

# Microbiology

— Lecture no. —

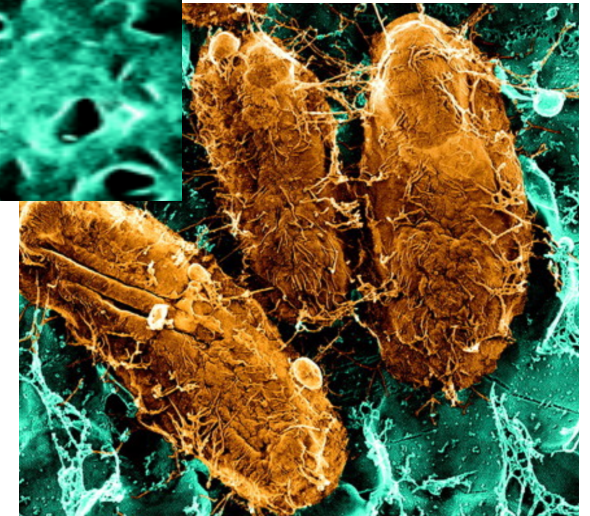
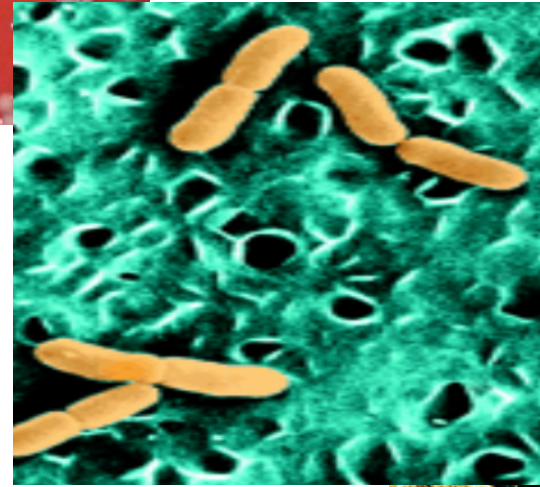
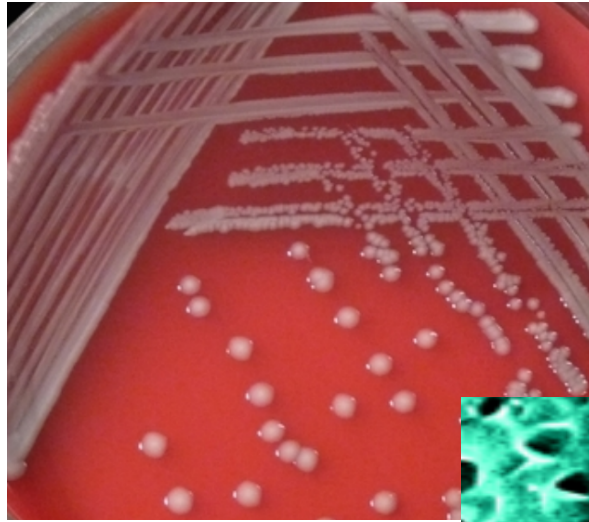
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# Microbiology of Urogenital system

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Sexually transmitted diseases

Genital infections encompasses a variety of clinical entities, including :

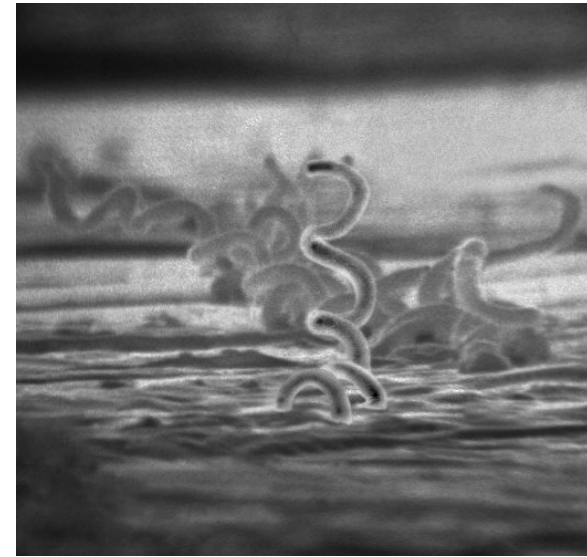
- **Bacterial vaginosis**
- **Chancroid**
- **Gonorrhoea**
- **Chlamydia**
- **Syphilis**
- ***Mycoplasma genitalium***
  
- **Trichomoniasis**
  
- **Vulvovaginal candidiasis**
  
- **Genital warts**
- **Human immunodeficiency virus.**
- **Genital herpes**

## SEXUALLY TRANSMITTED AND SEXUALLY TRANSMISSIBLE MICROORGANISMS

BACTERIA	VIRUSES	OTHER <sup>a</sup>
Transmitted in Adults Predominantly by Sexual Intercourse		
Neisseria gonorrhoeae	HIV (types 1 and 2)	Trichomonas vaginalis
Chlamydia trachomatis	Human T cell lymphotropic virus type 1	Pthirus pubis
Treponema pallidum	Herpes simplex virus type 2	
Haemophilus ducreyi	Human papillomavirus (multiple genital genotypes)	
Klebsiella (Calymmatobacterium) granulomatis	Hepatitis B virus <sup>b</sup>	
Ureaplasma urealyticum	Molluscum contagiosum virus	
Mycoplasma genitalium		

Syphilis / etiology (this lecture's diseases are more serious however, they're less common)

- Spirochetes are **thin**, helical **gram-negative** bacteria (has outer and inner membrane). The most important (common) treponemal species that causes human disease is *Treponema pallidum*, the causative agent for Syphilis (helix made due to the presence of active filaments between 2 membranes)
- *T. pallidum* has not been cultured regularly in vitro because they are dependent on host cells for many metabolites (e.g. purines, pyrimidines, amino acids). Moreover, they're extremely sensitive to oxygen (microaerophilic or anaerobic), these 2 factors make it extremely fastidious to the point that it can't be cultured.



dark field (can't be seen with LM)



Immunofluorescence

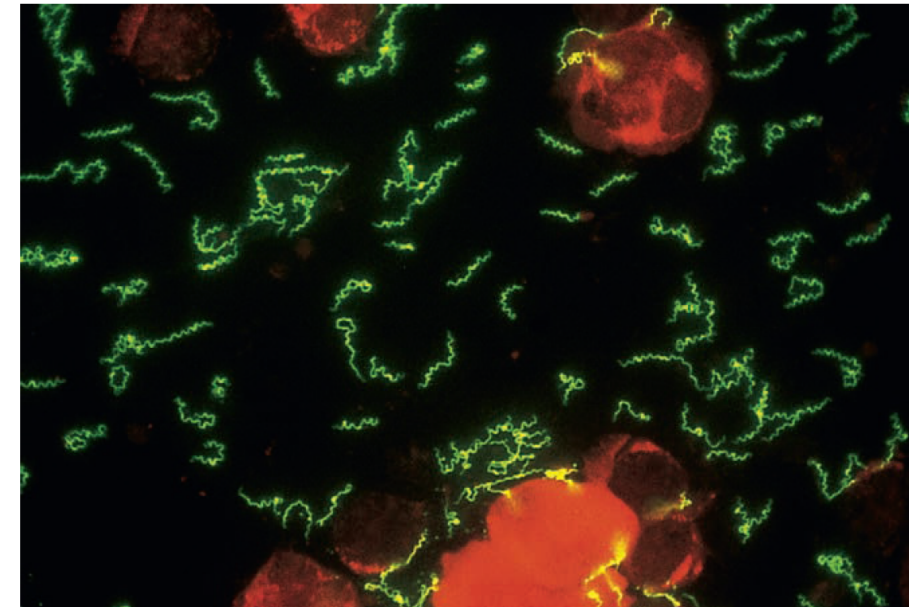


FIGURE 32-3 *Treponema pallidum* in the direct fluorescent antibody test for *T. pallidum*. (From Morse SA, Ballard RC, Holmes KK,

## Syphilis / epidemiology

- Between 2000 and 2012, the incidence of newly acquired disease has **increased** each year.
- Patients infected with syphilis are at **increased risk for transmitting and acquiring HIV** when genital lesions are present
- Syphilis **cannot be spread through contact with inanimate objects (fomites)** such as toilet seats (since the bacteria is very labile to drying and disinfectants) . The most common route of spread is by **direct sexual contact**.
- Other routes include **congenitally** (from an infected mother) or by **transfusion** with contaminated blood.



The face of a newborn infant displaying snuffles indicative of congenital syphilis



Portrait of Gerard de Lairesse by Rembrandt van Rijn, circa 1665–67, oil on canvas - De Lairesse, himself a painter and art theorist, had congenital syphilis that deformed his face and eventually blinded him.<sup>[54]</sup>



Secondary stage rash on the palms of the hands.

## Syphilis / signs and symptoms

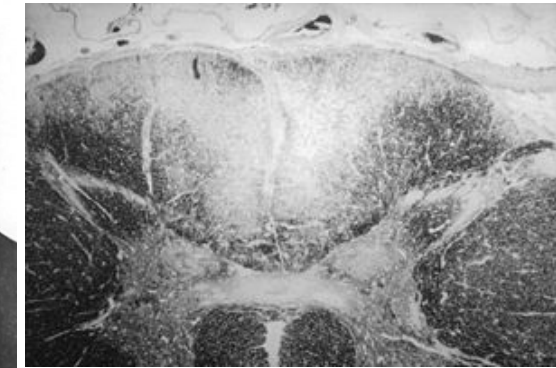
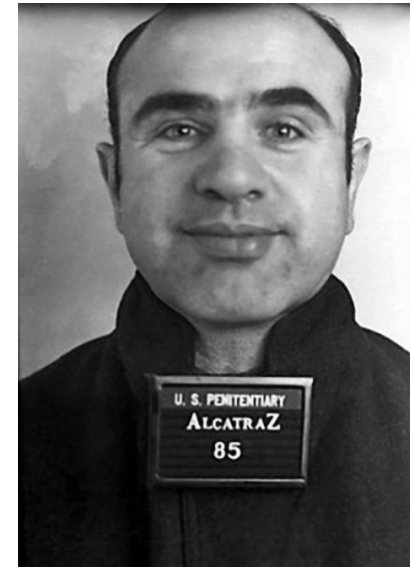
- The clinical course of syphilis evolves through three phases. If the patient is not treated, syphilis cause **systemic devastating damage**.
- Most investigators believe that the tissue destruction and lesions observed in syphilis are primarily the consequence of the patient's immune response to infection.



**primary phase** is characterized by skin lesions (**chancres**) at the site where the spirochete penetrated  
(Usually on the penis and vagina)



In the **secondary phase**, the clinical signs of disseminated disease appear, (e.g. **skin lesions** over the entire body, fever, headache).  
(Damage to small blood vessels under the skin) Symptoms resolve within weeks.



<https://www.youtube.com/watch?v=MxV-ljxcSxQ>

- Late syphilis severely damages organs involved (e.g., **CNS**, **neurosyphilis**, tabis dorsalis, cardiovascular syphilis) leading to various symptoms (e.g. **dementia** or **blindness** , can cause chronic meningitis )

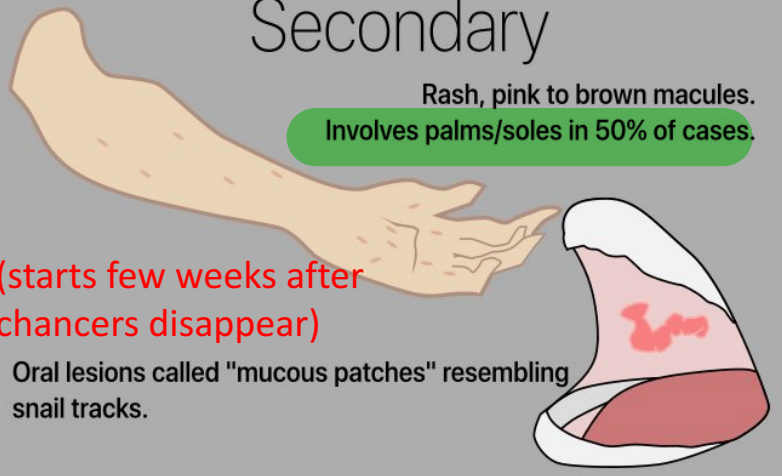
# The Stages of Syphilis

## Primary



The chancre lesion is the hallmark of primary syphilis. It may appear 10-90 days after exposure. Common sites include penis and labia. Other sites include anus, oral mucosa. Without treatment, chancre disappears in 2-8 weeks.

## Secondary



Rash, pink to brown macules. Involves palms/soles in 50% of cases.

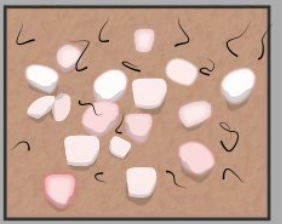
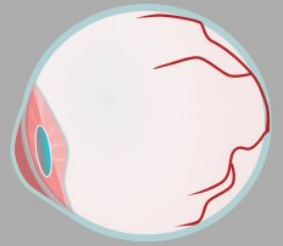
(starts few weeks after chancres disappear)

Oral lesions called "mucous patches" resembling snail tracks.



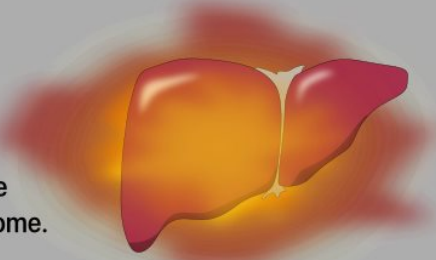
Ocular syphilis manifestations including anterior or posterior uveitis.

Symptomatic early neurosyphilis, cranial nerve deficits and/or aseptic meningitis presentation.



Genito-inguinal rashes, including tinea-mimicker or heaped-up wart-like lesions called condyloma lata.

Less common internal organ manifestations including acute hepatitis and nephrotic syndrome.



## Latent

Latent syphilis refers to asymptomatic infection after the period of primary and secondary syphilis (noticed or unnoticed) has passed.

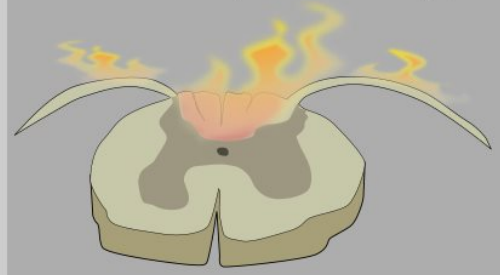
### Early Latent

Early latent refers to asymptomatic patients with positive testing, in whom history can confirm exposure to or symptoms of primary or secondary syphilis within the last year. This is group may receive single-dose penicillin like primary or secondary.

### Late Latent

Late latent patients have positive serology but do not meet criteria for early. Thus, multiple doses of penicillin.

## Late (Tertiary)



Late Neurosyphilis, including tabes dorsalis, gait impairments, and dementia. Tabes dorsalis damages the dorsal columns and sensory nerve roots, causing a syndrome of pain and sensory deficits similar to those of B12 deficiency.

Gumma are ulcerating granulomas on skin, bone, and internal organs. (Unique ulcer)



Cardiovascular effects of late syphilis include aortic aneurysm and coronary arteritis.

## Syphilis / diagnosis and treatment

- **Darkfield microscopy, immuno-fluorescent stains, or PCR** can be used on immediate samples (from a chancre) for visualization and diagnosis.
- Serology is the most important tool; (when the patient isn't in the first stage "no chancre" we use serology "the pathogen is within the blood" ).

**non- treponemal/ cardiolipin tests**, e.g. venereal disease research laboratory (VDRL)/ Rapid plasma regain test (RPR). A quantitative test should be done to **screen**, stage the disease and monitor treatment. (these tests look for antibodies "**IgA,IgM,IgG**" against the antigens that are produced when treponema damages cells and destroy them "**not antigens against the pathogen**" , those antigens maybe present with other disease like: (SLE, Anti phospholipid syndrome, etc) so the tests are not specific, used mainly for screening. If they are positive we do the next test).

**specific treponemal tests** *Treponema pallidum* particle agglutination (**TP-PA**) test can be used for **diagnosis**



- Syphilis be controlled only through the practice of **safe-sex** techniques and adequate **treatment with antibiotics** (UDRL, RPR are also used to stage and monitor treatment decrease pathogen, decrease damage to cell, decrease t antigen's, decrease antibodies (the titer decrease 4 times)
- **Penicillin is the drug of choice.** (Benzathine benzylpenicillin / Penicillin G) , treated with a **single dose of Penicillin.**
- <https://escholarship.org/uc/item/5gs4q6wz>



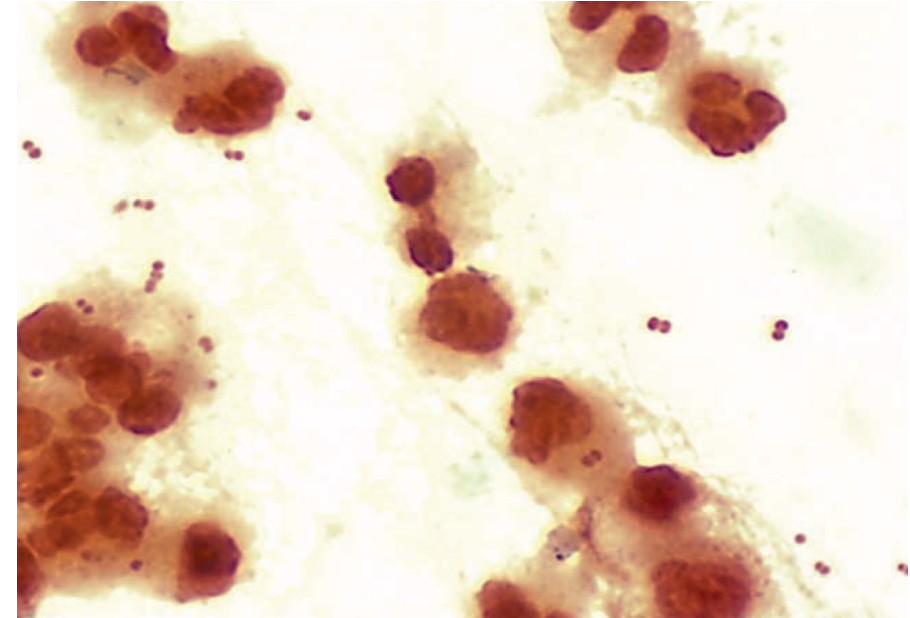
**In this case a woman came with this Gamma (tertiary's syphillis )**



**After treatment**

## Gonorrhoea / etiology

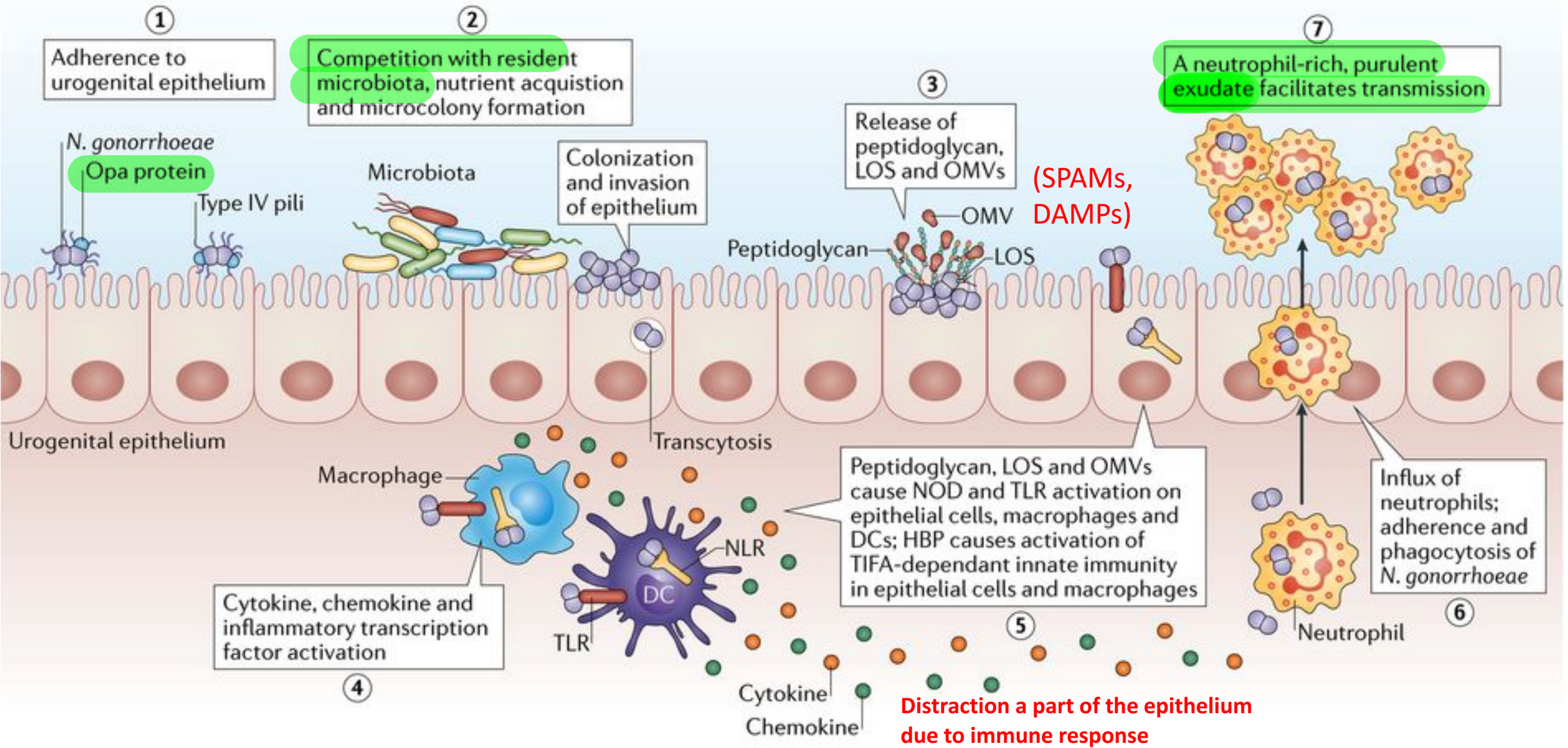
- A **purulent infection** of mucous membranes (e.g. urethra, rectum, cervix, conjunctiva, pharynx) caused by *N. gonorrhoeae*, **has the ability to attach to epithelial membranes.**
- *Neisseria* species are aerobic **gram-negative** bacteria, typically coccoid shaped arranged in pairs (**diplococci**)
- The presence of *N. gonorrhoeae* in a clinical specimen **is always considered significant.** In contrast, strains of *N. meningitidis* can **colonize the nasopharynx of healthy people** without producing disease.
- *N. gonorrhoeae* is *fastidious* and only grows on enriched **chocolate agar** and other supplemented media.



It is the second commonest STI in the UK, affecting predominantly young people (peaking in males aged 20– 24 years and females aged 16– 19 years). The recent increase in incidence and **growing prevalence of antimicrobial resistance** have made it a major public health concern

**Note: Syphilis and Trichomoniasis** have a little anti microbial resistance, while its more common in **Gonorrhoea and Chlamydia**.

# Gonorrhoea / pathophysiology



Distraction a part of the epithelium due to immune response

## Gonorrhoea / signs and symptoms

- Genital infection in men is primarily restricted to the **urethra**. A purulent urethral discharge and dysuria develop after a 2- to 5-day incubation period. **Virtually all infected men have acute symptoms.**
- As many as half of all infected women have mild or **asymptomatic** infections.
- Retrograde spread may occur, causing **salpingitis/ endometritis, PID**, and **tubo-ovarian abscesses** in up to 20% of women with cervicitis.

### *Neisseria gonorrhoeae*

**Gonorrhea:** characterized by purulent discharge for involved site (e.g., urethra, cervix, epididymis, prostate, rectum) after 2- to 5-day incubation period

**Disseminated infections:** spread of infection from genitourinary tract through blood to skin or joints; characterized by pustular rash with erythematous base and suppurative arthritis in involved joints

**Ophthalmia neonatorum:** purulent ocular infection acquired by neonate at birth

### **S.Aureus is the main cause of septic arthritis**



MALE



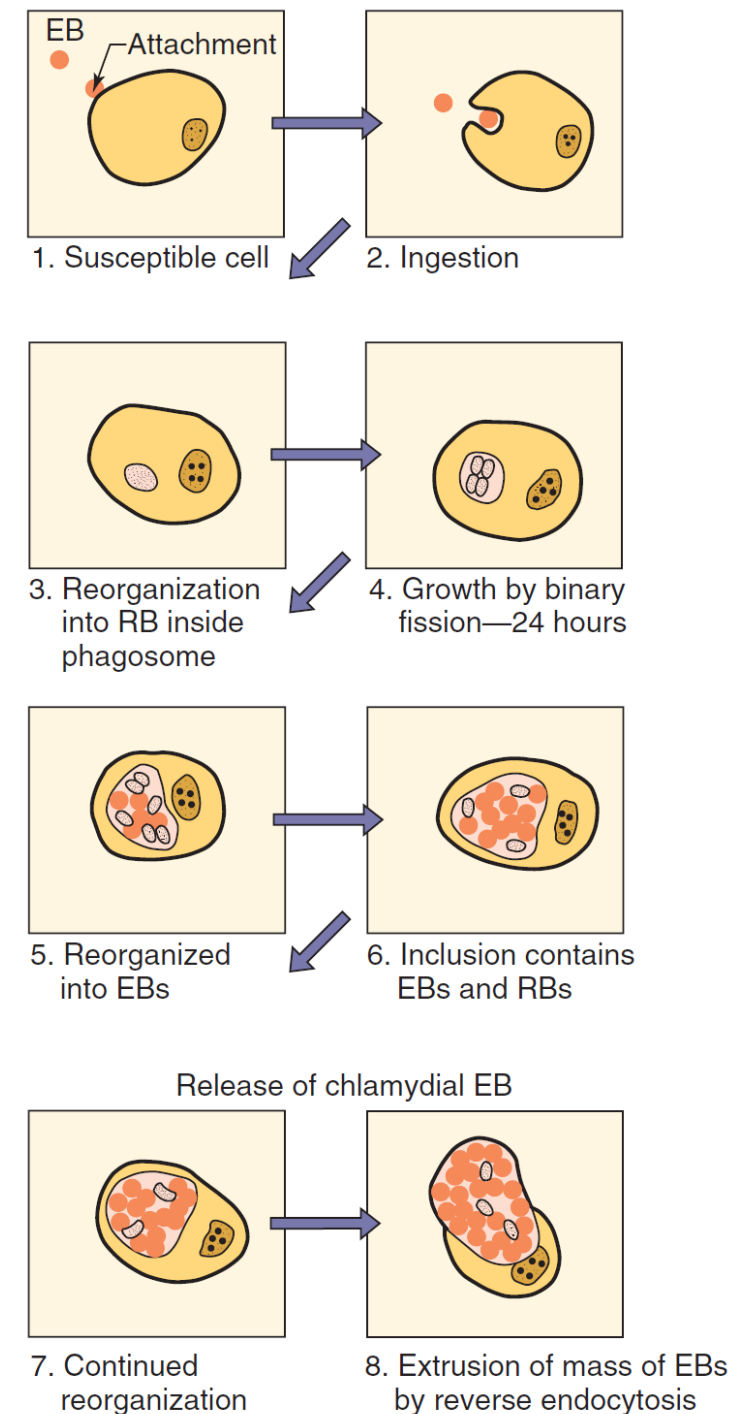
FEMALE

- Samples include **Exudates** (by a swab into urethra), **urine, cervical or throat swabs**
- **Microscopy**— provides rapid, near- patient diagnosis in symptomatic patients and shows **Gram- negative diplococci** within polymorphonuclear cells.
- **Culture**— all infected areas should be swabbed and plated onto selective media, both to confirm diagnosis and to provide antibiotic susceptibility data, **chocolate agar**.
- **Nucleic acid amplification tests** (NAATs)— these have become the screening test of choice for asymptomatic individuals with urethral and endocervical infection, and for rectal and pharyngeal infection in MSMs.
- Treatment should include **patient and sexual partner/s**.
- First- line therapy is **ceftriaxone** 500mg IM single dose plus **azithromycin** 1g PO single dose, **unless the bacteria is resistant**

## Chlamydia / etiology

- A common STD caused by *Chlamydia trachomatis*. An **obligate intracellular parasites**, 0.3 microm in diameter, with a unique life cycle.
- Infects epithelial cells, which are found on the mucous membranes of **the urethra, endocervix, endometrium, fallopian tubes, anorectum, respiratory tract, and conjunctivae.....** makes spreading even more.
- Metabolically inactive **infectious forms (elementary bodies [EBs])**, makes spreading Easy and metabolically active **noninfectious forms (reticulate bodies [RBs])**.

After replication it escape from the cells in the form of elementary body and infect other cells again.



- Chlamydia infections are the **most common bacterial sexually transmitted diseases** in humans and are **the leading cause of infectious blindness** worldwide
- Other than **sexual transmission**, **eye-to-eye transmission** of trachoma is by **droplet, hands, contaminated clothing**, and flies (**in endemic regions**) that transmit ocular discharges from the eyes of infected children to the eyes of uninfected children.
- **Trachoma** is the **leading cause of preventable blindness**. Infections occur predominantly in children, who are the chief reservoir of *C. trachomatis* in endemic areas.



## Chlamydia / signs and symptoms

- Most genital tract infections in **women** are **asymptomatic** (as many as 80%) while most in **men** are **symptomatic**, as many as 25% of the infections will be inapparent.
- infection may **persist** for many years if untreated, infection can spread to the upper genital tract in women causing **pelvic inflammatory disease** which may result in future infertility or ectopic pregnancy (**if not treated**)
- It can cause **cervicitis** in women and **urethritis** and **proctitis** in both men and women.
- Other presentations— **Lymphogranuloma venereum** LGV (the cause of 10% of genital ulcers in tropical countries)



Inflammation of the cervix in a female from chlamydia infection characterized by mucopurulent cervical discharge, redness, and inflammation.

### *Chlamydia trachomatis*

**Trachoma:** chronic inflammatory granulomatous process of eye surface, leading to corneal ulceration, scarring, pannus formation, and blindness

**Adult inclusion conjunctivitis:** acute process with mucopurulent discharge, dermatitis, corneal infiltrates, and corneal vascularization in chronic disease

**Neonatal conjunctivitis:** acute process characterized by a mucopurulent discharge

**Infant pneumonia:** after a 2- to 3-week incubation period, the infant develops rhinitis, followed by bronchitis with a characteristic dry cough

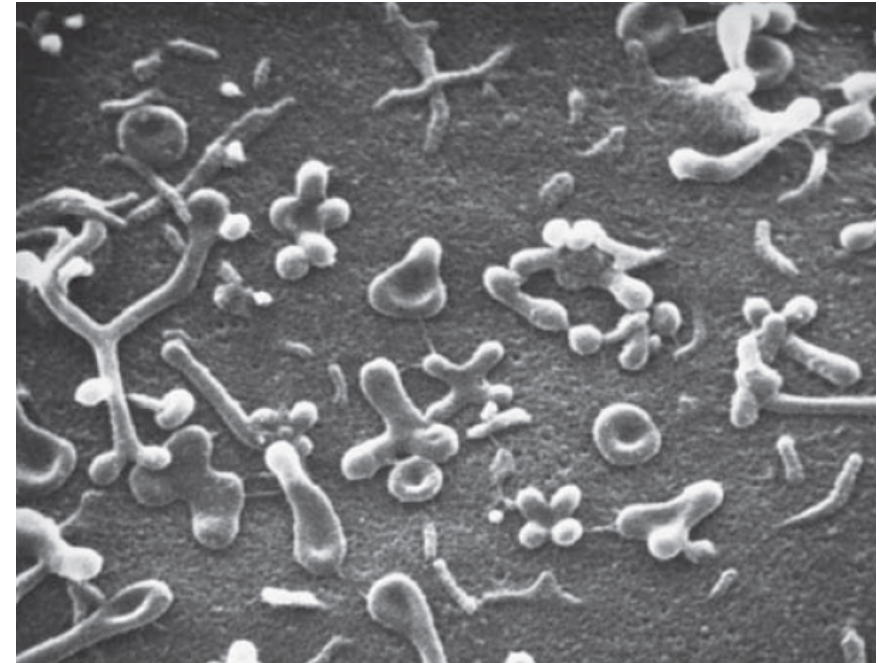
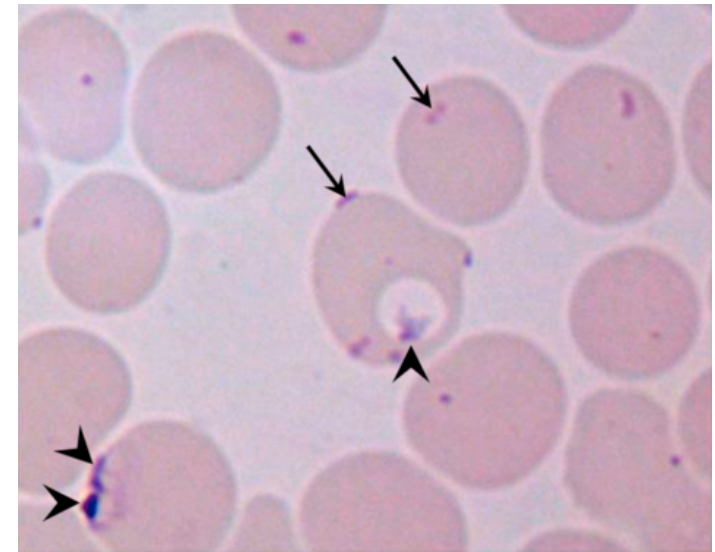
**Urogenital infections:** acute process involving the genitourinary tract with characteristic mucopurulent discharge; asymptomatic infections common in women

**Lymphogranuloma venereum:** a painless ulcer develops at the site of infection that spontaneously heals, followed by inflammation and swelling of lymph nodes draining the area, then progression to systemic symptoms

- Samples include **Exudates** (by a swab into urethra), **first catch urine, cervical or throat swabs**
- **Culture**— not routinely recommended, with low sensitivity and expensive.
- **Nucleic acid amplification tests (NAATs)**— these have become the diagnostic test of choice, as they are highly sensitive (90– 95%).
- Treatment should include **patient and sexual partner/s**.
- The drug of choice for reasons of compliance is **doxycycline** 100mg bd PO for 7 days or **azithromycin** 1g single dose

Nongonococcal urethritis caused by Mycoplasma

- ***Mycoplasma*** and ***Ureaplasma*** organisms are the **smallest free-living bacteria**. They are unique among bacteria because they **do not have a cell wall** and their cell membrane contains **sterols**.
- ***M. genitalium*** and ***Ureaplasma urealyticum*** can cause **nongonococcal urethritis (NGU)** and **pelvic inflammatory disease**.



## Nongonococcal urethritis caused by Mycoplasma

- The most sensitive diagnostic tests are **PCR amplification** tests of species-specific gene targets.
- Absence of the cell wall renders the mycoplasmas resistant antibiotics that interfere with synthesis of the cell wall (e.g. Penicellins).
- Rising incidence and emerging antimicrobial resistance are a major concern these days.
- The poor clinical outcomes with **doxycycline** therapy led to the use of **azithromycin** as the primary drug of choice

**As you know, penicillin doesn't work here because Mycoplasma lack cell wall !!!**

Organism	Site	Human Disease
<i>Mycoplasma genitalium</i>	Genitourinary tract	Nongonococcal urethritis, pelvic inflammatory disease
<i>Ureaplasma urealyticum</i>	Respiratory tract, genitourinary tract	Nongonococcal urethritis, pyelonephritis, spontaneous abortion, premature birth

## Urethritis in adult males

- Urethritis, or inflammation of the urethra, is a common manifestation of sexually transmitted infections among males. Infectious urethritis is typically caused by a sexually transmitted pathogen; thus, most cases are seen in young, sexually active men.
- **Neisseria gonorrhoeae** and **Chlamydia trachomatis** are commonly identified in cases of urethritis. **Mycoplasma genitalium** has also been strongly associated with urethritis.
- In a study of 768 males screened for STIs at 11 different clinic settings in the United States in 2012, the prevalence of *N. gonorrhoeae* ranged from 21.6 percent among symptomatic to 1.4 percent among asymptomatic males
- **Coinfections with other sexually transmitted pathogens are common.** In a study of more than 3800 heterosexual males and females attending an STI clinic, chlamydial coinfection was demonstrated in 20 percent of males and 42 percent of females with gonorrhea

## Urethritis in adult males

- **Dysuria**, or discomfort with urination, is usually the chief complaint in males with urethritis and is reported in the majority of males with gonorrhea and over half of patients with nongonococcal urethritis (NGU).
- Other complaints include **pruritus, burning, and discharge at the urethral meatus**. Urethral discharge can range from mucoid or watery to frankly purulent. However, **not all males with laboratory evidence of urethritis have symptoms**. Five to 10 percent of cases of laboratory-documented gonococcal urethritis and up to **42 percent of males with NGU are asymptomatic**.
- Urethritis can occur in conjunction with other infectious processes of the lower urogenital tract, including **epididymitis** or **prostatitis**. Males with urethritis should be questioned about and evaluated for the presence of fever, testicular pain and swelling, obstructive urinary symptoms (dribbling or hesitancy), perineal or pelvic pain, which may suggest involvement of the epididymis or prostate. **(may lead to infertility , Reversible if treated)**

A 26-year-old male patient came to the dermatology clinic of Tanta University hospital complaining from severe burning sensation during urination and dysuria for 4 days. Additionally, he was suffering from penile discharge and testicular tenderness. He had a history of multiple heterosexual relationships with a last contact 8 days ago. On physical examination, vital signs showed: blood pressure 110/79, pulse 75, and temperature 37.6°C. There was mucopurulent cloudy discharge from urethra. Swollen testicles were also observed. When the patient asked about any other symptoms, he mentioned feeling fatigue with pain in the knee joints and ankles 2 weeks ago but he did not receive any medical remedy until the appearance of severe irritation, redness in the eye, as well as edema in the eyelid with the presence of copious discharge (conjunctivitis). These symptoms seem to be unrelated to a degree that may obscure the diagnosis.

Following counseling, urethral and ocular swabs, and blood sample were aseptically obtained and streaked immediately on Thayer Martin and chocolate agar plates then incubated overnight at 37°C in the presence of 5% CO<sub>2</sub>. Following the incubation period, Grayish white, transparent to opaque, slightly raised colonies with 1–2 mm diameter were observed. After Gram-staining, **pink to red diplococci** with coffee bean-shaped cells opposing each other on the concave sides. This result was sufficient for the presumptive identification of *N. gonorrhoeae*. Furthermore, numerous polymorphonuclear cells with intracellular diplococci, were

The results of susceptibility testing were interpreted according to CLSI. It revealed multiple drug resistance to ampicillin, ampicillin/clavulanic acid, cephradine, cefotaxime, cefepime, cefuroxime, ceftriaxone, ciprofloxacin, chloramphenicol, sulfamethoxazole, trimethoprim, tetracycline, doxycycline, and spectinomycin. Only gentamicin, rifampicin, and azithromycin were active against the test pathogen





## History

- 17-year-old white female
- College student
- Seeking advice about contraception
- Shy talking about her sexual practices
- Has never had a pelvic exam
- Has had two sex partners in past six months
- Does not use condoms or any other contraceptives
- Her periods have been regular, but she has recently noted some spotting between periods. Last menstrual period was 4 weeks ago.
- Denies vaginal discharge, dyspareunia, genital lesions, or sores

## Physical examination

- Vital signs: blood pressure 118/68, pulse 74, respiration 18, temperature 37.1° C
- Breast, thyroid and abdominal exam within normal limits
- The genital exam reveals normal vulva and vagina
- The cervix appears inflamed, bleeds easily with swab insertion for diagnostic testing, and there is a purulent discharge coming from the cervical os.
- The bimanual exam is normal without cervical motion pain, uterine or adnexal tenderness.

3. Which laboratory tests should be ordered or performed?

- Pregnancy test
- Test for *Chlamydia trachomatis*
- Test for *Neisseria gonorrhoeae*
- Syphilis screen with RPR or VDRL
- Saline wet mount, pH and KOH preparation of vaginal secretions
- Counseling and testing for HIV

## Laboratory Test Results for Suzy Jones

- NAAT for *Chlamydia trachomatis*: positive
- NAAT for *Neisseria gonorrhoeae*: negative RPR: non-reactive
- Wet mount: pH 4.2, no clue cells or trichomonads but numerous white blood cells (WBCs)
- KOH preparation: negative for "whiff test"
- HIV antibody test: negative
- Pregnancy test: negative

A 39-year-old man presented to the emergency department reporting several weeks of generalized weakness, headache, nausea, and migratory arthralgia. The patient had exclusively had sex with men, had participated in condomless anal insertive and receptive intercourse, and had been in a monogamous relationship during the past 6 months.

Physical examination revealed a painful ulcerated plaque on the upper lip, a macular rash with three crater-like scarred painless lesions (considered to be healing chancres) on the glans, a nonpruritic hyperkeratotic maculopapular palmar rash and bilateral submandibular lymphadenopathy. No alopecia, gummas, neurologic deficits or ocular or cardiovascular abnormalities were noted.

Ulcerated plaque on the upper lip. Results of laboratory testing included a positive reactive syphilis immunoglobulin G (IgG) enzyme immunoassay and a positive rapid plasma reagin (RPR) test (titer 1:256). Human immunodeficiency virus (HIV) testing was negative, and serologic testing demonstrated prior immunization to hepatitis B virus. Given the clinical presentation and laboratory findings, secondary syphilis was considered the most probable diagnosis.

The patient was treated with benzathine penicillin G 2.4 million units intramuscularly.





## Clinical Case 23-1 Gonococcal Arthritis

Gonococcal arthritis is a common presentation of disseminated *Neisseria gonorrhoeae* infection. Fam and associates (*Can Med Assoc J* 108:319–325, 1973) described six patients with this disease, including the following patient, who has a typical presentation. A 17-year-old girl was admitted to the hospital with a 4-day history of fever, chills, malaise, sore throat, skin rash, and polyarthralgia. She reported being sexually active and having a 5-week history of a profuse yellowish vaginal discharge that was untreated. Upon presentation, she had erythematous maculopapular skin lesions over her forearm, thigh, and ankle, and her metacarpophalangeal joint, wrist, knee, ankle, and midtarsal joints were acutely inflamed. She had an elevated leukocyte count and sedimentation rate. Cultures of her cervix were positive for *N. gonorrhoeae*, but blood specimens, exudates for the skin lesions, and synovial fluid were all sterile. The diagnosis of disseminated gonorrhea with polyarthrititis was made, and she was successfully treated with penicillin G for 2 weeks. This case illustrates the limitations of culture in disseminated infections and the value of a careful history.

A patient has been diagnosed with primary syphilis (Stage I). When assessing the patient, which of these findings will the healthcare provider anticipate?

Choose 1 answer:

- 
- (A) Reddish rash on the palms of the hands
- 
- (B) Firm and painless genital ulcers
- 
- (C) Sore throat and swollen lymph glands
- 
- (D) Muscle weakness and visual changes
-

## Further reading:

- Oxford handbook of infectious diseases and microbiology-  
Part4: Clinical syndroms  
Chapter 18: Sexually transmitted infections
- Harrison's Infectious Diseases 3rd Edition  
SECTION III Infections in organ systems  
Chapter 35