Capacity Building Program on Clinical Aspects of HIV/AIDS for Nurses and other Health Workers

CASA

Face-to-face training
March 2019

Co-infections in HIV
Sexually Transmitted Diseases (STDs)

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TIGRAY HEALTH BUREAU

AGENZIA ITALIANA PER LA COOPERAZIONE ALLO SVILUPPO

WELCOME BACK!

Just tell me…

What expectations do you have from this training?

Write 3 of them at the end of your notebook

Table 1. Training modules and schedule for nurses and other health workers

YEAR. TOPIC	SCHEDULE
2018. HIV/AIDS Treatment and Prevention	
WHO HIV Guidelines Update	1 day face-to-face training 4 months distance learning
Clinical, immunological and virological monitoring of patients on ART	1 day face-to-face training 4 months distance learning
2019. Co-infections in PLHIV	
Sexually Transmitted Diseases	1 day face-to-face training 4 months distance learning
Tuberculosis: Advanced Aspects	1 day face-to-face training 4 months distance learning
Opportunistic Infections (excluding TB): Advanced Aspects	1 day face-to-face training 4 months distance learning
2020. Comorbidities in PLHIV	
Cardiovascular and Metabolic Comorbidities in PLHIV	1 day face-to-face training 4 months distance learning
Cancers in PLHIV	1 day face-to-face training 4 months distance learning
Liver and Kidney Diseases in PLHIV	1 day face-to-face training 4 months distance learning

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Match the STDs! What's the images stand for?

Syphilis (Lues)
Treponema pallidum

Urethritis, lymphogranuloma venereum
Chlamydia trachomatis

Genital herpes infection
HSV 1/2

Gonorrhea (the clap)
Neisseria gonorrhoeae

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Sexually transmitted diseases (STDs) are passed for one person to another through sexual activity including vaginal, oral, and anal sex. They can also be passed from one person to another through intimate physical contact (heavy petting), though this is not very common.

It is important to know that STDs are preventable. If you have sex, know how to protect yourself and your sexual partner from STDs (ex condom!).

CDC, 2016

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Global epidemiology of STDs

- 1 million sexually transmitted infections (STIs) are acquired every day worldwide.
- More than 500 million people are estimated to have genital infection with herpes simplex virus (HSV).
- More than 290 million women have a human papillomavirus (HPV) infection.
- STIs such as HSV type 2 and syphilis can increase the risk of HIV acquisition.
- Over 900 000 pregnant women were infected with syphilis resulting in approximately 350 000 adverse birth outcomes including stillbirth in 2012.
- Drug resistance, especially for gonorrhoea, is a major threat to reducing the impact of STIs worldwide

World Health Organization

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Why is important to speak of STDs?

- These epidemics have a profound impact on the health and lives of children, adolescents and adults worldwide.
- Complications due to sexually transmitted infections have a profound impact on sexual and reproductive health.
- It needs to define the specific populations that are most affected by sexually transmitted infection epidemics (MSM, sex workers and their clients, PLHIV, adolescents, women, drug users, people affected by conflict and civil unrest)
- Counselling and behavioural interventions offer primary prevention against STDs and can improve people's ability to recognize the symptoms of STIs and increase the likelihood they will seek care or encourage a sexual partner to do so.

World Health Organization

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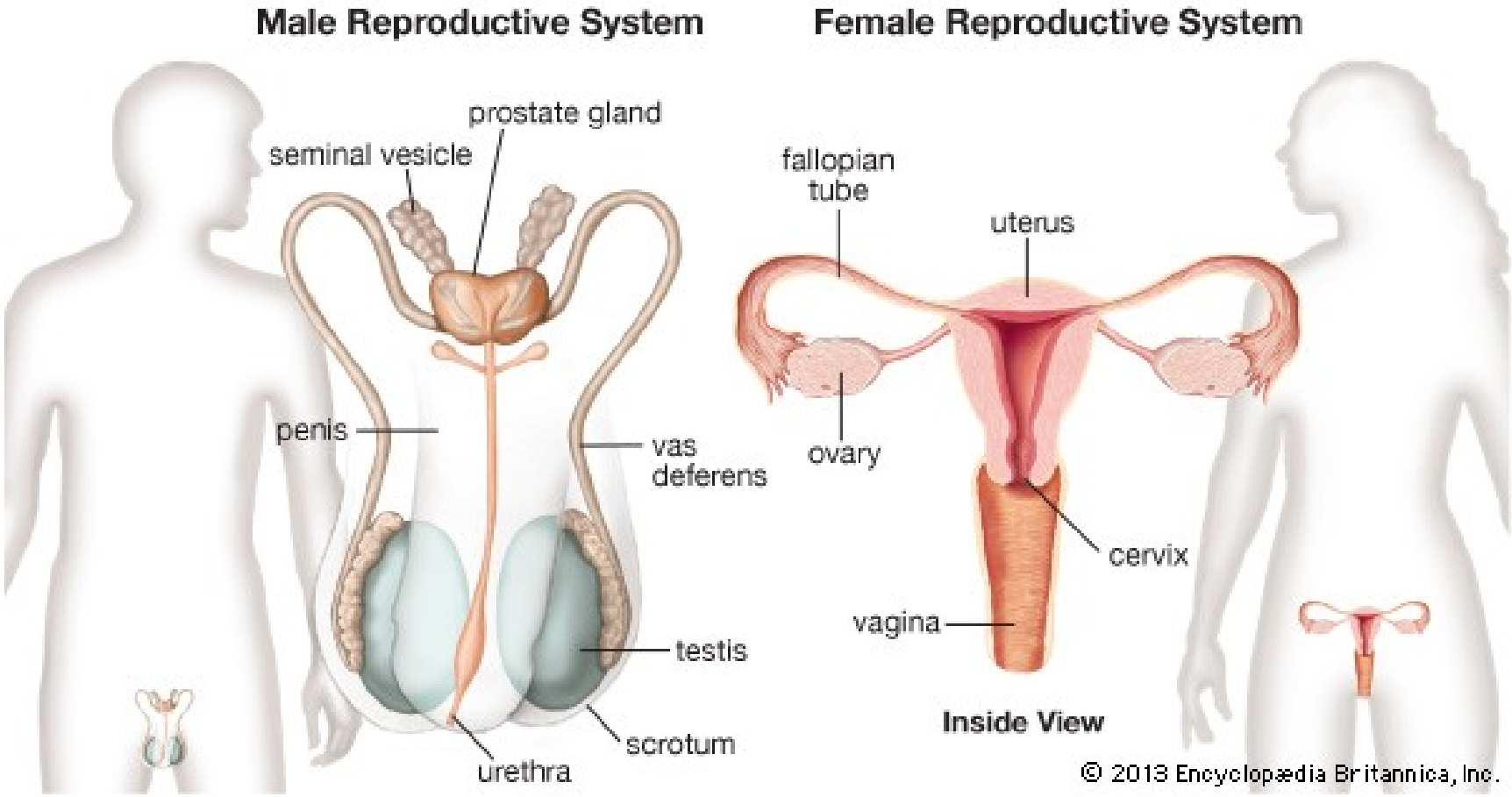
Anatomy in STDs



1- Clinical Case - Hakim

24 year- old man

Reporting a single, small, painless sore on the penis (like a button) since two days. Small lymph node on the left groin. No recent fever, no other specific sign or symptoms.

The man reported unprotected sexual intercourse 3 weeks before the ulcer appearance.

What type of STDs do you suspect in this patient?

1) Genital ulcer (chancroid)

2) Primary syphilis

3) Genital Herpes infection

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1- Clinical Case - Hakim

What could be the appropriate approach to this situation?

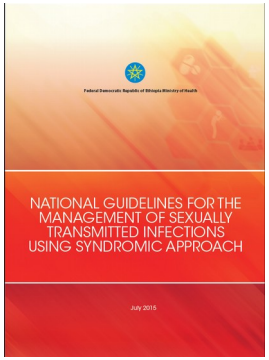
1) Give him the treatment with penicillin i.m. (without testing other STDs)

2) «wait and see». May be everything will be resolve in few days

3) Tested as soon as possible for HIV infection and ask to the patient if there were other manifestation correlated with STDs. Then, give the appropriate treatment.

STDs and HIV: always do test!

- STDs facilitate HIV transmission by breaching protective mucosal barriers and recruiting susceptible immune cells to the site of infection.
- Ulcerative and non-ulcerative STDs also create portals of entry for HIV to access susceptible cells.
- HIV alters susceptibility of STI pathogens to antibiotics
- Syphilis is related to both increased concentrations of HIV RNA in blood plasma and decreased CD4 cells
- Some STDs can easily worsening when co-esist with HIV (tertiary syphilis)



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Sex Transm Infect. 2011 April ; 87(3): 183–190.

1- Clinical Case - Hakim

HIV test: positive!!
CD4+ cell count: 335
cell/mmc

Weight: 56 kg

Start TDF/FTC(3TC)/EFV + penicillin 2,4 milion units IM (one time)

1- Clinical Case - Hakim

Syphilis (Lue)

- Etiological agent: *Treponema pallidum*
- Disease progresses in stages (*primary, secondary and tertiary syphilis*)
- May become chronic without treatment
- Sexual and vertical; also blood trasfusion
- Most contagious to sex partners during the primary and secondary stages.

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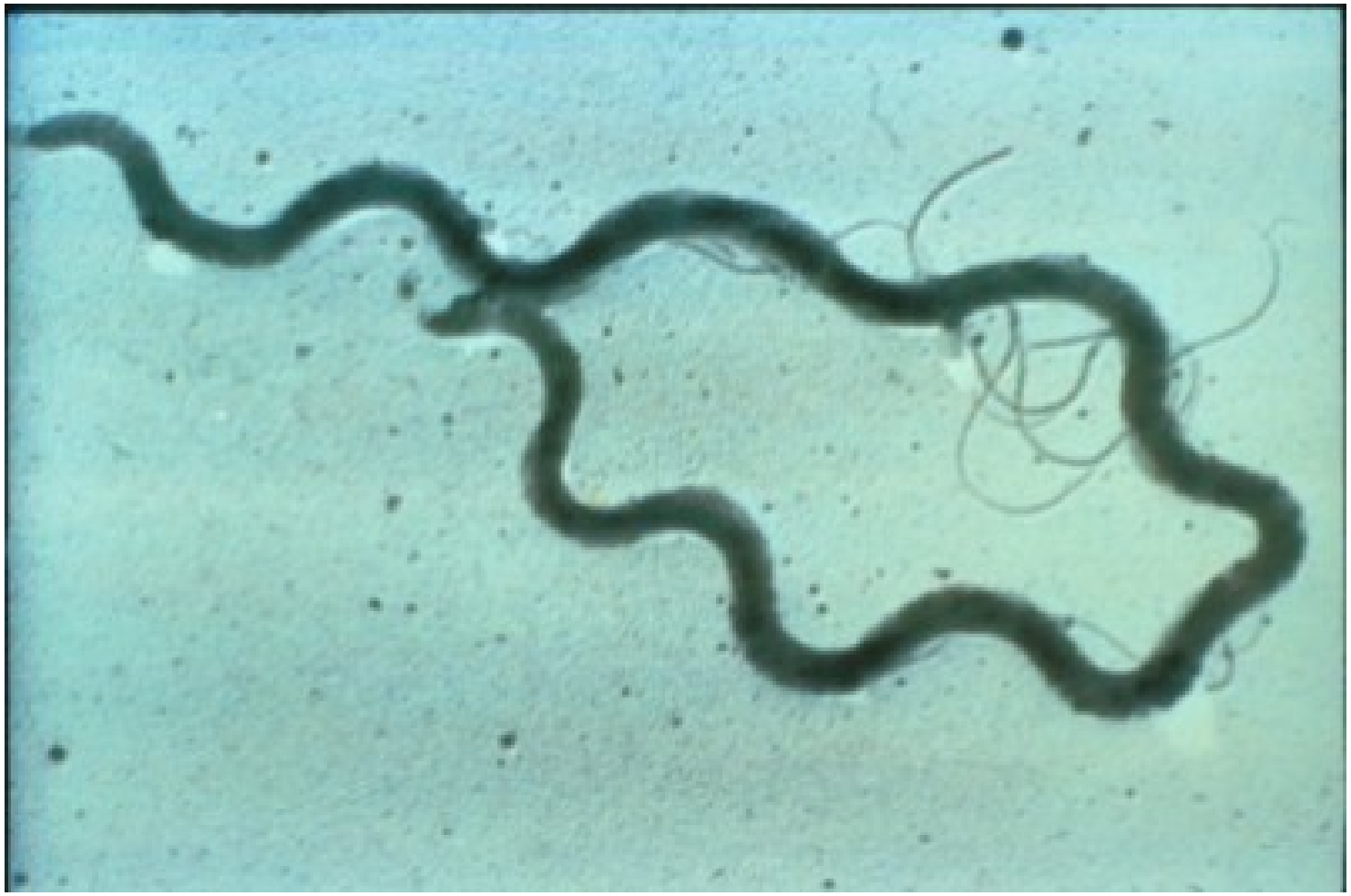
Treponema pallidum



Electron photomicrograph, 36,000 x.

Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

Pathology

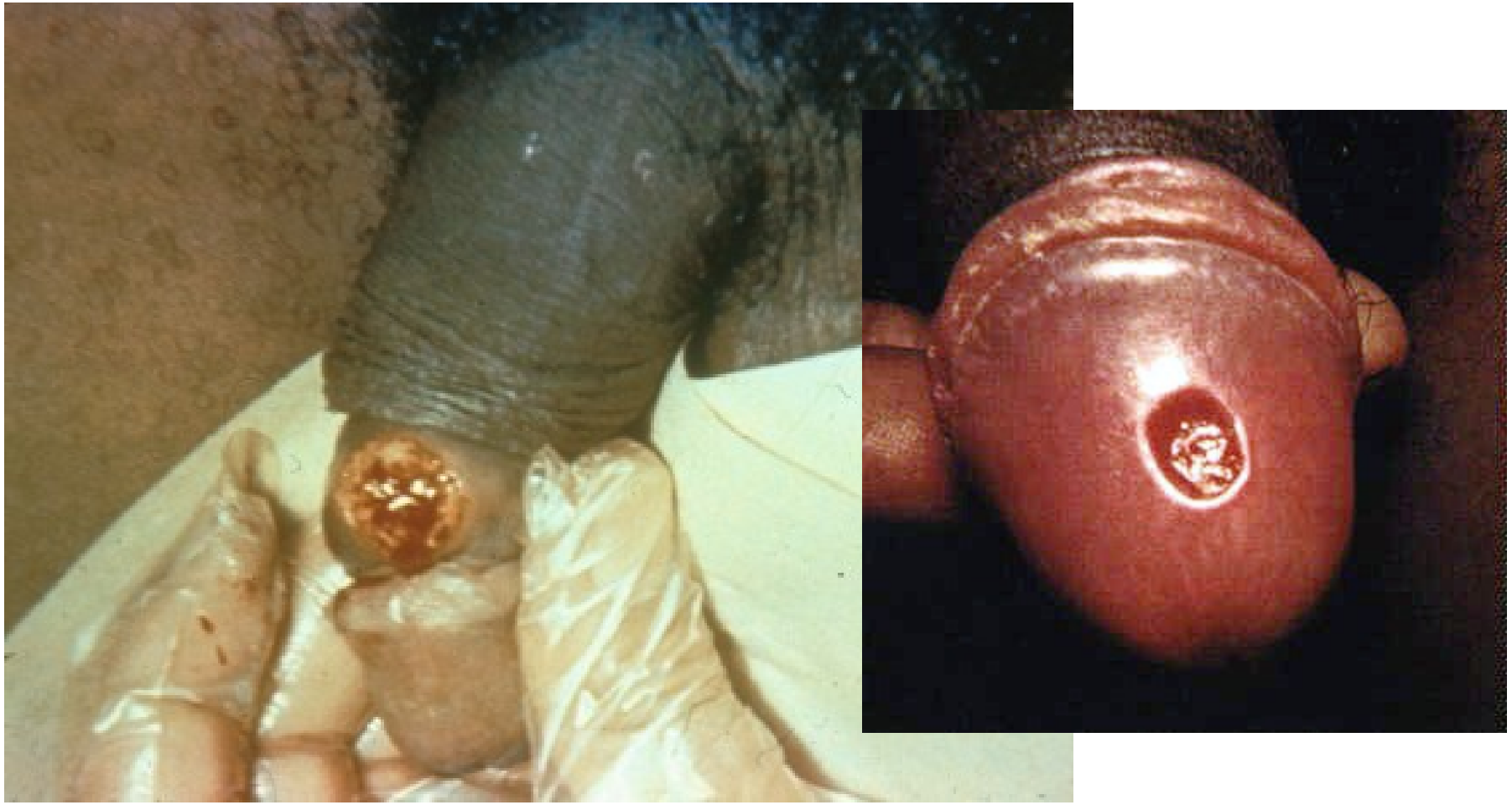
- Penetration:
  - *T. pallidum* enters the body via skin and mucous membranes through abrasions during sexual contact
  - Spread through placenta from mother to fetus during pregnancy

- Dissemination:
  - Travels via the circulatory system throughout the body
  - Invasion of the central nervous system (CNS) can occur during any stage of syphilis.

Primary syphilis

- Primary lesion or "chancre" develops at the site of inoculation.
- Chancre
  - Progresses from macule to papule to ulcer;
  - Typically painless, indurated, and has a clean base;
  - Highly infectious;
  - Heals spontaneously within 3 to 6 weeks; and
  - Multiple lesions can occur.
- Regional lymphadenopathy: classically rubbery, painless, bilateral
- Serologic tests for syphilis may not be positive during early primary syphilis.

Primary syphilis- penile chancre

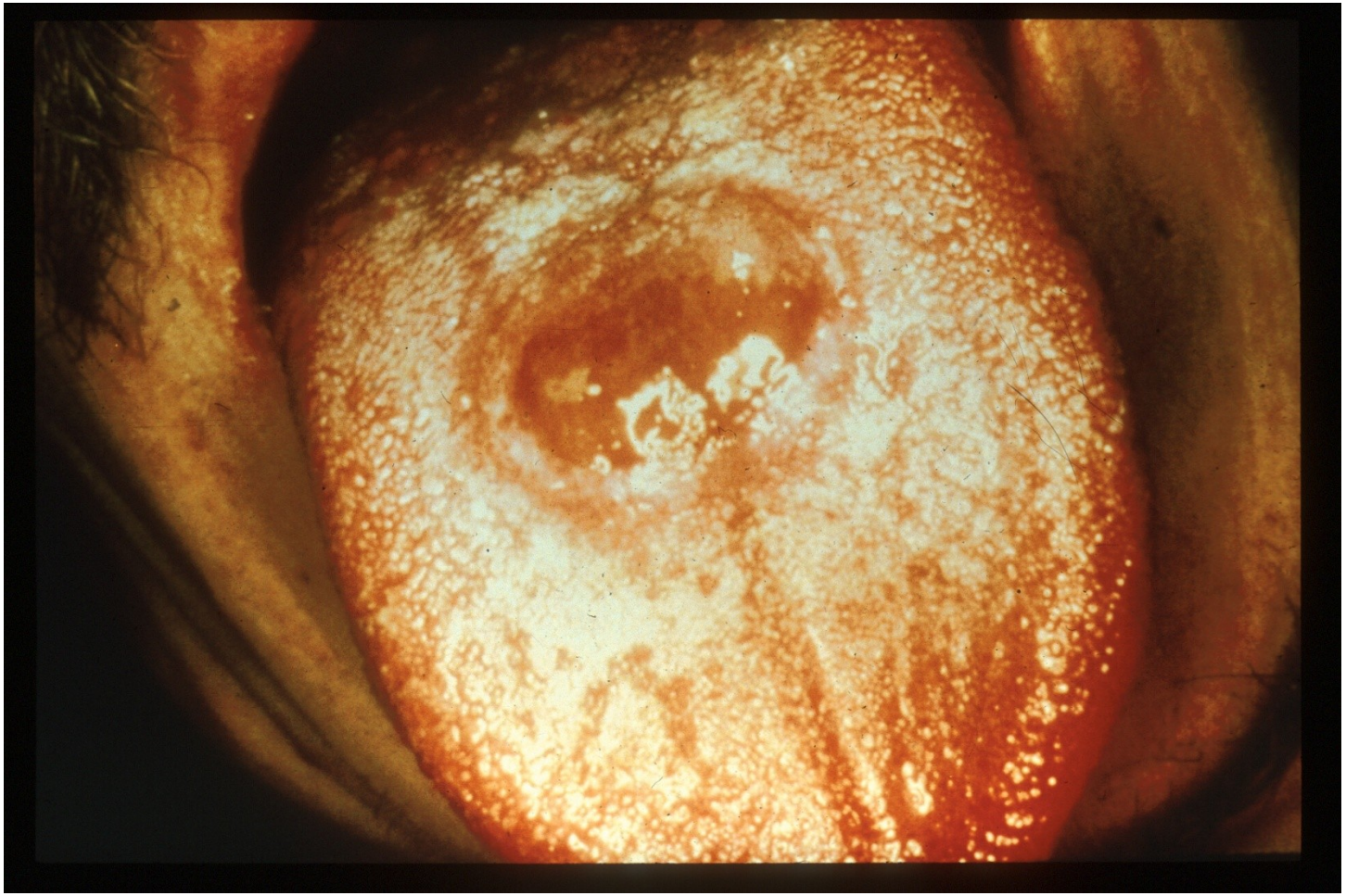


Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

Primary syphilis- labial chancre

Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

Primary syphilis- tongue chancre



Source: CDC/ NCHSTP/ Division of STD Prevention /STD Clinical Slides

2- Clinical Case - Aynalem

Three months later Hakim's story…

22 years-old woman.

Since 2 days skin rash on both sides round, red, non-itchy fat pathces 5-10 mm in diameter. Were involved also palms and sore.

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2- Clinical Case - Aynalem

Serological test for T. pallidum (RPR): positive

HIV test: negative

It' a case of secondary syphilis!

Should we…

1) Treat with penicillin (different from primary?)
2) Test for pregnancy, screen the partner and treat both
3) Treat syphilis to her, screen the partner and eventually treat

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2- Clinical Case - Aynalem

Pregnancy test was positive.

Treatment: penicillin G 2,4 milion units i.m. (one time)

The patients was fine and after nine months she gave birht a healthy baby.

Partner was positive to RPR. HIV test negative
He was treated with penicillin G but weekly for 3 weeks

Secondary syphilis

- Secondary lesions occur several weeks after the primary chancre appears; may persist for weeks to months.
- Primary and secondary stages may overlap
- Mucocutaneous lesions most common
- Clinical Manifestations:
  - Rash (75%–100%)
  - Lymphadenopathy (50%–86%)
  - Malaise
  - Mucous patches (6%–30%)
  - Condylomata lata (10%–20%)
  - Alopecia (5%)
  - Liver and kidney involvement can occur
  - Splenomegaly is occasionally present
- Serologic tests are usually highest in titer during this stage.

Treatment: penicillin G 2,4 milion units i.m. (one time)

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Latent syphilis

- Host suppresses infection, but no lesions are clinically apparent
- RPR test positive
- May occur between primary and secondary stages, between secondary relapses, and after secondary stage.
- Categories:
  - Early latent: <1 year duration; 25% will have a relapse of secondary stage signs. During this stage, patients are considered to be infectious due to the possibility of unrecognized relapse!!!
  - Late latent: ≥1 year duration; evaluate for clinical evidence of tertiary and ocular disease (CSF exam, if necessary!)

Treatment early latent: penicillin G 2,4 milion units i.m. (one time)
Treatment late latent: penicillin G 2,4 milion units i.m. q wk for 3 weeks

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Tertiary Syphilis

- Approximately 30% of untreated patients progress to the tertiary stage within 1 to 20 years.

- Rare because of the widespread availability and use of antibiotics.

- Manifestations
  - Gummatous lesions
  - Cardiovascular syphilis
  - NOT NEUROSYPHILIS

Treatment: penicillin G 2,4 milion units i.m. q wk for 3 weeks

Tertiary syphilis-ulcerating gumma

Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

Tertiary syphilis-gummata on forearm

Source: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

Neurosyphilis

- Occurs when *T. pallidum* invades the central nervous system (CNS)
- May occur at any stage of syphilis
- Can be asymptomatic
- Early neurosyphilis occurs a few months to a few years after infection (acute syphilitic meningitis, meningovascular syphilis, and ocular involvement)
- Neurologic involvement can occur decades after infection and is rarely seen (general paresis, tabes dorsalis, and ocular involvement)

Treatment: aqueous crystalline penicillin G 18-24 million units IV administered as 3-4 million units IV q4h x 10-14 d.

Number of small vesicles to come up on the mucous membranes of the genitalia (glans, penis, labia, cervix).
Vesicles burst and shallow ulcers develop. ARE VERY PAINFUL!
Near the ulcer the mucous membrane is red.

Any idea?

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Herpes genitalis

- Etiological agent: *Herpes simplex* type 2 (HSV2)
- Exists worldwide; in Ethiopia the prevalence range fro 39% to 41%.
- HSV2 is the most common cause of genital ulcer disease (GUD)
- Different clinical presentation from primary infection to recurrences
- HSV is capable of establishing latent infection in neuronal cells
- Sexual and vertical transmission
- HIV and HSV-2 co-infections are very common and both infections can facilitate acquisition of the other
- Genital herpes in pregnancy causes significant maternal morbidity, with an increasing number of infections due to oral–labial transmission.

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Sex Transm Infect. 2011 April ; 87(3): 183–190

International Journal of Infectious Diseases 79 (2019) 50–57

Pathology

- Penetration:
  - *HSV2* enters through mucosal surfaces or kin breaks and replicate locally, often with no clinical manifestations, during sexual contact
  - Fetal usually acquired intrapartum. Oral-labial transmission often post-partum.

- Dissemination:
  - Virus infects neurons and travel via the nerve; during recurrances HSV spreading peripherally along sensory nerve.
  - Can complicate in systemic infection

Herpes infection and HIV

Effect of HSV2 on HIV

- ↑HIV acquisition
- ↑HIV transmission
- ↑HIV level in plasma & genital tract

Effect of HIV on HSV2

- More frequent, prolonged and atypical lesions
- ↑Frequency of HSV2 shedding
- ↑HSV2 acquisition & transmission
- Acyclovir resistance with CD4+<50 cells/mmc

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Herpes infection and HIV

- Active HSV2 infection, regardless of symptoms, involves high concentrations of activated CD4+ cells in the genital area and can lead to breaks in the mucosal layer through which HIV can enter.

In case of HSV infection,
ALWAYS test for HIV!

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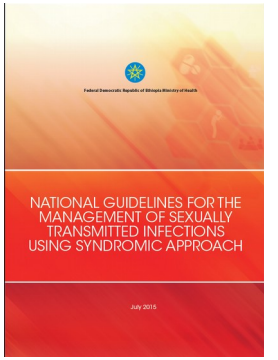
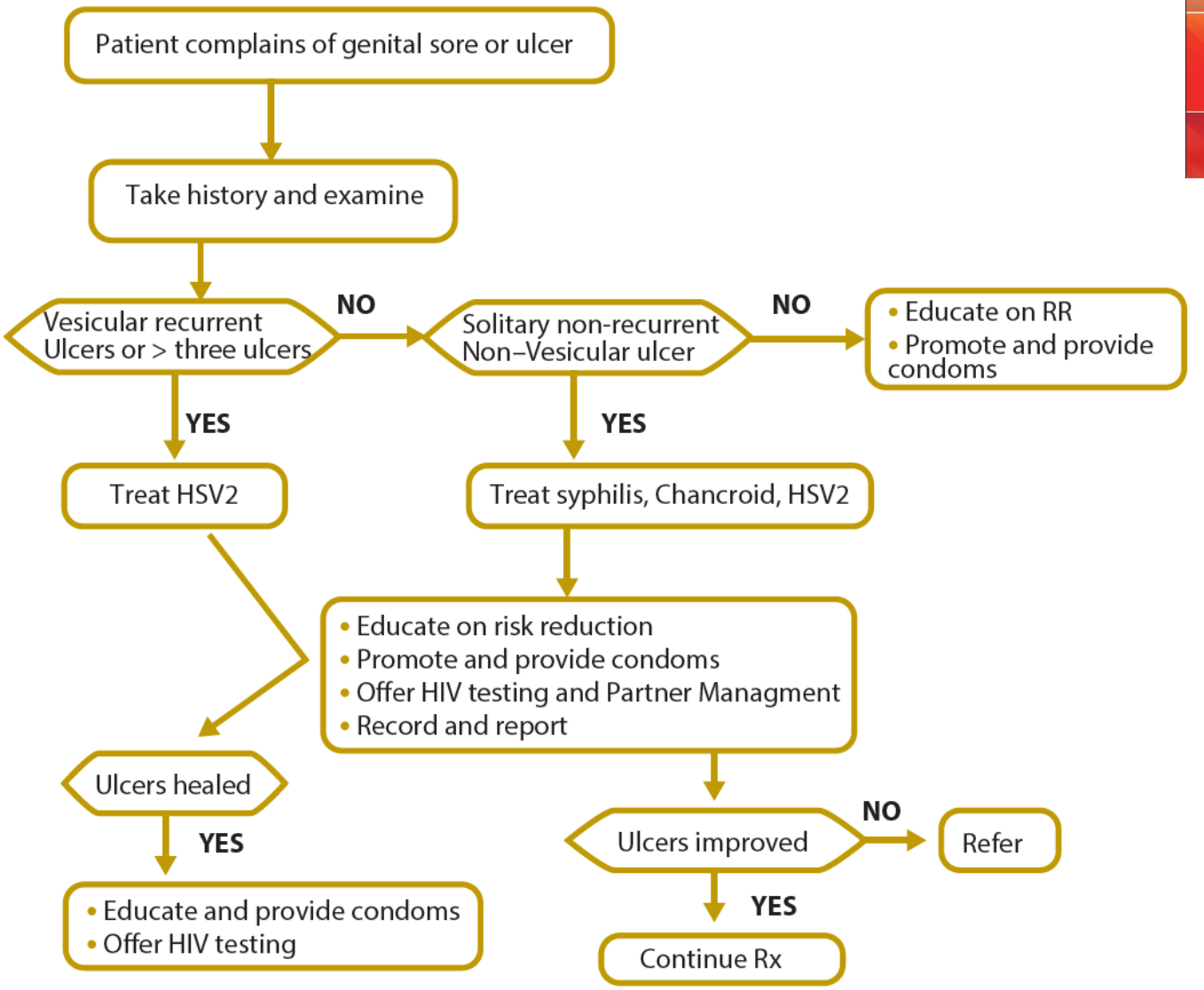
Figure 5. THE ALGORITHM OF SYNDROMIC CASE MANAGEMENT OF GENITAL ULCER SYNDROME





Treatment

1. **Treatment for Non- Vesicular Genital Ulcer**
   - *Benzathine penicillin 2.4 million units IM stat /Doxycycline(in penicillin allergy) 100mg bid for 14 days*

plus

   - *Ciprofloxacin 500mg bid orally for 3 days /Erythromycin 500mg tab qid for 7 days*

plus

   - *Acyclovir 400mg tid orally for 10 days (or 200mg five times per day of 10 day)*

2. **Treatment for Vesicular, multiple or recurrent genital ulcer**

Acyclovir 200 mg five times per day for 10 days

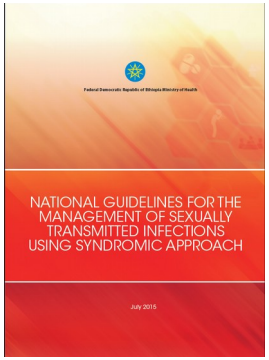
Or

Acyclovir 400 mg tid for 7 days

3. **Treatment for recurrent infection: Acyclovir 400 mg tid for 7 days**

Suppressive daily therapy for recurrence disease in PLHIV:

Acyclovir 400 mg bid or tid



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3- Clinical Case - Amadi

26 years- old man, HIV + since 1 year.
Therapy: TDF/FTC/EFV and CD4+ cell count 465/mmc

Since 4 days, report urethral discharge of yellow in copious amount; intensive pain with urine.

3- Clinical Case - Amadi

Patient said that had a unsafe sexual intercourse with a unkown partner one week before.

Physical exam: no fever, no vescicles on penis, no lymph node to the groin. Discharge from urethra was profuse and seems pus.

What do you suggest as diagnosis?

1) *Candida* infection
2) Gonorrhoea
3) Urinary tract infection

Gonorrhoea

Curr HIV Res. 2012 Apr; 10(3): 211-217

Ali et al. BMC Res Notes (2016) 9:439

- Etilogical agent: *Neisseria gonorrhoeae.*
- Is the second most common bacterial STI (*78 million new cases occurred in adolescents and adults aged 15-49 y.)*
- Global incidence rate of 19 per 1000 females and 24 per 1000 males
- In Ethiopia is the most common causative agents of urethral discharge syndrome (81%)
- Multiple sexual partners, sexually active age, unsafe sex practice, lower socio-economic status, urban residence and substance use are among the list of host related risk factors for acquiring the infection.
- In Africa the treatment of gonorrhea is almost empirical and antibiotics are generally given without considering sensitivity report

Curr HIV Res. 2012 Apr; 10(3): 211-217

Gonorrhoea

- Uncomplicated gonococcal infection manifests as urethritis in men and mucopurulent cervicitis in women.
- Pharyngeal infections in both men and women are largely asymptomatic. Proctitis, with anorectal pain, tenesmus and rectal discharge is one presentation of anorectal gonorrhea.
- Sexual and vertical transmission
- Gonococcal infections are often asymptomatic in women; unrecognized and untreated infection may lead to serious complications, including pelvic inflammatory disease, ectopic pregnancy and infertility.
- Untreated urethral infection in men can lead to epididymitis, urethral stricture and infertility.
- Infants of mothers with gonococcal infection can contract neonatal conjunctivitis, which may lead to blindness if left untreated.

But we have always to think about an other agent responsable for urethral discharge…

In Ethiopia, the second most frequent cause of urethritis is *Chlamydia trachomatis* (36.6%).

Symptoms are sub-acute (often asympthomatic or only dysuria) with scant discharge. If present, is white and mucoid (different from purulent of gonorrhea) .

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3- Clinical Case - Amadi

Our patients had definitely a gonorrhoea, but we can not exclude the presence of Chlamydia infection.

The signs and symptoms of complications, of the syndrome, if the infection is missed, are testicular pain and swelling, polyarthralgia, tenosynovitis, arthritis, skin lesions and constitutional symptoms (fever!).

Treatment: ceftriaxone 250 mg IM stat + azithromycin 1 gm p.o. stat

- Risk reduction
- Treatment compliance
- Proper and consistent use of condom
- Partner notification and management
- Importance of HIV testing
- Abstinence from sex till all symptoms resolve

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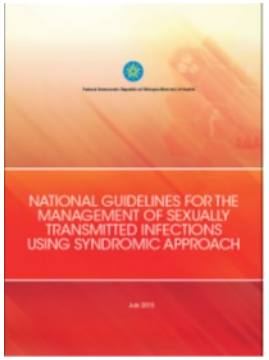
Figure 3. The algorithm of syndromic case management of urethral discharge syndrome



Urethral discharge syndrome flow chart in men

Complains of Urethral discharge or dysuria

Take history and Examine *(Milk urethra if necessary)*

Discharge present?

NO

Other STIs?

NO

- **Educate on RR**
- **Promote and provide condoms**

YES

- Treat for GC and CT
- Educate and counsel on risk reduction
- Offer HTC
- Promote the use and provide condoms
- Partner management
- Record and reporting
- Advise to return in 7 days if symptoms persist

YES

Use appropriate flow chart

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Neisseria/Chlamydia and HIV

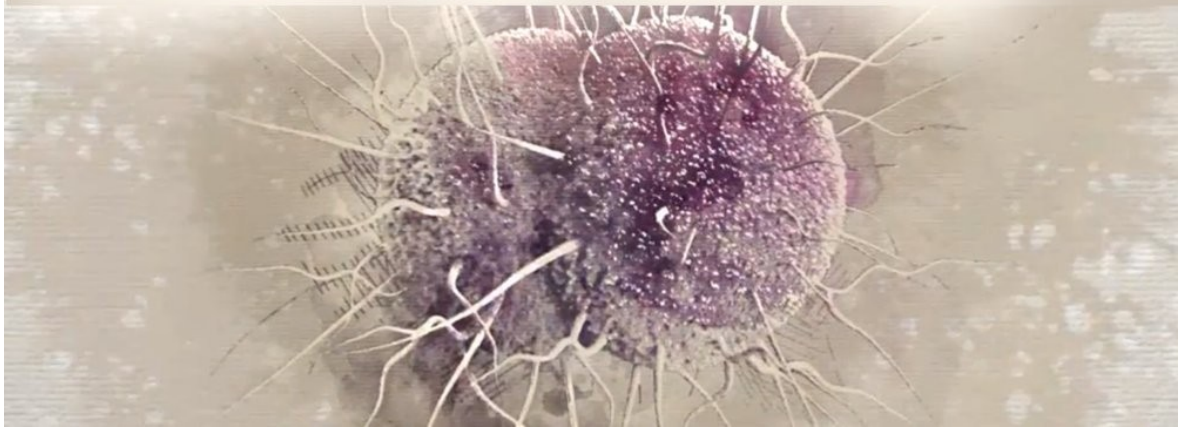
HIV concentrations in semen and vaginal fluids are directly associated with number of leukocytes (white blood cell) migrating to the genital tract. A dose-relationship exists between leukocyte concentrations, a marker for inflammatory processes, and HIV viral shedding.

HIV treatments reduce blood plasma viral load and may reduce infectiousness, but in presence of STDs, HIV shedding in the genital tract is well documented in men and women who have undetectable blood plasma viral load.

Gonorrhea and *Chlamydia*, for example, are associated with high concentrations of leukocytes in the genital tract, and therefore greater HIV shedding.

DRUG-RESISTANT GONORRHEA

AN URGENT PUBLIC HEALTH ISSUE



1930s: Introduction of sulfanomide antimicrobials to treat GC

1940s: Due to increasing resistance, sulfanomides no longer recommended for GC treatment; penicillin becomes treatment of choice

1980s: Due to increasing resistance, penicillin and tetracycline no longer recommended to treat GC

1990s: Fluoroquinolones become predominant treatment

2007: Fluoroquinolones no longer recommended; cephalosporins (incl. injectable ceftriaxone and oral cefiximine) become backbone of GC treatment

2012: Cefixime no longer recommended as first-line regimen, leaving ceftriaxone-based dual treatment as last recommended treatment

2015: Ceftriaxone plus azithromycin is the only recommended treatment for treating GC

1930 1940 1950 1960 1970 1980 1990 2000 2010 2015

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A ntibiotic susceptibility profile of *N. gonorrhoeae* isolates from S eptember 2006 to J une 2012, ANRS, E thiopia

Antimicrobial agent	Percent non-susceptibility	95% confidence intervals
Ceftriaxone	27.8	(9.7, 53.5)
Penicillin G	94.4	(72.7, 99.9)
Tetracycline	92.6	(75.7, 99.1)
Ciprofloxacin	40.9	(20.7, 63.6)
Ceftriaxone and Penicillin G	35.7	(12.8, 64.9)
Ceftriaxone and Tetracycline	31.3	(11.1, 58.7)
Ceftriaxone and Ciprofloxacin	20	(4.3, 48.1)
Penicillin G and Tetracycline	87.5	(61.7, 98.4)
Penicillin G and Ciprofloxacin	66.7	(34.9, 90.1)
Tetracycline and Ciprofloxacin	38.1	(18.1, 61.6)
Multi drug non-susceptibility	27.8	(9.7, 53.5)
Other triple non-susceptibility	63.6	(30.8, 89.1)
All four drugs non-susceptibility	27.3	(6.0, 61.0)

The most important recommendation to give to patients is:

COMPLIANCE TO TREATMENT AND COUNSEL ON RISK REDUCTION!

The most important thing to remember for a health worker:

TRY TO IDENTIFY THE PARTNER(S), SCREEN AND TREAT ALL

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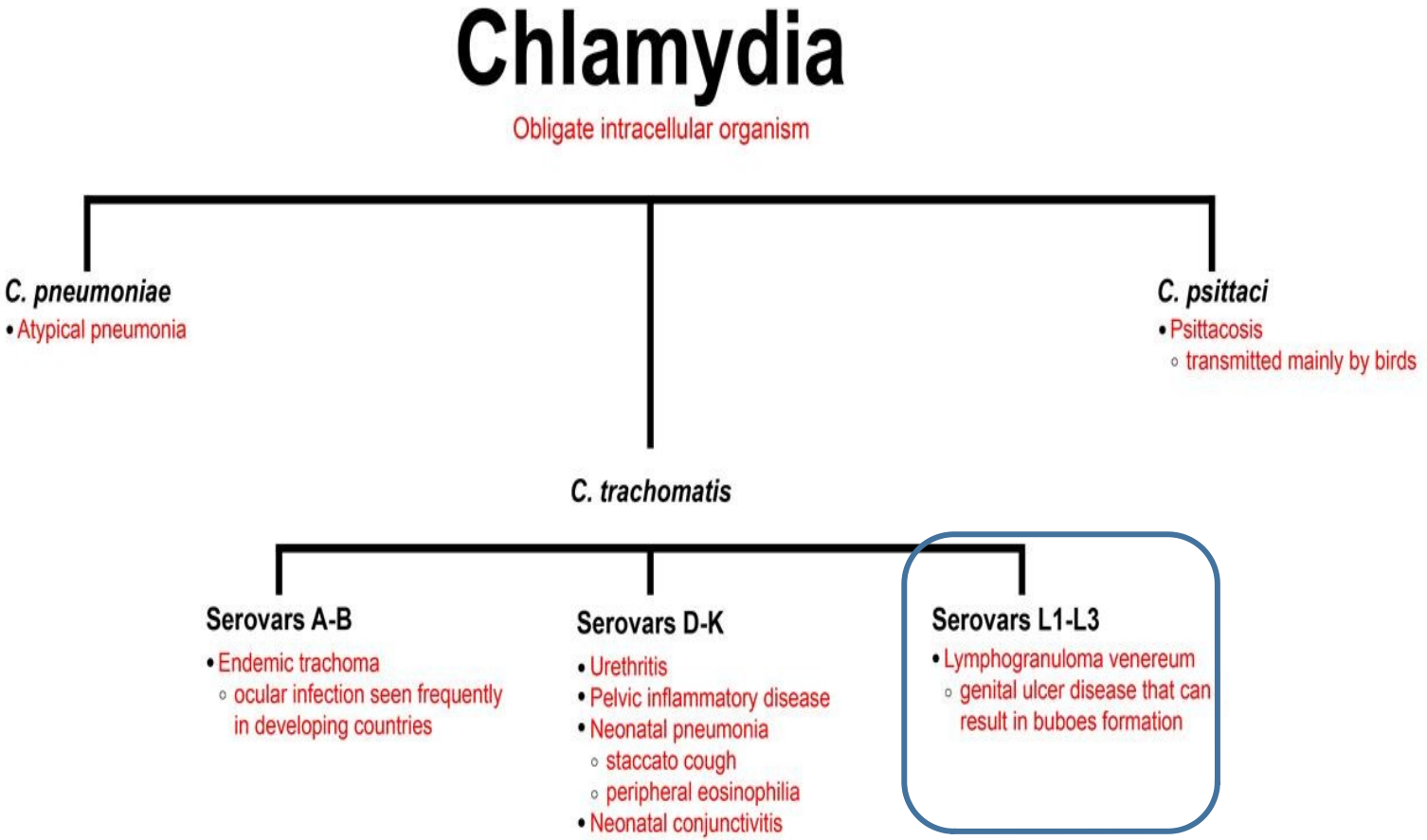
Do you remember *Chlamydia trachomatis* in the last case?
Urethritis is not the only syndrom cause by this agent…

Lymphogranuloma venereum
(swallen glands)

Lymphogranuloma venereum is caused by *Chlamydia trachomatis serovar L1-L2-L3*



Lymphogranuloma venereum

- One to three weeks after infection: small blister or ulcer appears on the genitalia (also anal region) which is usually not noticed (differential diagnosis with syphilis or HSV2!)

- 2-6 weeks later: lymph nodes in the groin become enlarged and inflamed. Pus forms in the lymph nodes which then burst. Abscesses can join to make large ulcers. Rarely complications of this stage include febrile arthritis, pneumonitis, and perihepatitis

COMPLICATIONS

- Fistula or sinus formation
- Extensive ulceration of genitalia
- Proctocolitis with tenesmus and bloody purulent discharge.
- Chronic untreated LGV may result in lymphatic obstruction, elephantiasis of the genitalia.

National guidelines for management of STDs in Ethiopia- 2015

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Treatment

Doxycycline 100 mg bid orally for 14 d/Erythromycin 500 mg orally qid for 14 d

In HIV + patients:

- Use the same regimen (doxycycline and erythromycin) as in HIV-negative persons.

- Prolonged therapy may be needed due to delay in resolution of lesions.

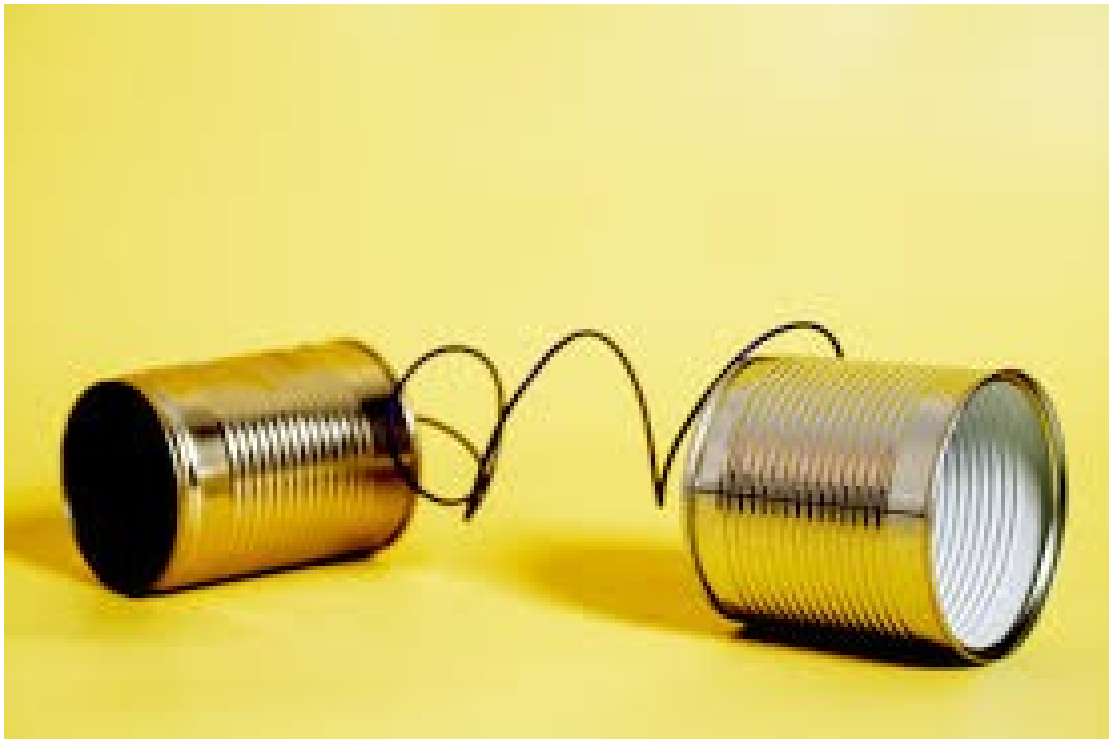
Health education and counselling

In health education, the aim is to make the patient better informed, so that he/she can make an informed choice of sexual behavior and practices.

Counseling relates more to issues of anxiety and coping with the infection or its biomedical as well as social consequences.

The AIM of risk reduction counseling and education for STI patients include:

- Help patients re-examine long-standing habits and situation that are putting them at risk
- Prevent further transmission to others
- Remain free of infection in the future
- Promote partner notification, treatment and education
- Promote treatment adherence
- Enhance coping with the STI and its social consequences




There Is No Judgement Here....

Health Workers attitude

Service providers have been faced with the realities of the HIV epidemic and the critical role of sexual risk reduction behavior.

STIs and HIV cannot be addressed effectively without a FRANK AND DIRECT dialogue about sexual practices.

Health care providers should be aware that the following issues can make sexual practices difficult to discuss:

- Cultural taboos: to discuss explicit sexual practices
- Discomfort: in both service provider and client
- Biases: perceptions about "the sort of clients who are infected with a STI"
- Personal values: allowing personal views and attitudes to interfere with their professional obligation to provide non-judgmental and respectful services to clients
- Lack of Knowledge: unfamiliarity with local preferences and customs

Primary prevention

(Measures that can employ to avoid STIs)

Abstinence: «wait until you feel ready…

Mutually faithful sexual relationship

Correct use of condoms

Safe sex practices: no unsafe sex!

Secondary prevention

(Promoting STI care-seeking behavior)

Promoting non-stigmatizing and non-discriminatory health services

Making correct diagnosis of STDs

Providing correct antimicrobial therapy for STDs

Offer voluntary HIV testing and counseling

Educate on treatment compliance

Advise on how the patient's partner may be treated

Take home messages

Any suggestions? Help me to formulate!!!

-

-

-

-

thank you

novella.cesta@gmail.com