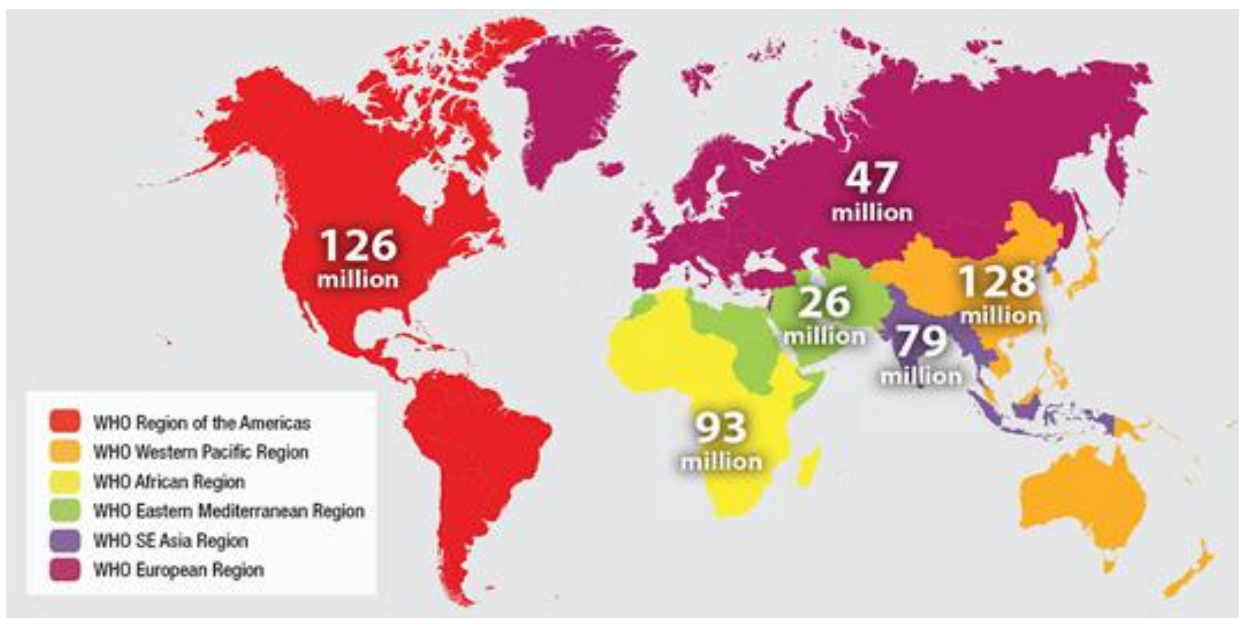


# Sexually Transmitted Diseases

Sources : sexually\_transmitted\_diseases-2015 (edited+some notes from last year sheet)

## Introduction ;

- More than 1 million people acquire a sexually transmitted infection (STI) every day.
- Each year, an estimated 500 million people become ill with one of 4 STIs: **Chlamydia, gonorrhoea, syphilis and trichomoniasis**.
- More than 530 million people have the virus that causes **genital herpes (HSV2)**.
- More than 290 million women have a **human papillomavirus (HPV)** infection.
- The majority of STIs are present without symptoms.
- **STIs** can have serious complications beyond the immediate impact of the infection itself, through **mother-to-child transmission** of infections and **chronic** diseases.
- **Drug resistance**, especially for gonorrhoea, is a major threat for reducing the rate STIs worldwide.
- **STIs** are caused by more than **30 different bacteria, viruses and parasites** and are spread predominantly by sexual contact, including vaginal, anal and oral sex.
- Many STIs—including **chlamydia, gonorrhoea, hepatitis B, HIV, HPV, HSV2 and syphilis**—can also be transmitted from mother to child during pregnancy and childbirth
- World Map STDs



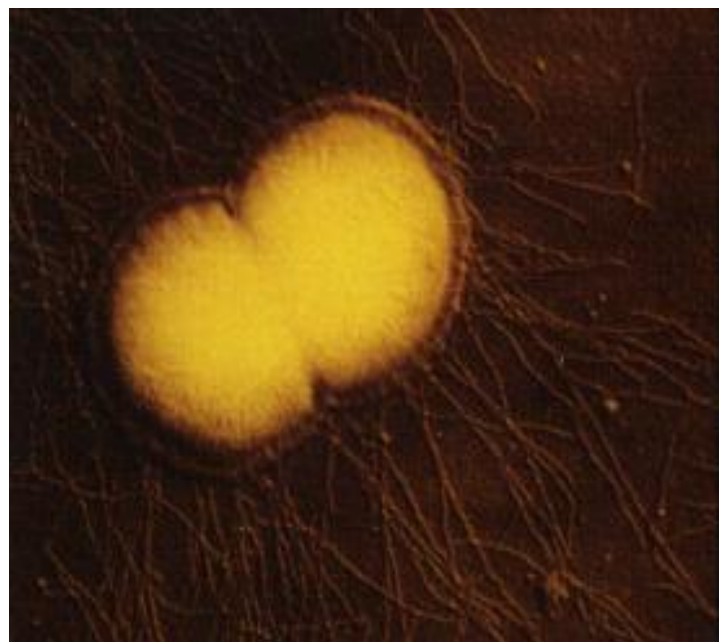
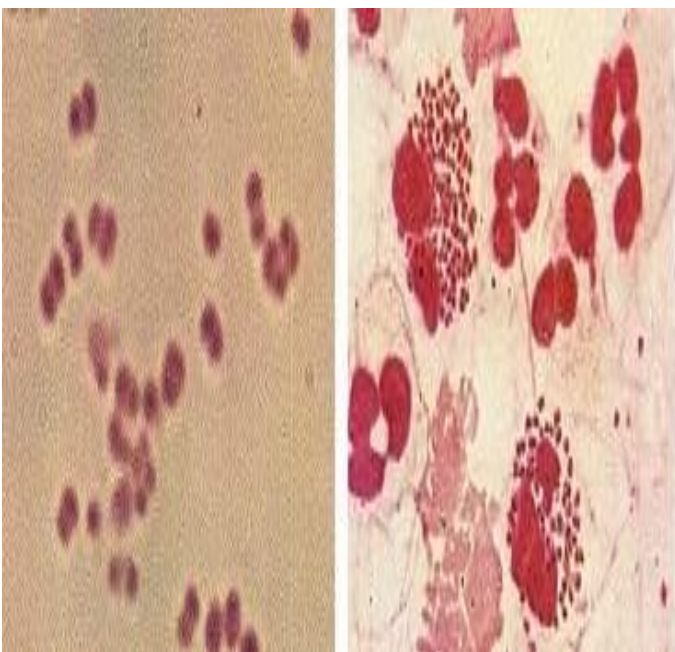
\*STDs are associated with infertility.

## Common Bacterial & Fungal Agents of STDs:

1. *Neisseria gonorrhoea*: Gonorrhoea
2. *Chlamydia trachomatis*, *Mycoplasma genitalium* /*Ureaplasma urealyticum* → cause nonspecific urethritis, vaginitis, salpingitis, pelvic inflammatory disease by one or more organisms.
3. *Treponema pallidum* : Syphilis
4. *Haemophilus ducreyi* : Chancroid
5. *Gardnerella vaginalis* : Vaginosis, Mixed bacterial infection
6. *Candida spp.*: Vaginitis

## Gonorrhoea

- ***N. gonorrhoeae*** :Gram-negative diplococci , killed rapidly outside human host. Presence of pili & surface cell outer membrane proteins support cells attachment. Generally the pathogenicity of N.G is related to presence **oligolipopolysaccharides** that are smaller than the lipopolysaccharides of gram negative bacteria. infect & cause local inflammation of mucosa of genital tract, throat, rectum in both men and women.. Acute & chronic stages. The only way of transmission is direct sexual contact, rarely acquired by other means.
- In women: vagina & cervix are the first infected →infection can spread into the uterus & fallopian tubes, resulting in Pelvic Inflammatory Disease (PID)/ endometritis and salpingitis .
- **Common complication:** Ectopic pregnancy & infertility in about 10% of chronic infected women.
- Mother to child →New born eye-infection is common in asymptomatic infected mother →**Ophthalmia neonatorum** → cornea damage & blindness without treatment.
- *Neisseria Gram-ve diplococci*



## SYMPTOMS:

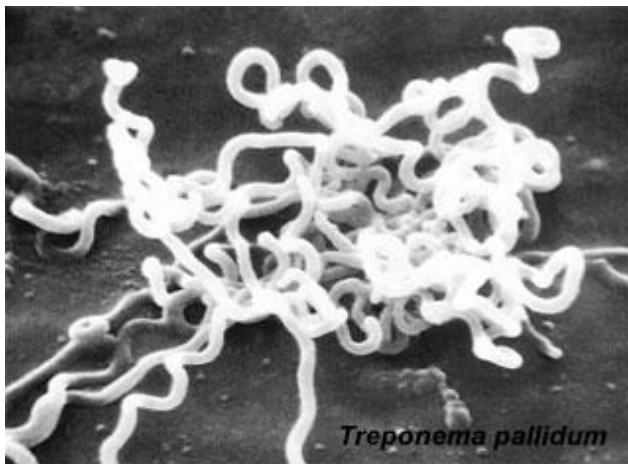
- Infection in **women: first** ,Mostly mild without symptoms (80%). bleeding can be associated with vaginal intercourse.  
**Later**, chronic infection.. painful burning sensations during urinating, occasionally yellow or bloody purulent vaginal discharge.
- Infection in **men**: Develop mostly as acute **urethritis** with symptoms **more** often than women including: fever, burning sensations, abdominal pain. Urethral discharge/ white/ yellow pus with mild to severe pain.. anal infection & itching. **Incub. period 2-10 days.**
- **Disseminated *N.gonorrhoea*** may cause epididymitis, proctitis ,orchitis → infertility.  
Complications: Rarely blood sepsis, meningitis, endocarditis, dermatitis-arthritis syndrome.
- gonorrhoea is recognized in acute form in males but In females it's mostly chronic and asymptomatic
- It can be acute, subacute or chronic inflammation in the mucosa of the genital tract. Acute and subacute stages are always easily treated with anti microbial drugs. Chronic inflammation is more difficult and more serious. The infection is usually related to genital tract but it might be demonstrated in the oral cavity or rectum of infected men or women.

## DIAGNOSIS & TREATMENT:

- Direct Gram-Stain smear from urethral/vaginal discharge .( we should not rely on the Gram stain alone )  
presence of **intracellular Gram-negative diplococci** resembling *Neisseria* in polymorphonuclear leukocytes .  
#If there is a vaginal or urethral discharge you have to collect it and prepare a gram stain to demonstrate the presence of gram negative diplococci, however, this is not enough you have to demonstrate the presence of intracellular gram negative diplococci inside the WBCs. Demonstration of Extracellular gram-negative diplococci is not a diagnosis for Gonorrhoea
- Rapid culture of specimens-discharge-cervical swabs, rectal swab /throat →in **Blood/ Chocolate agar (Thayer-Martin blood agar** includes certain antibiotics; to inhibit the growth of contaminants.), for 24-48 hrs.  
micro- aerobic incubation, biochemical sugar test & +ve oxidase & +ve catalase.  
Further testing to differentiate the species includes testing for **oxidase** (all clinically relevant *Neisseria* species show a **positive** reaction) and the carbohydrates maltose, sucrose, and glucose test in which *N. gonorrhoeae* will oxidize only the glucose.
- Antimicrobial drugs.. mostly (80%) **Resistant** –penicillin(not used any more). Relatively Effective drugs are used Cefixime, Ceftriaxone, Ciprofloxacin, Doxycycline . 2nd and 3rd generation cephalosporins. Physicians mostly use the 2nd generation. →susceptibility test should be done.
- No immunity after infection ,**No vaccine** is available

## Syphilis :

- ***T. pallidum*** has a characteristic helical/Spiral shape, part of the spirochete family, 4-15 um, Related to Gram-negative bacteria. can't be demonstrated by Gram-stain; it has a few amounts of lipopolysaccharides in its wall but they are not enough to demonstrate the gram negativity in the gram stain test. Since we can't use the gram stain we use the dark field microscopy or silver stain to recognize it but stains are usually not so accurate in demonstrating it, we can obtain the specimen from the fluids inside the lesions on the external genitalia then we can see under the microscope that it's spiral, highly motile and exists in clumps.
- Treponema cell wall contains **peptidoglycan layer rich in Lipids(side effects on CNS) & Endoflagella (attachment)** within outer membrane → Responsible for motility.
- Treponema cells are very sensitive to drying, heat and disinfectant.. survive few minutes outside the human body.. **Infect only human host.**
- **Pathogenicity:** Hyaluronidase, high lipids enhance invasiveness , contributes to granulomatous lesions & autoimmune reaction during progressive infection.
- Can't be cultured in vitro, but it can be isolated in Rabbit testicles for research.
- Morphology of Treponema



### General Feature:

- **Transmission:** Sexual contact(99%), blood, body fluids of infected person.
- Bacteria pass infected **skin or mucous membranes** usually of genital area, lips, mouth, anus.
- Treponema active cells penetrate and reside in epithelial cells.. multiply slowly.. **2-6 Weeks**
- **Syphilis** has so many clinical symptoms
- Presence HIV infection at the same time can change the symptoms and course of syphilis.
- **Syphilis** other than congenital syphilis, occurs in 3-4 stages that sometimes overlap over many years.

- Once its passed from a fresh lesion of an infected individual to the **skin** or **mucous** membrane of other individual it will produce **hyaluronidase** which allows the organism to penetrate the sub mucosa and reside in the epithelial cells to produce localized infection (primary infection), this localized infection is demonstrated by the presence of lesions called **chancre** usually found on the external genitalia in men and inside the vagina or uterus in women, they might disappear later in the course of infection. However if these lesions didn't appear on the external genitalia of male then it would be very difficult to diagnose the first primary infection of syphilis in this male because other symptoms of syphilis such as temperature, lymphadenopathy, headache, sore throat are common in other diseases. In other words, syphilis is not easily recognized without the presence of extragenital lesions because the wide range of symptoms it has might mimic other types of infections. The primary disease is even more difficult to be recognized in women.

### Primary Syphilis-1 :

- Primary syphilis is often a small, round firm , **painless ulcer /chancre/ lesion..** Highly infectious
- Most lesions appears on Extra Skin Genitalia / Vagina, but ulcers can also develop on the cervix, tongue, lips, or other parts of the body,can be easily overlooked without symptoms.. **No fever.**
- There is often only **one ulcer..** nearby swollen lymph nodes .. The ulcer usually appears about 3 weeks after infection, but it can occur any time within **3 months** after exposure to infection & disappears after 4 weeks .

### Secondary syphilis-2 :

- If primary syphilis is not treated→mostly progress to the **Secondary stage.** (associated with more clinical features)
- Most persons with secondary syphilis have **red maculopapular skin rash**, including often palms of hands and soles of feet.. Associated with moist lesions.. **Candylomas** which occur in the anal or genital areas as a flat soft lesions.
- Other common symptoms include:** Sore throat, fatigue, headache, swollen lymph glands. Less frequent symptoms include fever, hepatitis, meningitis, glomerulonephritis, weight loss, hair loss, lesions (cold sores) in the mouth or genital area.  
Most lesions of secondary syphilis contain many **Active Treponema..** Patients is highly infectious.
- During the primary phase the infectious rate is high, it is even more in the secondary stage.
- Diffuse skin rash associated with Syphilis



## Congenital Syphilis

- Pregnant woman with secondary syphilis may infect fetus vertically in utero during first trimester & at birth.. Infection may cause miscarriage, premature babies & stillbirth.
- Few percentage of infants with **Congenital syphilis** have symptoms at birth.. but the majority develop symptoms later→After 2 years.
- Untreated babies may have facial & tooth deformities.. delays in growth or seizures along with many other problems such as rash, fever, swollen liver and spleen, jaundice, anemia, including damage to their bones, teeth, eyes, ears, brain.
- Congenital syphilis does not necessarily result in death.

## Latent/Tertiary Syphilis-3

- As with primary syphilis.. secondary syphilis will disappear even without treatment→infection will progress to the **next hidden stages**.
- If the primary or secondary infections are not treated with antimicrobial drugs and the body has not managed to resist the infection by the humeral antibodies and cell mediated immunity then the 3rd stage might develop. It is known as the latent stage (not associated with internal organ damage) and later might develop into the last stage . Few % infected people develop Tertiary Syphilis
- **latent syphilis**: Positive blood syphilis test.. often without clinical signs or symptoms.. Rare transmission of Infection.. Without treatment will progress slowly over many years to **Tertiary syphilis**
- During this stage antibodies, cell-mediated immunity, hypersensitivity developed to Treponema antigens.. play a role in immunity.. But not sufficient to stop the development of disease complication in each case.
- tertiary syphilis (associated with granulomatous lesions in any part of the body)
- Latent syphilis is mostly related to developing of antibodies and hypersensitivity to T.pallidum antigens but they are not sufficient to stop the progress of the disease, these autoimmune conditions might lead to organ damage. At this stage the patient cannot be cured. Latent syphilis is associated with low transmission of Infection or even absent transmission. In case of no treatment, latent syphilis in a minority of people will progress to Tertiary syphilis, the most serious stage of the disease.
- Tertiary phase means the damage has been already established in internal organs. The patient is not really infectious at this stage because there is no living T.pallidum.  
primary and secondary stages are infectious but the latent and tertiary are not. The damage mostly starts in the CNS, so first symptoms might be related to the mental behavior, later on it might affect the eyes, bones, jaws or any part of the body. The damage might be in the form of granulomatous lesions (gummatos syphilis) which means there is progressive destruction that might spread all over the body, it develops slowly over 5-30 years and it's not necessarily recognizable in the early years but in the end it will lead to severe damage and often the end result is the death. Tertiary syphilis is associated with high mortality. Primary and secondary are mostly not associated with any death.

- Tertiary Syphilis is **autoimmune reaction** to Treponema antigens.. Which damages heart, eyes, brain, nervous system, bones, joints.. almost any other part of body by developing **Gummas** (granuloma that is characteristic of an advanced stage of syphilis)
1. **Gummatos syphilis**.. progressive destructive granulomatous lesions over many years.. Mostly skin, bones, Liver, mucocutaneous tissues.. Lesions are free of *Treponema* → Noninfectious.. High mortality.
  2. **Neurosyphilis** :meningovascular syphilis, degenerative CNS, brain or spinal cord damage.. is one of the most severe signs of this stage → Paralysis and Death
  3. **Cardiovascular syphilis**.. affects heart muscles → fatal aortic aneurysm.

## Non-sexually transmitted Treponema

1)Pinta-Yaws. both are contagious, non-venereal (non genital) infection caused by *T. pertenue, T. carateum* .

- Human infection occurs mainly in children less than 15 years.. Following direct skin to skin contact with infected person → causing depigmentation skin lesions in legs, finger, face, chest, abdomen.
- The disease occurs primarily in warm, humid, tropical subtropical areas of Africa, Asia, South America.

2)Bejel is non-venereal syphilis-like disease, called **endemic Syphilis** caused by *T. endemicum*.

- but it's a rare disease and not found in our countries.
- Transmission: Direct contact.. First soft oral & skin lesion in face, later may affect Nasopharynx and bones.. Diagnosis & Treatment similar to Syphilis.

## Lab Diagnosis

- It is very difficult to diagnose syphilis based on clinical symptoms without the presence of the first genital ulceration or skin rash.
- Symptoms and signs of the disease might be absent or be confused with those of other diseases.
- Direct Dark Field Microscopy can detect *Treponema* spiral forms and motility from fresh collected exudates-lesions
- *T. pallidum* can't be observed in Gram-stain, **Sliver-stain** can be used in biopsy.. No Culture in vitro
- Serology Screening Tests, Non-Specific tests:

**1-VDRL** , Venereal Disease Research Laboratory --> not enough because it only gives +ve or -ve result. (presence of the Ag)

**2-RPR** – Rapid Plasma Reagin(IgE) .{ more accurate and more specific}. Both used antigens include Cardiolipin + cholesterol+ Lecithin

- Both detect **anti-lipid IgG & IgM** in host Serum after infection 2-4 weeks .. After disappear the skin lesions

( Primary / Secondary Syphilis).



- Both tests become negative after antibiotic treatment and in Tertiary Syphilis. The test may give positive results with other diseases.. Collagen vascular disease, Acute febrile disease, Recent bacterial vaccination.

Even if there are clinical features present & positive screening test you have to confirm this by another tests, the specific confirmatory tests.

### Specific Confirmatory Tests:

- **Fluorescent Treponemal Antibody Absorption- FTA-Abs test** (Killed Treponema cells +Patients serum+ Labeled antihuman gamma globulin) .. Detects presence of **IgG & IgM** in Serum & CSF. Highly specific and sensitive for all stages. it often gives positive result if the infected patient is in the primary or secondary stage and might give positive in the tertiary stage but it is often used to confirm the primary and secondary stages. It might give negative result in an infected patient if the patient is treated with antimicrobial drugs.
- **T.pallidum Micro-hemagglutination Assay** detects **syphilis antigens**.. specific and sensitive..confirm most stages of infection . it often gives positive in all the syphilis stages, the primary, secondary and tertiary.
- All tests can't distinguish Syphilis from other non-sexually transmitted Treponema infections.. Yaws & Pinta, Bejel. They are skin infections not true Syphilis. They produce similar immunological reactions and might result in developing of granulomatous lesions on the skin.

### Treatment & Prevention:

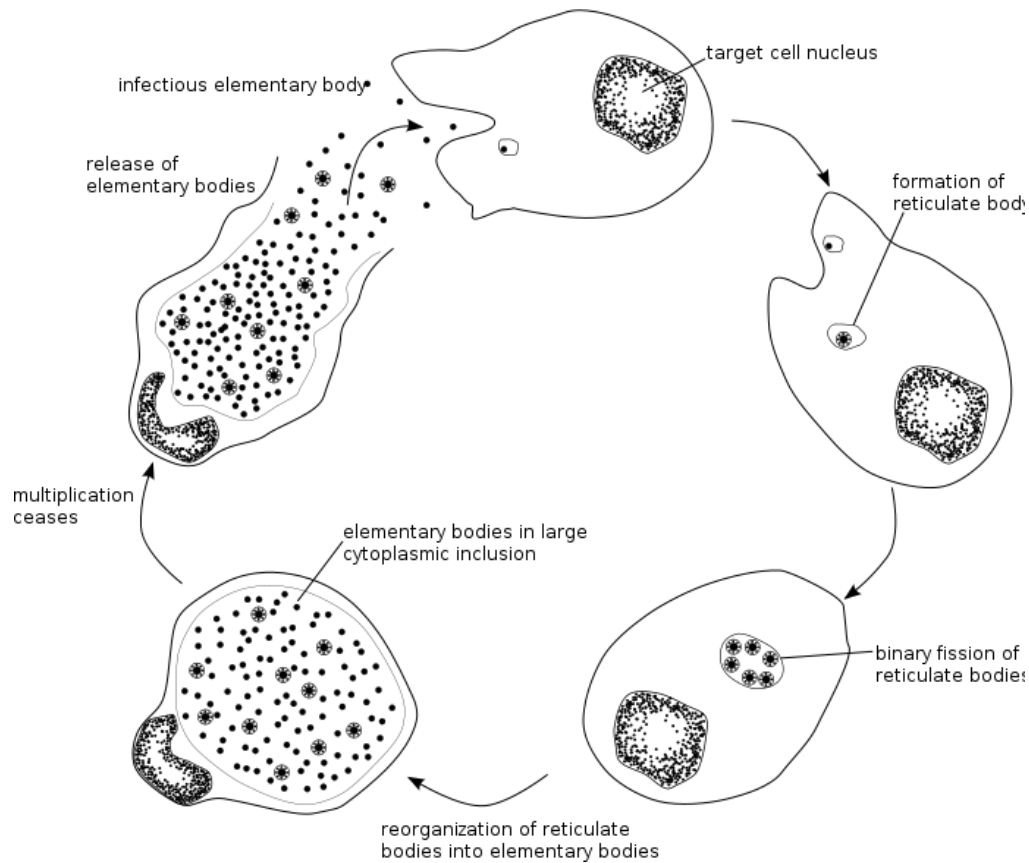
- Syphilis is easy to cure in its early stages.. Intravenous Penicillin is the best treatment for syphilis.
- Doxycycline can be given.. For Penicillin allergic persons.
- Always both partners should be treated
- Late syphilis, Can't be reversed.. Untreated syphilis in women can cause miscarriages.. premature births, stillbirths, or death.. No Vaccine is available

## Chlamydia trachomatis:

- **C. trachomatis** is one of the most widespread bacterial of STDs , About 50 Million of new cases each year worldwide (also common in Jordan)..Human natural host, Genital serotypes.  
Intracellular Growth.. Elementary bodies→Infectious stage.  
Reticulate bodies replicate in infected mucosal tissue as inclusion bodies.
- The life cycle of Chlamydia trachomatis consists of two stages: **elementary body** and **reticulate body**. The **elementary body** is the dispersal form. The dispersal form induces its own endocytosis upon exposure to target cells. It is this form that prevents phagolysosomal fusion, which then allows for intracellular survival of the bacteria. Once inside the endosome, the elementary body germinates into the **reticulate body** as a result of the glycogen that is produced. The reticulate body divides through binary fission. After division, the reticulate body transforms back to the elementary form and is released by the cell by exocytosis. One phagolysosome usually produces 100-1000 elementary bodies



- Chlamydial infection followed vaginal/anal sexual contact with an infected partner. Sexual Infection is more asymptomatic in women than men (80%)..Incub.1-3 weeks.
- In men**, most early symptoms are mild, few pus cells- dysuria, nonspecific urethritis. Non-treated infection may progress slowly over years to cause epididymitis, proctitis, proctitis (Inflammation of the rectum )& Infertility.
- In women** infection causes cervicitis, urethritis, Proctitis, endometritis, salpingitis.. pelvic inflammatory disease (PID).. Pelvic adhesion & Infertility.



- Newborn baby may be infected during delivery → develop eye infection.. inclusion conjunctivitis.. **Ophthalmia neonatorum**.
- Another route for acquiring this infection in infants : the oral cavity contaminated with amniotic fluid contains the chly.tra reaching after that to the lung ending with chlamydia trachomatis pneumonia this is rare and more common with other organisms>
- Symptoms of conjunctivitis, which include discharge and swollen eyelids, usually develop within the first 10 days of life.
- Complication:** Trachoma, Blindness.. Rarely cause Neonatal atypical pneumonia.
- Adult infection inclusion conjunctivitis is due to spread from genitalia to eye by contaminated fingers.

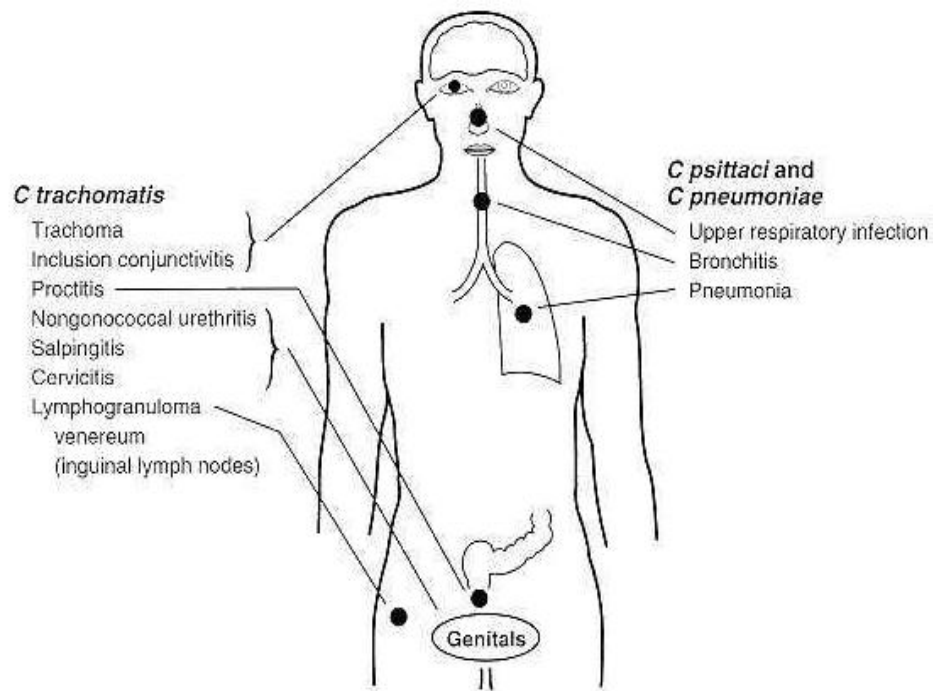
# Chlamydia Elementary- and Reticulate bodies



- Chlamydia symptoms-2

## Chlamydia diagnosis

- Detection Chlamydia Plasmid/DNA in urine/cervical swabs/ urethral swabs by PCR test.
- Elementary bodies of Chlamydia can be identified by direct smear prepared from discharge.. stain with monoclonal antibodies, detected by fluorescence microscopy by **Direct** immunofluorescent test .



- Chlamydia antigen test** is a rapid test that detect the Chlamydia antigen from female cervical swab, male urethral. **MaCoy cell tissue culture** used for isolation & antibiotic susceptibility
- Serological test is not significant for detection genital infection.
- Chlamydia trachomatis resembles Gram –ve bacilli but it can't be demonstrated using gram stain and it can't be cultured by artificial medium, we have to use special culture medium like . MaCoy cell tissue culture due to the fact this organism is INTRACELLULAR organism that means it can't replicate outside in the artificial medium as the other types of bacteria.
- NOW in last 10 years a new test has been relied on detection of specific plasmid within the cytoplasm of the chlamydia ,this plasmid only found in Chlamydia so they prepare primers to detect this plasmid and this plasmid is detected as DNA by using PCR this test is proved to be very accurate ,very specific and now the most common test used to detect Chlamydia infection.

## Chlamydia (DDx,Tx)

- Chlamydia is easily confused with gonorrhoea in women because the symptoms of both diseases are similar and both diseases may occur together.
- Lymphogranuloma venereum**, *C. trachomatis*.. serotypes L1-L3.. Common in tropical countries..Infection starts as genital ulcer with Lymphadenopathy.. spread to genitourinary and gastrointestinal tract.. causing inflammation & strictures in genital tract.
- Treatment: Doxycycline.. Erythromycin
- No vaccine**

## Other genital Infections

NOW other 3 types of organisms which might associated with ST infections despite the fact these organisms might be part of UGT flora ,it might be preset without signs & SYMPTOMS & Only under certain condition- still some of these conditions unknown – it might develop genital tract infection often in association with non specific urethritis ,nearly these **Mycoplasma genitalium/ M. hominis, Ureaplasma urealyticum** all of these 3 types may cause the same specific symptoms or 2 ,3 together contribute on the same symptoms ,infection by 2 out of these organism would be more extensive than the infection by 1

- ***Mycoplasma genitalium/ M. hominis, Ureaplasma urealyticum***: These can be present without any symptoms in about 20% genital tract males/females.. Single or more organisms may cause up to 25% of cases of **non-specific urethritis** ..mostly *M. genitalium* in men.. Mild discharge few pus cells, burning and pain during urinating.
- **In women**, cases of mucopurulent cervicitis & PID can be associated with *M. hominis/ M. genitalium*

**Vaginitis** → inflammation of vagina result in discharge, itching, burning, pain due to change in the normal balance of vaginal bacteria → **reduced lactobacilli or estrogen levels after menopause**.. Also associated with **Candida spp.** or mixed infection.

- **Bacterial vaginosis (BV)**: Mixed bacteria is the most common cause of vaginitis.
- ***Gardnerella vaginalis***: Part of vaginal flora.. may cause vaginosis in association with anaerobic or other bacteria .

*Gardnerella vaginalis* which is part of vaginal flora in addition to lactobacilli, again this organism under certain condition especially following administration of antibiotics or steroids drugs, the flora might within the vagina changes due to changes in the PH and might increases in numbers especially *Gardenella* increases with alkaline medium than neutral or acidic medium. Bacterial vaginosis associated with the infection and gives the impression of the patient is infected with STD but it's in fact due to activation of **endoflora** of vagina and often it can be treated with drugs that used to treat anaerobic infection like metronedazole or chlindamycin. So it not recognized as STDs but it gives the impression of that

- **Diagnosis**: Direct Gram-stain..presence of numerous "**clue cells**" (cells from the vaginal lining.. coated with numerous gram-variable bacteria, pus cells & fishy odor.. Culture urine / cervical swabs
- **Vaginitis treatment of Mycoplasma** : Doxycycline.. Erythromycin
- **Vaginosis treatment**: metronidazole or clindamycin

## YEAST INFECTION

- Vaginal yeast infection, or **vulvovaginal candidiasis**, is a common cause of vaginal irritation, discharge
- This common fungal infection occurs when there is an increase in presence of one or more ***Candida albicans* or others *C. glabrata, C. tropicalis, C. krusei***
- Although this infection is not considered an **STI**, 10 to 15 percent of men/women develop symptoms after sexual contact with an infected partner.

- *Candida spp.* are always present in the vagina in small numbers, Several factors are associated with increased yeast infection in women, including: Pregnancy, using oral contraceptives , using steroid drugs/ antibiotics, having uncontrolled diabetes mellitus.
- Wearing tight, poorly ventilated clothing and synthetic underwear may contribute to vaginitis.
- The most frequent symptoms of yeast infection in women are itching, burning, and irritation of the vagina. Painful urination are common.
- Vaginal discharge is not always present and may be a small amount. The thick, **whitish-gray discharge is typical.** it can vary from watery to thick discharge.
- Re- occurrence of vaginal candidiasis is very common.
- In males candidiasis is very rare and if it presents this means there is obstruction in the genital tract & maybe in immunocompromised patient but in females is very common it can be occur each month, 2-3 months .
- The only way to prevent the devolvement of vaginal candidiasis is to restore the vaginal flora by less use of wide spectrum antimicrobial drugs & other drugs which might enhance the growth of Candida.
- Rarely for Candida or for other STD's causative agent **except for Chlamydia** to reach blood stream unless there is obstructions also rarely to reach the upper urinary tract, kidneys producing complications.

## Diagnosis & Treatment

- Microscopic examination of discharge/urine

Presence of numerous yeast cells.. **Pseudohyphae.**

- Culture on **Sabouraud Dextrose Agar**, **ChromCandida Agar**, Serum Germ Tube test.
- Various antifungal vaginal drugs are available to treat yeast infections.
- Antifungal creams can be applied directly to the area.. oral or vaginal cream of fluoconazole, miconazole, clotrimazole.

## ▪ **Candida albicans Pseudohyphae**

Done by:  
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