SEXUALLY TRANSMITTED INFECTIONS

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Chancroid

- Genital papule or pustule
- Painful ulcer.
- May have “kissing” ulcerations.
- Painful, unilateral lymphadenopathy
- Hemophilus ducreyi (gram negative bacillus). Requires X factor (hematin) and a 5% CO_2 atmosphere for growth.
- Polysaccharide capsule as virulence factor.
- Produces IgA protease.
- Responds to azithromycin or ceftriaxone
- Should treat sexual partner as well.
- Condom use.

Chancroid

Painful ulcer with marked surrounding erythema and edema.

(Courtesy of Prof. Alfred Eichmann, MD.)

Fig. 30-27 Accessed 07/01/2010

Bacterial vaginosis

- Thin, homogeneous discharge that adheres to the vaginal walls
- Elevated pH > 4.5 (anterior vaginal fornix)
- Addition of KOH to discharge elicits characteristic fishy odor
- Presence of clue cells on microscopic examination of wet mount (epithelial cells studded with large numbers of bacteria, Gardnerella vaginalis, which obscure the cells border)
- If woman has three episodes of bacterial vaginosis with same sexual partner, the partner should be treated as well with metronidazole.
- Condom use.

Syphilis

- Treponema pallidum
- Spirochete
- An obligate pathogen.
- May be visualized with darkfield microscopy.
- Lipopolysaccharide outer membrane.
- Produce hyaluronidase (facilitate perivascular entry) and is coated with host-cell fibronectin (preventing phagocytosis).
- B-cell response leads to inflammatory damage of small vessels and obliterative endarteritis.
- T-cell response leads to granuloma formation.

Primary syphilis

A 28-year-old male with penile lesion for 7 days. Painless ulcer on distal penile shaft with smaller erosion on the glans. The ulcer is quite firm on palpation.

Fig. 30-18 Accessed 07/01/2010

Primary syphilis

- Painless chancre develops at inoculation site.
- 3-4 week incubation (10-90 day range).
- Begins as papule then erodes to painless ulcer with raised borders.
- Usually present on genitalia.
- Ulcer is highly contagious as is the site of replicating spirochetes.
- Darkfield exam is positive.
- Painless regional lymphadenopathy develops weeks after chancre.
- Ulcer heals on its own by 2 mos.
- RPR or VDRL likely negative in primary syphilis.

Secondary syphilis

- Early latent.
- Exposure less than one year and no clinical signs.
- RPR or VDRL positive
- FTA confirmation.

Secondary syphilis

- Secondary. Exposure less than a year and clinical signs of ulceration or rash.
- Begins as flu-like syndrome usually 4-10 weeks after appearance of chancre.
- Several days later a copper-colored rash (macular, papular, or pustular) can cover entire skin surface including palms and soles.
- Resolves after several months.
- Rash is highly infectious.
- May manifest with optic neuritis, arthropathy.
- Responds to penicillin.

Secondary syphilis

B

A

Papulosquamous truncal eruption (left); palmar eruption (right). May see mucosal lesions as well. Occur up to 3 months following primary infection.

Figs. 30-21B and 30-22A Accessed 07/16/2010

Tertiary syphilis

- Late Latent. Exposure more than one year and no clinical signs. RPR or VDRL may be negative; FTA confirmation.
- Aneurysm of thoracic aorta. Blindness and dementia may also be presenting signs in tertiary syphilis.
- The gumma is a scar-like granulomatous lesion that may be found on skin or in other organs.
- Endarteritis and a plasma cell infiltration are clues to its origin.

Tertiary syphilis

- Tertiary.
- Without neurologic signs.
- RPR or VDRL may be negative
- FTA confirmation.
- With neurologic signs.
- RPR or VDRL may be negative
- FTA confirmation.

Treatment

- Responds to penicillin.
- All sexual contacts require treatment.
- Though there is no clinical trial to demonstrate efficacy, tetracycline is used if the patient is allergic to penicillin.
- Worsening of symptoms with antibiotic therapy is the Jarisch-Herxheimer reaction.

Chlamydia

- Clear discharge
- Often asymptomatic
- Obligate intracellular parasite.
- Cannot make own ATP.
- No peptidoglycan.
- Infective form is an elementary body that reproduces in phagosomes.
- Initial body found only in phagosome
- Reverts to elementary body as host cell dies.
- C. trachomatis visualized as glycogen filled cytoplasmic inclusion in cells.

Chlamydia

- DNA Probe analysis for C. trachomatis
- Type L causes lymphogranuloma venereum
- Responds to azithromycin or doxycycline
- Should treat sexual partner as well.

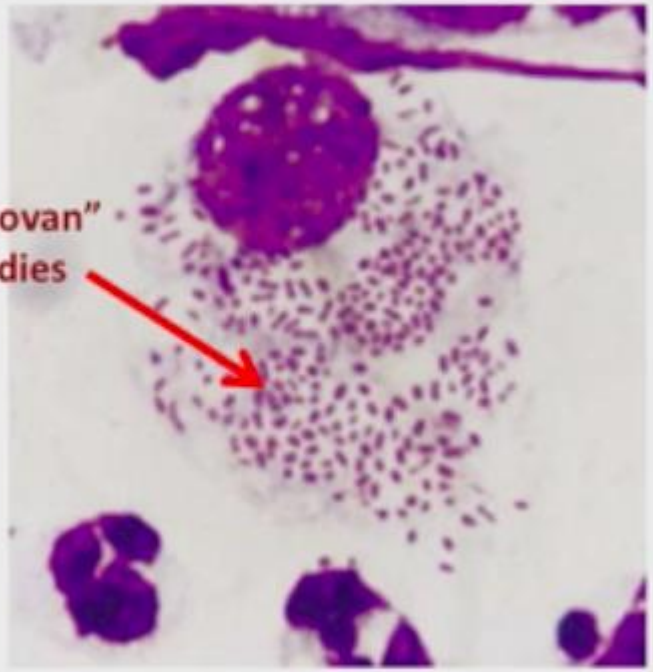
Lymphogranuloma venereum

- Caused by serotypes L1, L2 and L3.
- Acquired by abrasions.
- Characterized by transient papules on external genitalia followed by 1-2 months by painful swelling of inguinal and peri-rectal lymph nodes.
- The affected lymph nodes are those that drain the primary site of infection.
- The lesions that develop become necrotic and attracts granulocytes.
- Responds to azithromycin.

Granuloma inguinale

- Occurs in tropical regions
- Painless, slowly progressive ulcerative lesions on the genitals or perineum without regional lymphadenopathy
- Subcutaneous granulomas (pseudobuboes) may be seen.
- The lesions are highly vascular (i.e., beefy red appearance) and bleed.
- Extragenital infection can occur
- “Donovan bodies” are blue-black chromatin condensations in cytoplasm of large mononuclear cells
- Responds to azithromycin

Clinical Syndromes



Giemsa staining of
K. granulomatis in genital lesion

A penile ulcer by
K. granulomatis

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Gonorrhea

- Dysuria, discharge.
- Women may be asymptomatic.
- Gram negative intracellular diplococci.
- Growth on Thayer-Martin media.
- Acid production with glucose metabolism. Proliferates in phagocytic vacuoles.
- Produces IgA protease.
- Attach by pili.
- Lipo-oligosaccharide wall (no capsule).
- Protein-1 and OMP1 inflammatory mediators.
- DNA Probe analysis for N. gonorrhoeae

Gonorrhea

- Ceftriaxone or cefixime as drug of choice.
- Tetracycline (spectinomycin) if penicillin sensitive.
- Concomitant treatment for chlamydia
- Should treat all sexual contacts.

Ureaplasma urealyticum

- No murein cell wall.
- Distinct from Mycoplasma because of the urease activity.
- Main reservoir is the genital tract of sexually active men and women.
- Rarely found before puberty.
- Occurs in 80% of individuals who have had >3 sexual partners.
- Estimated that half of the cases of Non Gonococcal Urethritis in men are caused by Ureaplasma.
- In women, Ureaplasma is associated with chorioamnionitis and postpartum fever.

Non-specific urethritis/cervicitis

- Most common STD in US.
- Highest prevalence among sexually active teens
- Rate exceeds 5% in men and 10% women
- One third to one half of all male contacts of females with cervicitis develop urethritis after 2-6 weeks
- Penile discharge, dysuria, itch in men
- Vaginal discharge, itch in women
- Gram stain with 5 or more WBC's per high power field
- AND no organism identified on culture.
- Responds to single dose azithromycin or use of doxycycline for 7 days

Candidiasis

- White creamy or “cottage cheese” vaginal discharge OR
- Reddening of glans penis (Balanitis).
- Buds or pseudohyphae on wet mount
- Fluconazole once orally should eradicate infection
- Vaginal suppository may relieve immediate symptoms.
- Balanitis may be treated with topical steroid and antifungal.
- Should treat sexual partner as well.

Trichomonas

- Frothy green or gray vaginal discharge (women)
- Urethral itch with frothy discharge (men)
- Men may be asymptomatic
- Visualization of Trichomonas vaginalis on wet mount preparation diagnostic
- Responds to single dose of metronidazole (given orally or rectally or vaginally)
- Should treat sexual partner as well.
- Condom use.

Herpes simplex virus-1

- Illness begins with abrupt onset of fever, anorexia.
- Lasts 2-3 weeks with virus shedding beginning 7-10 days post-infection.
- May be aysmptomatic during this period.
- 12 to 96 days after constitutional symptoms, mouth becomes sore (Gingivitis).
- May complain of sensation of “swallowing glass.”
- Pathognomomic are vesicles that become ulcers
- Found on mucosal tissues
- Virus transmitted with oral sex.
- Treated with acyclovir.
- Infect trigeminal ganglion.

Herpes simplex virus-2

- 2-7 day incubation period.
- In men, painful vesicles appear on the glans penis or the penile shaft.
- May be multiple
- In women
- Painful vesicles in cervix, vagina.
- May complain of burning sensation.
- Profuse watery discharge.
- Extragenital lesions may appear on thigh, buttocks, perineum.

Herpes simplex virus-2

- Fever, dysuria, bilateral inguinal and pelvic adenopathy
- The development of headache and photophobia may be the result of HSV-2 infecting the sacral dorsal ganglia and ascending to the CNS.
- First episode treated with valacyclovir.
- If recurrent, may use suppressive therapy with famciclovir or valacyclovir
- Treat sexual partner.
- Condom use.
- May be transmitted to infant transiting vagina.
- Active infection may be a reason for C-section.

Human papillomavirus

- Human papilloma viruses 1 and 4 are the most common causes of verrucae.
- Appearance of verruca depends upon which viral strain infects and the site of infection.
- Regress over time.
- Papillomas of oropharynx, larynx are commonly cuased by HPV-6, HPV-11.
- Anogenital warts (condylomata accuminata) are generally caused by HPV-6 or HPV-11.
- Present as papules but may have cauliflower appearance.
- Cervical dysplasia and neoplasia are associated with HPV-16 and HPV-18.

Human papillomavirus

- The virus does not have an envelope.
- E6, E7 proteins inactivate p53 and RB genes (upregulate cyclin E) respectively as well as induce centrosome duplication.
- E6 also upregulates telomerase.
- Perinuclear halo noted in cervical cells on Pap smear.
- May be reported as atypical cells of unknown significance.
- DNA probe for HPV

Human papillomavirus

- External genitalia warts and perianal warts respond to Imiquimod.
- Imiquimod activates the body's immune response through the toll-like receptor. Imiquimod disrupts cytokine activity and simultaneously attacks the body's mucus membrane tissues.
- Imiquimod does not prevent the emergence of new warts.
- Cryotherapy (liquid nitrogen or cryoprobe)
- Podophyllin (not to be used with anal warts) or topical 5-FU for non-mucosal lesions
- Consider administration of HPV vaccine to patient as well as sexual partner.

Condyloma lata

Fig. e5-20 Accessed 07/01/2010

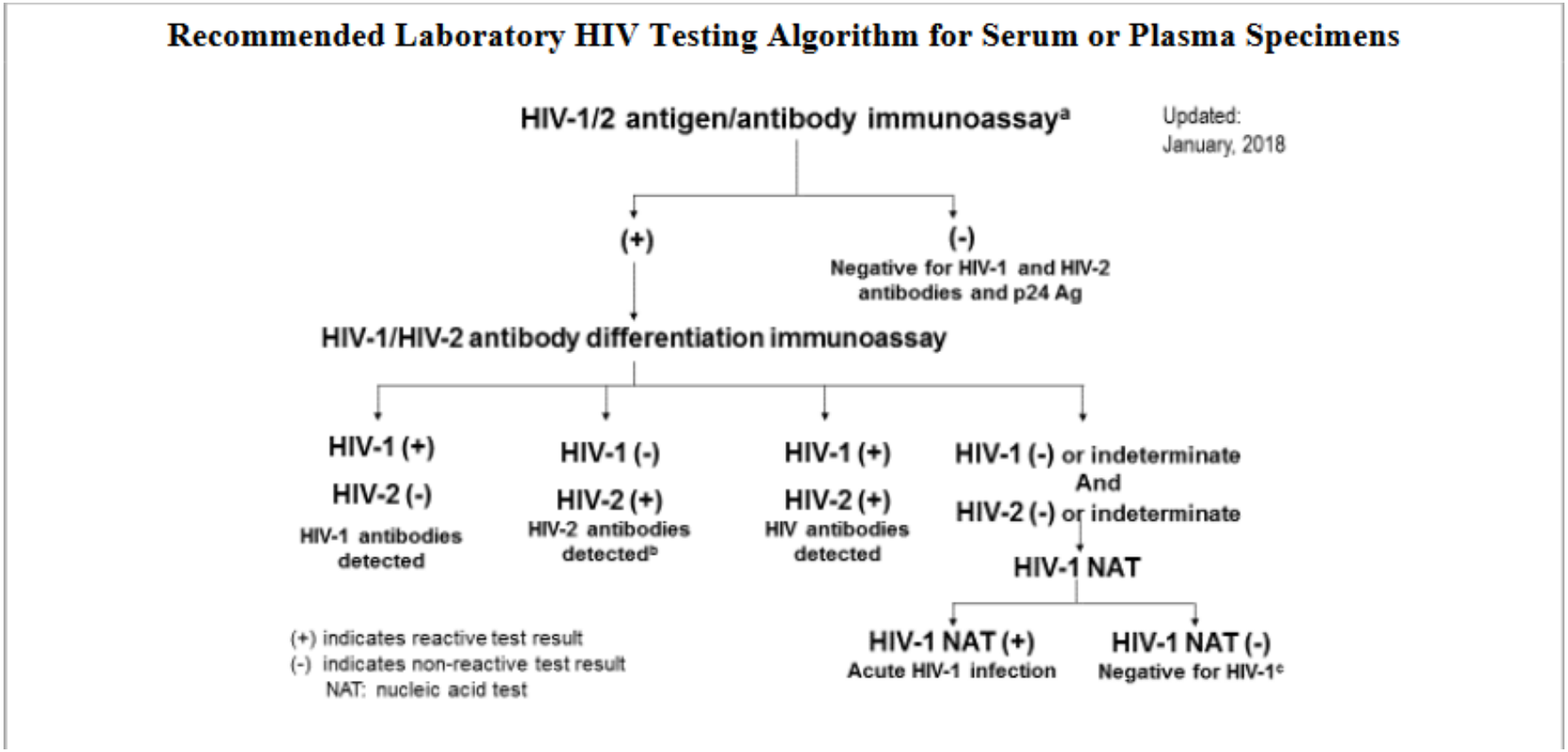
HIV

- Initial infection may present as flu-like syndrome with generalized adenopathy.
- HIV Tropism
- T and M-Tropic R5 virus in 90%
- Attracted to CCR5 co-receptors (macrophages)
- Allows entry early in infection.
- T-Tropic X4 virus.
- Attracted to CXCR4 co-receptors (T-cells)
- Allows entry
- Occurs late in infection.
- Correlates with rapid progression to AIDS.

HIV

- Very rapid decrease in GALT CD4 lymphocytes.
- Slow progressive decrease in circulating CD4 lymphocytes.
- 70% of patients experience a “mononucleosis syndrome” of fever, rash, sore throat, lymphadenopathy, and a flu-like syndrome with athralgia, headache, and diarrhea.
- EBV VCA and CMV antibody negative as clues.

Antibodies to gp41 and p24 antigens are the first detectable serologic markers following HIV infection



https://stacks.cdc.gov/view/cdc/50872

Percentage of patients progressing to AIDS within 3 years if untreated

	HIV RNA <500 copies/ml	HIV RNA >3000-10,000 copies/ml	HIV RNA >10,000-30,000 copies/ml	HIV RNA >30,000 copies/ml
CD4 >750 cells/uL	0	3.2	9.5	32.6
CD4 <750 cells/uL	3.7	8.2	40.1	47.9

When to initiate ART

- The optimal time to initiate antiretroviral therapy in adult patients with CD4 count >350 cells/μl is not well defined.
- For HIV-infected patients older than 50 years of age, antiretroviral therapy (ART) is recommended for all, regardless of CD4 cell count.
- Older patients frequently have a blunted immune response
- Older patients have high virologic response rates.
- Older patients have relatively poor CD4 cell increases in response to antiretroviral therapy as measured by an increase of CD4 count by 100 cells/fl

When to initiate ART

- Older HIV-infected patients have a greater risk of developing serious non-AIDS complications.
- Patients >55 years old may be at higher clinical risk even after starting therapy
- The administration of ART during pregnancy or intrapartum significantly reduces the risk of mother-to-child transmission
- A 96% reduction in transmission between sero-discordant heterosexual couples when the positive partner was receiving ART

ART complications

- ART initiation is associated with a risk of immune reconstitution inflammatory syndrome (IRIS).
- IRIS is a clinical syndrome characterized by new or worsening infectious and non-infectious complications observed after the initiation of ART
- The risk of IRIS increases when ART is begun:
- At low CD4 cell counts (<100 cells/fl)
- With the presence of cryptococcal or TB meningitis
- With cutaneous Kaposi’s sarcoma

When to initiate ART therapy in children

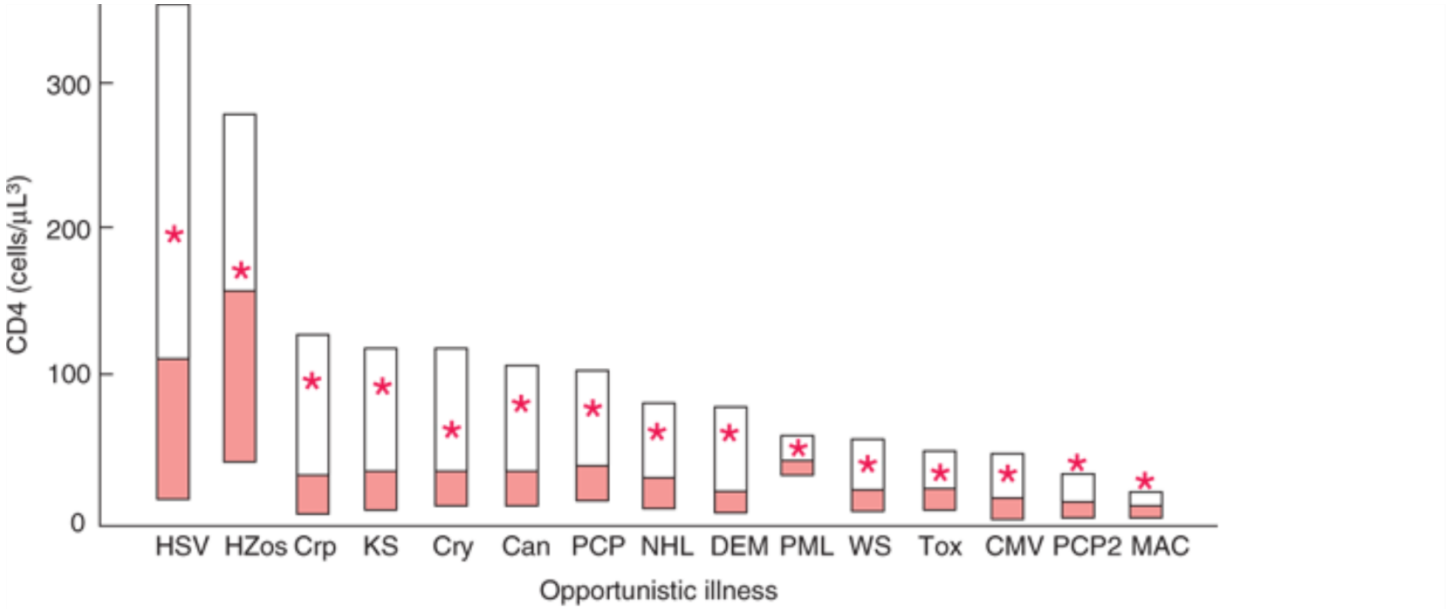
- Antiretroviral therapy is initiated in infants <12 months of age regardless of clinical status, CD4 count, or viral load.
- The 1-year risk of AIDS or death is substantially higher in younger than older children at any given level of CD4 count, particularly for infants age <12 months.
- Always test for drug resistance.

Pre-exposure protection

Table 10: Recommended Oral PrEP Medications

Generic Name	Trade Name	Dose
Tenofovir disoproxil fumarate (TDF)	Viread	300 mg
Emtricitabine (FTC)[a]	Emtriva	200 mg
TDF + FTC	Truvada	300mg/200 mg

CD4 counts and development of opportunistic infections



Boxplot of the median (line inside the box), first quartile (bottom of the box), third quartile (top of the box), and mean (asterisk) CD4+ lymphocyte count at the time of the development of opportunistic disease. Can, candidal esophagitis; CMV, cytomegalovirus infection; Crp, cryptosporidiosis; Cry, cryptococcal meningitis; DEM, AIDS dementia complex; HSV, herpes simplex virus infection; HZos, herpes zoster; KS, Kaposi's sarcoma; MAC, Mycobacterium avium complex bacteremia; NHL, non-Hodgkin's lymphoma; PCP, primary Pneumocystis jiroveci pneumonia; PCP2, secondary P. jiroveci pneumonia; PML, progressive multifocal leukoencephalopathy; Tox, Toxoplasma gondii encephalitis; WS, wasting syndrome. (From RD Moore, RE Chaisson: Ann Intern Med 124:633, 1996.)

Accessed 02/03/2016