Review and Update – *UTIs and STIs*

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Learning Objectives

- List differential diagnoses for urethritis/cervicitis.
- Identify dermatologic manifestations of sexually-transmitted infections (STIs).
- Summarize current treatment recommendations for STIs and urinary tract infections (UTIs).
- Describe possible sequelae from untreated infections.
- Recognize and avoid certain language that may discourage patient openness in discussing sexual health.

What this presentation is…

- Case-based review of diagnosis of most STIs and UTIs with current treatment guidelines (CDC 2015, ISDA 2011, EAU 2015).

What this presentation is not…

- Screening recommendations
- Treatment after sexual assault
- HIV or Hepatitis A/B/C
- Immunizations or prophylaxis against STIs (e.g., Gardasil, Truvada)
- Cervical or testicular cancer

Part 1:
Let’s talk about sex, baby

Epidemiology

- *The US has the highest rate of STIs in the industrialized world*
  - Approximately 20 million new cases annually
  - This costs the healthcare system $16 billion each year
- Between 2003 and 2017, there has been:
  - 196% increase in cases of syphilis
    - Highest rates (2017) Nevada, California, and Louisiana
  - 66% increase in cases of gonorrhea
    - Highest rates (2017) in the South (and Alaska!), but increasingly in the Southwest
  - 95% increase in cases of chlamydia
- In 2018, England saw its first case of drug-resistant gonorrhea

Case #1: Appropriate language

- Charlie, a 38 year-old Caucasian transgender man, presents to the Emergency Department for lower abdominal pain.
- His medical record does list his preferred name, but also indicates his gender as female.

- *How would you approach this situation?*

- *How might you evaluate his need for a urine pregnancy test and/or pelvic exam?*

Eliciting a sexual history

- Make sure the patient is comfortable with anyone who may be in the room
- Use open-ended questions and neutral words that avoid implied judgment or a "correct" answer (e.g., rather than, "Do you use condoms?," ask, "What do you do to keep yourself safe when you have sex?")
- Normalizing language, taking the focus off the individual a bit, may also be helpful (e.g., "Some people worry about whether a particular symptom means they have a sexually-transmitted infection. Where do you go for information?")

Quallich, CDC 2015

The 5 P's

- Partners
  - Gender and number of partners
- Practices
  - Condom usage
  - Oral, vaginal, and anal sex
- Protection from STIs
- Past history of STIs
  - Last STI testing (if ever)
  - Exposures to STIs
  - Other risks (e.g., IVDU, involvement in the sex trade)
- Pregnancy
  - Other forms of birth control

CDC 2015

Word choice matters

- Sex – assignment based on genetics (XX, XY) and/or anatomic features at birth
- Cisgender – those whose gender identity and/or expression align with cultural expectations of assigned birth sex
- Transgender female (MTF) – biologic male whose gender identity is female
- Transgender male (FTM) – biologic female whose gender identity is male
- Nonbinary – those who do not identify as either male or female (can identity with both, neither, or a combination); may call themselves queer, agender, or genderfluid

Avoid assumptions

- Gender identity/expression ≠ sexual orientation/practice
- Sexual practice may change over time
- Orientation ≠ practice
- One risk does not necessarily beget another
- Avoid heteronormative questions and, separately, “slut shaming” (criticizing someone for falling outside of societal expectations regarding sex, or the perception of such)

- *When in doubt, ask for clarification* (e.g., “Can you explain that to me?”)

Slang changes

- In the 17th century, people might fadoodle, put the devil into hell, dance the Paphian jig, play at rantum-scantum, join giblets, lerricompoop, or ride a dragon upon Saint George.

- Now we have side chicks and cougars, pitchers and catchers, bugchasers and serosorters, pegging and parTying, bears and chickenhawks. We swipe right and hope to get to third base; we send text messages asking, “DTF?” or “Netflix and chill?”

Part 2:
The birds and the b(acteria)s

Case #2a: Dysuria

- Natasha, a 20 year-old African-American woman, presents to your Urgent Care with the chief concern of dysuria.
- She endorses suprapubic pain and pressure, as well as urinary urgency and frequency.
- She denies gross hematuria, vaginal discharge, or flank pain.
- Her last menstrual period (LMP) was 2 weeks ago.
  She is not sexually active.

- *What's your differential?*
- *How would you further evaluate her symptoms?*

Diseases of the urinary tract (♀)

- Urinary tract infection (UTI)
- Interstitial cystitis (IC)/ bladder pain syndrome (BPS)
- Hemorrhagic cystitis
- Pyelonephritis
- Nephrolithiasis

- Gonorrhea (GC)
- Non-gonococcal urethritis (NGU)
  - Chlamydia (CT)
  - Mycoplasma/ureaplasma
  - Trichomonas
  - Herpes simplex virus

Workup for dysuria

- POC urinalysis ("clean catch" sample) reveals:
  - 1+ leukocyte esterase, positive nitrates, and trace blood
- Urine culture pending (and will likely return within 3 days).
- Urine pregnancy test negative.
- Urine GC/CT not sent.

- *Is this UTI complicated or uncomplicated?*
- *How would you treat this patient?*

Symptomatic uncomplicated UTIs

- Gram-negative aerobic bacteria (e.g., *E. coli*) most common; gram-positive bacteria (e.g., *Staph saprophyticus*) possible

- Treatment of *uncomplicated* UTIs:
  - Trimethoprim-sulfamethoxazole (TMP-SMX) 160/800mg (Bactrim DS), 1 tab PO BID x3d
  - Nitrofurantoin (Macrobid) 100mg PO BID x5-7d
  - Fosfomycin 3g PO x1

  - Ciprofloxacin (Cipro)* 250mg PO BID x3d
  - Amoxicillin/clavulanate (Augmentin)* 500/125mg PO BID x3-7d
  - Cephalexin (Keflex)* 500mg PO BID x3-7d

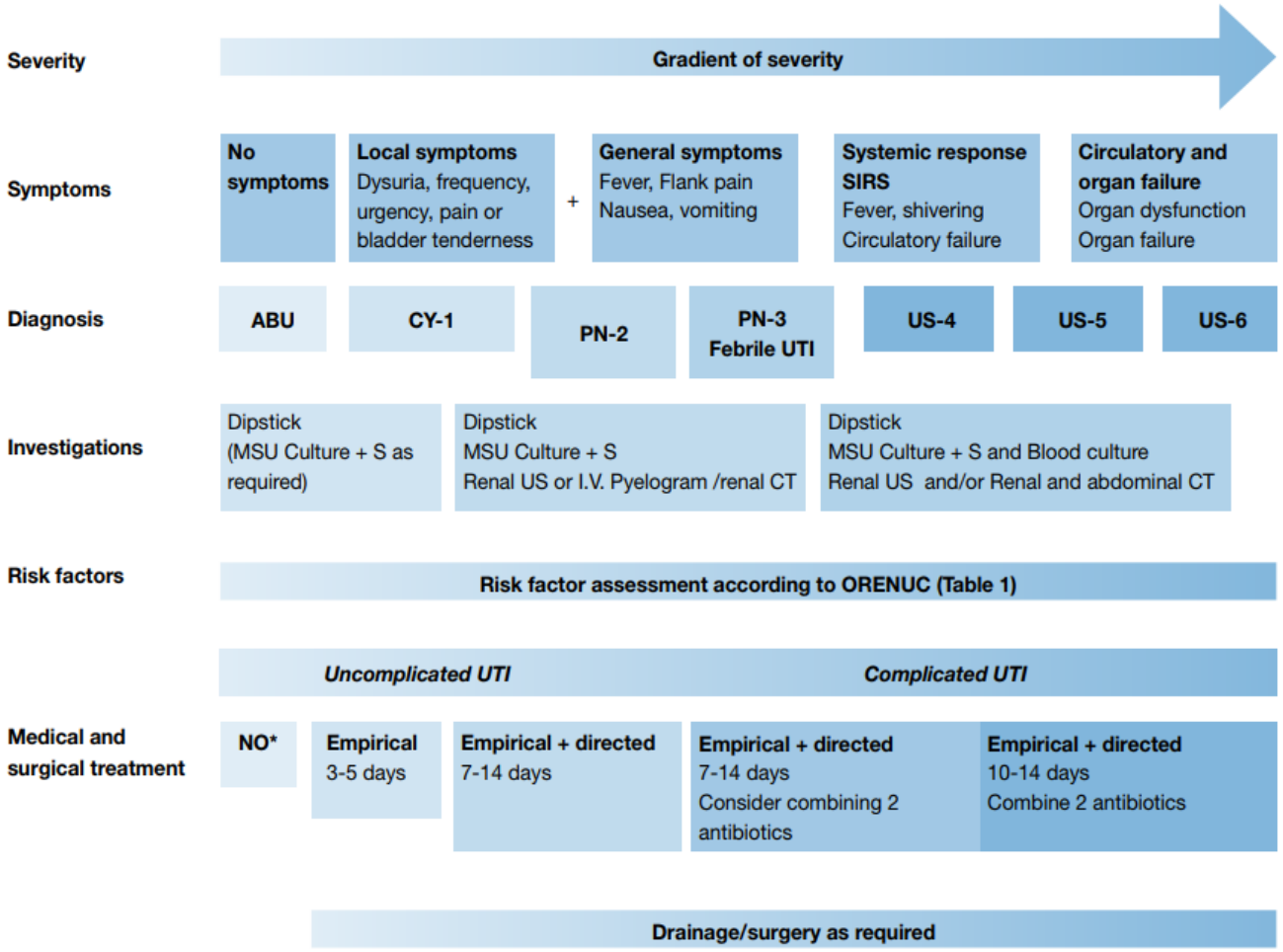
IDSA 2011

Complicated UTIs/pyelonephritis

- Complicated UTIs = persistent, recurrent, or predisposition to infection or treatment failure
  - Recurrent UTIs (≥3/y) may warrant daily or post-coital antibiotic prophylaxis

- Treatment of *complicated* UTIs:
  - Trimethoprim-sulfamethoxazole (TMP-SMX) 160/800mg (Bactrim DS), 1 tab PO BID x3-14d
    - For severe infections, TMP-SMX 8-10mg/kg/day TMP PO divided q6-12h x14d
  - Ciprofloxacin (Cipro)* 500mg PO BID x7-14d
    - Alternative = ciprofloxacin 400mg IV q12h x7-14d

Classification of UTIs



* *Two presently accepted exceptions: during pregnancy and prior to urological surgery.*

EUA

Other situations

- Asymptomatic bacteriuria (ASB) +/- pyuria
  - May be more common in older adults, but screening and treatment generally not recommended (?pregnant women)
- Pregnant women
  - Avoid TMP-SMX and fluoroquinolones
- Children
  - 3rd generation cephalosporins preferred
- Elderly
  - Vaginal atrophy may contribute to recurrent UTIs
- Renal impairment
  - Adjust dose based on creatinine clearance
  - Do not use nitrofurantoin

Beveridge, Rowe, EAU

Case #2b: Urethral discharge

- Humberto, a 24 year-old Latino man, presents to your STI clinic with the chief concern of dysuria and penile discharge.
- He reports mild testicular discomfort.
- He denies other urinary symptoms.
- He is uncircumsized and engages in unprotected vaginal intercourse with several female partners.

- *What's your differential?*
- *How would you further evaluate his symptoms?*

Diseases of the urinary tract (♂)

- Similar differential diagnosis as before, but with some anatomic differences:
  - UTI may be less likely due to length of urethra
  - The prostate gland may be involved (*prostatitis*)
  - The glans penis and/or foreskin (prepuce) may also be involved (*balanoposthitis*)

Workup for urethral discharge

- Physical exam reveals scant creamy, off-white penile discharge with mild urethral inflammation. No rash or genital lesions. Mild generalized testicular discomfort with palpation. Cremasteric reflex is intact.
- Empiric treatment discussed, but patient declines. He is advised to refrain from sexual contact until his urine GC/CT tests (“dirty urine” sample) return.
- 3 days later, the labs reveal infection with *gonorrhea*.

- *How would you treat his infection?*

Gonorrhea (GC)

- *Neisseria gonorrhoeae*
- Treatment for uncomplicated genital, rectal, or pharyngeal infections includes *dual therapy* with ceftriaxone 250mg IM x1 and azithromycin 1g PO x1. This regimen can also be used in pregnant women.

- Untreated, GC can cause epididymitis, infertility, pelvic inflammatory disease (PID), or disseminated gonococcal infection (DGI). It can also increase one's risk of acquiring or transmitting HIV.

NCSD, CDC

Unlucky twins

- Humberto's twin brother Arturo reports similar symptoms (dysuria, penile discharge, and testicular pain), but his testing reveals *chlamydia*.

- *How is his treatment different?*

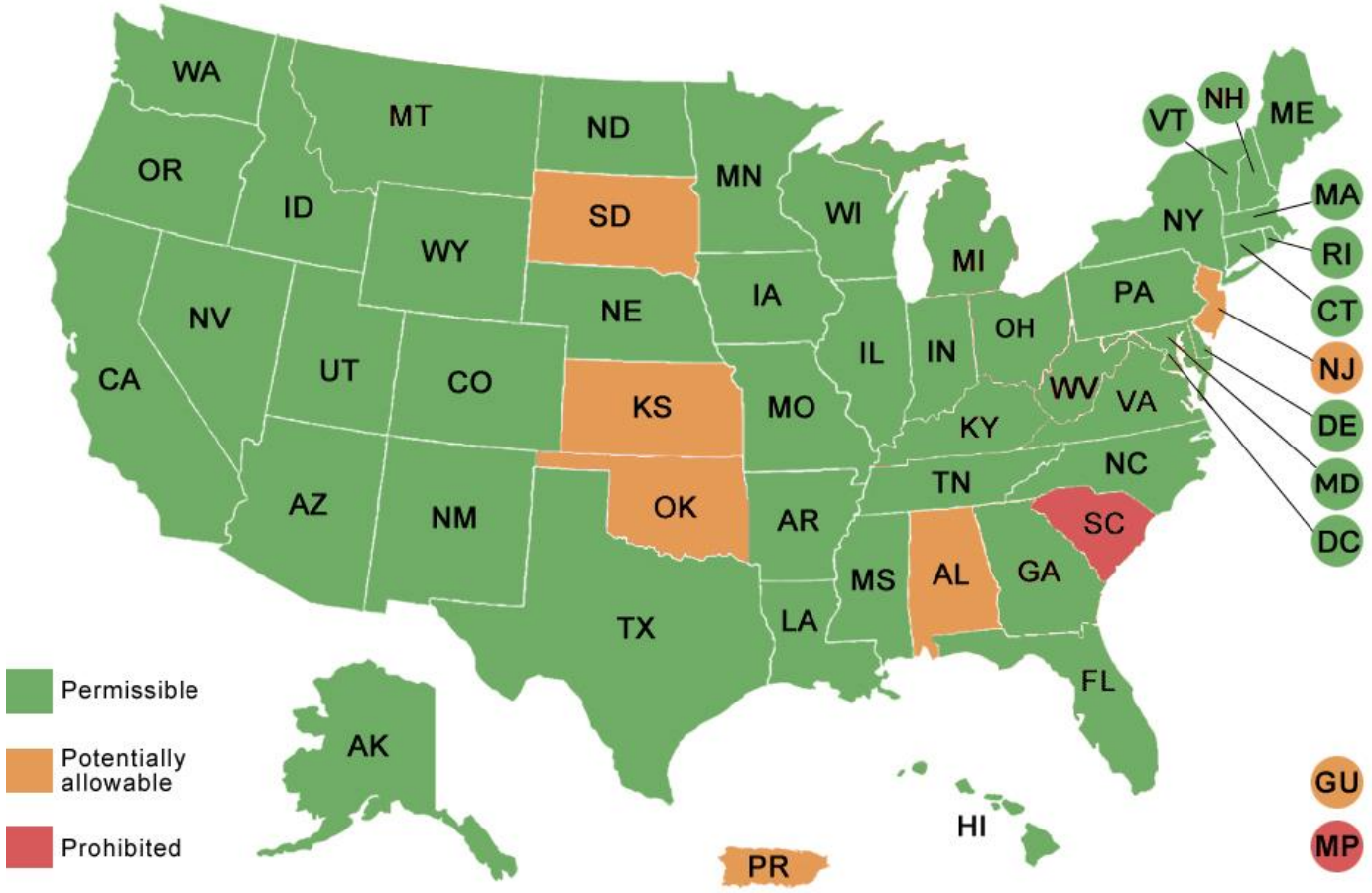
Chlamydia (CT)

- *Chlamydia trachomatis*
- Treatment for uncomplicated genital or pharyngeal infections consists only of azithromycin 1g PO x1. This regimen can also be used in pregnant women.
  - Alternative = doxycycline 100mg PO BID x7d
    (*not* for pregnant women, ?preferred for rectal infection)

- *C. trachomatis* can also cause lymphogranuloma venereum (LGV), which manifests as genital papules or ulcers and inguinal lymphadenopathy. It is rare in industrialized countries. Treatment: doxycycline 100mg PO BID x21d.

NCSD, CDC

Expedited partner therapy (EPT)



CDC (2019)

Case #2c: Vaginal discharge

- Rangi, a 21 year-old woman of South Pacific Islander heritage, heard about Arturo's infection and presents to your STI clinic with the chief concern of malodorous vaginal discharge.
- She denies vaginal pain or bleeding.
- She engages in unprotected vaginal intercourse with male and female partners.

- *What's your differential?*
- *How would you further evaluate her symptoms?*

Diseases of the vagina/cervix

- Gonorrhea (GC)
- Chlamydia (CT)
- Trichomonas
- Mycoplasma/ureaplasma
- Bacterial vaginosis (BV)
- Candidia

- Syphilis
- Chancroid
- Herpes simplex virus (HSV-1/-2)
- Human papillomavirus (HPV)

Workup for vaginal discharge

- Pelvic exam reveals fishy-smelling, tacky grey vaginal discharge with positive “whiff test.”
- Wet prep (saline) reveals clue cells. KOH prep shows neither spores nor pseudohyphae.

- *Could any other tests have been performed?*
- *How would you treat this patient?*

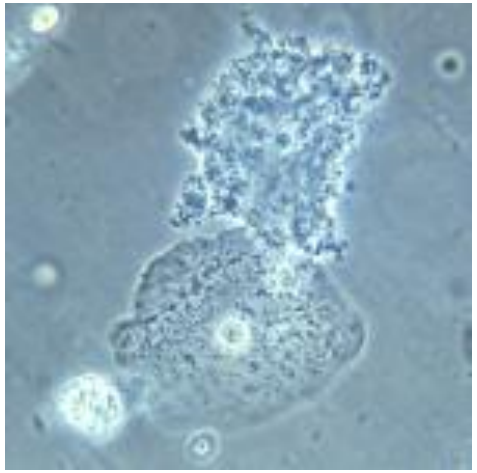
- *What if her exam/testing had different findings?*

Bacterial vaginosis (BV)

- Imbalance of vaginal flora, but associated with *Gardnerella vaginalis*

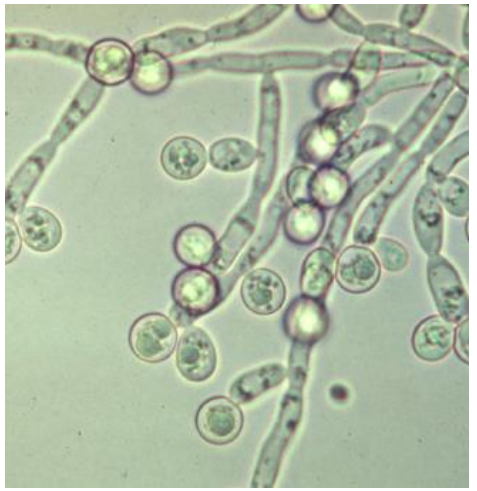
- Many treatment options:
  - Metronidazole 500mg PO BID x7d
  - Metronidazole gel 0.75% one applicator (5g) PV daily x5d
  - Clindamycin cream 2% one applicator (5g) PV qhs x7d

  - Tinidazole 2g PO daily x2d
  - Tinidazole 1g PO daily x5d
  - Clindamycin 300mg PO BID x7d
  - Clindamycin ovules† 100mg PV qhs x3d



CDC

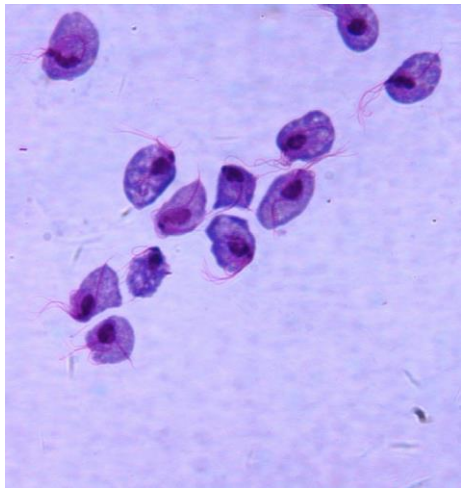
Candidiasis



- *Candida albicans* → candidiasis
  - Thick, white curd-like vaginal discharge
  - Superficial candidial skin infections
    usually feature a hot, itchy, and/or painful flat red rash
  - Multiple treatment options, including fluconazole 150mg PO x1 or terconazole 80mg PV daily x3d

CDC

Trichomoniasis



- *Trichomonas vaginalis* → trichomoniasis
  - May be asymptomatic or present with vaginal discharge (malodorous, purulent, frothy), vaginal odor, and/or itch
  - Treatment options include metronidazole 2g PO x1‡ or tinidazole 2g PO x1
    - Persistent or recurrent infections may be treated with metronidazole 500mg PO BID x7d

CDC

Vaginitis

	Bacterial vaginosis	Candidiasis	Trichomoniasis
Symptoms	Odor, itch, discharge	Itch, thick discharge, dysuria, discomfort	Often asymptomatic; itch, discharge
Vaginal discharge	Adherent, thin, milky-white, “fishy”	Thick, clumpy, white “cottage cheese”	Frothy, grey or yellow-green, malodorous
Saline wet mount	Clue cells, no/few WBCs	WBCs (few to many)	Motile flagellated protozoa, many WBCs
KOH wet mount		Pseudohyphae, budding yeast	
KOH “whiff test”	Positive	Negative	Often positive

CDC (2013)

Other causes of, and treatments for, vaginal discharge

- *Mycoplasma genitalium*
  - New/emerging pathogen
  - Less common than CT but more common than GC; coinfection with chlamydia not uncommon
  - Current treatment is azithromycin 1g PO x1, but there may be increasing resistance/declining efficacy
- *Mycoplasma hominis*
  - Doxycycline 100mg PO BID x7-14d
- *Ureaplasma urealyticum*
  - Doxycycline 100mg PO BID x7-14d
    - Macrolides like azithromycin or fluoroquinolones like moxifloxacin may be alternatives

Part 3:
The skin you’re in

Case #3a: Genital itch

- Pooja, a 30 year-old South Asian transgender woman, presents to your Urgent Care with the chief concern of itching in the genital area.
- She denies new soaps, detergents, clothing, etc.
- She reports taking estrogen hormonal therapy and has not had vaginoplasty.

- *What else would you want to know?*
- *What's your differential?*

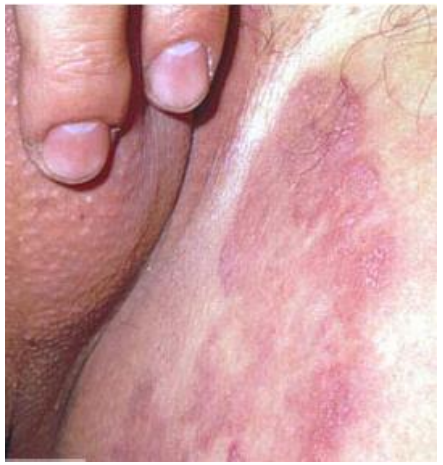
Diseases of the (genital) skin

- Candidiasis
- Tinea cruris/corporis
- Pubic lice (pediculosis pubis)
- Scabies

- Herpes simplex virus
- Anogenital warts (HPV)
- Molluscum contagiosum
- Syphilis
- Chancroid
- Donovanosis (granuloma inguinale)

Tinea

- *Trichophyton rubrum, T. mentagrophytes* → tinea cruris
  - Treatment consists of topical antifungals like terbinafine, clotrimazole, and ketoconazole applied BID x10-14d
  - Itraconazole 200mg PO daily or terbinafine 250mg PO daily x3-6 weeks may be used for refractory cases



Merck

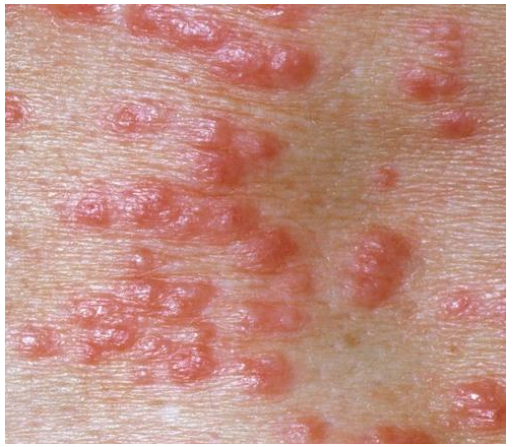
Pubic lice

- *Phthirus pubis* → pubic lice (pediculosis pubis)
  - Permethrin 1% cream or pyrethrins with piperonyl butoxide applied to affected areas and washed off after 10min
  - Alternative treatments include malathion 0.5% lotion applied to affected areas and washed
    off after 8-12h or ivermectin 250 µg/kg
    PO x1 and repeated after 2 weeks

CDC

Scabies

- *Sarcoptes scabiei* → scabies
  - Permethrin 5% cream applied from the neck down and washed off after 8-14h or ivermectin 200 µg/kg PO x1 and repeated after 2 weeks (not for use in children <10yo)
  - Lindane 1%, an alternative treatment, is not for use in children and may be banned/restricted
    in some areas due to toxicity



CDC

Case #3b: Genital bumps

- Saahirah, a 35 year-old woman of Middle Eastern heritage, presents to your Urgent Care with the chief concern of bumps on her genital tissue.
- She denies having had this issue before. She denies ulcers.
- She is married and monogamous. She does not suspect her husband of extramarital affairs.

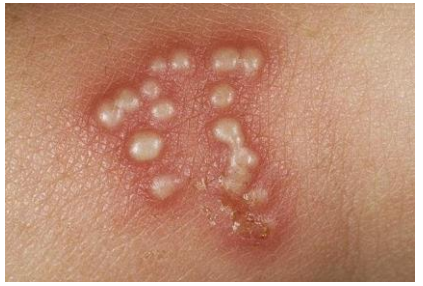
- *What else would you want to know?*
- *What's your differential? (What's more likely now?)*

Diseases of the skin (revisited)

- Herpes simplex virus
- Anogenital warts (HPV)
- Molluscum contagiosum
- Syphilis
- Chancroid
- Donovanosis (granuloma inguinale)

- Pubic lice (pediculosis pubis)
- Scabies
- Candidiasis
- Tinea cruris/corporis

Genital herpes: testing and types

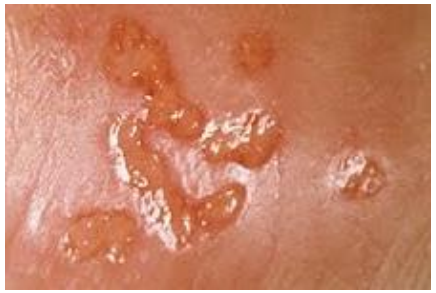


- Limitations of testing for herpes simplex virus (HSV-1/-2):
  - Swab can only be done for an active lesion; relatively high rate of false negatives (especially if lesion small or already healing)
  - Blood test may be difficult to interpret; though IgM appears first, only IgG tests can distinguish between HSV-1 and -2
- Treatment dosage and duration depends on the number and frequency of outbreaks; topical analgesia should be offered
- Cold sores (herpes labialis) and mat herpes (herpes gladiatorum) are typically caused by HSV-1 and treated differently

CDC

http://www.ashasexualhealth.org/stdsstis/herpes/herpes-testing/

Genital herpes: treatment

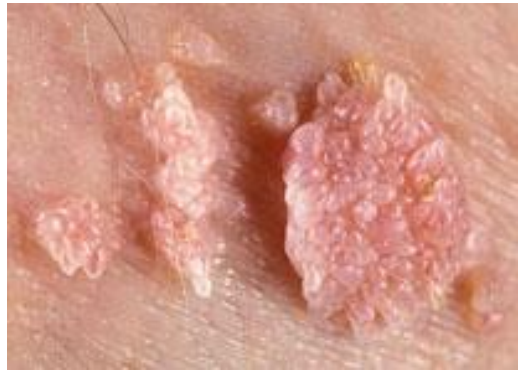


- WHO (2016) favors acyclovir over valacyclovir or famciclovir (but their guidelines use a lower dose of valacyclovir)
- First episode:
  - Valacyclovir 1g PO BID x7-10d
  - Acyclovir 400mg PO TID x7-10d
  - *Treatment may be extended if healing incomplete after 10d*
- Recurrence (episodic outbreaks):
  - Valacyclovir 500mg PO BID x3d
  - Acyclovir 800mg PO BID x5d
- Daily suppressive (if >4-6 outbreaks/yr or severe symptoms):
  - Valacyclovir 1g PO daily
  - Acyclovir 400mg PO BID

CDC

Human papillomavirus (HPV)

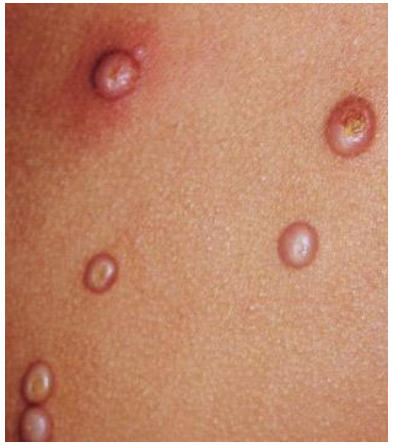
- Human papillomavirus (HPV) → anogenital warts
  - Soft, moist, raised (sometimes pedunculated) polyps that may cause itching, burning, or discomfort
  - Cryotherapy or surgical removal (e.g., shave, curettage, laser) or trichloracetic acid (TCA) or bichloracetic acid (BCA) 80-90% solution[§]
  - Patient-administered treatment options for external warts include:
    - Imiquimod 3.75-5% cream[†] or
    - Podofilox 0.5% solution or gel or
    - Sincatechins 15% ointment[†]



CDC

Molluscum contagiosum

- Molluscum contagiosum (poxvirus)
  - Smooth, small (2-5mm in diameter) papules, usually in clusters and with a central umbilication
  - Treatment can also be through mechanical methods or topical irritants



Case #3c: Genital ulcers

- Quinn, a 42 year-old Caucasian man, presents to your STI clinic for evaluation of a painless ulcer on his penis.
- He reports practicing unprotected anal penetrative and receptive intercourse with male partners.

- *What else do you want to know about his symptoms?*
- *What's your differential?*
- *How would you further evaluate his symptoms?*

Diseases of the skin (revisited)

- Herpes simplex virus
- Syphilis
- Chancroid
- Donovanosis (granuloma inguinale)
- Anogenital warts (HPV)
- Molluscum contagiosum

- Pubic lice (pediculosis pubis)
- Scabies
- Candidiasis
- Tinea cruris/corporis

Workup for syphilis

- *Treponema pallidum*

- Syphilis serology:
  - Nontreponemal tests (e.g., VDRL, RPR)
    - Screening test in the “classical” testing algorithm
  - Treponemal tests (e.g., FTA-ABS, TP-PA)
    - Detect antibodies specific for syphilis
    - *Treponemal antibodies remain detectable even after successful treatment*

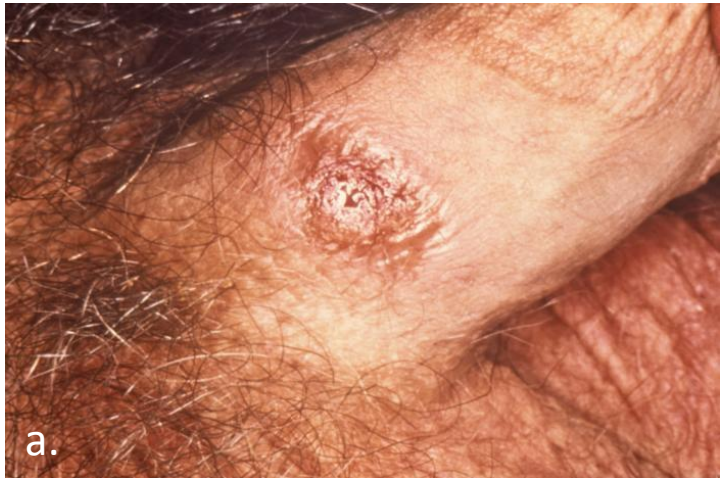
CDC (2017)

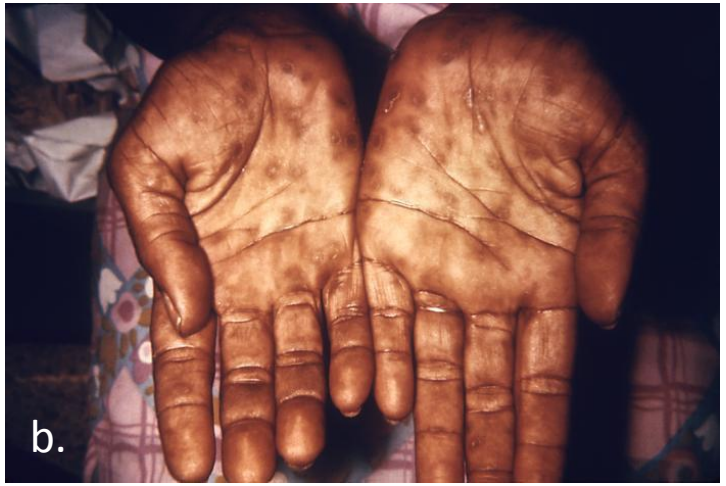
www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm
French P. *BMJ*. 2007;334:143-147.

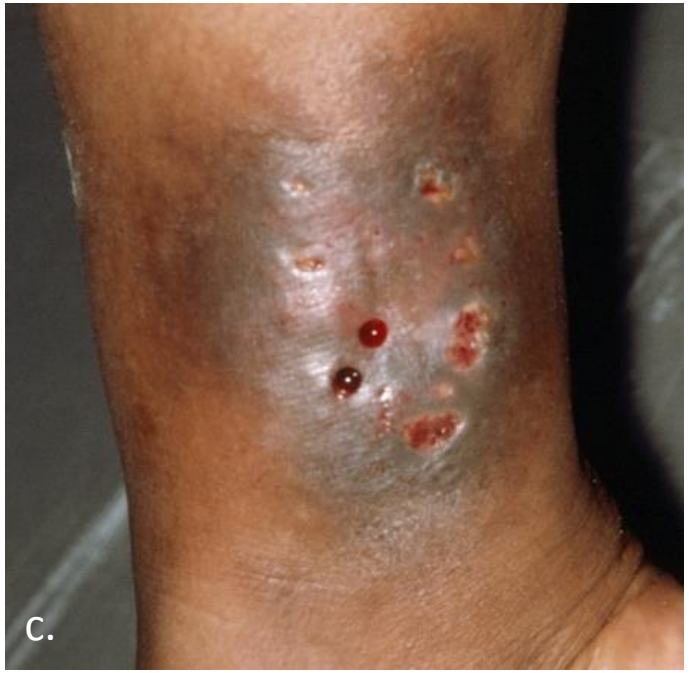
Syphilis: progression

Stage	
Primary	• Painless ulcer(s) lasting 3-6 weeks • Frequently associated with localized nontender LAD
Secondary	• Nonpruritic rash (rough spots) on palms/soles while primary chancre is healing, or several weeks later • Nonspecific symptoms such as fever, HA, LAD, sore throat, patchy hair loss, weight loss, myalgias, and fatigue
Latent	• Early latent syphilis = infection within previous 12 months • Late latent syphilis = infection more than 12 months ago
Tertiary	• Variable presentation affecting heart, liver, kidneys, and bones/joints • Appears 10-30 years after initial infection; can be fatal
Neurosyphilis	• When bacterium enters nervous system; can occur at any stage • Symptoms include altered behavior, dementia, ataxia, and paralysis • Ocular syphilis can lead to blindness

Syphilis: progression *(con't)*







a. Chancre (1° syphilis)
b. Syphilitic dermatitis (2° syphilis)
c. Gumma (late/3° syphilis)

Syphilis: treatment

- Primary, secondary, and early latent syphilis (<1y)
  - Benzathine PCN G 2.4 M units IM x1
- Late latent syphilis (or latent syphilis of unknown duration) and tertiary syphilis
  - Benzathine PCN G 2.4 M units IM weekly x3 (i.e., 7.2 M units total)
- Neurosyphilis and ocular syphilis
  - Aqueous crystalline PCN G 18-24 M units/day (3-4 M units IV q4h or continuous infusion) x10-14d

www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm
French P. *BMJ*. 2007;334:143-147.
Willeford WG, Bachmann LH. *Trop Dis Trav Med Vacc*. 2016;2:20.

Genital ulcer diseases (GUD)

- *Hemophilus ducreyi* → chancroid
  - Papules, painful ulcers, and suppurative inguinal lymphadenopathy
  - Azithromycin 1g PO x1 or ceftriaxone 250mg IM x1 or ciprofloxacin 500mg PO BID x3d or erythromycin base 500mg PO TID x7d
- *Klebsiella granulomatis* (formerly *Calymmatobacterium granulomatis*) → donovanosis (granuloma inguinale)
  - Rare in the US; beefy-red bumps give way to nodules and erosion of genital/anal tissue
  - Azithromycin 1g PO weekly x3+ or azithromycin 500mg PO daily x21+ (and until all lesions have completely healed)

Part 4:
Take me home, country roads

Infections by class

Bacterial	Viral	Fungal	Parasitic
Chlamydia	HSV-1/-2	Candidiasis	Trichomonas
Gonorrhea	HPV	Tinea	Pubic lice
Syphilis	Molluscum contagiosum		Scabies
Chancroid			
Mycoplasma			
Ureaplasma			
BV			
UTIs/Pyelo			
Donovanosis			

Complications and their treatment

- Lymphogranuloma venereum (LGV): doxycycline 100mg PO BID x21d
- Disseminated gonococcal infection (DGI): ceftriaxone 1g IM/IV daily x7d [or more] + azithromycin 1g PO x1
- Cervicitis: azithromycin 1g PO x1 *or* doxycycline 100mg PO BID x7d
  - Same as treatment for nongonoccal urethritis (NGU)
- Pelvic inflammatory disease (PID): ceftriaxone 250mg IM x1 + doxycycline 100mg PO BID x14d +/- metronidazole 500mg PO BID x14d
- Epididymitis: ceftriaxone 250mg IM x1 + levofloxacin 500mg PO daily x10d
- Proctitis: ceftriaxone 250mg IM x1 + doxycycline 100mg PO BID x7d

Take-home points

- There is substantial overlap in symptoms for STIs and UTIs, but infections may also be *asymptomatic*.
- Recommended treatment may differ based on various factors, and not all professional guidelines agree. When in doubt, consult a specialist.
- Similarly, be familiar with the laws in your place of practice, with regard to treatment of minors, EPT, etc.
- Patients can sense when you're nervous. Normalize sensitive questions for you and for them.

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