Sexually Transmitted Infections (STI) / Clinical aspect

Learning Objectives: By the end of this lect., you need to:

1- **Understand the importance of sexually transmitted infections (STIs).**
2- **Learn how to take a sexual history.**
3- **Describe the outlines of testing, diagnosis, and transmission of common STIs and blood-borne viruses (BBVs).**
4- **Understand how patients need to be supported to undertake screening.**
5- **Demonstrate its effect on women health and pregnancy outcome.**
6- **Describe the care for the HIV-positive mother and child.**

Overview:

There are several conditions now classified as sexually transmitted infections (STD) which are a major public health concern. The subject is frequently misunderstood and the impact on affected women, their partners and at times their children may be considerable.

STIs are often asymptomatic but can still be transmitted to others and cause significant problems at the time of infection or in the future; for example, human papillomavirus (HPV) infection and cervical cancer. STIs often coexist and when one is found, screening for others is required.

Respecting and maintaining patient confidentiality is vital when managing women with an STI or HIV diagnosis. STIs may be difficult to control & treat because of social nature of disease transmission.

Taking a sexual history:

History taking is the first step to identify and treating STIs. It allows the health care professional to quantify risk, decide which tests are required and whether they need to be repeated later, and gather information needed for treatment.

Rational for questions	Points to cover in the questions
Assessment of clinical need & symptoms	Why the woman attending, what are the symptoms, any specific features, and any history of past or current STIs.
Any sexual exposure to guide testing decisions	Any sexual exposure in the last 3 months, barriers as condoms used, and partner details, including history of STI. Other exposures: intravenous drug used, high risk tattoos or piercing or medical procedures.
Contraception needs &	Menstrual history, current pregnancy risk, and need for

pregnancy risk assessment	contraception
Other sexual health needs	Cervical cytology if indicated, vaccine HPV or hepatitis if indicated
Assessment of risk behaviors	Alcohol, smoking or others
Assessment of possibility of violence or abuse	Any forced sex or violence or abuse by sexual partner

Testing for STIs and associated conditions:

Technological advances have facilitated accurate, non-invasive testing for most STIs. Table below summarizes appropriate screening and diagnostic tests:

Bacterial vaginosis	Microscopy of vaginal discharge or Amsel's criteria / Not required if asymptomatic
Candidiasis	Microscopy of vaginal discharge +/- culture, not required if asymptomatic
Trichomoniasis	Nucleic acid amplification test (NAAT) test from vulvovaginal swab Culture or wet mount microscopy of vaginal discharge alternative Not required if asymptomatic
Chlamydia	NAAT test from vulvovaginal swab Oral or anal swab, if sex practice from these sites
Gonorrhea	NAAT test from vulvovaginal swab Culture required if test positive before treatment Oral or anal swab, if sex practice from these sites
HIV	Serology for combined & HIV 1+2 antibodies with HIV p24 Ag. Test also available of dried blood spot & saliva sample.
Syphilis	Serology for treponema test (usually enzyme linked immunoassay (EIA), if positive, then non-treponemal test titre).
Hepatitis B & C	Serology for hepatitis B core Ab or surface Ag or both, hepatitis C Ab. These tests done for women from a high prevalence area or at additional risk of infection (known or likely exposure, intravenous drug use, sex work).

These infections can be categorized in groups:

Infective causes of vaginal discharge:

1- Bacterial vaginosis (BV):

The commonest cause of abnormal vaginal discharge, a definitive cause is not determined, depletion of the lactobacilli dominant in the healthy vaginal flora is observed, with an elevation

of vaginal pH to > 4.5. Risk factors include douching, black race, smoking, having a new sexual partner.

Symptoms: include an **offensive vaginal** discharge that is often reported as having a 'fishy' malodour, and on examination a homogenous off-white vaginal discharge with a high pH is observed.

BV is associated with a number of pathologies including **pelvic inflammatory disease (PID)**, post-hysterectomy vaginal cuff cellulitis and, in **pregnancy**, preterm birth and rupture of membranes and miscarriage. An increased risk of HIV infection is observed in women at risk with BV.

Treatment: Oral or intravaginal metronidazole or clindamycin are indicated in women with symptoms. Women with BV should be advised that vaginal douching or excessive genital washing should be avoided.

2- Vulvovaginal candidiasis

This condition occurs when **yeast** of the Candida species, most frequently C. albicans, cause vulval and vaginal inflammation. The vagina is colonized with Candida sp. in up to **20%** of women in their **reproductive years**, rising to **40% in pregnancy**, and is most often asymptomatic. C. albicans is part of the normal flora and can grows in normal vaginal PH of 4.0.

When symptoms occur: they include itching, irritation and a typically white, curdy vaginal discharge. On examination, signs of inflammation, including erythema, oedema and fissuring of the vulva and vagina, together with the discharge may be observed. Symptoms may be more frequent and persistent when the woman is **diabetic**, **immunocompromised** and in **pregnancy**. **Treatment**: with topical intravaginal pessaries and topical application which has fewer side effects than systemic treatment. Oral imidazoles also effective.

Candidiasis can be introduced in the body through sexual contact but usually it is not an STI and partners without symptoms do not require treatment.

3- Trichomoniasis

Vaginal and urethral infection with the flagellate **protozoan** Trichomonas vaginalis (TV) causing results in symptoms of vaginal discharge with a variable appearance usually copious, yellowish and symptoms and/or signs of vulvovaginitis. Less commonly it infects the male urethra, prostate & seminal vesicles, producing a white discharge. Trichomoniasis is the most common protozoal urogenital tract infection in human. Its prevalence remains high in many developing countries where are many as 20-30% carrying the infection. The disease is largely sexually transmitted.

Asymptomatic infection is observed in up to 50% of women and most of their male sexual partners. Simultaneous treatment of sexual partners is required. There is some evidence of an association with pregnancy outcome: preterm birth, low birthweight and maternal postpartum sepsis. **Treatment** is with a systemic metronidazole regime.

Cervicitis and pelvic inflammatory disease (PID):

1- Gonorrhoea:

This condition is caused by infection with the **bacteria Neisseria gonorrhoea**. Infection occurs through sexual contact and simultaneous treatment of current sexual partners is required. Endocervical infection is asymptomatic in up to 50% of cases, with altered vaginal discharge (mucopurulent) the most common symptom and lower abdominal pain in up to 25%. Rectal infection occurs through transmucosal spread through anal sex, and pharyngeal infection through oral sex; the latter is nearly always asymptomatic.

Examination: is often normal, although cervicitis with or without a mucopurulent discharge may be seen. Ascending infection may result in PID (gonococcal salpingitis) which may lead to tubal scaring and infertility.

Rarely hematogenous spread can cause disseminated gonococcal infection with a purpuric rash and/or an arthralgia or arthritis that is typically monoarticular in a weight-bearing joint & meningitis & endocarditis. **Ophthalmic infection**: occurs due to inoculation from infected genital secretions, and neonatal infection occurs when the mother has endocervical infection at the time of delivery.

In males, urethral infection (gonococcal urethritis), purulent discharge and pain during urination. But could be asymptomatic.

Testing is indicated: in symptomatic women or those who have another STI. NAAT tests are highly sensitive and specific, and if N. gonorrhoea is identified it is important to obtain a sample for culture and sensitivity testing as there has been a development of widespread antimicrobiological resistance.

Screening for other STIs need to be done, particularly for C. trachomatis, as dual infection is common. Dual treatment of uncomplicated infection with a parenteral third- generation cephalosporin plus azithromycin.

In pregnancy: if the woman is penicillin allergic, then cephalosporin used and if the neonate develops eye infection, then topical and systemic antibiotics according to the sensitivity.

2- Chlamydia:

Chlamydial infection is the **most common bacterial STI**, with women under 25 years of age most frequently affected. Infection with C. trachomatis is **often asymptomatic** but can still result in subclinical PID and subsequent complications. For this reason, screening programmes for this age group have been developed and there is some evidence that they reduce the rates of PID.

Testing is also indicated in women with other risk factors, including a new sexual partner, or those with symptoms that include altered vaginal discharge, intermenstrual or postcoital bleeding or abdominal pain.

Examination: is often normal, but **cervicitis with mucopurulent discharge** may be present. Infection at other mucosal sites occurs as in gonorrhoea and similarly neonates born to mothers with cervical infection may develop **conjunctivitis.** A **reactive arthritis** that is typically monoarticular affecting the weight-bearing joints may occur but is more common in men.

Repeated and chronic exposure can lead to sterility and ectopic pregnancy in female.

This organism may cause subclinical enodmetritis which may predispose to early pregnancy loss, chorioamnionitis, preterm birth and clinical postpartum endometritis with failure of implantation of (In Vitro Fertilization) IVF. Such women and their partner should be screened.

Men developed nongonococcal urethritis and possible other infections (as prostate or rectum).

Treatment: For uncomplicated genital chlamydia, equally effective treatment regimens include azithromycin or doxycycline; the benefit of the former is that it is single dose and well tolerated. Simultaneous treatment of sexual partners is required. During pregnancy use Erythromycin or Azithromycin as a single 1 g dose is licensed for such treatment.

The neonate is treated with tetracycline ointment and 2 weeks coarse of erythromycin syrup because of the risk of Chlamydia pneumonitis.

Pelvic inflammatory disease:

This occurs when there is ascending infection from the endocervix to the higher reproductive tract. It usually complication of chlamydia and less frequently of gonorrhoea.

The diagnosis of PID:

- Usually made clinically and symptoms typically include lower bilateral abdominal pain, dyspareunia, altered vaginal discharge and intermenstrual bleeding or postcoital bleeding. Systemic symptoms of infection may be present.

- Characteristic clinical findings include lower abdominal and cervical motion tenderness and cervicitis.
- Testing for all STIs is required, Exclusion of pregnancy need to be done and Laparoscopy may be needed.

Where PID is suspected empirical treatment should be started immediately, as delay increases the risk of complications. These include the sequelae of endometrial and fallopian tube inflammation and damage such as subfertility, ectopic pregnancy and chronic pelvic pain. Right upper quadrant pain due to perihepatitis is an unusual complication called Fitz-Hugh–Curtis syndrome.

Treatment regimens: should cover all common pathogens and are 2 weeks in duration; they usually include doxycycline plus metronidazole with a parenteral third-generation cephalosporin at the start. Sexual partners require simultaneous screening and empirical treatment, usually with azithromycin. Women require clear information regarding possible sequelae from their infection.

Viral STIs and systemic manifestations

1- Genital herpes

There are two types of herpes virus that cause this condition:

- Herpes simplex virus (HSV) type 1 (HSV-1); causes oral cold sores & keratitis, and is often acquired in childhood, also could be a cause of genital herpes.
- Herpes simplex virus (HSV) type 2 (HSV-2); causes of genital herpes blisters.

Following infection with the virus, the virus establishes latency in the local sensory ganglia and may reactivate, resulting in shedding of the virus, with or without symptoms. Primary infection is the first infection of either HSV-1 or -2; non-primary infection is subsequent infection with the other type. The majority of initial infections are asymptomatic, although the individual may still be infectious, and subsequent recurrences may be symptomatic. Recurrence rates are significantly higher with HSV-2 and reduce in frequency with time.

Clinical presentation: include genital pain and dysuria, in addition to systematic symptoms as fever, malaise & myalgias. On examination there are typically multiple superficial tender ulcers with regional lymphadenopathy.

Diagnosis:

- Detection of the virus from the genital lesions by gently taking a swab. The test of choice is a polymerase chain reaction (**PCR**) test that types the virus.
- **Serology**, testing for immunoglobulin (Ig) G and M to HSV-1 and -2, can be helpful in establishing whether or not an individual is at risk of infection or if the infection is

primary, non-primary or a recurrence. In clinical practice this is useful when assessing women and their sexual partners in pregnancy.

Neonatal herpes:

Is a severe infection with a mortality rate of up to 30% and consequent lifelong neurological morbidity in up to 70%. It is most often acquired during delivery if the mother has primary or non-primary initial infection within the third trimester and especially the last 6 weeks, when reported neonatal infection rates are as high as 41%. IgG to the virus in the serum crosses the placenta and provides neonatal protection from infection, and the risk of neonatal herpes when the mother has lesions of recurrent infection present at delivery is less than 3%. The recommended mode of delivery for women with first attach of genital herpes in the third trimester is prelabour caesarean section, and in those with proven recurrent lesions, vaginal delivery may be appropriate if other obstetric factors allow.

Treatment of the symptoms of genital herpes:

Course of aciclovir, which is very safe and effective, including in pregnancy. Information for patients, including the lifelong nature of the infection, **asymptomatic shedding** and therefore risk to sexual partner and the need for disclosure, the effectiveness of condoms (up to 50%) and antivirals in limiting transmission, are important.

2- Genital warts

These are benign epithelial tumours caused by Human papilloma virus (HPV) infection. There are over 100 genotypes of HPV and types 6 and 11 cause over 90% of genital warts. Infection with HPV in the genital epithelium via sexual transmission is extremely common, with the majority of cases being subclinical.

Infection with the oncogenic genotypes including types **16 and 18** is also through sex, but these cause anogenital dysplasia and cancer, not warts.

HPV vaccination is available as a bivalent (against types 16 and 18) or quadrivalent (types 6, 11, 16 and 18) vaccine.

Diagnosis: By clinical examination.

Treatment:

Include ablative therapies such as application of liquid nitrogen or surgical techniques or patient-applied topical therapies, including podophyllotoxin- containing preparations or the local immune modulator imiquimod. As these are benign lesions treatment is optional. When genital warts are present **in pregnancy** treatment is limited to ablative options. Rarely, warts may become very large and obstruct the birth canal, necessitating caesarean delivery.

Screening for other STIs is required and screening for cervical cancer is as usual.

3- Molluscum contagiosum:

Is a highly-contagious STI– It is caused by pox virus producing painless hard pearly papules with central umbilication, up to 5mm in diameter, on the mons, buttocks or inside of the thighs.

Diagnosis: made on the appearance but on squeezing the lesion a cheesy white material appears → under light microscope → the presence of rounded molluscum bodies (Kopner phenomenon).

Treatment: local damage by excoriation with a needle and application of phenol, silver nitrate or antiseptic paint.

4- Cytomegalovirus: CMV:

It is the most common intrauterine viral infection and the most common viral infection of the neonates. Human CMV can be transmitted through tears, saliva, urine, semen or vaginal secretion or breast milk. It is type of herpes virus, so has the ability to establish latency. In temperate countries it can be transmitted by sexual contact. In tropical countries most children are infected at childhood so few pregnant women are susceptible.

The primary infection may produce no symptoms or mild non-specific symptoms, so the incidence in pregnancy is not accurate but it's around 1/200 pregnancies and 40% result in fetal infection. Infection later in pregnancy is more likely to result in fetal morbidity.

Main features are:

Microcephaly, blindness and deafness. Others are pneumonitis, chorioretinitis, cerebral calcification, developmental delay, hepatosplenomegaly, jaundice & purpura. Sometimes the only presentation is a child born with sensorineural hearing loss.

Diagnosis: is rare before delivery since most of the cases are asymptomatic.

Definitive diagnosis of congenital infection:

Isolating the virus in cell culture from throat swab, urine, blood or CSF in the first 3 weeks of life. Serological test by rising titer of IgG Ab. Or specific IgM Abs persists for few weeks to a few months. And specific IgA antibodies from a few months to a year. In utero by amniocentesis and PCR as it is concentrated in the urine.

Differential diagnosis of congenital manifestations are Toxoplasmosis, rubella, HS, & syphilis.

Treatment: Specific antiviral available but not use in pregnancy only in immunosuppressed patient and it is not indicated in infants with congenital defect. Rehabilitation may be needed for congenital abnormalities.

5- Hepatitis B:

Is a severe infection that may follow by chronic carriage and disease ending in cirrhosis. Transmitted sexually, through blood products and through vertical transmission from infected mother. Most acute infections are not clinically recognized as only 20% will have jaundice. The earlier in life the infection, the more likely the person becomes a carrier.

In some countries, pregnant women are screened at booking. In In acute infection: (HBsAg) & (HBeAg) are detectable in the serum. Hepatitis B core Ab appear after 6 weeks and remain detectable thereafter as a marker of exposure.

Treatment: Interferon under the guidance of liver specialist with antiviral drug with special activity against hepatitis B.

Vertical transmission: can be prevented by vaccination of the neonate born to the mother with hepatitis B. Haptitis B Ig at birth if the mother is e Ag positive. Countries with high rate of hepatitis infection has a policy of universal vaccination of all infants.

6- Hepatitis C:

An RNA virus which causes chronic hepatitis. The prevalence varies widely across the world, with the highest incidence in Egypt and in patients with a history of intravenous drug use with low occasion transmitted sexually. Vertical transmission also uncommon.

Syphilis:

Syphilis is caused by infection with the **bacterium Treponema pallidum** subspecies pallidum,

Transmission:

Through direct contact with secretions from an infective lesion, or via transplacental passage of the bacteria during pregnancy.

This infection is multisystem and has many clinical features that may mimic other conditions. Untreated it can relapse, and remit and late complications can present many years after the original infection. Infectivity declines with time and treatment with penicillin-based regimens are curative, although reinfection may occur.

Those living in African and Asian countries and Eastern Europe are more often affected. The infection is classified as **congenital or acquired**, and each of these as **late or early**.

In acquired early syphilis: the initial manifestation is the '* **chancre**', which develops at the site of exposure (skin or mucous membrane). This is usually a single, genital lesion but is increasingly seen at other sites such as the oral cavity and may be multiple. Typically, the lesion is painless, indurated and exudes serous fluid containing T. pallidum, and there is regional lymphadenopathy. This resolves within a few weeks and following this as the bacteria disseminate there will be variable clinical symptoms and signs. These include a widespread erythematous rash typically including the palms and soles and that can result in alopecia, oral and genital mucous lesions and raised lesions, usually in the anogenital area, termed '***condylomata lata'**.

Complications: include neurological involvement, resulting in meningitis, an eighth nerve palsy and consequent deafness or tinnitus and ophthalmic involvement, most often uveitis.

This stage also spontaneously resolves as the host immune response is effective in controlling the infection, although relapse may occur for up to 2 years.

***Late complications include:**

- Gummatous lesions: granulomatous, locally destructive lesions typically affecting skin & bone.
- Cardiovascular involvement: usually affecting ascending aorta, resulting in aortic valve incompetence.
- Neurological involvement: classified as meningovascular disease, tabes dorsalis and a progressive dementing illness, general paresis.

Congenital infection: occurs when the microorganism transmits across the placenta and cause fetal death, spontaneous miscarriage, or live with symptoms of congenital syphilis, that include many of central nervous and structural abnormalities. The riskiest time for congenital infection is when syphilis is acquired either very soon before or during pregnancy. Screening for syphilis in pregnancy is well established, allowing effective treatment of most women, although infection may occur in pregnancy after this.

Diagnosis:

- **Dark field microscopy** or, more recently, by **PCR** testing detecting T. pallidum in infectious lesions.
- **Non- treponemal serological tests** include the **rapid plasma reagin (RPR) & Venereal Disease Reference Laboratory (VDRL)**, which demonstrate rising titers during acute, active infection that drop with time and following treatment, and so can be used to monitor treatment. They may be negative in early infection, falsely positive in other physiological (such as pregnancy) or disease (including several rheumatological conditions), and so require confirmation by **non-treponemal tests** such as **enzyme or chemiluminescence immunoassays (EIA/CLIA) or T. pallidum particle or haemagglutination assays (TPPA/TPHA)**. These treponemal tests may also be

negative in the very early stages of disease, and should be repeated if negative 4–6 weeks later if this is suspected.

- Serological tests for syphilis may be positive for life, although reinfection results in the non-treponemal titer rising rapidly

Treatment:

- Depot preparations of penicillin; different regimes for differing stages of infection are the treatment of choice.
- Simultaneous treatment of current sexual partners is required.
- Testing of partner, and where applicable children, is required.

Human immunodeficiency virus

General information:

- Infection with HIV results in an initial acute viral illness followed by a chronic decline in cellular immunity due to progressive depletion of CD4-positive T-lymphocytes, and eventually resulting in one or more illnesses defined as the acquired immune deficiency syndrome (AIDS). These are listed in Table e below.
- HIV infection disproportionately affects those living in or originating from sub-Saharan Africa and their partners, homosexual men and intravenous drug users without access to clean injecting equipment.
- Highly active retroviral therapy (HAART) has transformed the lives of HIV-positive people and their families, making early diagnosis and treatment possible to allow maintenance of that individual's own health and to protect their partners and children from infection.
- For this reason some countries recommend offering HIV testing to all those aged 13–64 accessing medical care and antiretroviral therapy to all those found to be HIV positive.

Bacterial infections, multiple or recurrent*
Candidiasis of bronchi, trachea or lungs
Candidiasis of oesophagus†
Cervical cancer, invasive§
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (>1 month's duration)
Cytomegalovirus disease (other than liver, spleen or nodes), onset at age >1 month
Cytomegalovirus retinitis (with loss of vision)†
Encephalopathy, HIV related
Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis or oesophagitis (onset at age >1 month)
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (>1 month's duration)
Kaposi sarcoma†
Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex*†
Lymphoma, Burkitt (or equivalent term)
Lymphoma, immunoblastic (or equivalent term)
Lymphoma, primary, of brain
Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extrapulmonary†
Mycobacterium tuberculosis of any site, pulmonary,†§ disseminated,† or extrapulmonary†
Mycobacterium, other species or unidentified species, disseminated† or extrapulmonary†
Pneumocystis jirovecii pneumonia†
Pneumonia, recurrent†§
Progressive multifocal leucoencephalopathy
Salmonella septicaemia, recurrent
Toxoplasmosis of brain, onset at age >1 month†
Wasting syndrome attributed to HIV

Gynaecological complications in HIV-positive women:

- Women with HIV infection are more likely to have infection with HPV 16 or 18 and have a higher prevalence and incidence of cervical cancer, cervical intraepithelial neoplasia (CIN) grade 2/high-grade squamous intraepithelial lesion (HSIL) or above and vaginal intraepithelial neoplasia. For this reason, annual cervical cytology is recommended.
- Other anogenital malignancies resulting from oncogenic HPV infection also occur more frequently and at a younger age in HIV-positive people.
- PID requires longer courses of antibiotics in women with HIV.
- Postpartum endometritis is common in women with HIV.
- Eruptions of secondary genital herpes may become widespread, severe and persist for weeks with deep, painful ulceration.

Contraception and preconception management:

- Many antiretrovirals interact with hormonal contraceptives, resulting in reduced contraceptive efficacy. Non-hormonal contraception such as condoms and IUDs are appropriate.
- Prior to attempting pregnancy, the health of a HIV-positive woman and her partner should be optimized. This includes standard health promotion and for serodiscordant couples advice regarding prevention of HIV transmission. This is achieved by optimal HIV control as transmission between sexual partners is extremely low when the positive partner has undetectable HIV ribonucleic acid (RNA) levels (termed the 'viral load') in the serum.
- Screening for and treating coexistent STIs and, and can offer fertility treatment when this is indicated to couples where one or both are HIV positive within regulatory frameworks.

Management of the HIV-positive mother and her child:

- All pregnant women must know their current HIV status, and those who are positive require access to high-quality medical and obstetric care. Effective antiretroviral therapy, ensuring an undetectable viral load in serum towards the end of pregnancy, provides excellent protection of the neonate.
- Most mother-to-child transmission (MTCT) occurs during birth or breastfeeding.
- Intrauterine infection is unusual and the risk of this is increased by an intervention that disrupts the placenta (for example, amniocentesis).

- Delivery by prelabour caesarean section reduces MTCT rates when the HIV viral load is detectable.
- Obstetric risk factors that increase the risk of transmission include prolonged rupture of membranes, procedures that breach the infant's skin (such as fetal scalp electrodes) or increase maternal blood in the birth canal; however, these risks are reduced by effective control of maternal HIV.
- Even in the presence of well-controlled HIV, transmission rates to the infant during breastfeeding are up to 3%, so in circumstances where formula feeding is safe, this is preferable.

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