Sexually transmitted diseases (STD)

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Definition- STD are group of diseases (bacterial , viral and chlamydial) which are acquired by sexual contact (contagious) , although they may be transmitted by other routs (non-sexual contact) . They can present as :

1. **Genital ulcer .**
2. **Urethritis .**
3. **Cervecitis .**
4. **Vaginal discharge .**
5. **Papules .**

Genital ulcer : an ulcer on the genital area in both sex , which may be caused by sexually or non-sexually transmitted disease , the **sexual** includes :

	Chancroid	**Granuloma inguinal**	**Lymphgranuloma venereum**	**Primary syphilis**	**Herpes simplex**
Aetiology	Haemophilus ducrey	Calymmatobacterium (Donovania) granulomatis	Chlamydia	Treponema pallidum	Herpes simplex hominis virus
Incubation period	12h-3d	3-6wk	3d-several wks	3wks	3-10d
Initial lesion	Single or multiple round to oval deep ulcers with ragged and under mined edges , purulent base , tender lesions	Soft , non-tender papule(s) that forms irregular ulcer with beefy-red , friable base and raised rolled border .	Evanescent ulcer (rarely seen)	Non-tender , eroded papule with clean base and raised , firm , indurated, border , multiple lesions occasionally seen	Primary lesions are multiple , oedematous , painful erosions with yellow – white membranous coating . recurrent have grouped vesicles on erythematous base
Duration	Undetermined (months)	2-6days	3-6days	3-6wks	Primary 2-6wks , recurrent 7-10ds
Site	Genital , perianal	Genital , perianal , inguinal	Genital , perianal or rectal	Genital , perianal or rectal	Genital , perianal

Regional lymphadenopathy	Unilateral or bilateral , tender , matted , fixed , may become soft and fluctuant	Subcutaneous perilymphatic granulomatous lesions , produced inguinal swelling and are not lymphadenitis (pseudo buboes)	Unilateral or bilateral firm painful inguinal lymphadenopathy , with overlying dusky skin , may become fluctuant and develop grove in the groin (bubo)	Unilateral or bilateral firm movable , non-suppurative , painless inguinal adenopathy	Bilateral tender inguinal adenopathy in primary and may or may not present in recurrent
Diagnostic tests	Smear , culture or biopsy of lesion , smear from aspirated unrptured lymph node	Biopsy , touch preparation from biopsy stained with Giemsa	LGV , complement fixation test , culture	Dark-field examination , VDRL , FTA-ABS	Tzanck smear , culture
Treatment	Azthromycin 1g once orally , ceftriaxone 250mg once IM.	Doxyciclin 100mg 2/d for 3wks , methprime double –strength 2/d for 3wks	Doxyciclin 100mg2/d for 21ds	In syphilis therapy	Acyclovir , famcyclovir , valcyclovir

Syphilis:

Definition- it is a human infectious disease caused by bacterium called *Treponema pallidum* , transmitted by direct contact with a lesion in patient with **primary or secondary stage , in utero (congenital) transplacental route or during delivery** , as the baby passes through an infected birth canal . The bacterium is fragile and dies when removed from the human environment , it may infect any organ of the body , causing an indefinite number of clinical presentation (**one who knows syphilis knows medicine) .** The **annual incidence is** 12.2million cases /world , mostly in developing countries , **incidence in USA was 3.2-8.1/100000people , in UK 0.3-0.6/100000 .**

Aetiology- syphilis is caused by *Treponema pallidum* , which is a very small , spiral bacterium (**spirochete) ,** whose form and **corkscrew** rotation motility can be observed only by dark –field microscopy . The **reproductive time is estimated to be 30-33ho ,** in contrast to most bacteria which replicate every 30min. , so **serum levels of antibiotics** must there for persist for at least 7-10days to kill all replicating organisms , the **Gram stain** cannot be used , and culturing of the bacteria is difficult .

Clinical features- syphilis is classified into two types :-

A. **Endemic syphilis (Bejel):** non-venereal (non-sexual) , infectious , contagious , chronic relapsing disease , transmitted by direct contact with the bacterium . After **incubation period of 3wks** , **primary stage of oral lesion on the lips ,** which persist for 3mo. , followed by secondary stage (similar to secondary stage of sexual type , consist of skin rash , gummata and lymphadenopathy) , **treatment is similar to sexual type .**

B. **Sexual (venereal) syphilis : Which is divided into :-**

1. **Acquired syphilis .**
2. **Congenital syphilis .**

1. <u>Acquired syphilis :</u> The greatest risk of transmission occurs during the **primary , secondary and early latent stages of disease ,** which required abrasion in skin or

mucous membrane , i.e. the patient is most infectious during the 1-2 years of infection , and those patients with **secondary syphilis** are the most contagious , because of the large number of lesions , **10-60% of individuals acquired the syphilis from an infected partner , one third (1/3)** of persons with single exposure to early syphilis will become infected . **The incubation period is 3wks (**range from 9-90days) .

The **clinical presentation** of syphilis is extremely divers and may occur decades after initial infection . **Untreated syphilis** may pass through **two stages :-**

a. **Early stage –** which is divided into: ***Primary ,** ***Secondary (both are infectious** and seldom last more than 2years , but do not exceed 4years) , and ***Latent syphilis , divided into early latent (infectious) and late latent (non-infectious) ,** which may last from 5-50years .
b. **Late stage syphilis –** non-infectious , start after 2years of infection , only 25-30% of patients progress to this stage .

After 4wks of infection , inguinal lymphadenopathy may develop , in one and in both groin after 5wks of infection . **Reactive reaginic serological tests are** detectable at 5.5-6wks , **the macular rash at 8wks , papular lesions at 3mo. , and condylomas at 6mo.** . Syphilis there for can be transmitted by **blood transfusion** , and as a result of deep inoculation by accidental puncture , i.e. there is no primary lesion , this is called **syphilis d'emblee' .**

***Primary syphilis (chancre):** it appears at the site of initial treponemal invasion of the dermis , as papular lesion , which ulcerate rapidly . It may occur on any skin or mucous membrane surface and is usually situated on the external genitala , the **ulcer is presented as hard , button-like , with regular edge and regular base** up to 1cm in diameter , painless , unless become secondarily infected , the ulcer is often surrounded by a narrow , red border , 1-2mm wide , usually solitary , but may be multiple (not uncommon) . In female most cases of primary syphilis pass to secondary stage with out diagnosis (hedin on the cervix) , in **men , glans , frenum , underside of the prepuce , shaft , pubic region and meatus .** The **extragenital chancres** accounts for 6% of all chancres , most commonly on the lips and the oral cavity , anal canal , anus , and transmitted by kissing or orogenital sex . With out **treatment** the chancre heals with scarring in 75% of cases , with in 3-8wks , and in 25% of cases progress directly to the secondary stage .

Diagnosis- genital herpes simplex , other ulcerative STD , infected traumatic ulcers , Behest's syndrome , tertiary syphilis , chancre redux (recurrent primary sore at its original site) , TB ulcer , SCC , BCC , Bowen's disease , scabietic papules or nodules (when ulcerate by scratching) . On lip DD. herpes simplex , carcinoma , traumatic ulcer on the tongue , Behest's syndrome , aphthus , whitlow , paronychia , anal fissure , anal warts , haemorrhoids , anal discharge , cancer .

***Secondary syphilis :** Only 25% of primary syphilis progress to secondary , it is the stage of the disease , when generalized manifestations occurs on the skin and mucous membrane , **serological tests are always positive** in immunocompetent persons . The rash in 2ry syphilis have three common features :- ***They do not itch ,** ***They are coppery red ,** ***The lesions are symmetrically distributed .** The rash firstly appears at around 8wks (rang 2wks-6mo.) of infection , with flue like constitutional symptoms consists of **fever , headache , sore throat , bone and joint pain** , that are more pronounced at night , and hepatosplenomegaly . **The clinical criteria of secondary syphilis are :-**

1. Rash – are the commonest feature , initially **macular , and become papular by 3months ,** and last for 2-10wks , which include :-

a. Macular syphilide (roseolar rash) – this is the earliest generalized syphilid , appears symmetrical , coppery red , round and oval spots , predominantly seen on the **trunk , palms and soles** . It is easily overlooked , especially in deeply pigmented skin , **non-scaly , non-itchy .** When a roseolar rash fad , it some times leaves a pattern of **depigmented spots on hyperpigmented background ,** which is called **leukoderma syphiliticum** , most commonly located on the back or sides of the neck (formerly known as 'the necklace of Venus') .

b. Papular syphilide – the papule is the basic lesion of secondary syphilis , individual papules seldom exceed 0.5cm in diameter , more usually early papular are in fact **maculo-papular , a**nd generalized all over the body . The typical papule is **firm , round or oval , 2-5mm in diameter** , early papules tend to be shiny , some times gradually a thin layer of scales forms , and quickly shed , this is the typical **papulosquamous syphilide . In the late phases** of a papular syphilide , the lesions tend to be more pigmented , and a large **nummular** lesions (1-3cm in diameter) , and covered by massive layers of scales , which may closely resemble psoriasis (**psoriasiform)** , but the scales are easily removed , due to underlying exuding serum , commonly on the palms and soles , also annular and circinate papular rash may be seen .

On the macerated skin surfaces and mucous membranes , for e.g. periano-scrotal junction , there may be small , eroded papules , flush , hypertrophic and may coalesced to form **condylomata lata ,** more commonly seen around the anus and the vulva . In men the papules frequently occupy the entire surface of the glans penis , coronal sulcus and the inner aspect of the purpuce , which may result in partial or complete phymosis . In women , in the axillae and beneath the breast , small superficial , eroded , about 0.3cm papules , are some times seen , but more typical are hyperkeratotic papules , which may affect the adjacent mucous membrane , and in the last stages of pregnancy , hypertrophic coalesced , sodden –surfaced papules , may be very pronounced . **Later on , the papules** are more irregularly distributed , but sho**ws a predilection** for certain sites , such as the **corners of the mouth , angles of the nose , palms , soles and body folds** , such as beneath the breast or in the axillae .

The face is often affected , particularly if the patient has greasy skin , so it involves the seborrhoeic areas , and may form a line along the hair margin called **corona veneris .**

Hypertrophic lesions of the palms and soles , may flake , peel and fissure , and between the toes may resemble sever **tinea pedis .**

Micropapular and miliary eruptions – are especially seen late in the second stage i.e. about year or more after infection , called lichenoid syphilide , which are small papules tend to be arranged in groups of varying size over the body . A lesion called **corymbose syphilide ,** in which a large central papule surrounded by small satellite papules .

c. Pustular ulcerative syphilide – these are now , a rare lesions which consist of crusted papules on the scalp , which by brushing ooze serum and become secondary infected, and may heal with scars formation .

d. Syphilitic alopecia – 5% of cases patchy hair loss is characteristic of syphilis , which consists of small , scattered , irregularly thinned , mouth –eaten patches of semi-baldness , which may involve the eye brows and beard area .

e. Nails – syphilitic paronychia .

2. Lesions of the mucous membranes - occurs in about 30% (1/3) , of cases , which consist of gray , round , or oval mucous patches on the palate , inner aspect of the lips and cheeks , which may coalesce to form **'snail-track' ulcers** , some times sharply

defined , round or oval lesions devoid of dead epithelium , and may be associated with flattened papillae , may appear on the tongue . Bilateral syphilitic **tonsillitis may coexist ,** as may syphilitic laryngitis associated with eroded papules and hoarseness .

3. Generalized lymphadenopathy – occurs in 50% of cases of secondary syphilis , the nodes are **painless , discrete , mobile , rubbery** and vary in size from about 0.5-2cm .

4. Neurological involvement – CNS may be involved during the secondary stage , CSF shows raised cell count , increased protein in at least 15% of cases , less often , serological testes are positive . The patient may complain of headache only , occasionally , meningitis may be present as paralysis of one or more cranial nerves , meningitis with paraplegia and double incontinence is rare .

5. Other systemic features – includes panuveitis , periostitis , joint effusion , glomerulonephritis , hepatitis , gastritis and myocarditis .

The lesions of 2ry syphilis resolve spontaneously in a variable time period , and most patients enter the latency stage within the first year of infection . Approximately 25% of untreated patients with secondary syphilis may experience **relapse** , most of them (approximately 90%) , during the first year , a small percentage in the second year , and non after the fourth year , also **primary stage may relapse ,** especially the immunocompromised .

***Diagnosis* – in DD.** macular rash – from measles , rubella , PR . , **papular rash** – from seborrhoeic dermatitis , psoriasis , LP . acne vulgaris , leprosy and TB. , **condylomata lata –** from haemorrhoids , condylomata acuminate , balanitis cercinata , genital herpes , **micro-papular rash – from** keratosis pilaris , scrofulosorum , trichophytide and lichenplanopilaris , **palms and soles rash –** from psoriasis , scaling mycosis , LP , **oral lesions** –from apathies , tonsillitis , herpes simplex

***Latent syphilis :-** In which there are no clinical stigmata of active disease , although disease remains detectable by positive serological testes , it includes :

a. Early latent stage – is the stage of latent syphilis with in 2years of infection , vertical transmission of infection may still occur , but **sexual transmission is less likely** , in the absence of muco-cutaneous lesions . **About 25%** of patients with latent syphilis develops clinical manifestations of **late syphilis** , often decades later , **early latent syphilis can be diagnosed if ,** with in the year preceding the evaluation , they had :

1. A documented seroconversion (i.e. RPR , VDRL) , without evidence of active disease (reactive serological test) , normal CSF and chest X-ray .

2. Unequivocal symptoms of primary or secondary syphilis .

3. A sex partner documented to have 1ry , 2ry , or early latent syphilis .

b. Late latent syphilis – is the stage of latent syphilis after 2years of infection , have the same diagnostic criteria of early latent stage , but the titer of reactive (reagent) serological tests is low (non-treponemal tests) .

***Diagnosis*-** in DD. *biological false positive reactions (tests-BFP) , *other treponemal diseases e.g. Yaws , Pinta .

***Late syphilis :-** After a period of latency of up to 20years , manifestations of late syphilis can occur , it became rare in many parts of the world because of treponemicidal antibiotics therapy , it includes :

1. Tertiary syphilis – is late skin syphilis , which appears in two forms :

a. Superficial or nodular or tubercular syphilide – the lesions are **protruding , firm , coppery red nodules** (>0.5cm in diameter) , on dependent limbs , they may be cyanotic . The nodules appears in groups with tendency to a circinate arrangement , with central healing and peripheral extension , so that the outline may be **horseshoe**

shaped , **tongued , kidney shaped or serpiginous** , with histology resembles 2ry syphilis , some time the abundance of waxy scales gives the eruption a **psoriasiform** appearance , other nodulo-ulcerative eruptions are covered by massive crusts . These nodular lesions can appear any where on the body , but favor the extensor surfaces of the arms , the back and the face , they are symptomless , central scarring is a feature .

b. Gummata- are the characteristic lesions of 3ry syphilis appear 3-10years after infection and consisting of granuloma . **Clinically** appears as cutaneous **plaques or nodules** of irregular shape and out line and are often **single** lesion on the **arms , back , and face** , have a tendency for central necrosis and ulceration and for peripheral healing with **tissue-paper scarring** . They most often originate in the subcutis and growing in all directions to involve the dermis and epidermis , also may start in bone and muscles and ulcerate to **'punched out' appearance .**The **gammata not infrequently** attacks the **mucous membrane of both hard and soft palate** , which may cause destruction and scarring , also nasal septum destruction , pain less testicular swelling , portal hypertension , glossitis , leukoplakia and fissuring of the tongue , which are **precancerous .**

Diagnosis- In DD. **face** – lupus vulgaris , epithelioma , Bowen's disease , bromides and iodides , DLE , sycosis barrbae , rosacea . **Trunk and limbs –** circinate psoriasis , leukemic infiltrations , mycosis fungoides , venous ulcer , erythema induratium . **Tongue –** congenital scrotal tongue , carcinoma .

2. Cardiovascular syphilis –may tack 20 or more years to be clinically evident , the typical lesion is aortitis , affecting ascending aorta , appears 10-30years after infection , may be asymptomatic , or it may lead to stretching and incompetence of the aortic valve , left ventricular failure or aneurysm formation , other symptoms includes angina pectoris .

3. Neurosyphilis – the onset can occur weeks or decades after treponemal dissemination , may be :

a. Asymptomatic neurosyphilis – accounts 1/3 of all neurosyphilis , it occurs in 10% of those with latent disease and has a peak incidence at 12-18months after infection , it cure spontaneously in 70% of patients .

b. Meningial neurosyphilis – occurs in 2ry syphilis , with features of meningitis .

c. Meningo-vascular syphilis – occurs most frequently between 4-7years after infection , as hemiparesis , seizures , aphasia , due to tissue infarction .

d. Gammata neurosyphilis – typical features of a space occupying lesion .

e. Paranchymatous syphilis –generalized paralysis , from disease of brain parenchyma 10-20years after infection , with psychiatric symptoms .

f. Tabetic neurosyphilis –this was the most common form of neurosyphilis in the preantibiotic era , 15-25years after 1ry infection , called **tabes dorsalis , with pain in the lower limbs** , parasthesia , progressive ataxia , bowel and bladder dysfunction .

2. Congenital syphilis :

Is the infection of the fetus in utero , by the transmission of *T. pallidum* a cross the placenta , which may occur at any stage of pregnancy . **In untreated cases** , stillbirth occurs in 19-35% of reported cases , 25% die shortly after birth , 12% are with symptoms at birth , and 40% will have late symptomatic congenital syphilis . **Adequate therapy** of infected mother before the 16wks of gestation usually prevents infection of the fetus , treatment after 18wks may cure the disease , but not prevent irreversible neural deafness , interstitial keratitis , bones and joints changes in the newborn . The fetus is at greatest risk when maternal syphilis is of less than 2years duration , the annual incidence in USA varies from 3-107/100000 of live births . **Clinically** , congenital syphilis occurs in an **early and late forms :**

a. **Early congenital syphilis –** is defined as syphilis acquired in utero , that become symptomatic during the first **2years** of life , usually appears in the first week of life . The skin eruptions are those of **exaggerated of acquired secondary syphilis ,** there are influenza-like respiratory symptoms in 20-50% of cases , hepatosplenomegaly or lymphadenopathy in 50-75% and mucocutaneous changes in 40-50% . The maculopapular rash and desquamating erythema of the palms and soles are common , deep fissures at the angle of the mouth (split papules) , a highly infectious hemorrhagic nasal discharge , **snuffles ,** are a characteristic early signs . A **vesiculobullous variant (pemphigus syphiliticus)** may occur with vesicles , bullae and erosions . **Osteochondritis with ''saw tooth''** metaphysic on radiographs and periostitis appear with tender limbs and joints , non-tender generalized adenopathy , alopecia , iritis and failure to thrive occur less frequently .

b. **Late congenital syphilis (stigmata) –** the symptoms and signs of this stage usually become evident after the age of 5years (at any time , after 2years of age) , with average age of 30years . It may be difficult to distinguish from acquired syphilis . The most important signs (stigmata) **are : frontal bossaeing 87% , saddle nose 74% , short maxilla 83% , high arched palate 76% , mulberry molars (more than four small cups on a narrow lower molar of the second dentition) , Hutchison's teeth** (peg-shaped upper central incisors of permanent dentition **appears after the age** of 6years) , sternoclavicular enlargement (periostitis) 39% , and rhagades (linear scars radiating from the angles of the eyes , nose , mouth and anus 8% . Hutchinson's triad is Hutchinson's teeth , interstitial keratitis and cranial nerve 8 deafness , considered pathognomonic of late congenital syphilis , **mucosal and skin lesions are those of late acquired (nodules and gamma) ,** cardiovascular and neurosyphilis rarely occurs .

<u>Tests used to confirm clinical diagnosis of syphilis :</u>

1. Dark-field microscopy – scraping from the lesions (1ry,2ry, and early congenital) , examined directly under dark-field microscopy , to see the *T.pallidum* , which has a characteristic morphology and motility . It is **diagnostic , confirmatory and specific test** , before serological tests to become positive .

2. Lesion biopsy for histopathology – these changes are the same in early and late disease , which consists of a **perivascular infiltration of lymphocytes and plasma cells , accompanied by intimal proliferation in both arteries and veins (endarteritis obliterans) .**

3. Molecular amplification tests –PCR and RNA amplification is more sensitive than PCR , and results are indicative of living organisms .

4. Serological tests – are divided into:

A. Reaginic (Non-treponemal) tests – these are tests which detected IgM and IgG antibodies to lipoidal material released from damaged host cells and to lipoidal-like antigens of *T.pallidum* . There are four tests available , all are **quantitative** and useful to asses **treatment , which include .**

a. Venereal disease research laboratory (VDRL) antigen (consisting of cardiolipin , cholesterol and lecithin) , it is **quantitative** test and is useful in assessing response to treatment . It became positive with in 1-4 wks after the

appearance of chancre (1ry syphilis) , titers are highest in secondary syphilis . **The prozone phenomenon** occurs in 2% of sera (undiluted sera give negative results because of antibody excess) , the titer slowly declines after 4wks following the appearance of the chancre and may be spontaneously become negative in some cases of **latent syphilis and neurosyphilis , VDRL slide test** is widely used and requires the microscopic demonstration of antigen-antibody flocculation in heat –inactivated serum .

b. Unheated serum antigen (USR) test – is similar to the VDRL , but dose not require preheated serum , because the antigen has been stabilized .

c. Rapid plasma regain (RPR) test .

d. Toluidine red unheated serum test (TRUST) – use either charcoal or red paint pigmented added to the USR reagent to enhance visualization of the Ag-Ab flocculation , which is visible macroscopically , can be performed in consulting rooms .

B. Specific (treponemal) tests – these are used as confirmatory testing , they detect antibodies to antigenic determinants of treponemes , are **qualitative procedures** and are not helpful in assessing treatment responses , once positive , they tend to remain positive for life , irrespective of treatment , also used to differentiate true-positive from false-positive in the standard non-treponemal antibody tests , which include :

a. *T. pallidum* immobilization test (TPI) , 99% of cases are positive and 100% specific , but it is time consuming , performed by adding of serum from syphilitic patients to media contain virulent *T.pallidum* obtained from rabbits , so the antibodies in the patients sera inhibit the normal movement of *T. pallidum* , which is observed by dark-field microscopic examination . The **TPI** became positive a few days to a week later than to regain tests i.e. later in primary stage , and in the late stage . it is almost always positive (negative results may occur) . With early treatment of syphilis , the TPI may become negative , but if the disease has been untreated for more than 5-6mos , the reaction is likely to remain positive for the rest of the patients life , despite any later treatment , the TPI became a gold standard .

b. The fluorescent treponemal antibody absorption (FTA-ABs) test and the FTA-BBs double –staining (FTA-ABs DS) , are both IFT (indirect immunofluorescent tests) , 1% of cases give false –positive tests (**biological FBT) .**

c. The *T. pallidum* haemagglutination assay (TPHA) – it is very sensitive and specific , more sensitive than FTA-ABS .

d. Treponemal enzyme immunoassay (EIA) –as confirmatory test .

e. Western blot – has similar sensitivity and specificity to FTA-ABS , used for research .

Screening can be performed by either EIA or the combination of VDRL &TPHA .

Biological false positive reactions (BFP):

All the tests in use can produce BFP **results , regains** can be found in the blood of most normal people . Biological false positive reaction may be **:a. acute or b. chronic ,** i.e. they last less than or more than **6months :- VDRL , FTA and FTA-ABS** are the commonly seen .

- **a. Acute BFP reactions -are usually give persistently** low titer positive regain tests (with negative treponemal tests) , and rarely last more than 3mos . They are commonly seen in associations with **malaria , leprosy (especially LL) , typhus , respiratory infections (pneumonias) , infectious mononucleosis , active** pulmonary **T.B , hepatitis ,** subacute **bacterial endocarditis , measles**

, chickenpox , filariasis , leptospirosis , trypanosomasis , relapsing fever , pregnancy and narcotic addiction .

b. Chronic BFP reactions – are usually strongly positive , last more than 6mos and associated with **collagen autoimmune diseases , dysgammaglobulinaemia , SLE , polyarteritis nodosa , rheumatoid arthritis .**

5. Examination of CSF – is indicated in : *neurological , ophthalmic or auditory symptoms and signs , *clinical evidence of active infections e.g. aortitis , gamma , iritis , *treatment failure , *HIV infection , *serum non-treponemal titer of more than 32 , if duration of syphilis is over one year , and *non-penicillin –based treatment regimen planned . **CSF examination** is done in **: a. 2ry syphilis after 1-2years post-treatment follow up , b. in untreated asymptomatic syphilis . The typical** CSF findings in neurosyphilis are : moderate mononuclear pleiocytosis (10-400cells/ml) , elevated total protein (0.46-2g/L) , and positive CSF VDRL (highly specific and rarely give false positive results) .

Management of syphilis :

Reactions which may develop during treatment of syphilis are :

1. **Penicillin reactions – anaphylactic reactions .**
2. **Jarish-Herxheimer reaction –** is an acute febrile reaction that occurs in many patients with 2hos of commencing treatment , mediated by cytokines , with headache , myalgia , bone pain and an exacerbation of skin lesions with fever and controlled by antipyretics , and some clinicians advocated , a short course of steroid (prednisoline 30-60mg/day for 3days , and beginning antisyphilis therapy on the 3rd day . **In pregnancy** may induce abortion , early labour or fetal distress , in neurosyphilis and cardiovascular syphilis may be fatal .

Follow –up – clinical and serological assessment should be done at **3,6 and 12mos ,** after the completion of treatment in early syphilis .

***Reagin non-treponemal tests (VDRL) ,** titers correlate with disease activity and become negative with time after successful treatment .

***The treponemal antibody tests (specific)** , will continue to remain positive for long life after successful treatment (except 25% treated during 1ry phase) .

In late , latent and 3ry benign syphilis – 2years follow up at 3,6mos and every 6mos.

In neurosyphbilis and cardiovascular syphilis – followed up for life .

Treatment of syphilis

Stage	**First line therapy**	**dose**	**Penicillin allergies**	**Dose**
Early syphilis	***Aqueous procaine , benzyl penicillin , or benzathin penicillin***	***600000-900000IU, IM/day for 10d*** ***2.4MU,IM , in single dose***	***Doxycycline*** ***Erythromycin*** ***Azithromycin*** ***Oxyterracycline*** ***Ceftriaxone***	***100mg,2/d orally for 14ds*** ***500mg,4/d orally for 14ds*** ***500mg/d , orally for 14ds*** ***500mg,4/d,for 14ds*** ***500mg/d ,IM or IV, for 10ds***
Late syphilis	***Aqueous porcine penicillin or benzathin***	***600000-900000IU/d,IM for 15-21ds*** ***2.4MU/wk , IM***	***Doxycyclin*** ***Oxytetracycline***	***100mg 2/d orally for 28ds*** ***500mg 4/d for 14ds***

	penicillin or ***amoxicillin*** ***plus probenecid***	***for 3wks*** ***2g 3/d orally for 28ds*** ***500mg 4/d orally for 28ds***		
Neurosyphilis	***Benzyl penicillin G or*** ***aqueous porcine penicillin +probenecid*** ***or amoxicillin +probenecid***	***1.8-2.4g/d for 21ds(as 0.3-0.4gIV every 4ho*** ***2.4MU/d,IM for21ds*** ***500mg4/d orally for 28ds*** ***2g3/d orally for 28ds***	***Consider penicillin desensitization or ceftriaxone*** ***or doxycycline***	***2g/d IM or IV for 10-14ds*** ***200mg 2/d orally for 28ds***
Congenital syphilis-early Late congenital syphilis >2years **, the same as late acquired syphilis in children**	***Crystalline penicillin*** ***or porcine penicillin*** ***or benzathin penicillin***	***50000IU/kg every 12ho for first 7ds of life &every 8ho thereafter for a total of 10ds*** ***50000IU/kg/d IM for 10ds for infants with normal CSF*** ***50000IU/kg as single IM dose***		

Treatment failure – is suggested by a four folds increase in titer , or less than a four folds decrease in pretreatment with in 12-24mos and development of symptoms or signs of syphilis . All required CSF examination and treated by double doses .

Prognosis- cure rate in treated early syphilis is 95% , HIV positive patients carry poor prognosis . All sexual contact followed up for 3mos in primary , 6mos in 2ry and 1year in early latent syphilis .

Gonorrhea:

Definition – it is an infection of mucous membranes and or skin by ***Neisseria gonorrhoeae*** (Gram-negative coccus) , it is transmitted only by sexual contact (**genital , genital-oral or genital-rectal)** , with an infected person , and not transmitted through toilet seats or the like . It most commonly infects superficial mucous membranes and initially produce discharge and dysuria .

Aetiology- gonorrhea is caused by *Neisseria gonorrhoeae (Gram-negative diplococcic)* , which creates a purulent discharge , and phagocytosed by polymorphonuclear leukocytes , it is a fragile organism that survives only in humans and quickly dies if all of its environmental requirements are not met , **survive only in blood and on mucosal surface ,** including the urethra , endocervix , rectum , pharynx , conjunctiva and prepubertal vaginal tract , but not survive on the stratified epithelium of the skin and postpubertal vaginal tract . It required body temperature

and a slightly alkaline medium to survive , it causes most commonly urethritis in males and endocervisitis in females , also may enter the blood stream from the primary source of infection and cause a disseminated gonococcal infection , it may cause asymptomatic male carriers .

Clinical features :

1. **Genital infection in males – the risk of infection for a man after a single exposure** to an infected women is about 20-35% , after an incubation period of 3-5days , most of infected men have a sudden onset of burning , frequent urination , and a yellow , thick , purulent urethral discharge (some times delayed for 5-14days) . About 5-50% of cases are asymptomatic and become chronic carriers for months . **Infection may spread to the prostate , seminal vesicles and epididymis .** The **diagnosis** of the disease can be confirmed by finding in urethral exudates , a gram-negative intracellular **diplococci .**
2. **Genital infection in females –** most cases occurs in between 15-19years , the risk of infection for a women after a single exposure to an infected men is about 50-90% , only 40-60 % of infected women developed symptoms of urethritis and or endocervicitis , these infections includes :

a. Urethritis – begins with frequency and dysuria after a 3-5days incubation period , these symptoms are of variable intensity , pus may be seen exuding from the red external urinary meatus , or after the urethra is milked with a finger in the vagina .

b. Cervecitis- endocervical infection may appear as a nonspecific , pale-yellow vaginal discharge , but in many cases , this is not detected or is accepted as begin a normal variation . The cervix may appear normal , or it may show marked inflammatory changes with cervical erosions and pus exuding from the ose , **Skene's glands** , which lies on either side of the urinary meatus , exude pus if infected .

c. Bartholin ducts – when infected , shows a drop of pus at the gland orifice , which open on the inner surfaces of the labia minora , at the junction of their middle and posterior thirds near the vaginal opening . After occlusion of the infected duct , a swollen , painful mass palpated deep in the posterior half of the labia majora , which cause discomfort while walking or sitting . **The diagnosis** of acute urethritis can be made and confirmed by detection of Gram-negative intracellular diplococci in the purulent exudates from the urethra .

d. Pelvic inflammatory disease (PID) – is infection of **uterus , fallopian tubes , and adjacent pelvic structures by gonococci** , which spread from the cervix and vagina , it occurs in 10-20% of gonococcal infection .

3. **Rectal gonorrhea –** it is acquired by anal intercourse , women with genital gonorrhea may also acquired rectal gonorrhea from contamination of the ano-rectal mucosa by infectious vaginal discharge , **a history of anal intercourse** is the most important clue to the diagnosis because the symptoms and signs of rectal gonorrhea are in most cases nonspecific . **Clinically** most of patients had non-specific signs and symptoms , consists of **pain on defecation , blood in stool , pus on undergarments , or intense discomfort while walking ,** anoscopic examination revels generalized exudates in 54% of cultured – positive patients and 37% of culture-negative patients , and reveal proctitis , not involve segments of bowl beyond the rectum , i.e. about 2.5CM inside the anal canal .

4. **Gonococcal pharyngitis –** it is acquired by penile-oral sex , and rarely by **kissing** , and most commonly in homosexual . **Most cases are asymptomatic ,** but in those with symptoms , which ranged from **mild sore throat , or sever pharangitis with diffuse erythema and exudates . Diagnosis** is made by culture , if exudates are present (***Nisseria meningitides is a normal inhabitant of the pharynx) .***
5. **Disseminated gonococcal infection (DGI – ARTHRITIS – DERMATITIS SYNDROM) . It is** the most common cause of acute septic arthritis in young sexually active adults . **The classic clinical triad is : *dermatitis , *tenosynovitis , *and migratory polyarthritis . It follows** a genito-urinary , rectal , or pharyngeal mucosal infections , develops in approximately 1-3% of patients with mucosal gonorrhea . **Usually develops** within 2-3wks of the primary infection , more likely haematogenous dissemination occurs within one week of the onset of the menstrual period , commonly in women (due to asymptomatic infection) , also **pregnancy** increased the risk . **Migratory polyarthralgias are the** most common presenting symptoms , occurring in up to 80% of patients . Less than 30% have symptoms or signs of localized gonorrhea , **cervical cultures in women with DGI are positive in 80-90% of cases** , and men's urethral culture are positive in 50-75% of cases . Most patients have involvement of less than 3joints , fever and skin rash and tenosynovitis developed , 25% have chills , >50% fever , pain , redness and swelling of 3-6 small joints with out effusion . Skin lesions are seen in 2/3 of cases , start after termination of chills and fever , as painless , non-pruritic , tiny , red papules or petechiae , that either disappear or evolve through vesicular and pustular stages , with a grey necrotic and then haemorrhagic center which represent the embolic focus of the gonococcus , these lesions heal in a few weeks , and new lesions may appear even after antibiotic therapy. Most commonly seen on the extensor surfaces of the hands and dorsal surfaces of the ankles and toes , also on the trunk . **Diagnosis is made clinically and confirmed** by isolation of gonococci from primary mucosal infection , and culture of **joints , skin lesions and blood to isolate the bacteria .**

***Treatment* –** urethral , cervical , rectal and pharyngeal gonorrhea are treated by **cefixime 400mg orally once ,or ciprofloxacin 500mg once orally , or ofloxacin 400mg once orally , or ceftriaxone 125mg once IM . Alternative spectinomycin 2g once IM .**

<u>Lymphogranuloma venereum :</u>

Definition & aetiology* -** it is a rare sexually transmitted disease , affecting mainly the lymphatic tissue , that spreads to tissue surrounding it . It is **caused by the obligatory intracellular *Chlamydia trachomatis (serotypes L1,L2 and L3) . It is more common in men (15-40years) , a symptomatic female carriers are probably the primary source of infection , men presented with ulcers or tender inguinal and or femoral lymphadenopathy usually unilateral .

Clinical features:

Primary lesion : after an incubation period of 5-21days , a small painless papule or herpetiform vesicle occurs on the penis , fourchette , posterior vaginal wall or cervix . The lesion evolves rapidly to a small , painless erosion that heals without scarring within a week . The lesion in most cases is **innocuous** and most patients will not remember it , and rarely seen in women .

Inguinal stage : unilateral or some times bilateral inguinal lymphadenopathy accompanied by headache , fever and migratory polymyalgia and arthralgia appears from 1-6wks after the primary lesion heals . In **a short time the lymph nodes became tender and fluctuate and referred to as buboes** , when ulcerate and discharge purulent material , inflammation spreads to adjoining nodes and leads to matting , abscesses formation and rupture result in sinus tracts , which eventually heals with scarring . **Buboes** are common in males , but occurs in only 1/3 of infected females , enlargement of inguinal nodes above and femoral nodes below creates the **groove sign** in about 1/5 of the patients , which is considered **pathognomonic sign** . **In women** only 20-30% of cases developed inguinal lyphadenopathy .
Genito-ano-rectal syndrome : this late stage occurs more often in **women** , who were previously asymptomatic , **proctocolitis or inflammatory involvement** of perirectal or perianal lymphatic tissues may lead to perirectal abscesses , fistulas , strictures , and stenosis of the rectum and ulceration of the labia , rectal mucosa and vagina . **Chronic oedema , elephantiasis of the female external genitals is a late manifestation of lymphatic obstruction .**
Diagnosis- clinical criteria are supported by **serological tests** , the organism is difficult to culture , **complement fixation test** become positive within 1-3wks (LGV-CFT) and titers >1:64 are indicative of active LGV .
Treatment – the drug of choice is doxycycline 100mg-2/d , orally for 21days . Erythromycin 500mg -4/d for 21days is also effective , fluctuant L.N.s should *be aspirated through healthy adjacent normal skin ,* **incision and excision of L.N.s** delays healing and is contraindicated , stricture and fistula may require surgical intervention .

Chancroid (soft chancre) :
Definition & aetiology- it is one of the common sexually transmitted disease all over the world , especially USA , Africa , Caribbean , Southwest , Asia . It is considered to be the most common cause of genital ulceration (in Iraq rare) . It is caused by **short Gram-negative rod called *Haemophilus ducreyi*** , male: female is 10:1 . It predominantly affects **heterosexual men** , and most cases originate from prostitutes , who are often carriers without symptoms , it is a cofactor of **HIV disease** transmission . About 10% of patients who have chancroid could be co infected with ***T. pallidum or HIV* .**
***Clinical features* –** after an incubation period of 3-5days , a painful **, red papule** appears at the site of contact and rapidly become **pustular** , and ruptures to form an irregular shaped **ragged ulcer** , with a red halo , **deep , bleeds easily , undermined edge** , and a base covered by **yellow-gray exudates .** The ulcer is highly infectious , and multiple lesions appears on the **genitals . Untreated** cases may resolve **spontaneously** , or more often progress to cause deep **ulceration** , sever phimosis and scarring . **Anorexia , malaise , and low grad fever** are occasionally present . **Females may** have multiple , painful ulcers on the labia and fourchette , and less often on the vaginal walls and cervix , autoinoculation results in lesions on the thighs , buttocks and anal areas . **Female carriers** usually are asymptomatic , 50% of untreated patients develops **unilateral or bilateral inguinal lymphadenopathy** , beginning approximately 1week after the onset of the initial lesion , the **nodes** then resolve spontaneously or they suppurate and break down .
Diagnosis- by clinical criteria and exclusion of other causes of genital ulceration (e.g. syphilis , herpes simplex -----) , **by serological and HIV infection tests .** The diagnosis is **confirmed by culture of *H. ducreyi*** on **Mueller – Hinton agar** , has

supplemented with chocolate horse blood and **Isovitalex (MH-HBC) ,** also **Gram-stain , Wright and Giemsa stain** , give Gram-negative cocco-bacilli (false positive result is possible) .
Treatment- azithromycin 1g orally in single dose , ceftrixone 250mg IM in a single dose , erythromycin 500mg 4/d orally for 7days , or ciprofloxacin 500mg 2/d orally for 3days .

Granuloma inguinale (Dovanosis) :
Definition & aetiology- it is an endemic disease in tropical areas , chronic , superficial , ulcerating disease of the **genital , inguinal , and perianal areas ,** mildly contagious , **caused by *Calymmatobacterium granulomatis*** , a Gram-negative , facultative , obligate – intracellular , encapsulated bacillus .
Clinical features – the incubation period is unknown , but 14-50days is suspected , the disease begins as **a single or multiple papules , nodules or ulcers** on the genitala and then evolves into a painless , broad , superficial ulcer with a distinct , raised , rolled margin and friable , beefy , red , granulation tissue like base raised above the skin surface . The **ulceration spreads contiguously** causing progressive mutilation and destruction of local tissue . **Autoinoculation produces** lesions on adjacent skin termed **kissing lesions . The disease** progresses to the genitocural and inguinal folds in males , and the perineal and perianal areas in females , and remains confined to moist stratified epithelium areas , sparing the columnar epithelium of rectal area . **Ulcers bleed** to touch and are not usually associated with inguinal lymphadenopathy . In females the **vulva** is the most frequent site involved , and cervical involvement usually presented as a **proliferative growth and mimic carcinoma** . **Systemic haematogenous dissemination** can occur , which is the cause of constitutional symptoms , distant disease and **death . Delay in treatment** results in significant local destruction , fistula , and abscesses formation , scarring and mutilation .
Diagnosis- culture is very difficult , the most reliable method of diagnosis , involves **direct visualization** of the **bipolar-staining intracytoplasmic inclusion bodies called Donovan bodies** (with in histiocytes of granulation tissue smears or biopsy specimens) , by using 20% **Giemsa stain , Wright's or Leishman's stains are also** suitable .
Treatment- trimethoprim –sulfamethoxazole , one double-strength tablet 2/d orally , and doxycyclin 100mg 2/d orally , for at least of 3wks , if there is no response in the first few days of therapy , the addition of **gentamicin 1mg/kg IV every 8ho. , should be considered .**

Non-gonococcal urethritis (NGU) – Non-specific :
Definition & aetiology – NGU and cervecitis are the most common sexually transmitted diseases in USA . *About 1/2 of cases are caused by genital **chlamydial infection ,** ****Ureaplasma urealyticum*** **and** ***Mycoplasma genitalium*** may cause 10-30% of cases , ****Herpes viruses , Trichomanis vaginalis , Haemophilus*** **species , and anaerobic bacteria account** for less than 10% of cases , and in approximately 1/3 of cases , *noninfectious cause can be found . Most women with cervical chlamydial infection , most homosexual men with rectal chlamydial infection , and as many as 30% of heterosexual men with chlamydial urethritis have few or no symptoms .
Clinical features :

1. ***NGU in males –***begins with dysuria and urethral discharge within 7-28days after sexual contact with smarting sensation , while urinating and a mucoid discharge . About 2/3 of the acute idiopathic

epididymitis in sexually active men younger than 35years are caused by ***Chlamydia trachomatis* .**

2. ***NGU in females* –** the signs and symptoms are even more non-specific , and may be asymptomatic or begins with a mucopurulent endocervical exudates or a mucoid vaginal discharge .

Diagnosis* –** is made by confirming the presence of urethritis , demonstrating the presence of ***Chlamydia trachomatis and excluding gonococcal infection , **Gram-stain** of urethral discharge or smear from urethra , 2CM beyond the meatus (4ho. After urination) , to exclude the gonococcal urethritis , also culture is done for gonococci .

***Treatment* -** doxycyclin 100mg 2/day for 7days , alternative , erythromycin 500mg 4/day , for 7days . Azothromycin 1g once orally , alternative , ofloxacin 300mg 2/day orally for 7days .

Criteria	**NGU**	**GU**
I.P.	**7-28 days**	**3-5 days**
Onset	**Gradual**	**Abrupt**
Dysuria	**Smarting**	**Burning**
Discharge	**Mucoid or purulent**	**Purulent**
Gram-stain of discharge	**Polymorph nuclear leukocytes**	**Gram-negative intracellular diplococci**

AIDS AND THE SKIN :

AIDS (acquired immune deficiency syndrome) : is a viral disease caused by human immunodeficiency virus (HIV) , which is acquired : * **sexually ,** *__from blood or blood products ,*or vertically from an infected mother during pregnancy , birth ,or breast feeding .__ The virus infects immunocompetent cells including CD4 T-cells and macrophages . It creates variable patterns of disease in **individuals , groups and races ,** but all are characterized by **, evolving , some times fulminant immunodysfunction (AIDS) , affecting many systems of the body , including the skin and mucous membrane .**

There are two main types of HIV infects human , HIV-1 and HIV-2 .

HIV-1 is by far the commonest cause of AIDS . **HIV-2 appears to cause AIDS more slowly than HIV-1 ,** and is less infectious with lower rates of either sexual or mother –to child transmission .

Pathology- HIV is a single –stranded RNA virus (nuclear proteins , envelope and reverse transcriptase) , which by adherence (fusion) of its envelope protein to the CD4 receptor and co-receptors on monocytes / macrophages . This process of fusion and inward passage of genetic material of the virus is accomplished by the trasmembrane envelope protein coming into contact with the cell surface . **Within the cell** , the nuclear protein (RNA) trasverse to circular DNA by reverse transcription , and transported to the nucleus of the cell , which is cleaved by integrase and inserted it into the host cell-DNA , and replication occurs , and RNA release .

***Immunology:1.*Specific humoral** or antibody response – neutralizing antibody to the envelope proteins of the virus , and other non-neutralizing antibodies against the nuclear proteins , which are usually measurable by 12weeks after infection .

***2. Cellular responses (specific T.lymphocyte)* –** cytotoxic T.cells (CD8) form the primary component of the cellular immune response , which develop within 5-10days after antigenic stimulation , which have the major role in the control of HIV infection.

CD4 T-cell response induced by HIV infection provide help to both HIV-specific CD8 and B-cells , CD4 is activated through MCH (HLA class-2) molecules on the surface of antigen –presenting cell (dendritic cell) , in response to a variety of HIV proteins in early disease , **but** immunological abnormalities in T-helper (CD4) function occurs very early in HIV infection , even before CD4 T-cell number diminish , as a result of HIV infection and destruction , which is responsible about many infection by other pathogens .

AIDS case definition : Clinical category

CD4 T-cell count	**A: asymptomatic persistent generalized lymphadenopathy or acute HIV infection**	**B: symptomatic**	**C: AIDS indicator condition**
1. >500 multiply 1000000**/L(>29%) >500/ML**	**A1**	**B1**	**C1**
2. 200-499/ML(14-28%)	**A2**	**B2**	**C2**
<200/ML(<14%)	**A3**	**B3**	**C3**

All patients in categories A3,B3,C1,C2 and C3 are considered to have AIDS on the AIDS indicator conditions and / or a CD4 T-cell count of /200/ML .

Natural history of AIDS:

The course of HIV disease may vary considerably in different individuals , thus some individuals develops AIDS within 2-3years and termed **rapid progressors , and others** remains free from AIDS for more than 10-15years and are termed **long-term non-progressors (long –term survivors) .** In the absence of treatment the average time from seroconversion to the development of AIDS is 8-11.6years , with a median time of approximately 10years . **Rate** of progression appear similar by sex , race , and risk category .

Many clinical and laboratory factors are known to predict the rate of HIV disease progression to AIDS :

1. **Transmission risk group :** time from HIV seroconversion to AIDS is approximately 7years in transfusion recipients , 10years for hemophilia's , 10years for IV drug users and 10-12years for homosexual men .
2. **Age at onset of infection :** for patients aged 16-24years the time of HIV from seroconversion to AIDS is 15years , where as for those aged over 35years at seroconversion is 6years .
3. **Clinical indicators :** patients with symptomatic primary HIV infection progress more rapidly than those with symptomatic seroconversion , other clinical markers of progression are oral thrush , oral hairy leukoplakia , herpes zoster , constitutional symptoms and weight loss .
4. **CD4 T-**cell count and their decline over time are very important predictors of disease progression , on average the CD4 T-cell count decrease by 40-80/ml annually , an acceleration inCD4 T-cell decline heralds progression of disease , CD4 T-cell count of <200/ml is diagnostic of AIDS , and the median survival time in an untreated patient with a CD4 T-cell count of <200/ml is 38-40mo .

5. **Viral load :** progressively increasing HIV RNA concentrations can signal the development of advancing immunodeficiency AIDS , the combined measurement of CD4 T-cell count and viral load is an extremely accurate method for assessing the prognosis of infected patients .
6. **Other factors :** the size and route of initial inoculum of virus , pathogenicity , virulence and genotype of the infecting virus .

***Treatment of HIV disease* – 3 groups of drugs are used ,** combination therapy give better result and no resistance develop .

1. **Nucleoside analogue reverse transcriptase inhibitors :** zidovudine , zalcitabine , disanointed , stavudine , lamivudine , abacavir .
2. **Non-**nucleoside reverse transcriptase inhibitors : nevirapine , deavirdine.
3. **Protease inhibitors :** ampenavir , indinavir , nelfinavir , ritonavir , saquinavir and lopinavir .

Dermatological manifestation of HIV infection :

The number of mucocutaneous disease like the CD4 T-cell count is a prognostic indicator of the development of AIDS and over all survival . In general HIV dermatology presents **four broad challenges to the dermatologists which are :**

a. **The opportunity to make the initial diagnosis of HIV in patients with a seroconversion illness or with subtle or florid manifestations of one or other dermatosis associated with underlying HIV infection .**
b. **Differentiating whether a skin problem is caused by HIV infection or by HIV therapy .**
c. **The dermatologist's therapeutic imagination and experience is occasionally tested .**
d. **The implications of HIV –associated skin disorders for the better understanding of the skin in health and disease .**

The clinical manifestations of acute primary HIV disease are :

Fever >38degree in 77% , fatigue in 66% , erythematous maculopapular rash in 56%% , oral ulcer in 29% , odynophagia in 28% , myalgia in 55% , headache in 51% , pharangitis 44% , cervical adenopathy in 39% , arthralgia 31% , axillary lymphadenopathy in 24% , weight loss in 24% , nausea in 24% , diarrhea in 23% , night sweat in 22% , cough in 22% , anorexia in 21% , inguinal lymphadenopathy 21% , abdominal pain 19% , oral candidiasis 17%, vomiting in 12% , photophobia in 12% , sore eyes in 12% , genital ulcer in 7% tonsillitis in 7% , depression in 6% and dizziness in 6% .

Dermatological manifestation of HIV seroconvertion are :

Exanthema , enenthema , urticaria , toxic erythema , EM , oropharyngeal candidiasis , acute genitocrural intertrigo , oral ulceration and genital ulceration.

***Diagnosis of primary HIV infection* –** clinical criteria supported by :

1. **Essential – * ELISA –enzyme-linked immunosorbent assay .**
   ***Western blot ,*HIV-1 –P24 antigen testing , *HIV-DNA or RNA –PCR .**
2. **Supplementary test (indicated in inconclusive ELISA results) - *HIV-DNA or RNA-PCR , *HIV-RNA quantification , *T-cell subset enumeration , *exclusion of other viral illnesses .**

<u>Established skin HIV infection</u>(AIDS) :

***Pruritis , xerosis , ichthyosis –** are common in HIV and can be variably symptomatic (DD. scabies , AD ----) .

***Inflammatory dermatoses are rare – erythroderma , photosensitivity , ACD** , chronic actinic dermatitis , prurigonodularis , urticaria , persistent , insect bite –

reaction , granuloma annular , PRP , lichen spinulosus , pityriasis lichenoides , PR , acne , hydradenitis suppurativa , lichen amyloid , varicose ulcer , perniosis , EN , vasculitis , anetoderma , autoimmune bullous diseases , acrodermatitis enteropathica , cutaneous mucinosis , atypical cutaneous lympgoproliferative disorder and thrombocytopenic purpura .

***Seborrhoeic dermatitis –** only 1-3%of the general population have SD , compared with 20-85% of HIV patients .

***Atopic dermatitis** or AD-like condition is common in children with HIV disease .

***Psoriasis –**it's prevalence in general population is 2% , in HIV patients it is 1-5% more prevalent .

***Eosinophilic folliculitis –** is an HIV **specific disorder** , occurs at CD4 T-cell counts of 250-300/ml , and therefore identifies patients at immediate risk of developing opportunistic infections . The eruption consists of centripetal (face &trunk) , pruritic , erythematous , perifollicular papules and pustules (mimics staph-or pityrosporum folliculitis and acne vulgaris) . There may be peripheral eosinophilia and elevated level of IgE , lesions are sterile , the lesions are treated by phototherapy , topical steroid , oral erythromycin , tetracycline , co-trimaxazole , oral antihistamine , oral dapson , oral isotretinoin and antiviral therapy .

***Pruritic papular eruption-** is a common cutaneous manifestation of HIV , the prevalence is 10-45% with some similarity to papular eruption of pregnancy , papular urticaria is also common , it is a sign of an advanced degree of immunosuppression , occurring at CD4 T-cell count below 100-200/ml , may be the first sign of HIV , it consists of **excoriated erythematous urticarial papules , elevated IgE and peripheral eosinophelia . Treated by phototherapy or thalidomide .**

***Infections :**

1. Bacterial infections – includes : folliculitis , impetigo , ssss , erysipelas , pseudomonas infection , panniculitis , ecthyma gangrenousm .

* Bacillary angiomatosis : is caused by Gram-negative **cat-scratch disease organism (*Bartonella henselae)*** , consists of purple , papular and nodular vascular lesions resemble **Kaposi's sarcoma** , diagnosed histologically , which shows **abnormal endothelial epitheloid cells proliferation** , rather than spindle cells , and predominant neutrophilic infiltrate , **treated by oral erythromycin** alone or in combination with **INH , rifampicin , Ethambutol or Clofazimine .**

*Syphilis – 1ry , 2ry , papilosqumous and gamma , yaws , leprosy , Lyme disease , TB , atypical mycobacterial infections .

2. Viral infections – HSV-1 & HSV-2 (sever chronic , ulcerative , perianal disease) **,** treated by systemic antiviral drugs , Varicella-zoster virus (ophthalmic and sacral HZ) , Cytomegalovirus , HPV (wart in 5-30% of patients with HIV) and MC .

3. Fungal infections – Candidiasis (oral , esophageal , paronychia) , Dermatophytosis – ***T, rubrum in 30%*** , onychomycosis , Cryptococcosis 5-10% of patients in USA & UK , and 40% in Africa , Histoplasmosis 20-50% of cases in endemic areas .

4. Protozoal infections – *Pneumocystic carinii* pneumonia , disseminated amoebiasis , scabies with unusual clinical features (Norwegian) .

***Neoplasm –** Kaposi's sarcoma , melanoma , actinic keratosis , SCC , BCC , lymphoma .

***Hair &nails abnormalities –** acquired **trichomegaly (of eye lashes) , AA , AU , onychomycosis , tinea capitis , hypertrichosis of eye lashes , curly hair , clubbing , half and half nails , Beau's lines , loss of lunula , leukonychia , blue nails and onycholysis .**