CDC) recommends that all pregnant women with symptoms be treated with oral medications because the medications are safe and work better than vaginal creams or gels.

GENITAL MYCOPLASMAS

- Three Mycoplasma species,
  - *Mycoplasma hominis,*
  - *Mycoplasma genitalium,*
  - *Ureaplasma urealyticum.*

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

Ureaplasma urealyticum

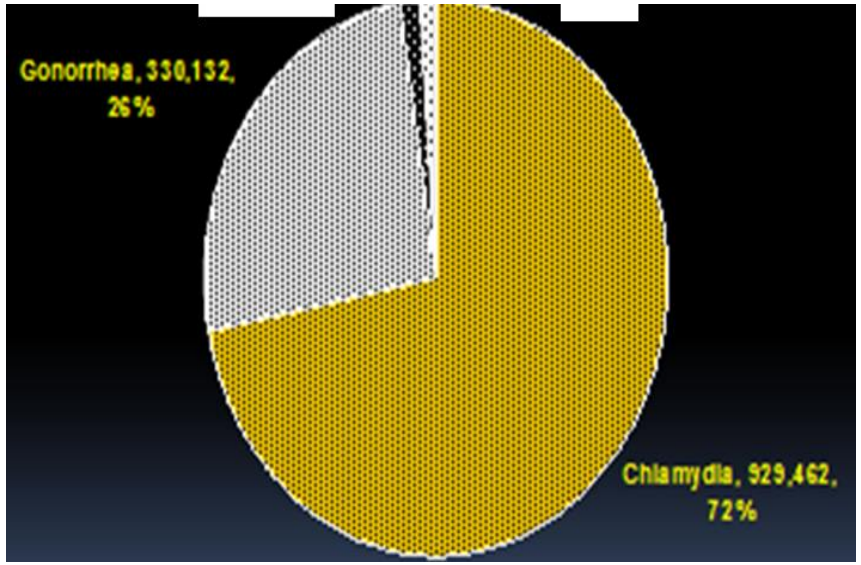
- is part of the normal genital flora of both men and women in about 70% of sexually active humans.
- It stains gram negative, that is because it lacks a cell wall.
- Symptoms can be "silent" or can cause noticeable symptoms such as fishy odor discharge, NGU and bacterial vaginosis.
- *Ureaplasma urealyticum* is a common cause of urethritis when neither gonococcus nor chlamydia can be demonstrated, particularly in men.
- 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.
- The infants are often colonized, and *Ureaplasma urealyticum* has been isolated from the infant’s lower respiratory tract and CNS both with and without evidence of inflammatory response.

Ureaplasma urealyticum

- It had been associated with a number of diseases, including non-specific urethritis (NSU), infertility, stillbirth, premature birth.
- 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.
- **Diagnosis;** A biopsy or swab, which is tested in a lab plus symptoms and signs of infection, is used to diagnose Ureaplasma. The biopsy or swab may be taken from the vagina, uterine lining, urethra, or urine sample. Due to its small size, Ureaplasma is nearly impossible to see under a microscope. The urine sample or swab is subjected to a PCR test that looks for the DNA of the bacteria
- Treatment:
    - A tetracycline, such as doxycyline, is effective for specific treatment

Chlamydia, Epidemiology

- Is a STDs
- In USA over 900,000 cases are reported each year, which is three times the number for gonorrhea (2004)
- The cases among males and females are higher than in gonorrhea
- Prevalence in pregnant women 6% - 12%
- Reinfection is frequent



Reported Sexually Transmitted Diseases, United States, 2004

Chlamydia

- Obligatory intracellular bacteria
- Intracellular replication that results in the death of the cell
- weakly Gram-negative bacterium. It is ovoid in shape and nonmotile
- Three species: ***C. trachomatis,*** *C. psittaci, C. pneumoniae*

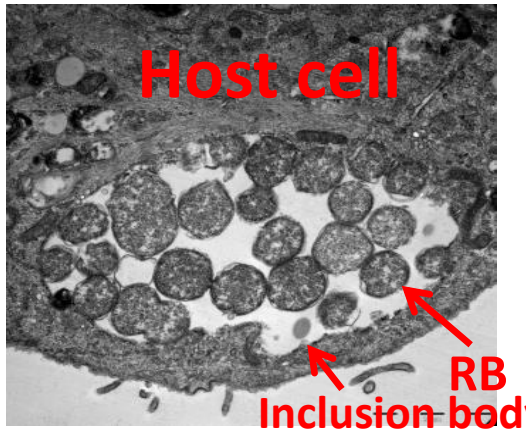
Q: Why *Chlamydia* is an obligatory intracellular parasite?

- No flavoproteins or cytochromes, therefore, lacking ATP-generating ability
- Need to obtain ATP from the host cell.
- Called energy parasites

Chlamydia

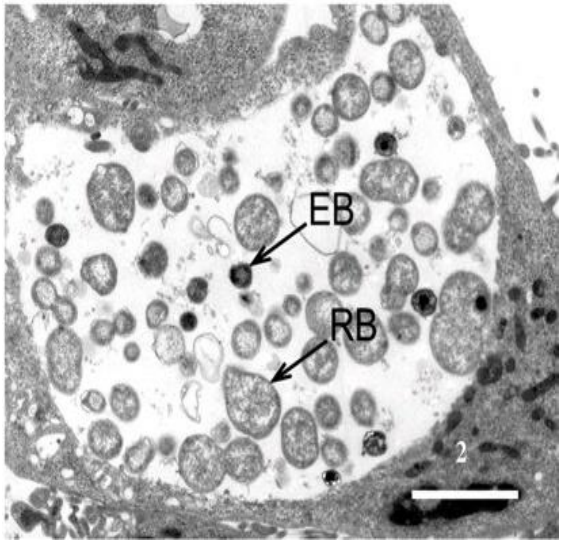
Chlamydial Morphologies and life cycle

Takes on two forms in its life cycle:



1- <u>Elementary body</u>

- about 0.3 um in diameter
- infectious nonreplicating
- condensed genetic material
- released from ruptured infected cells



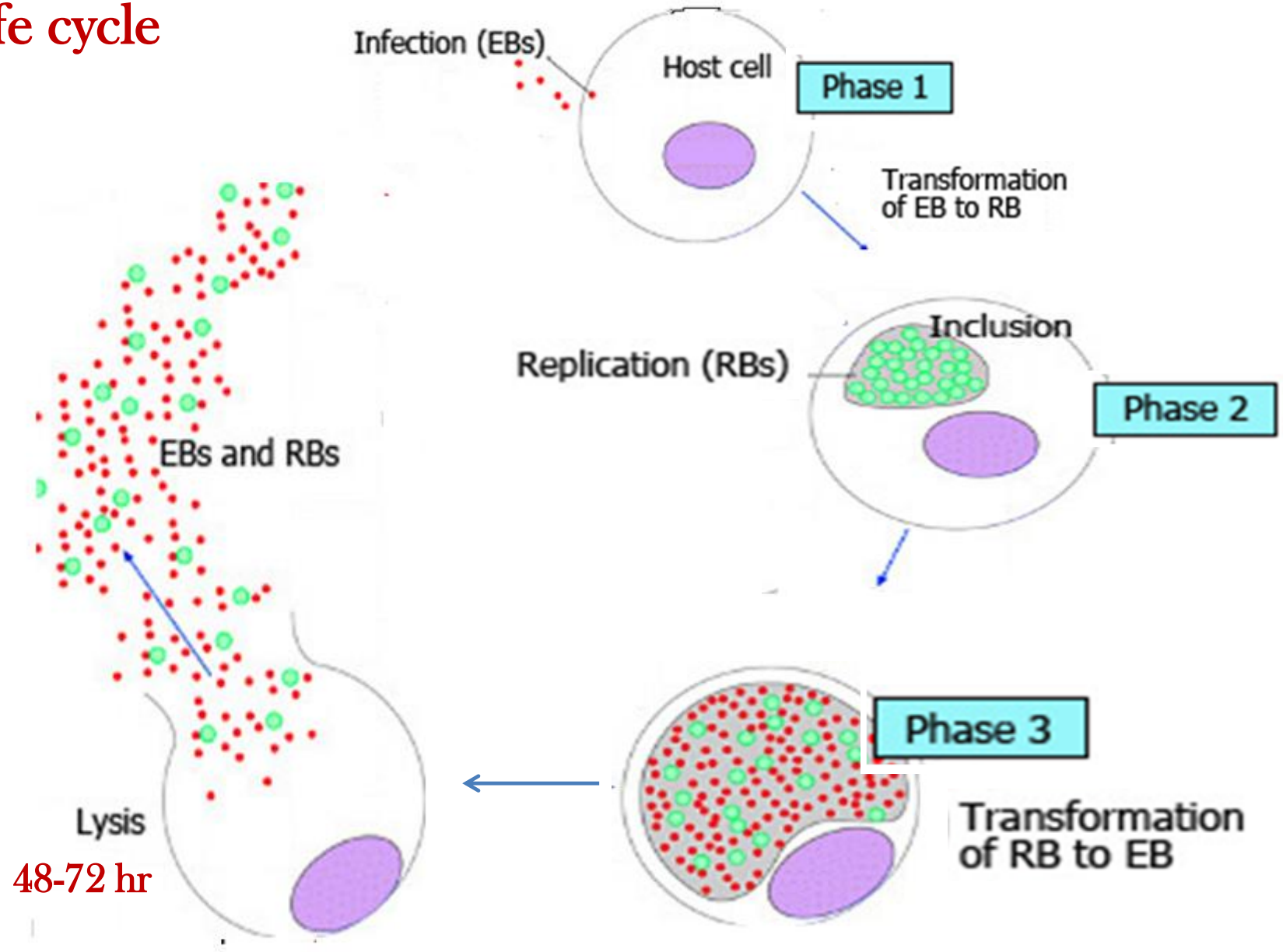
48h post infection

2- <u>Reticulate Body</u>

- intracytoplasmic form 0.5 - 1.0 um
- non-infectious replicating form
- replication and growth in an inclusion body
- diffuse genetic material

Chlamydia

Life cycle



Clinical syndromes

Strains causing human diseases

C. trachomatis strains	Associated diseases
Ocular strains (A, B, Ba, C)	Conjunctivitis, trachoma, infant pneumonia,
Genital strains (D-K)	Nongonoccocal urithritis, Mucopurulent cervicitis, pelvic inflammatory disease (PID)
Genital strains (L1, L2, L3)	Lymphogranuloma venereum (LGV)

Clinical syndromes

Clinical syndromes caused by *C. trachomatis*

	Local Infection	Complication	Sequelae
Men	Conjunctivitis Urethritis Prostatitis	Reiter's syndrome Epididymitis	Chronic arthritis (rare) Infertility (rare)
Women	Conjunctivitis Urethritis Cervicitis Proctitis	Endometritis Salpingitis Perihepatitis Reiter's syndrome	Infertility Ectopic pregnancy Chronic pelvic pain Chronic arthritis (rare)
Infants	Conjunctivitis Pneumonitis Pharyngitis Rhinitis	Chronic lung disease?	Rare, if any

Pathogenesis

- Chlamydiae have a tropism for epithelial cells of the endocervix and upper genital tract of women, and the urethra, rectum and conjunctiva of both sexes.

- Once infection is established, there is a release of proinflammatory cytokines by infected epithelial cells.

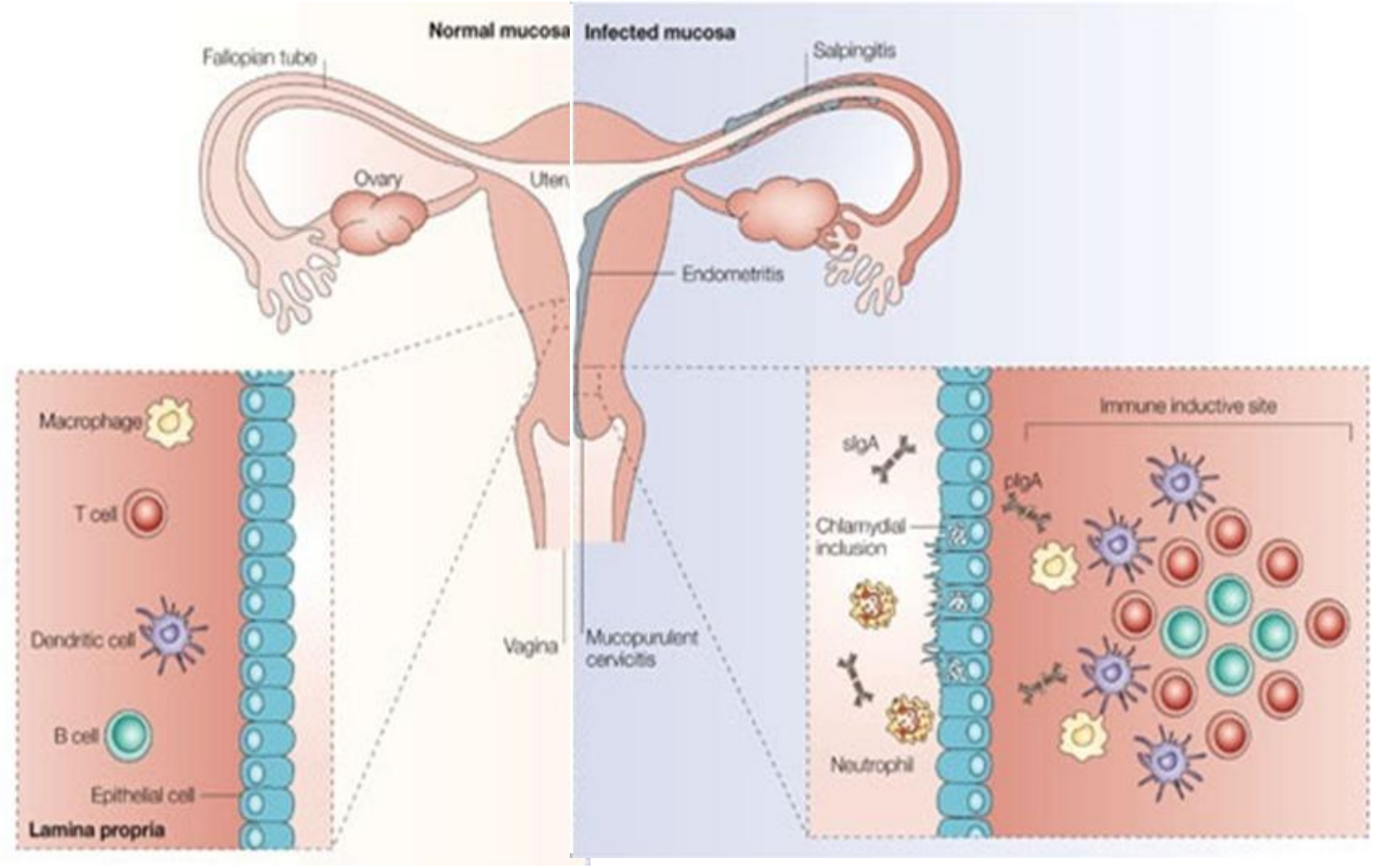
- This results in early tissue infiltration by PMNs, later followed by lymphocytes, macrophages, plasma cells and eosinophils.

- If the infection progresses further (because of lack of treatment and/or failure of immune control), aggregates of lymphocytes and macrophages (lymphoid follicles) may form in the submucosa; these can progress to necrosis, followed by fibrosis and scarring.

Pathogenesis

Normal

Infected



Pathogenesis

How does Chlamydia affect pregnancy?

- Chlamydia can cause a **pregnant** woman to go **into labor** early or **deliver a low-birth weight baby**.
- Chlamydia can spread fr**om mother to baby during birth**. This can cause **pneumonia** or a **serious infection** in the baby's eye that may lead to **blindness**.
- A pregnant woman can be **treated** to prevent transmission to the baby.

Clinical syndromes

In Men

Urethritis

- The most **common cause of nongonococcal urethritis (NGU)** in men (40 to 96 percent)
- More common than gonococcal infection
- Majority (>50%) are asymptomatic
- The **incubation** period is variable but is typically **5 to 10** days after exposure
- Symptoms
  - ✓ mucoid or clear urethral discharge with bad smell
  - ✓ dysuria
- Sometimes the **discharge is so scant (thick, white, odorless, and curd-like) like cottage cheese** . This is in contrast to the more copious and purulent urethral discharge and shorter (two to seven days) incubation period for gonococcal urethritis

Clinical syndromes

In Men

Epididymitis

Men with acute epididymitis typically have testicular pain and tenderness, hydrocele, and palpable swelling of the epididymis.

Prostatitis

Symptoms included

- dysuria
- urinary dysfunction
- pain with ejaculation
- pelvic pain

Clinical syndromes

In woman

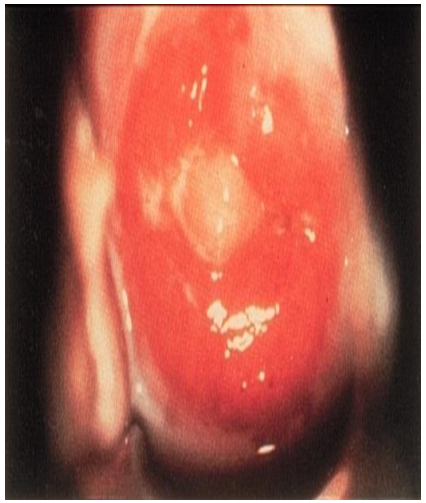
Urethritis

- Usually asymptomatic
- Signs/symptoms, when present, include dysuria, frequency, pyuria

Cervicitis

- Majority (70%-80%) are asymptomatic
- Local signs of infection, when present, include:
  - mucopurulent endocervical discharge
  - cervical edema with erythema and friability

Cervicitis

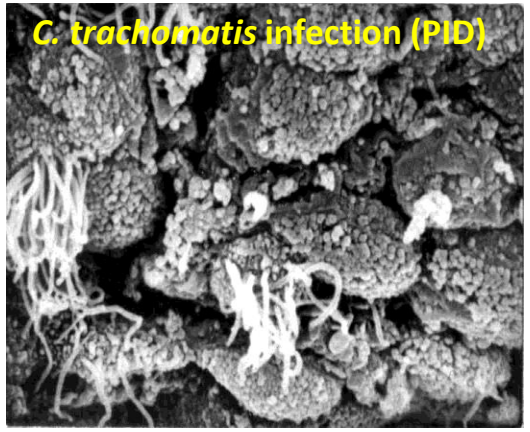


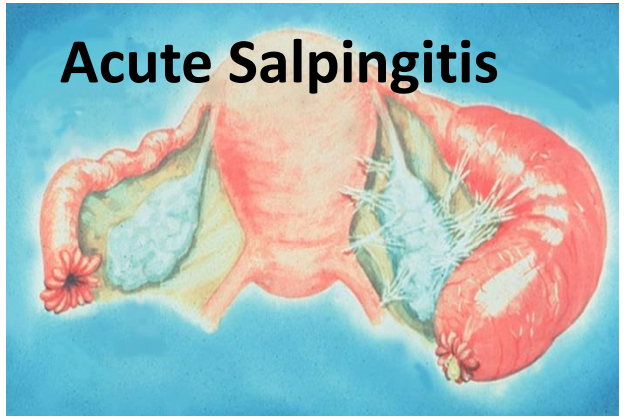
Clinical syndromes

In woman

Complications in Women

- Pelvic Inflammatory Disease (PID)
  - Salpingitis
  - Endometritis





Clinical syndromes

Proctitis

- Defined as inflammation of the distal rectal mucosa
- The clinical presentation depends on the infecting chlamydial serovars
  - LGV serovars: anorectal pain, mucopurulent exudate, tenesmus, rectal bleeding and constipation. If left untreated, can lead to rectal fistulae and strictures
  - The non-LGV: the infections are usually asymptomatic

Reiter's Syndrome (reactive arthritis)

Characterized by a triad of

- Arthritis
- nongonococcal urethritis
- conjunctivitis

Clinical syndromes

Lymphogranuloma venereum (LGV)

- primarily an infection of lymphatics and lymph nodes
- It gains entrance through breaks in the skin, or it can cross the epithelial cell layer of mucous membranes.
- The organism travels down to multiply in the lymph nodes

Stages

Primary stage

- A self-limited painless genital ulcer that occurs at the contact site 3–12 days after infection
- Unobserved in most cases
- Heals in a few days

Clinical syndromes

Secondary stage

- occurs **10–30 days later**, but can present up to six months.
- The infection **spreads** to the **lymph nodes** through lymphatic drainage pathways.
- causing **tender** inguinal and/or femoral Lymphadenopathy
- These changes may progress to **necrosis**

Third stage

- Healing of necrosis takes place by **fibrosis**.
- This can result in varying degrees of lymphatic obstruction and chronic edema
- Causing genital elephantiasis

STDs comparison

Syphilis	▪ firm painless ulceration ▪ 5–15 mm and sharply demarcated ▪ often, a painless nontender inguinal lymphadenopathy
***Herpes* genitalis**	▪ group of vesicles on an erythematous base ▪ after rupturing, they form an ulcer ▪ heal within 1–4 weeks
H. ducruyi	▪ soft Painful deep purulent ulcers (2–20 mm) ▪ painfull Lymphadenopathy. ▪ Swollen lymph nodes can break through the skin and lead to large abscesses (collections of pus) that drain
LGV	•painless ulcer (2–10 mm). • the genital ulcers heal spontaneously. •tender and painful lymphadenopathy is a typically symptom of LGV

diagnosis

- The preferred method for chlamydia testing is the nucleic acid amplification test (**NAAT**) that detects the genetic material (DNA) of Chlamydia trachomatis
- **A urine test.** A sample of your urine is analyzed in the laboratory for presence pyurea but no bacteria.
- **A swab.** For women, your doctor takes a swab of the discharge from your cervix for culture or antigen testing for chlamydia.

diagnosis

- Typical intracytoplasmic inclusions in Giemsa-stained cell.
- Positive culture in McCoy or HeLa cells of body fluids or secretions.
- Serology test in patients with presumed lymphogranuloma venereum.

Treatment

- Tetracycline
- Azithromycin
- Erythromycin in children