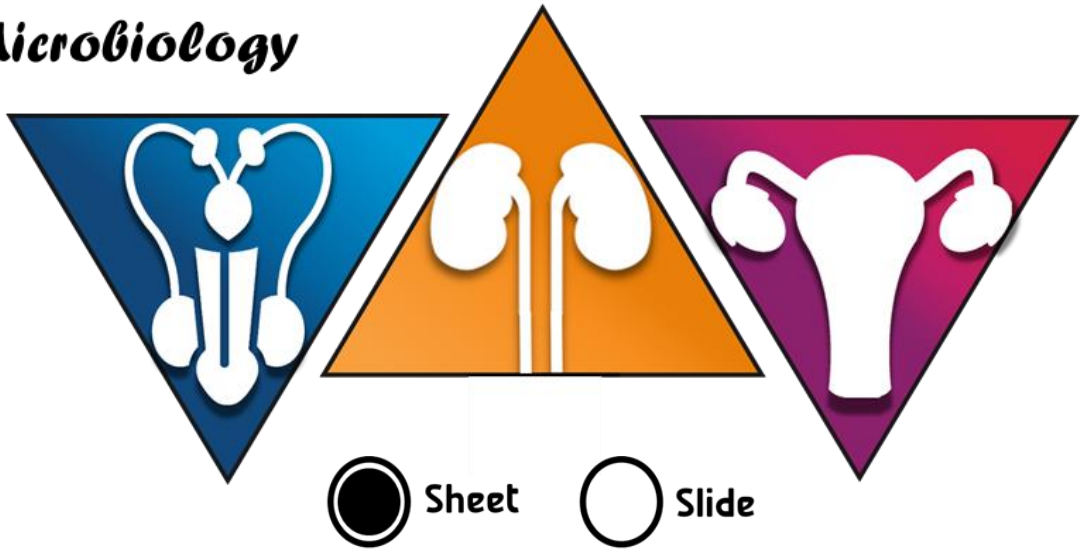
Urogenital system

Microbiology



Number: - 4

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Since the Professor usually gets questions from what he mentions in his lectures, this sheet solely contains what the professor has mentioned. **You must refer to the slides.**

*The professor started with a quick **revision** from the last lecture:*

- We mentioned in the previous lecture the epidemiology of STIs and how wide spread they are.
- We also mentioned how in the past 10 years or so there has been an increase in most STIs. This increase might be because of the relaxed sexual behaviour among individuals as a result of knowing that STDS are curable by antibiotics so they become less careful.
- He also repeated that there is a gender and a regional variation concerning STIs and that the spread of STIs among the Arab region is relatively low.
- We talked about the risk factors, signs and symptoms we expect to see in patients with urogenital infections or STDs.
- He also mentioned that there is an overlap in the signs and symptoms therefore the diagnosis is not always simple.

Bacterial vaginosis (BV)

- Linked to abnormal flora
- Discharge
- Maybe itching
- Clue cells when it's examined by microscope.
- Treated with metronidazole
- Some will revert to normal flora while others will experience recurrences

Trichomoniasis

- Caused by a protozoa
- One of the common non-bacterial STDs
- Discharge
- May be itchy and smelly
- Dyspareunia
- Dysuria
- Under the microscope we see the protozoa swimming around

Syphilis

- Caused by Treponema pallidum

- Can be **congenital** however the most common route of spread is by **direct sexual contact.**

  Stages:
  1. Primary -----> chancres
  2. Secondary -----> More systemic involvement. T. Pallidum reaches the blood. Skin lesions(maculopapular rash)
  3. Late (Tertiary) ------> Affects CNS and the heart
     (Going from primary to tertiary the infection becomes more systemic)
- Diagnosis using dark-field microscopy , or through Non Treponema screening tests like venereal disease research laboratory (VDRL) or Rapid plasma regain test (RPR). Or through specific treponemal tests like Treponema pallidum particle agglutination (TP-PA) test that used to look for antibodies against Treponema antigens.
- Penicillin G is the drug of choice

Now we will move on to the first entity of this lecture:

Gonorrhoea:

Gonorrhoea is caused by **Neisseria Gonorrhoea.**

(Recall Neisseria meningitidis which we took during the meningitis lectures.)

The word gonorrhoea gives you an indication on how it will present. The suffix -rrhea means flow or discharge so, we will expect gonorrhoea to present with **discharge** especially urethral discharge.

Morphology:

- Gram negative.
- Diplococci

-N. Gonorrhoea can affect **various mucous membranes** in the body such as the urethra, rectum, cervix, conjunctiva, pharynx

-Unlike, N. meningitidis which can colonize the nasopharynx of healthy people without producing disease (Normal Flora) N. gonorrhoeae is a clinical specimen so, once we find it in a culture it is significant. (Not part of the flora like other Neisseria)

-Similar to other Neisseria specifies it is **fastidious** (requires specific nutritional requirements) and only grows on **enriched chocolate agar**. This helps in identifying Neisseria Gonorrhoea **since when we see a diplococci on chocolate agar it gives a presumptive identification that it is** Neisseria Gonorrhoea**.**

-It is the second commonest bacterial STI following chlamydia.

There is a major public health concern as a result of the growing prevalence of antimicrobial resistance among Gonorrhoea strains.

Pathophysiology:

1. The diplococci attach to the epithelium via the pili.
2. This will affect the microbiota competing with them for nutrients and results in changing the whole environment of the Vagina.
3. After colonization, Gonorrhoea can transcytose (grow deeper) and interact with immune cells such as macrophages, dendritic cells and even epithelial cells
4. Gonorrhoea will be detected by PRRs (Pattern Recognition Receptors) of the immune cells and cause them to release cytokines and chemokines
5. These cytokines and chemokines will attract **Neutrophils**
6. Gonorrhoea enters the **Neutrophils** and become intracellular. Neutrophils are able to transcytose outside the epithelium outside into the vagina. So, the Neutrophils infected intracellularly by the bacteria will be excreted in the form of a purulent exudate.
7. The pus coming out from an infected vagina is expected to have neutrophils with diplococci inside them.

In men:

Virtually all infected men have acute symptoms which involve urethral discharge and dysuria

In women:

Half of all (Majority) infected women have mild or asymptomatic infections. Therefore, a discharge is not always present, or it is sometimes unnoticed.

Gonorrhoea causes several diseases related to each other:

1.) Gonorrhoea: Patients with Gonorrhoea present with purulent discharge not only in the urogenital system (urethra, cervix) but also in

the conjunctiva, pharynx, rectum. This depends on site where the pathogen has infected.

2.) It can progress to disseminated infection, especially in women since it can go unnoticed. This occurs as the pathogen goes from the site of infection to the blood to the skin and joints. (Remember that G.meningitidis after it colonize in the nasopharynx it could go to the bloodstream and cause infection and meningitis).Disseminated infection is characterized by pustular rash. Joints can be affected causing suppurative arthritis.

3.) Similar to how UTI can ascend to the kidney causing cystitis and Glomerulonephritis, STIs and Gonorrhoea in particular can ascend to the: cervix then to uterus or fallopian tube as well as other components of the pelvis. Depending on the site, we have different names for each infection.

Salpingitis ------> fallopian tube

Endometritis ------> lining of the uterus
PID(pelvic inflammatory diseases)---→ inflammation in the pelvis

4.) Also, Gonorrhoea, can cause tubo-ovarian abscesses

How do we diagnose gonorrhoea?

We take the discharge (Exudates) by a swab into urethra, urine, cervix, urethra or throat. In other words, we take a swab where we expect the pathogen to be. And then it should be sent to the microbiology lab to be examined.

Microscopy and culture help in presumptive identification. Microscopy provide rapid diagnosis and shows Gram-negative diplococci when the bacteria are stained. Culture media should be chocolate agar. However the **screening test of choice** is **Nucleic acid amplification tests (NAATs)** as in many other STDs.

Treatment:

Ceftriaxone works well against Neisseria so it's the drug of choice here. If you remember, Ceftriaxone also was part of the empirical treatment in suspected bacterial meningitis. It should be kept in mind that we have to treat the sexual partner.

Chlamydia

The first and most important feature of Chlamydia is that the pathogen goes intracellularly and hides in the cells.

Chlamydia can infect several epithelial types such as epithelial cells in the urethra, endocervix, endometrium, uterus, fallopian tubes and conjunctivae (The doctor focused on conjunctivae and said it is an important part of the transmission of chlamydia)

Chlamydia has a unique life cycle compared to other bacteria as it has **two forms in its cycle**. The first one is the elementary bodies which is metabolically inactive infectious form (this form is like spores in other bacteria). Also, this form **can survive extracellularly.** After it goes inside the cells, it is reorganized into metabolically active non-infectious form, reticulate bodies [RBs], which is the second form. It should be kept in mind that the second form is the form which enable the bacteria to replicate and grow.

Pathophysiology:

The elementary bodies infect the cell and will grow and form reticulate bodies which divide inside the cell. The cell will explode and cause the reticulate but more importantly the elementary bodies to be released and infect other cells.

Chlamydia is usually asymptomatic, and unlike T.Pallidium which cannot survive on inanimate objects, elementary bodies of chlamydia can survive extracellularly and infect through these objects. These characteristics make chlamydia a **successful pathogen in transmission**

-The reservoir of chlamydia is endemic area are the eye (conjunctivae) of children.

Transmission:

Transmission can occur through sexual transmission, or through eye-to-eye transmission by droplets, hands, and contaminated clothing. Here please notice that the transmission could occur through innate objects because elementary bodies of chlamydia can survive on them. That is unlike in case of syphilis which can't be transmitted through objects.

In the eye, it causes Trachoma which is the leading cause of preventable blindness. Blindness caused by Trachoma occurs mainly in rural areas

where healthcare systems are not accessible. Unfortunately, although Trachoma can be solved by a single dose of antibiotics it is still common to this day.

Diseases:

Like in Gonorrhoea, a Chlamydia infection in women is usually asymptomatic while in men it is symptomatic. Also similar to Gonorrhoea, it can ascend and cause PID. Depending on where it infects in can cause cervicitis in women and urethritis and proctitis (rectum) in both men and women

A disease caused by a serotype of chlamydia is called lymphogranuloma venereum: it shows in the form of painless ulcers, other than painless ulcer or chancre that we find in syphilis.

Sample:

1.) **Exudates or discharge by swab into urethra.**
2.) **First catch urine,** unlike mid catch urine in UTIs. We are looking at the pathogen that is first pushed out by urine than find in the urethra.

Tests:

Culture is not recommended since the pathogen is intracellular so culture will be expensive.

1.) Nucleic acid amplification tests (NAATs)— these have become **the diagnostic test of choice**, as they are highly sensitive (90–95%).

Treatment:

Treatment should include patient and sexual partner/s.

1.) The drug of choice for reasons of compliance is **doxycycline**
2.) **Azithromycin**

Urethritis is sometime classified as gonococcal and non-gonococcal.

If Chlamydia or trichomanias vaginalis causes urethritis it is classified as non-gonococcal.

Many pathogens can cause this such as Mycoplasma and Ureaplasma, which are the smallest free-living bacteria. These pathogens lack a cell wall (not stained by Gram stain) and because of that, they have different shapes (not cocci or bacilli). Similar to gonorrhoea and Chlamydia they can cause PID if they ascend upwards. PCR (NAAt) are important diagnostic tests for these pathogens. They are a concern also due to antimicrobial resistance similar what we face in chlamydia and gonorrhoea.

Nonbacterial STD:

Vulvovaginal candidiasis

-Occurs **mainly** in women and **rarely transmit to** males partners.

-Candidiasis is an infection caused by *Candida albicans* which is part of the normal flora (gut flora and vaginal flora) that is opportunistic when it overpopulates.

Clinical picture:

Candidiasis usually presents as a Rash + White plaques and exudate

Pruitis (itch)

Pain on urination

Cottage cheese discharge

pH is still acidic (unlike in trichomonal and bacterial vaginosis were pH increased (less acidic))

Sample:

Take swab of the white plaques and quickly put it in wet mount with KOH.(Note: KOH is important in lysis the epithelium surrounding the candida). Look under the microscope to find the yeast and hyphae of candida albicans.

-Some women that have recurrences usually self-diagnose. One study demonstrated that only 34% of those women self-diagnosing candida infection actually had it. (Therefore self-diagnosing is unreliable)

29– 49% of premenopausal women reporting at least one episode of candidiasis

*In many of the sporadic cases,*There is genetic susceptibility. With this susceptibility there is a high risk of recurrence.

Factors that increase risk of infections are diabetes, HIV due to immune suppression , antibiotic use which affect the vaginal flora and pregnancy (due to changing the vaginal ecology)

Treatment:

You give Peroral or topical antifungal

If the patient doesn't respond to a short treatment course, you should increase the course for two weeks.

You do not give peroral antifungal in pregnancy because it's contraindicated you give tropical.

Case #1

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.

1.) Pain on urination (In the previous lecture we said that a male patient coming in with these symptoms we start thinking of prostatitis so keep this in mind.)

2.) Penile discharge and testicular tenderness. This gives an indication that we should start thinking that it is an STD

3.) Looking at the sexual history we see that he has had multiple heterosexual relationships in the last 8 days. This is an important risk factor in STDs "multiple sexual partners"

4.) Normal BP, pulse however there is mucopurulent cloudy discharge from urethra as well as swollen testicles when examining him

5.) Fatigue, pain, knee joint

6.) edema in the eyelid with the presence of copious discharge (conjunctivitis). So conjunctivitis (we start thinking in gonorrhoea and chlamydia)

What do we do? We take swabs

Following counselling, 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% CO2. 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 (which means gram negative 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 microscopically detected in the urethral smear.

7.) **Culture:** First thing we do is put the exudate on chocolate agar and Thayer Marten. If diplococci grow on Chocolate agar and on Thayer Martin. we know it is gonorrhoea. Which was the case here.

8.) **Microscope**: Gram-staining, pink to red diplococci (gram negative) + polymorphonuclear cells with intracellular diplococci ----> This result was sufficient for the presumptive identification of *N. gonorrhoeae*

After this we try to find what antibiotics the pathogen is susceptible to. We discover that the patient has a pathogen with multiple antibiotic resistance including ampicillin, ceftriaxone and cefotaxime, which as we said is an important public concern.

Case #2

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.

1.) Multiple sexual partners + younger age + no protection by condoms are all important risk factors for STDs.

2.) Good practice was done by the clinical such that although no sore, discharge or any clear manifestations were present the clinician went through a pelvic examination as a result of the risk factors. (Since many STD pathogens are asymptomatic in women)

3.) By doing so the clinician found: an inflamed cervix that bleed easily + there was purulent discharge from the cervix

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

We should test for all of them. Because if we suspect one STD we should test for other STDs as well.

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

The results show that:

1. She is positive for Chlamydia
2. Negative for syphilis (-ve RPR) and gonorrhoea
3. No clue cells so no bacterial vaginalis
4. No trichomonas

Whiff test is performed by adding KOH to the exudate, if the sample gives out a fishy smell we suspect **bacterial vaginosis**

Case #3

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.

1.) The patient falls under the risk factor of **MSM** (Men having sex with men) and condomless anal insertive and receptive intercourse. So his sexual practices put him in risk for certain diseases.

2.) Ulceration is present **orally**. These ulcerations are **painless and heal on their own** so termed **Chancres**. By this alone we assume **syphilis**

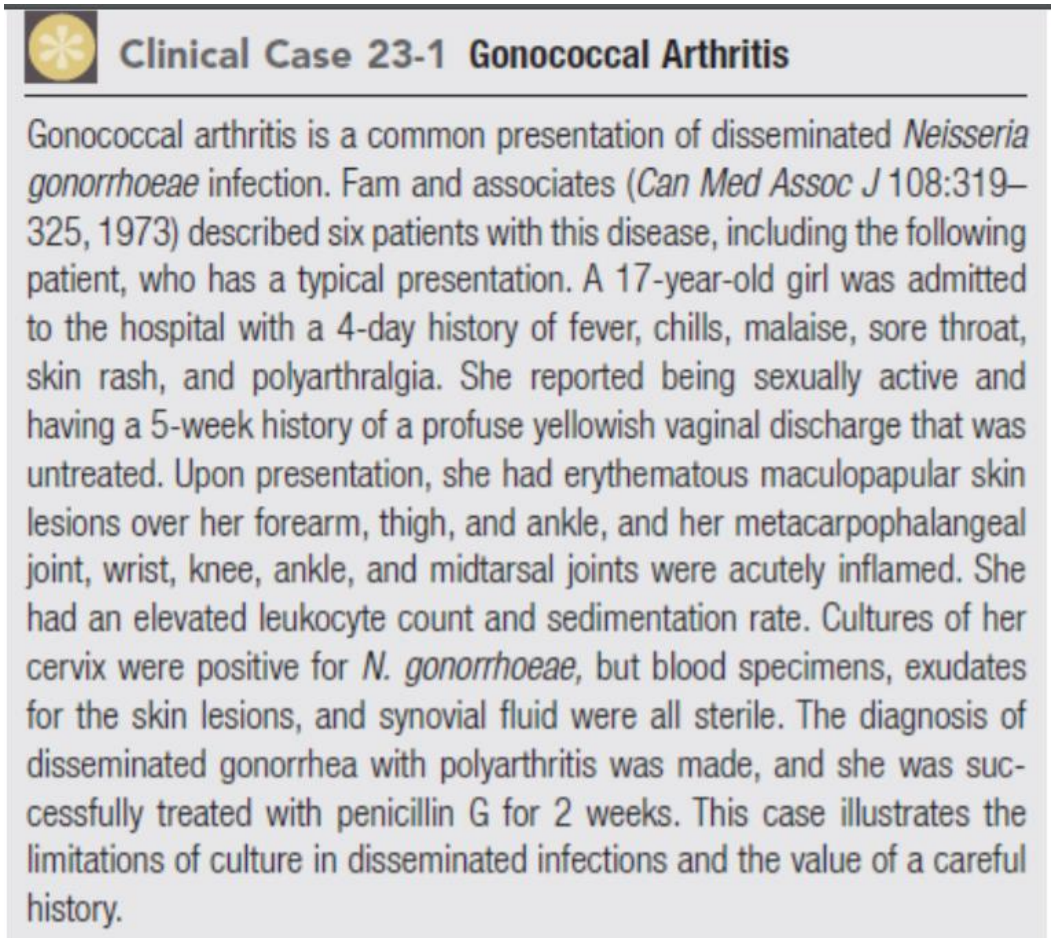
3.) The fact that the patient has **Maculopapular palmar rash** is indicative that he has reached **Secondary syphilis**. However, the **absence** of Neuro or Cardiac abnormalities gives an indication that it **has not progressed to tertiary syphilis.**

Tests:

The **RPR** test gives a positive result therefore the patient has secondary syphilis and is treated with **penicillin G**

His sexual behaviours also put him in risk of HIV + hepatitis B so we test for them. The results are negative may be because the patient was immunized against hepatitis B

Case #4



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 polyarthritis 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.

1.) The patient has a History of fever chills, (constitutional symptoms) which indicate disseminated infection because the bacteria enter the blood.

2.) She is Sexually active, so a risk of STDs is present

3.) She presents with perfuse yellowish vaginal discharge that wasn't treated from 5 weeks may be because of the stigma or maybe because it wasn't painful

4.) More importantly she has erythematous maculopapular skin lesions and polyarthralgi which are indicative of Disseminated infection.

5.) When blood specimens, skin lesions and exudates from synovial fluid were taken they were all sterile, may be because the way we culture these samples were not able to retrieve the pathogen

6.) Cultures for the cervix however were positive for chocolate agar (diplococci) so the pathogen is Gonorrhoea

7.) Treatment is **penicillin G for two weeks**

The take home message for this case is the **Limitation of cultures from blood** and the value of careful history **because of we didn't ask her about the perfuse yellowish discharge, then we couldn't suspect maybe gonococcal arthritis.**