

Sexually Transmitted Diseases

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Objectives:

1. Identify risk factors associated with sexually transmitted diseases (STDs)
2. Understand the incidence of STD's in relation to each other
3. Name the pathogen responsible for a given STD
4. Describe the hallmark signs and symptoms of a given STD
5. Recognize first line therapy for a given STD
6. Given a clinical scenario, be prepared to develop a specific drug treatment plan for the patient

I. ETIOLOGY

- A. Transmission of 20-24 organisms is possible through sexual contact between humans including:
 - Vaginal intercourse
 - Anal intercourse
 - Oral-genital intercourse
 - Oral-anal intercourse
- B. Common sites of infection include:
 - Genitals
 - Urinary tract
 - Pharynx
 - Rectum
 - Perineum
 - Eyes (children and adults)
 - Systemic
- C. Risk Factors
 - Sexually active < 25 years
 - Multiple sexual partners within the previous 6 months
 - Previous history of STD
 - Prostitutes, homosexuals, and drug abusers
 - Persons having sexual contact with prostitutes, homosexuals, and drug abusers
 - Inmates of detention centers
- D. Higher Risk
 - Young: two-thirds of all STD's occur in people in their teens and twenties
 - Single > separated > divorced > married
 - Male vs Female: rates are now thought to be similar due to higher number of asymptomatic infections in females
 - Number of sexual partners (more is not always better)
- E. Appropriate Care
 - History
 - Behavioral risk assessment
 - Physical exam
 - Laboratory exam
 - Diagnosis
 - Curative or palliative therapy
 - Counseling and education
 - Present episode of STD
 - Prevention of future episodes
 - Reporting of case when required
 - Sexual partner identification, notification, evaluation

F. Control of STD

- Education of persons at risk on the modes of disease transmission and the means for reducing the risk of transmission
- Detection of infection in asymptomatic persons and in persons who are symptomatic but unlikely to seek diagnostic and treatment services
- Effective diagnosis and treatment of persons who are infected
- Evaluation, treatment, and counseling of sex partners of persons with a STD

II. DISEASE BY CLASSIFICATION

A. Diseases characterized by genital ulcers:

- Chancroid
- Syphilis
- Lymphogranuloma venereum
- Genital Herpes Simplex

B. Diseases characterized by urethritis and cervicitis:

- Nongonococcal urethritis
- Gonococcal infections
- Mucopurulent cervicitis
- Chlamydial infections

C. Vaginal diseases:

- Trichomoniasis
- Vulvovaginal candidiasis
- Bacterial vaginosis

D. Miscellaneous:

- Epididymitis
- Pelvic inflammatory disease
- Sexually transmitted enteric infections
- Genital warts
- Ectoparasitic infections

E. HIV/AIDS

III. DISEASE BY PATHOGEN

Disease	Associated Pathogen
Bacterial	
Gonorrhea	<i>Neisseria gonorrhoeae</i>
Syphilis	<i>Treponema pallidum</i>
Chancroid	<i>Hemophilus ducreyi</i>
Enteric disease	<i>Salmonella</i> spp., <i>Shigella</i> spp.
Bacterial vaginosis	<i>Gardnerella vaginalis</i> , <i>Mycoplasma hominis</i>
Chlamydial	
Nongonococcal urethritis	<i>Chlamydia trachomatis</i>
Lymphogranuloma venereum	<i>Chlamydia trachomatis</i> , type L
Viral	
Herpes genitalis	Herpes simplex virus, types I and II
Hepatitis B	Hepatitis B virus
Condylomata acuminata	Human papillomavirus
Protozoal	
Trichomoniasis	<i>Trichomonas vaginalis</i>
Amebiasis	<i>Entamoeba histolytica</i>
Giardiasis	<i>Giardia lamblia</i>
Fungal	
Vaginal candidiasis	<i>Candida albicans</i>
Parasitic	
Scabies	<i>Sarcoptes scabiei</i>
Pediculosis pubis	<i>Phthirus pubis</i>

IV. GONORRHEA

Caused by *Neisseria gonorrhoeae*, an intracellular gram-negative diplococcus that attaches to non-ciliated columnar epithelial cells, penetrates, and multiplies on the basement membrane. Adherence is facilitated through pili and opa proteins. Gonococcal lipopolysaccharide stimulates the production of tumor necrosis factor, which causes cell damage.

A. Incidence: New cases have continued to decline over the last two decades, from 1 million in 1977 to 650,000 in 1996. However, rates remain disproportionately high among teens and ethnic minorities.

B. Transmission:

- Non-sexual transmission is possible but very rare
- Male risk of acquiring urethral infection
 - i. 20% after single exposure (vaginal intercourse)
 - ii. Moves to 80% after 4 exposures
- Female risk of acquiring cervical infection
 - i. 60-80% after single exposure
- Asymptomatic infection in males and females is an important reservoir of spread within the community

C. Presentation: Gonorrhea in women can involve any portion of the genital tract, the oropharynx or become disseminated. Infection in women is often asymptomatic compared to men who are asymptomatic only 10% of the time.

- Most common site of mucosal infection is the cervix.
- Approximately 50% of infected women with cervical infection are asymptomatic
- Symptomatic infection typically manifests as vaginal pruritis and/or a mucopurulent discharge
- Gonococcal infections in men can involve any part of the genital tract, either alone or in combination with other sites. Genital infections are generally symptomatic
- Urethritis is the most common symptom in men, including copious, spontaneous, mucopurulent penile discharge and/or dysuria.
- Epididymitis (unilateral testicular pain and swelling), proctitis, and pharyngitis occur less frequently

D. Diagnosis: Gram stain due to its high specificity and sensitivity is the most practical although culture for *N. gonorrhoeae* on Thayer-Martin agar remains the "gold standard"

E. Treatment:

- Adults – uncomplicated urethral, endocervical, or rectal infections
 - Ceftriaxone 125mg IM once
 - Cefixime 400mg PO once
 - **ALL must be followed by doxycycline 100mg PO twice daily for 7 days OR azithromycin 1000mg PO once**
 - Fluoroquinolones no longer recommended due to ↑ resistance
- Disseminated infection
 - Ceftriaxone 1g IM or IV every 24 hours
 - Cefotaxime 1 g IV every 8 hours
 - Ciprofloxacin 500mg IV every 12 hours
 - Regimen should be continued until 24-48 hours after symptoms resolve
 - Then follow with cefixime 400mg PO twice daily or ciprofloxacin 500mg PO twice daily for the remainder of 1 week.
- Meningitis and endocarditis
 - Ceftriaxone 1-2 g IV every 12 hours for 10-14 days
- Adult Gonococcal Ophthalmia
 - Ceftriaxone 1 g IM in a single dose with irrigation of the eyes with saline solution once
- Pregnancy
 - Ceftriaxone 125mg IM once
 - Spectinomycin 2g IM once (if penicillin allergic)

V. SYPHILIS

Caused by *Treponema pallidum*, an anaerobic bacteria 3–8 μm in length, with acute, regular, or irregular spirals and no obvious protoplasmic structure. It is solely a human pathogen and does not naturally occur in other species. Transmission occurs by penetration of the spirochetes through mucosal membranes and abrasions on epithelial surfaces. Incubation time from exposure to development of primary lesions averages 3 weeks but can range from 10-90 days. Lesions develop at the primary site of inoculation.

A. Incidence

- Rates of syphilis in the US are at the lowest levels in 20 years with only 70,000 cases annually (50% are male homosexual). Infection levels are so low that the CDC has concluded it is possible to eliminate syphilis in the United States.

B. Can spread transplacentally and infect unborn child

C. 50% of sexual contacts will be infected

D. Presentation: The presentation of patients with syphilis is variable (the great imitator)

- **Primary lesions (chancre) are painless**
 - 5-10% are painful
 - Penetrates the intact mucosa and reaches bloodstream via lymphatics
 - Usually heals in 3-6 week
 - Lymphadenopathy (unilateral or bilateral) may persist for months
- Secondary syphilis presents 6-8 weeks after chancre with a skin rash. The rash may be macular, papular, pustular, or mixed.
- Late syphilis
 - Seen in 1-10 years in 15% of patients
 - Cardiovascular involvement occurs in 10% in 10 years
 - CNS involvement occurs in 8% in 5-35 years

E. Diagnosis

- Presence of *T. pallidum* on dark-field microscopic exam of material from lesions
- Direct fluorescent-antibody test (DFA-TP) has greater sensitivity and specificity than dark-field
- Serologic tests are common but can be unreactive early in the disease
- Laboratory testing
 - Treponemal tests: once tests are positive they remain so for life and do not correlate with activity
 - Nontreponemal antibody titers (RPR) do correlate with disease activity

F. Treatment

- Primary and Secondary Syphilis
 - **Benzathine penicillin G 2.4 million units IM in 1 dose for adults**
 - Benzathine penicillin G 50,000 units/kg IM up to the adult dose in children
 - Penicillin allergic
 1. Doxycycline 100mg PO twice daily for 2 weeks
 2. Tetracycline 500mg PO 4 times daily for 2 weeks
- Early Latent Syphilis
 - Benzathine penicillin G 2.4 million units IM in 1 dose for adults
 - Benzathine penicillin G 50,000 units/kg IM up to the adult dose in children
- Latent Syphilis
 - Benzathine penicillin G 7.2 million units total (3 doses of 2.4 million units IM one week apart for 3 weeks)
 - Benzathine penicillin G 150,000 units/kg total (3 doses of 50,000 units/kg IM one week apart for 3 weeks)
 - Penicillin allergic
 1. Doxycycline 100mg PO twice daily for 2 weeks
 2. Tetracycline 500mg PO 4 times daily for 2 weeks
- Congenital syphilis
 - 100,000 – 150,000 units/kg of aqueous penicillin G daily (50,000 units IV Q12 hours during the first 7 days of life, then Q8 hours thereafter) for 10 days
 - 50,000 units /kg procaine penicillin G in a single dose daily IM for 10 days

VI. BACTERIAL VAGINOSIS

Caused by overgrowth of anaerobic organisms most commonly *Gardnerella vaginalis* and *Mycoplasma hominis*.

- A. Incidence:** The rate of occurrence depends upon the population studied: 17 to 19 percent in family-planning or student health clinics; 24 to 37 percent in STD clinics; and 10 to 35 percent among pregnant women in the U.S. Unlike most STDs, there is a high prevalence of infection among women who have sex with women (WSW)
- B.** May be associated with important complications of pregnancy and with pelvic inflammatory disease.
- C. Presentation:** Most women are asymptomatic.
- Those with symptoms present with an unpleasant, "fishy smelling" discharge that is more noticeable after unprotected intercourse
 - The discharge is off-white, thin, and homogeneous
 - Dysuria and dyspareunia are rare
 - Pruritus and inflammation are absent
- D. Treatment:**
- Recommended
 - Metronidazole 500mg PO twice daily for 7 days
 - Metronidazole gel 0.75% daily for 5 days
 - Clindamycin cream 2% qhs for 7 days
 - Alternatives
 - Metronidazole 2g PO once (not as effective)
 - Clindamycin 300mg PO twice daily for 7 days
 - Clindamycin ovules 100mg intravaginally qhs for 3 days
 - Pregnancy
 - Treat symptomatic women due to association with adverse pregnancy outcomes
 - Metronidazole 250mg every 8 hours for 7 days
 - Clindamycin 300mg every 12 hours for 7 days

VII. CHLAMYDIA

Caused by *Chlamydia trachomatis*, a small, gram-negative, obligate, intracellular bacterium not detectable by usual light microscopy. Distinct life-cycle:

- The small elementary bodies attach and penetrate into cells, changing into the metabolically active form (reticulate body) within six to eight hours post-exposure.
 - The reticulate bodies then reorganize into small elementary bodies, and within two to three days the cell ruptures, releasing newly formed elementary bodies.
- A. Incidence:** The number of reported chlamydia cases has risen in recent years but this is mainly due to ↑ screening rather than ↑ infections. Overall the number of new cases in the US has fallen from 4 million to about 3 million a year.
- B.** More common than gonorrhea and a major cause of involuntary infertility
- C.** Risk of transmission not established but probably less than gonorrhea
- D.** Non-sexual transmission is possible but not established (25-30% of non-sexually active children have antibodies)
- E. Presentation:** overlaps with gonorrhea and **coexisting infection very common**
- In women, cervical infection is the most common syndrome. However, more than 50% of women are asymptomatic. When symptoms occur, vaginal discharge, poorly differentiated abdominal pain, or lower abdominal pain are the most frequent.
 - Women with urethral infection present with symptoms of a urinary tract infection (UTI) such as frequency and dysuria, and occasionally of lower abdominal pain.
 - Approximately 30% of women with chlamydia infection will develop pelvic inflammatory disease (PID) if left untreated. While PID caused by *N. gonorrhoeae* infection may be more acutely symptomatic, PID due to *C. trachomatis* tends to be associated with higher rates of subsequent infertility.
 - In men, chlamydia presents as non-gonococcal urethritis (NGU), epididymitis and proctocolitis (homosexual men). The symptoms are considered milder than the gonococcal equivalent.

- F. Diagnosis:** Noninvasive screening options, such as urine testing or self-collected vaginal swabs are more acceptable to patients than traditional speculum examination.
- Tissue culture is expensive (only used in cases of forensic investigation eg, rape, child abuse)
 - Rapid diagnosis by monoclonal antibody techniques or nucleic acid amplification (NAAT)
 - Clinical practice guidelines strongly recommend routine chlamydia screening for sexually-active women below the age of 25
- G. Treatment:**
- **Azithromycin 1000mg PO once**
 - Doxycycline 100mg PO twice daily for 7 days
 - Pregnant woman
 - Erythromycin base 500mg PO four times daily for 7 days
 - Erythromycin ethylsuccinate 800mg PO four times daily for 7 days
 - Amoxicillin 500mg PO every 8 hours for 7 days

VIII. GENITAL HERPES

Caused by herpes simplex virus (HSV), a ubiquitous double-stranded DNA virus characterized by the following unique biological properties: neurovirulence (the capacity to invade and replicate in the nervous system), latency (the establishment and maintenance of latent infection in nerve cell ganglia), and reactivation of latent HSV induced by a variety of stimuli (eg, fever, trauma, emotional stress, sunlight, menstruation)

A. Incidence:

- HSV-2 in 70-90% of cases
- 3% (nuns) to 70% (prostitutes)
- Usually found in 20-30% of adults

B. Types I and II can cause genital ulcers

C. Presentation: The initial presentation can be severe with painful genital ulcers, dysuria, fever, tender local inguinal lymphadenopathy, and headache. In other patients, however, the infection is mild, subclinical, or entirely asymptomatic.

- Primary episodes are associated with systemic symptoms such as headache, photophobia, and malaise
- Lesions
 - **Typically cause pain** (5-10% are painless)
 - Occur 2-7 days after contact with infected secretions
 - Males – seen on glans or penile shaft
 - Females – seen on the vulva, perineum, buttocks, cervix and vaginal wall
 - Homosexuals – perianal and anus
- Infected persons without lesions can still transmit disease
- Increased abortion in pregnancy associated with active disease and babies should be delivered via Cesarean
- Diagnosis is made on clinical presentation or chemical immunological detection with a specific antibody or by cell culture

D. Treatment:

- First clinical episode of genital herpes:
 - **Acyclovir 400mg PO 3 times daily for 7-10 days or until clinical resolution**
 - Acyclovir 200mg PO 5 times daily for 7-10 days or until clinical resolution
 - **Valacyclovir 1000mg PO twice daily for 7-10 days or until clinical resolution**
 - Famciclovir 250mg PO 3 times daily for 7-10 days or until clinical resolution
- First clinical episode of herpes proctitis:
 - Acyclovir 400mg PO 5 times daily for 10 days or until clinical resolution
 - Little evidence exists that a higher dose of antivirals are needed to treat herpes proctitis
- Recurrent episodes:
 - **Acyclovir 400mg PO 3 times daily for 5 days, or**
 - Acyclovir 200mg PO 5 times daily for 5 days, or
 - Acyclovir 800mg PO twice daily for 5 days

- Famciclovir 1000mg PO twice daily for 1 day
- Valacyclovir 500mg PO twice daily for 5 days
- Daily suppressive therapy (patients with > 6 episodes per year)
 - Acyclovir 400-800mg PO twice daily
 - Famciclovir 500mg PO twice daily
 - Valacyclovir 250mg PO twice daily, 500mg once daily or 1000mg once daily
- Severe disease:
 - Acyclovir 5-10 mg/kg IV every 8 hours for 5-7 days or until clinical resolution

IX. GENITAL WARTS

Caused by *Condylomata acuminata*, a human papillomavirus (HPV). HPV infects epithelial tissues of skin and mucous membranes.

- A. Incidence:** 5.5 million cases occur each year resulting in nearly 20 million people in the U.S. infected
- B. Presentation:** Clinical manifestations of infection occur as cutaneous disease or anogenital disease, and can be clinically obvious or subclinical.
- C. Association with cervical dysplasia and carcinoma of the cervix**
 - Genotype 16 and 18 are the “high-risk” HPVs that cause most (70 percent) cervical cancers
 - Genotype 6 and 11 cause most (90 percent) genital warts
 - Gardasil[®] protects against these four genotypes
- E. Treatment:**
 - Podofilox 0.5% solution applied twice daily for 3 days followed by 4 days no therapy. This cycle is repeated for a total of 4 cycles
 - Imiquimod 5% cream applied 3 times weekly for up to 16 weeks
 - Cryotherapy with liquid nitrogen (don’t try this at home)

X. TRICHOMONIASIS

Caused by the flagellated protozoan *Trichomonas vaginalis*, which may be found in the vagina, urethra, and paraurethral glands of infected women. The flagellated parasite is approximately the size of a white blood cell, although size may vary based on physical conditions. The protozoal pathogen causes direct damage to the epithelium, leading to microulcerations.

- A. Incidence**
 - a. Most common curable STD among young, sexually active woman with an estimated 5 million new cases every year in the US and 180 million cases worldwide.
 - b. The organism also is detected in 30-40% of men who are exposed but are usually asymptomatic
- B. Patients with trichomoniasis are twice as likely to have gonorrhea as well**
- C. Presentation:**
 - a. Causes an intense inflammatory response
 - b. Purulent or homogenous vaginal discharge and vulvar or vaginal erythema are common
 - c. Colpitis macularis (strawberry cervix)
- D. Treatment:**
 - **Metronidazole 2g single dose, or**
 - Metronidazole 500mg PO twice daily for 7 days
 - a. Management of sex partners
 - Sex partners should be treated
 - Avoid intercourse until therapy is completed / patients are asymptomatic

Additional Resources:

1. Knodel, LC. (2005) Sexually Transmitted Diseases. Dipero, JT, Talbert, RL, Yee, GC et al. Pharmacotherapy: A Pathophysiological Approach (pp 2097-117)
2. Practice Guidelines from Centers for Disease Control and Prevention: <http://www.cdc.gov/std/treatment/2006/toc.htm>
3. Minnesota STD Statistics: <http://www.health.state.mn.us/divs/idepc/dtopics/stds/stdstatistics.html>
4. American Social Health Association: http://www.ashastd.org/learn/learn_statistics.cfm

Practice Cases:

MS, a 27 y/o male who presents to the internal medicine clinic where you are on rotation complaining of a 'sore' on his penis. He noticed it about 5 days ago, and says it's gradually been getting larger. It is not very tender to touch, and occasionally has seemed somewhat moist. He's never experienced anything like it, and is very concerned. He has no systemic symptoms such as rash or fever.

MS is currently sexually active primarily with men. Although he occasionally has sex with women, he has not done so in the last six months. In the last two months, he has had two male sex partners

On exam, a circular lesion is seen, about 1 cm in diameter. The ulcer is not tender to palpation.

Swabs and scrapings from the ulcer yielded spirochetes visible under dark-field microscopy. His RPR was 1:8 (positive)

The diagnosis of primary syphilis is made and the physician asks you to inform the 3rd year medical students what the drug of choice is for this ulcer.

Your reply:

- A. Azithromycin 2g slam in the office to ensure compliance
- B. Metronidazole 500mg PO twice daily for 7 days
- C. Benzathine penicillin G 2.4 million units IM
- D. Reinforce the "watch and wait" approach to see if the problem resolves on its own

JS is a 26 y/o male who presents with a 2-3 day history of urethral discharge and moderate-severe dysuria. He lives in Maple Grove with his wife and denies, denies, denies any other sexual contacts. He reports experiencing a similar problem occurring shortly after his bachelor party last summer.

On exam the physician notes the following:

- Normal oropharynx free from exudates or erythema
- No axillary lymphadenopathy
- No dermatologic findings on torso, extremities or genitals
- A yellowish urethral discharge
- Bilateral inguinal adenopathy, which is moderately tender to palpation
- Non-tender testes and epididymis without palpable swelling or masses
- No anal lesions

Gram stain of the discharge comes back positive for many gram-negative cocci in pairs. The physician wants to start JS on ciprofloxacin 500mg PO Q12 for 7-10 days. You pipe up and say:

- A. Great choice! Ciprofloxacin is the drug of choice for most round bacteria
- B. Ceftriaxone 125mg IM once
- C. Clindamycin ovules 100mg qhs for 3 days
- D. Famciclovir 250mg PO 3 times daily for 7-10 days or until clinical resolution

Being an expert in treating sexually transmitted diseases you also want to check JS for _____ and will recommend adding _____ anyway.

KG a 22 y/o female presents to Boynton for a routine annual physical examination. She complains of vaginal tenderness and occasional discharge. On exam KG is found to have significant vaginal erythema and microscopic, punctate haemorrhages of the cervix. A cytology specimen obtained indicated the presence of a flagellated protozoan.

What are your treatment recommendations for KG and her sex partner(s)?