

Skin in HIV

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Sexually Transmitted Infections in HIV Disease

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INTRODUCTION

Sexually transmitted infections (STIs) earlier known as Venereal diseases, as per definition made in 1917 included only syphilis, Gonorrhoea and Chancroid. Over the years the diseases like, non-gonococcal urethritis, trichomoniasis, Herpes genitalis and many more diseases were recognized as sexually transmitted [1].

A number of organisms can be transmitted through sexual contact. Most of these spread by sexual intercourse, while others can be transmitted both by sexual contact as well as by other modes of transmission [2].

Understanding the role of sexually transmitted diseases in the transmission of Human immunodeficiency virus (HIV), the role of STDs in progression of HIV disease, and the role of HIV infection in the alteration of natural history, diagnosis or response to therapy of STDs is critical to the development of optimal strategies for HIV control [3].

A consensus has grown that STDs increase the spread of HIV, a hypothesis suggested by Piot et al [4] in 1984, following which several reviews have explored the epidemiologic synergy between

STDs and HIV, concluding that the presence of either Genital Ulcer disease (GUD) or non ulcerative diseases (NUD) increase the transmission possibility of HIV [5-9].

The ulcerative STDs are major health problem in many developed and developing countries as a group of communicable diseases, but prevalence rate is higher in developing countries. The importance of ulcerative STD has increased considerably due to the fact that these lesions are a major cofactor in the transmission of HIV [10].

The risk of transmission of HIV infection is increased in ulcerative and non-ulcerative STIs with a two to five fold increase reported in most studies [11].

However the cross sectional survey of students from five large universities in Uganda revealed that there is a substantial risk for syphilis but little evidence of substantially increased HIV risk among them [12].

The availability of highly active antimicrobials helped in gradual decline in the number of bacterial STIs. However in present HIV era there is resurgence of some of the STIs. The surveillance reports of Syphilis, Chlamydia and Gonorrhoea has risen particularly in men who have sex with men (MSM) [13].

Since the clinical manifestations of STIs in HIV co-infected individuals most of the times is atypical, thereby they go under-recognized and under reported [14].

Hence various studies support guidelines recommending routine screening for STIs in a case of HIV infected patients and screening for patients with STIs for HIV infection, and highlights opportunities to provide relevant screening and education interventions [15].

The difficulty in arriving at appropriate diagnosis in most of the STIs with HIV co-infection is due to atypical presentation of STIs, lack of trained personnel especially in developing countries and inadequate laboratory facilities. Due to this most of the conditions are either under diagnosed or wrongly diagnosed, leading to wrong or inadequate treatment thereby allowing the infection to spread. This poses a great epidemiological threat for onward transmission of STIs as well as HIV. To overcome these shortcomings and to effectively control both HIV and STI, the WHO recommends use of syndromic management for patients presenting with GUDs in developing countries [16].

SYPHILIS AND HIV

Syphilis is an infectious disease caused by *treponema pallidum*, of great chronicity, the clinical manifestation of which resemble various dermatological and systemic diseases [17].

Syphilis and HIV share common risk factors like sexual transmission, transmission from mother to child and through blood transfusion. Syphilis infection increases the risk of HIV transmission and HIV infection in turn can alter the natural course of syphilis [18,19].

When syphilis occurs in an HIV infected individual the clinical course, laboratory diagnosis and response to therapy may be altered [20].

In developing countries AIDS mortality has played an important role in the decline of bacterial sexually transmitted infections, such as syphilis. It is estimated that AIDS associated mortality contributed to approximately one third of the decline in syphilis rates during the early 1990s. However there is a resurgence of syphilis and other STIs since 2000 as a consequence of ART therapy which has resulted in decreased mortality and increased longevity. Initiation of ART results in regaining immunity and resurfacing of the STIs which were otherwise asymptomatic or unrecognized [21-24].

The seroprevalence of syphilis in HIV infected individuals is high more so in men who have sex with men (30-60% high) [23].

The reason for this resurgence is multifactorial including the increased use of methamphetamine and sildenafil or both [24].

Risky sexual behaviour with new partner while travelling, internet dating and serosorting (HIV positive people searching for HIV positive sex partner). In addition the HAART era which has dramatically improved the quality of life for HIV infected patients has resulted in complacency and increased unprotected sex [25].

Syphilis is often the presenting infection in patients with concurrent HIV infection and HIV was found more commonly among patients with syphilis [10,20].

CLINICAL MANIFESTATIONS OF SYPHILIS

Although the number of unusual manifestations of syphilis is reported in HIV co-infected patients the classical presentation is still seen in few. The stage of the HIV disease, CD4 counts, ART therapy and other co morbid conditions determine the clinical outcome. A patient with normal CD4 counts generally will have classical presentation. Uncommon and varied presentations are seen when the CD4 count is less than 100. In HIV patients syphilis progresses more rapidly through its clinical stages [20].

PRIMARY SYPHILIS

The Hunterian chancre, a classical manifestation of primary syphilis in the form of painless, indurated, clean looking ulcer which heals over a period of 4-6 weeks with an atrophic scar is still seen in HIV infected individuals with normal CD4 count [26].

The atypical manifestations of primary syphilis like multiple ulcers which are painful, necrotic and associated with lymphadenopathy which can be phagedenic, haemorrhagic or perforating is seen in patient with very low CD4 count which generally do not show the tendency to heal [20].

Extra genital chancre are more frequently encountered in HIV co-infected individuals and sometimes chancre of the eyelid may be manifestation of primary syphilis [27].

SECONDARY SYPHILIS IN HIV INDIVIDUALS

Unlike in seronegative individuals where it manifests after 4 -6 week of primary stage in HIV positive individuals, secondary syphilis manifests very early within 2-4 weeks after development of chancre. Hence primary chancre is still present when secondary syphilis manifests.

The classical cutaneous manifestations like erythematous macular (roseolar), papular, papulosquamous lesions are seen in patients with asymptomatic HIV infection and normal CD4 count (Figure 9.1 and 9.2).



Figure 9.1: Erythematous papules and plaques over soles.

(Photo courtesy: Department of Dermatology,Bowring and Lady Curzon hospital)



Figure 9.2: Erythematous scaly papules over palms and flexor aspect of forearms.

(Photo courtesy: Department of Dermatology,Bowring and Lady Curzon hospital)

However unusual presentations like Lues maligna, rupioid like skin lesions and annular lichenoid plaques are 60 times more frequent in HIV individuals [28] (Figure 9.3).



Figure 9.3: Crusted lesion over left groin area – a case of secondary syphilis.

(Photo courtesy: Department of Dermatology, Bowring and Lady Curzon hospital)

Condyloma lata is also more frequently seen in these patients [29].

Palmo-plantar syphilis with uveitis and balanitis can mimic Reiter's syndrome in HIV positive patients [30].

Presence of bullous lesions in HIV negative individuals rules out acquired secondary syphilis. However in HIV co-infected patients bullous lesions can be manifestations of secondary syphilis [20].

The oral cavity lesions are seen more frequently in the form of white (ulcerative), papular and nodular lesions which can mimic aphthous ulcer, candidiasis, oral hairy leukoplakia, erythema multiforme and squamous cell carcinoma [31] can be seen in HIV co-infected patients in contrast to HIV negative patients where mucous patches and sometimes snail-track ulcers over the hard palate is seen in less than 1/3 of patients [32].

NEUROSYPHILIS

Treponema pallidum invades the CNS during the early stage of syphilitic infection [33].

Asymptomatic neurosyphilis is seen in 30-40% of persons with secondary syphilis which is demonstrated by abnormalities on CSF examination including VDRL reactivity. Acute syphilitic meningitis occurs within the first 2 years of infection. 10% of cases are diagnosed at the time of secondary rash [34].

Neurological complication of syphilis occurs more frequently and earlier in HIV infected patients, especially among those with CD4 <200/μL [35,36].

Early diagnosis and treatment of neurosyphilis is crucial due to potential persistent disabilities that can be easily treated or even prevented [37].

LAB DIAGNOSIS

Serologic tests for syphilis are the cornerstone of diagnosing syphilis infection, independent of HIV status [38].

Two types of serological tests are employed. Non treponemal tests including rapid plasma reagent test (RPR test) and VDRL test and the treponemal tests include FTA-ABS and TPHA. In HIV negative individuals non treponemal tests have 75% sensitivity in primary syphilis. In secondary syphilis sensitivity is 100% [39].

In HIV infected individuals, unusual syphilis serology is reported. Cases of seronegative syphilis is seen, although infrequently.

The non treponemal test titre may be higher in HIV positive patients than among HIV negative persons [40].

The median RPR titre among HIV infected patients with early syphilis is more than 1:128 in contrast to 1:64 among HIV negative patients [41].

Because of this, false negative results are seen in co-infected individuals (Prozone phenomenon) [42].

TREATMENT OF SYPHILIS IN HIV INFECTED PATIENTS

Primary, Secondary and Early Latent Syphilis

Injection Benzathine penicillin G 2.4 million units single dose IM is recommended. Some experts have recommended extra treatment (such as multiple doses of benzathine penicillin G, as recommended for latent syphilis or other supplemental antibiotics). However, these approaches have theoretical benefit only. Doxycycline (100 mg orally twice daily for 14 days) or Ceftriaxone 1g daily intramuscular or intravenously, for 8-10 days can be given [43].

Late Latent Syphilis

In these patients a CSF examination should be done and if it is normal, 3 weekly doses of Benzathine penicillin G 2.4 million units is given. If CSF shows abnormalities, it is treated as neurosyphilis [43].

Neurosyphilis

IV administration of aqueous crystalline penicillin G at a dose of 18-24 million units daily for 14 days [43].

HERPES AND HIV

Herpes simplex virus (HSV) infection is a common cause of ulcerative mucocutaneous disease in both immunocompetent and immunocompromised individuals [44].

Herpes simplex virus type-II is responsible for sexually acquired HSV infection and the seroprevalence rate ranges from 30-90% in patients with HIV [45].

Infection with herpes simplex virus is life-long, and currently there is no vaccine or drug to prevent or cure the infection.

HSV-2 infection affects approximately 500 million people around the globe and significantly increases the likelihood of acquiring HIV as well as its shedding, [46] by virtue of disruption of mucosal surfaces [47].

Oral and genital shedding of HSV occurs more frequently among those co infected with HIV [48,49].

HSV reactivation in HIV infected patients typically presents with vesicular and ulcerative lesions which can occur frequently and persist for longer periods (Figure 9.4 and 9.5). Chronic HSV infection of more than one month duration is classified as AIDS defining illness s by WHO. It may be widespread sometimes involving the whole perineum with deep seated ulcers particularly among those with low CD4 count [50] (Figure 9.6, 9.7).

The differential diagnosis of genital ulceration include syphilis, chancroid, LGV, recurrent varicella zoster infection, contact dermatitis, fungal infections and Behcets disease [51].

More serious and systemic manifestations of HSV infection include esophagitis, hepatitis, pneumonitis, meningoencephalitis, and retinal necrosis, all of which are relatively rare even in advanced HIV infection [51].

However atypical and disseminated HSV infection occurs relatively often in HIV positive patients [52].



Figure 9.4: Herpes genitalis- Persistent chronic ulcer over labia majora.

(Photo courtesy: Department of Dermatology, Bowring and Lady Curzon hospital)

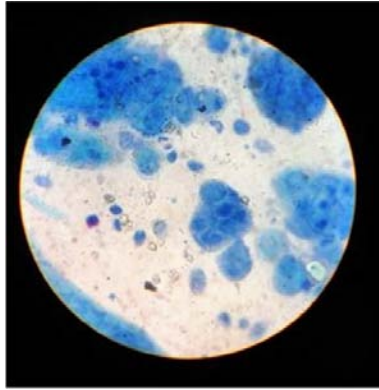


Figure 9.5: Tzanck smear showing multinucleated cell.

(Photo courtesy: Department of Dermatology, Bowring and Lady Curzon hospital)



Figure 9.6: Herpes genitalis presenting as large ulcer.

(Photo courtesy: Department of Dermatology, Bowring and Lady Curzon hospital)



Figure 9.7: Perianal herpes genitalis seen in homosexual man.

(Photocourtesy: Bowring and Lady Curzon Hospital, Bangalore.)

Atypical manifestations like hypertrophic herpes and sometimes progressive tumoral herpes simulating neoplasia can occur in HIV infection [53-55].

HSV DIAGNOSIS

Polymerase chain reaction (PCR) testing of samples taken from muco-cutaneous lesions yield consistently higher rates of HSV detection than those viral culture analysis and should be considered the gold standard for diagnosis of HSV infections in persons presenting with ulcerative disease [56].

For asymptomatic type specific serologic testing based on glycoprotein which can accurately distinguish HSV-1 and HSV-2 infections with high sensitivity and specificity can be carried out [56,57].

TREATMENT

Antiviral chemotherapy provides clinical benefits both as suppressive episodic treatment of symptomatic patients and as suppressive therapy for prevention of recurrent disease.

Episodic therapy for symptomatic reactivation of genital HSV can shorten the duration of lesions [57].

Suppressive therapy: Long term suppression is reported to reduce clinical outbreaks of genital Herpes and subclinical shedding by 80 and 95% respectively [58]. HSV-2 suppressive therapy with acyclovir 400 mg orally bid or Valacyclovir 500 mg bid for a period of 2 years reduced the risk of HIV-1 disease progression by 16%. However a recent study with Valacyclovir 1.5g bid has shown a more dramatic reduction in HIV-1 viral load in addition to effective suppression of HSV. The role of HSV-2 suppression in reducing HIV-1 disease progression prior to ART initiation warrants consideration [59].

In case of hypertrophic genital herpes with HIV co infection, Imiquimod should be considered in the therapeutic approach, as it is an effective, sure and well tolerated treatment [54].

ANTI-VIRAL RESISTANCE

The incidence of Acyclovir resistance in HSV-2 is the same in both HIV infected and unaffected individuals but drug resistant disease can be a serious problem for severely immunocompromised patients who show poor response to escalating dose of acyclovir [60].

The transmission of acyclovir resistant isolates from person to person has not been documented but due to increased use of acyclovir there is great concern that this transmission might occur in future [61].

LGV AND HIV

Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by Chlamydia trachomatis (CT) genotype (L1, L2, and L3).

Infections with Chlamydia trachomatis serotypes D-K are mostly associated with mild

symptoms or may be clinically silent. However infections with L genotypes are more invasive and induce anogenital ulcer or inguinal lymphadenopathy [62].

LGV is endemic in parts of Africa, Asia, South America and the Caribbean, but once was rarely observed in Western countries, where most cases were considered to be imported [63]. However, recent outbreaks have been reported in Europe, Australia, New Zealand, The United States and Canada, mainly among HIV positive men who have sex with men signaling LGV reemergence [63].

Clinical Features

The incubation period is short, generally less than one week but incubation period of 3-5 weeks and longer has been reported. The clinical course can be classically divided into early manifestations and late manifestations.

In the early manifestations primary genital lesion in the form of a papule or vesicle is seen and these lesions are transient and asymptomatic resolving within few days and sometimes the lesions are not observed, especially in females. This is followed by inguinal syndromes where superficial inguinal lymph nodes are affected and produce classical bubo.

In some patients of inguinal syndrome there may be fever, headache, anorexia, nausea, arthralgia and loss of weight.

Late manifestations of LGV (Figure 9.8, 9.9) may occur from a year to many years after the early stage which includes genital elephantiasis, anorectal syndrome and rarely malignancy as a sequel of genital elephantiasis and anorectal syndrome [64].



Figure 9.8: Inguinal Bubo in a patients who developed Fixed drug eruption to Doxycycline.

(Photo courtesy: Bowring and Lady Curzon Hospital, Bangalore)



Figure 9.9: Lymphogranuloma venereum.

(Photo courtesy: Bowring and Lady Curzon Hospital, Bangalore)

Recent cases are observed mainly among HIV positive people, often co-infected with HCV and other STIs, engaging in high-risk sexual practices. The main clinical picture is a relative new entity characterized by progressive ulcerative proctitis, the so called anorectal syndrome [63].

High index of clinical suspicion is a main stay of early diagnosis of LGV since the clinical presentation remains non-specific [65].

Clinical descriptions of male genital LGV are infrequent, even during the LGV proctitis epidemic, seen in Western countries in recent years. A diagnosis of LGV must be considered in the presence of sexually transmitted genital lesions even atypical, especially among HIV infected patients [66].

Clinical and endoscopic findings in LGV and inflammatory bowel disease resemble each other. A strong suspicion of LGV in men having sex with men should be considered as an important differential diagnosis in patients with IBD related symptoms [67].

By PCR technique on rectal swab specimen, *Chlamydia trachomatis* can be determined [65].

Pharyngeal localization of LGV could be independent of rectal involvement. It may remain asymptomatic or characterized by non-specific symptoms such as cervical adenopathy,odynophagia and tongue ulcer.

The inability to diagnose pharyngeal LGV because of which it remains untreated can act as a source of reservoir of infection among MSM [68].

Rarely LGV can manifest as acute seronegative polyarthritis and deep vein thrombosis especially in MSM with HIV infection [69,70].

Diagnosis

Although nucleic acid amplification test are well established in the diagnosis of urogenital chlamydia trachomatis infections in both male and females, culture is still regarded as standard for testing at extragenital sites. However in recent years studies have shown that nucleic acid amplification tests are much more sensitive than culture and should be the method of choice for detection of CT at extragenital sites in MSM [71-73].

Treatment of LGV

Centre for disease control, Atlanta, USA recommends:

1. Doxycycline 100 mg orally bid for 3 weeks or
2. Erythromycin base 500 mg orally qid for 3 weeks (especially in pregnant and nursing mothers, children under 8 years of age and patients sensitive to doxycycline) [74].

CHANCROID AND HIV

Chancroid which is also called as soft sore, soft chancre and ulcus molle is an acute localised, auto-inoculable infection of genitals caused by the *Haemophilus ducreyi* [75]. The disease has generated renewed interest because of its well established capacity to amplify the transmission of HIV infection [76,77] and the organisms emerging resistance to drugs [78-81].

The disease transmission is predominantly heterosexual, with male outnumbering females by ratio of 3:1 to 25:1 [82]. The causative organism has a short duration of infectivity and requires frequent contacts for spread within a population [83].

In women ulcers are often subclinical and sexual activity may continue, especially amongst commercial sex workers who constitute efficient reservoir for the infection [84].

Various clinico-epidemiological studies carried out to know the incidence of ulcerative sexually transmitted disease in HIV positive individuals has shown that the incidence of Chancroid is around 26% next only to HSV and primary chancre [10].

Clinical Features

The incubation period of *H. ducreyi* is between 4 and 7 days with no prodromal symptoms. This may be longer with pre-existing HIV infection. There may be a history of recent sexual exposure, possibly with a commercial sex worker [85].

The various clinical types of Chancroid are the follicular Chancroid, the transient Chancroid (chancre mou Volant), the papular Chancroid (ulcus molle elevatum), the giant Chancroid and the phagedenic chancroid [86] (Figure 9.10, 9.11).



Figure 9.10: Chancroid -A single tender ulcer over glans.

(Photo courtesy: Department of Dermatology,Bowring and Lady Curzon hospital)

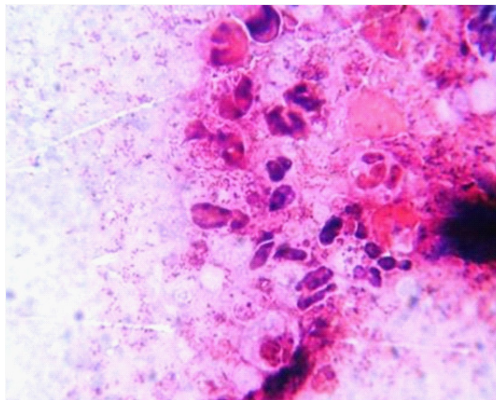


Figure 9.11: Histopathology of chancroid

(Photo courtesy: Bowring and Lady Curzon Hospital, Bangalore.)

Interactions between Chancroid and HIV

Subjects with HIV and concomitant Chancroid infection demonstrate increase infectiousness due to increase HIV shedding into genital tract from ulcer exudates [87], bleeding from ulcers during intercourse and increase plasma viral load from advanced disease or systemic immune activation by *H.ducreyi* [88].

Effects of HIV on Chancroid

HIV infection alters the clinical pattern of Chancroid by prolonging incubation period and increase in number of genital ulcers [85].

These ulcers heal slowly and poorly [89,90].

Extra genital sites are frequently affected [91-93].

Secondary invasion by Vincent organism leads to phagedenic chancroid [94-96].

Treatment

Early, appropriate and effective therapy for Chancroid will reduce the viral infectiousness of HIV and reduce the susceptibility of infection in their partner [97].

The antimicrobials used to treat Chancroid include ciprofloxacin, ceftriaxone, azithromycin and erythromycin. However, the WHO recommends syndromic management of genital ulcer disease to ensure all etiological factors are covered [97-100].

Treatment failures have been reported in individuals with immunosuppression caused by HIV [101].

ANOGENITAL WARTS

Infection with Human Papilloma Virus (HPV) is the most common sexually transmitted disease in the World. Among the 63 million new cases of HPV that occur each year, 30 million develop anogenital warts. There is a high prevalence of HPV/HIV co infection predominantly among men who have sex with men [102] (Figure 9.12, 9.13).

Co-infection with HIV and HPV

In patients infected with HIV, CD4 T lymphocytes, macrophages and Natural Killer Cells are reduced in number leading to changes in local immunity and modulating HPV infection [103,104].

Although HPV types detected in immunosuppressed patients have been found to be similar to those associated with warts in immunocompetent individuals a selective increase of high risk HPV types 6 and 11 were found to be associated with cancer in immunosuppressed patients [105].

HIV seropositive women were more likely to harbour high risk HPV types 16 and 18 than were HIV seronegative women. Cervical cancer which occurs in highly immunosuppressed individuals (CD4 <200) is considered as AIDS determining illness by WHO [106].



Figure 9.12: Anogenital wart in MSM.

(Photo courtesy: Department of Dermatology, Bowring and Lady Curzon hospital)



Figure 9.13: Multiple genital warts

(Photo courtesy: Department of Dermatology, Bowring and Lady Curzon hospital)

MOLLUSCUM CONTAGIOSUM

MCV is a common cutaneous pathogen in HIV infection. Prevalence is 5-18% of the HIV infected individuals. MCV tends to appear when CD4 cell count is below 200/mm³ and the severity of infection tends to parallel with the stage of HIV disease.

Molluscum contagiosum is caused by a pox-virus-Molluscum contagiosum virus.

Molluscum contagiosum in adults over the genital area is sexually transmitted. Transmission occurs through close skin to skin contact with infected persons or fomites.

Clinical Features

It is characterised by skin coloured or pearly white, dome shaped, umbilicated papules with a central pore from which the cheesy material can be aspirated.

Distribution of lesions of molluscum contagiosum in HIV infected individuals is on the face, neck, trunk and genitalia. Lesions may be numerous and of large size ranging from 1 cm to 10 cm. In HIV infected persons, multiple lesions may be found below the umbilicus and around the external genitalia [107] (Figure 9.14). These may be follicular. Mucosal lesions are seen when CD4 cell count is less than 50/mm³.

Diagnosis is often clinical and it has to be differentiated from disseminated cryptococcosis in HIV infected individuals. Other differentials include: Xanthoma, syringomas, plane warts, histiocytosis, penicilliosis etc.

Treatment

Apart from the conventional modes of treatment like needling and curettage, 5% potassium hydroxide, 5% imiquimod and initiation of HAART in HIV patients may lead to regression of lesions. The antiviral agent cidofovir, either given IV or topical 1-3% ointment has shown to be

effective in extensive lesions [108]. †Cefpodoxime is single dose of 200 mg oral.



Figure 9.14: Mollusum contagiosum on the genitals

(Photo courtesy: Bowring and Lady Curzon Hospital, Bangalore.)

GNORRHOEA IN HIV

Gonorrhea is a purulent infection of the mucous membrane surfaces caused by *Neisseria gonorrhoeae*. *N gonorrhoeae* is spread by sexual contact or through transmission during childbirth. The majority of Gonococcal -HIV coinfections occur among men.

Clinical Features

Gonorrhoea mainly causes urethritis (Figure 9.15) in males and cervicitis in females but can lead to complications like pelvic inflammatory disease, epididymitis, urethral strictures, rectal infection, disseminated gonococcaemia, gonococcal arthritis and ophthalmia neonatorum.

Complications of gonorrhea are increased in HIV disease. Risky sexual behaviors may directly increase the potential for infection with HIV and *N gonorrhoeae*. Rectal gonorrhea has been linked to an increased risk of HIV acquisition and *Neisseria gonorrhoeae* with reduced susceptibility to cephalosporins has emerged among MSM in multiple regions, further supporting the need for enhanced surveillance and intervention among this group [109].

Additionally, prospective epidemiologic studies show that gonorrhea in women and men is temporally associated with increased risk of acquiring HIV infection, and virologic studies too have shown that gonococcal urethritis is associated with increased urethral shedding of cell-associated HIV -DNA in urethral secretions, and with increased concentrations of HIV -RNA in semen, strongly suggesting that gonorrhea facilitates HIV transmission.

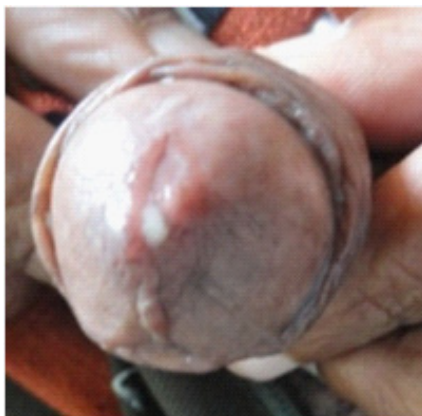


Figure 9.15: Gonococcal urethritis.

(Photo courtesy: Bowring and Lady Curzon Hospital, Bangalore.)

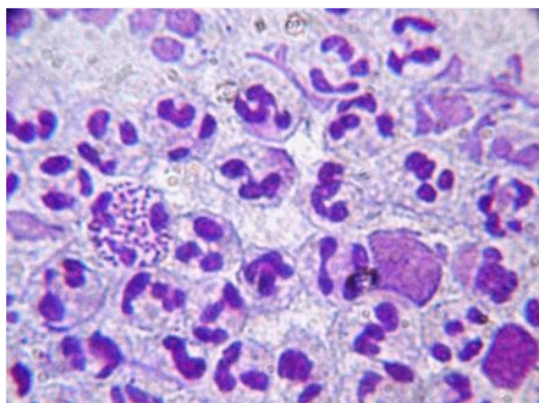


Figure 9.16: Gram negative Diplococci.

(Photo courtesy: Bowring and Lady Curzon Hospital, Bangalore.)

Diagnosis

Simple Gram stain of the discharge will reveal intracellular Gram negative diplococci (Figure 9.16). Nucleic acid amplification testing, typically used for urethral, cervical, and urine testing, can be used for the detection of gonorrhea infection in oral and rectal sites and should be incorporated into annual screening protocols for HIV-infected and noninfected MSM [110].

Treatment for gonorrhoea in HIV-infected individuals is the same as in those who are HIV-negative.

- Azithromycin 1g single oral dose.
- † Cefixime 400 mg oral as a single dose

- † Spectinomycin 2 g intramuscularly as a single dose
- † Other single dose cephalosporin regimens, cefotaxime 500 mg intramuscularly as a single dose or cefoxitin 2 g intramuscularly as a single dose plus probenecid 1 g oral.

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