



# Sexually Transmitted Infections: Other Diseases & Syndromes

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## Disclosures of Financial Relationships with Relevant Commercial Interests

- None

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### Of Note

- I have tried to use patient-first language throughout. When the terms 'women' and 'men' are used, I am referring to cis-gender women and men unless otherwise specified
- All photos are freely available from the following website unless otherwise noted:  
<http://www.cdc.gov/std/training/clinicalslides/slides-dl.htm>

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### Other STI Syndromes

- Urethritis/Cervicitis/Vaginitis
- Proctitis
- PID
- Epididymitis
- HPV
- Ectoparasites

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## Urethritis/Cervicitis/Vaginitis

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*
- *Mycoplasma genitalium*
- *Trichomonas vaginalis*
- Bacterial vaginosis

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## Question #1

PREVIEW QUESTION



A 32-year-old man presents complaining of a penile discharge. Gram's stain of the urethral discharge reveals intracellular Gram-negative diplococci. He reports an allergy to penicillins and cephalosporins.

**Which of the following regimens does the CDC recommend as the most appropriate therapy?**

- A. Azithromycin
- B. Azithromycin plus ceftriaxone
- C. Azithromycin plus gentamicin
- D. Ciprofloxacin
- E. Spectinomycin

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## Question #2

PREVIEW QUESTION



A man with persistent urethritis following doxycycline therapy is tested and found to be positive for *Mycoplasma genitalium*.

**Which of the following is the most appropriate therapy (assume today is his last day of doxycycline)?**

- A. Azithromycin 1g orally
- B. Azithromycin 500mg orally X1 followed by 250 mg daily on the subsequent 3 days
- C. Doxycycline 100 mg orally twice daily for 14 days
- D. Moxifloxacin 400 mg orally daily for 7 days

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## *Chlamydia Trachomatis:* Take-home Points

- Annual screening of all sexually active women aged  $\leq 25$  years is recommended for serotypes D-K, as is screening of older women with risk factors (e.g., new or multiple sex partners)
- High rate of reinfection for D-K
- Both D-K and LGV (L1-L3) cause proctitis/proctocolitis
- Longer duration of therapy (3 weeks of doxycycline) for L1-L3 serotypes **if symptomatic\*\*\***
- Association with reactive arthritis; prompt treatment reduces risk of reactive arthritis

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## Chlamydia Trachomatis

- Serological classification
  - A,B, Ba, C (Trachoma)
  - D-K (Genitourinary and ocular infections)
  - L1-L3 (Lymphogranuloma venereum)

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## Chlamydia Trachomatis D-K

### MEN

- Asymptomatic
- Urethritis
- Epididymitis (**70% of cases in young men**)
- Proctitis
- Conjunctivitis
- Pharyngitis (rare)
- **Reactive arthritis (urethritis, conjunctivitis, arthritis, skin lesions)**

### WOMEN

- Asymptomatic
- Cervicitis
- Urethritis
- **Pelvic inflammatory disease**
- Bartholinitis
- Proctitis
- Conjunctivitis
- **Reactive arthritis**

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## Chlamydia: Diagnostics

- Detection of WBCs on Gram's stain is not sensitive
- Cell culture (sensitivity 70%), direct immunofluorescence, non-amplified molecular tests (sensitivity ~85%), and **NAATs (gold standard; sensitivity >95%; specificity >99%)**
- FDA cleared for the detection of *C. trachomatis* on endocervical and urethral swab specimens, urine, vaginal swab specimens, throat and rectal swabs
- **Routine NAATs do NOT distinguish between D-K and L1-L3 serotypes. Multiplex tests do but are not commercially available.**

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## Chlamydia Trachomatis Treatment

- Duration of therapy depends on serotype:
  - D-K serotypes: **doxycycline 100mg PO BID X 7d is preferred**; alternate is 1 g oral azithromycin
  - L1-L3 serotypes (if moderate to severe proctitis): **Doxycycline 100 mg PO BID X3 weeks** (preferred); alternate is azithromycin 1g PO q week X 3 weeks
- Use of azithromycin is safe in pregnancy
- Test-of-cure (repeat testing 3–4 weeks after completing therapy) is **not** routinely recommended
- Screen all persons treated for chlamydia infection 3 months later (REINFECTION rates are high)

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## Azithromycin vs. Doxycycline

- **Urogenital** *C. trachomatis*
  - RCT in correctional facility: azithromycin=97% vs. doxycycline=100% (noninferiority of azithromycin was not established)  
Geisler NEJM 2015
- **Rectal** *C. trachomatis*
  - 2 RCTs: Efficacy difference in favor of doxycycline of 20%  
Dombrowski CID 2021; Lau NEJM 2021

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## Gonorrhea: Take-home Points

- IM ceftriaxone 500 mg is the preferred regimen for uncomplicated gonorrhea
- Pharyngeal gonorrhea: ceftriaxone is the only drug that is recommended; test of cure 7-14 days after treatment
- Disseminated gonococcal infection: patients may NOT have symptoms of urethritis
- Gonococcal conjunctivitis: 1g of ceftriaxone

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## *Neisseria Gonorrhoeae*

- Clinical presentation similar to that seen with *C. trachomatis*.
  - no association with Reiter's
  - responsible for **30% of cases of epididymitis in young men**
  - **MOST cases (>90%) of pharyngeal and rectal gonococcal infections are ASYMPTOMATIC**



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## Disseminated Gonococcal Infection (DGI)

- DGI frequently results in petechial or pustular acral skin lesions (< 12 lesions), asymmetrical arthralgia, tenosynovitis, or (monoarticular) septic arthritis
- The infection is occasionally complicated by perihepatitis and rarely by endocarditis or meningitis.
- Strains of *N. gonorrhoeae* that cause DGI may cause minimal genital inflammation
- **Risk factor for DGI: terminal complement deficiency (acquired form often seen in SLE) and with complement inhibitors (Eculizumab)**
- Differential diagnosis: meningococcemia, RMSF, dengue, staphylococcal endocarditis, Reiter's
- Treatment: Ceftriaxone IM/IV usually 5-7 days; longer with arthritis, meningitis, or endocarditis

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## DGI



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## Gonorrhea Diagnostics

- A negative Gram's stain should NOT be considered sufficient for ruling out infection in **asymptomatic** men. In addition, Gram's stain of endocervical specimens, pharyngeal, or rectal specimens are not sufficiently sensitive or specific to detect infection
- Sensitivity of culture ~80-90% from endocervical or urethral specimens in symptomatic persons; **<50% from throat/rectum**
- NAATs offer the widest range of testing specimen types because they are FDA-cleared for use with endocervical swabs, **vaginal swabs**, male urethral swabs, and female and **male urine**
- NAATs are FDA-cleared for specimens obtained from the rectum and pharynx; they are the 'tests of choice' for these sites

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## Gonorrhea Therapy

- The only first-line option for uncomplicated gonorrhea is **ceftriaxone (500 mg IM x1)**
  - 7% of isolates in the US in 2021 had elevated MICs to azithromycin so it was abandoned as first-line therapy

St Cyr MMWR 2020

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## Gonorrhea Therapy (Cont.)

- Second-line agents for urogenital or rectal infections:
  - Cefixime (800mg PO X1)
  - **Gentamicin 5mg/kg IM+ 2g azithromycin**
  - Azithromycin 2g PO X1 is no longer recommended
- **There are NO second-line recommendations for pharyngeal gonorrhea-** it's ceftriaxone or bust!
  - Gentamicin and cefixime have lower efficacy for pharyngeal infections Ross JDC, et al. *Lancet* 2019
  - All pharyngeal infections: must do a test of cure within 2 weeks after ceftriaxone therapy

St Cyr MMWR 2020

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## Gonorrhea Therapy (Cont.)

- **DGI:** Ceftriaxone 1g IM or IV until clinically better (can also use cefotaxime and ceftizoxime); then, can complete 7-day course of therapy with a PO cephalosporin (once results of antibiotic susceptibility testing are available)
- **Gonococcal conjunctivitis:** Ceftriaxone 1g IM X1

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## Extragenital Gonorrhea and Chlamydia

- 90% are asymptomatic
- NAATs, now FDA cleared, are the preferred (and most sensitive) diagnostic modality
- CDC recommends screening for both GC and CT at the rectum but screening for only GC at the throat
- Sexually active MSM should be screened at all sites of exposure
  - The majority of GC cases in MSM would be missed if genital-only testing were performed
- No formal extragenital screening guidelines for women

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## Non-gonococcal Urethritis (NGU)

- Gram stain of urethral secretions demonstrating  $\geq 2$  WBC per oil immersion field or positive leukocyte esterase test on first-void urine or microscopic examination of sediment from a spun first-void urine demonstrating  $\geq 10$  WBC per hpf
- More common etiologies:
  - *Chlamydia trachomatis* (25% cases)
  - *Mycoplasma genitalium* (30% of cases)
  - *Trichomonas vaginalis* (10-25% of cases; mainly MSW not MSM)
  - *Ureaplasma urealyticum* (controversial; do NOT test for this bacterium)
  - HSV
- Less common etiologies: anaerobes; enterobacteriaceae, Haemophilus, *Staphylococcus saprophyticus*, adenovirus
- NGU treatment: **doxycycline 100mg PO BID X 7d is now the preferred regimen**

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## Non-gonococcal Urethritis (NGU) (Cont.)

- If a person with NGU fails to respond to therapy, think of 4 possibilities: (1) Reinfection (2) *M. genitalium* that did not respond to above therapy (see next slide) (3) *T. vaginalis*- rare in MSM (treat with metronidazole) or (4) HSV

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## *Mycoplasma Genitalium*

- Strong association with non-gonococcal urethritis (NGU) [up to 30% of cases] and up to 35% of cases of persistent urethritis
- Moderate association with cervicitis and PID; weaker association with infertility
- **Test men with persistent urethritis or epididymitis; consider testing women with persistent cervicitis or PID (discuss with patient); consider testing in men and women with persistent proctitis symptoms; DO NOT SCREEN!**
- FDA-cleared diagnostic test now available
  - Combined molecular diagnostic with molecular detection of macrolide resistance is not yet FDA cleared but is available at a commercial laboratory in the US.

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## *M. Genitalium* Therapy

- **DUAL antibiotic therapy is now recommended**
  - Start with one week of doxycycline 100 mg orally BID (will decrease bacterial load) followed by either:
    - Azithromycin 500mg orally X1 followed by 250 mg daily on the subsequent 3 days (if macrolide sensitivity is known) OR
    - Moxifloxacin 400mg POX 7 days (if macrolide resistant or if macrolide resistance is unknown)
  - Emerging resistance to fluoroquinolones (~15% moxifloxacin resistance)
- **NOT FOR THE BOARDS:** In persons with FQ failures you can use minocycline (100 mg PO BID X 14 d) or ? tinidazole (2 g daily for 7 days); Pristinamycin (not available in US)

Int J STD AIDS. 2019;30(5):512-514

Clin Infect Dis. 2015;60(8):1228-36

<https://sti.guidelines.org.au/sexually-transmissible-infections/mycoplasma-genitalium/>

Sex Transm Dis. 2025. 1:52(2):e2-e4

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## Summary: Urethritis Approach

- All men presenting with urethritis should be tested for both GC and CT and treated with ceftriaxone and one week of oral doxycycline
- If the GC and CT tests are negative and the patient has persistent symptoms and signs:
  - If the patient is a MSW: Test for *M genitalium* and trichomonas and treat based on results
  - If the patient is a MSM: Test for *M genitalium* and treat based on results (trichomonas is rare in MSM)

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## Question #3

A 22-year-old woman is diagnosed with persistent cervicitis secondary to *Mycoplasma genitalium*. She is treated with one week of doxycycline followed by one week of moxifloxacin. She reports one male sex partner in the prior two months.

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### Question #3

Which of the following is the recommended approach to managing her sex partner?

- A. The CDC does not recommend routine partner therapy for *M genitalium*
- B. Test the partner for *M genitalium* only if symptomatic and, if positive, treat
- C. Test the partner for *M genitalium* irrespective of symptoms and, if positive, treat
- D. Treat the partner for *M genitalium* without testing using expedited partner therapy

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### Trichomonas Vaginalis

- May be asymptomatic in both men and women; causes vaginitis and NGU
- Diagnosis: culture and PCR; wet mount is not sensitive
- Vaginal pH usually >4.0
- Therapy: **Treat all women with metronidazole 500mg PO BID X 7 days OR tinidazole 2g PO X1** [do NOT use topical gel formulations]
  - RCT: 7 days of metronidazole superior to 2g single dose Kissinger et al. Lancet Inf Dis 2019
- **Therapy: Treat all men with metronidazole 2g PO X1 OR tinidazole 2g PO X1**
- Resistance: ~5% of strains have low-level resistance to metronidazole; <1% have high level resistance (see next slide)
- Partners in the preceding 60 days must be treated
- No need to screen asymptomatic pregnant women for trichomonas; **screen all women with HIV annually**

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### Trichomonas & Nitroimidazoles

- **Tinidazole** has a longer serum half-life and achieves higher tissue concentrations than metronidazole; MICs to tinidazole lower than to metronidazole
- Can use 2g of oral tinidazole to treat both men and women
- If patient fails Rx with metronidazole & reinfection is excluded:
  - Option 1: Tinidazole 2 g PO X1
- If patients fails option 1 above:
  - Option 2: Metronidazole 2g PO QD X 5d
  - Option 3: Tinidazole 2g PO QD X 5d

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### Bacterial Vaginosis

- Complex polymicrobial infection; causes vaginitis (thin, white, discharge with 'fishy' odor) and cervicitis; **may increase risk of PID**
- Dx: Nugent's score preferred in research settings; Amsel's clinical criteria performed in clinical settings: (1) discharge (2)pH>4.5 (3) clue cells (4) amine odor with KOH (whiff test)

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## Bacterial Vaginosis

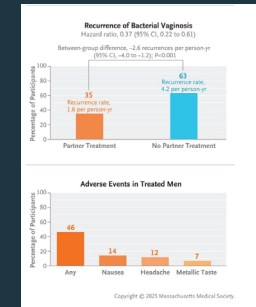
- Rx: Metronidazole 500mg PO BID X 7days OR Clindamycin 300mg PO TID X 7 days OR topical metronidazole gel or clindamycin cream OR Secnidazole 2g PO X1 dose
  - L. crispatus* supplements after topical metronidazole resulted in a 34% reduction in recurrence at 3m Cohen NEJM 2020
- Do NOT use metronidazole 2g PO X1**
- BV during pregnancy:** associated with preterm labor, PROM, post-partum endometritis
- Treat all **symptomatic** cases of BV during pregnancy; **screening asymptomatic pregnant women for BV if high risk for pre-term delivery (e.g., history of premature delivery) is no longer recommended**

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## Male-Partner Treatment to Prevent Recurrence of Bacterial Vaginosis

A Research Summary based on Voldreil LA et al. | 10.1056/NEJMoa2405404 | Published on March 6, 2025

- RCT; monogamous male partners of women with BV were treated with metronidazole 400-mg tablets and 2% clindamycin cream applied to penile skin, both twice daily for 7 days
- Trial stopped early by DSMB
- 80% of men were uncircumcised
- 7 prior studies did not show benefit, but none used topical clindamycin
- No change in recommendations in the US yet (but stay tuned)



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## Pelvic Inflammatory Disease (PID)

- Diagnostic criteria- only ONE of the following:
  - Cervical motion tenderness
  - Uterine tenderness
  - Adnexal tenderness
- Hospitalize
  - Pregnant
  - Tubo-ovarian abscess
  - Appendicitis cannot be excluded
  - Did not respond to PO antibiotics
  - Patient has nausea and vomiting, or high fevers/severe illness
  - Unreliable follow-up if treated as outpatient
- MOST patients with PID can be treated as outpatients (including first-episode PID and HIV positive women who do not meet above criteria)

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## Pelvic Inflammatory Disease (PID)

- Therapy**
  - Ceftriaxone 500 mg IM in a single dose **PLUS Doxycycline** 100 mg orally twice a day for 14 days **WITH Metronidazole** 500 mg orally twice a day for 14 days
  - Cefotetan 2 g IV every 12 hours **OR Cefoxitin** 2 g IV every 6 hours **PLUS Doxycycline** 100 mg orally or IV every 12 hours
- Additional recommended regimens can be found in the 2021 CDC STI Treatment Guidelines (online at cdc.gov)
- All patients treated with PO regimens should improve within 3 days otherwise, admit for parenteral antibiotics
- Treat all sex partners in preceding 60 days

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## Fitzhugh-Curtis Syndrome

- Perihepatitis: RUQ pain or pleuritic pain; usually NO LFT abnormalities (or very mild)
- Complicates ~10% of PID cases
- Pathophysiology: ?Direct extension of pathogens vs. immunological mechanism
- Rx: NSAIDs (+ treat PID)

## Epididymitis

- In young men:
  - *C. trachomatis* (70%)
  - *N. gonorrhoeae* (30%)
- In older men: *E. coli* causes majority of cases
- Therapy:
  - **Ceftriaxone 500mg IM X1 + Doxycycline 100mg PO BID X 10 days**
  - For acute epididymitis most likely caused by sexually-transmitted chlamydia and gonorrhea and enteric organisms (men who practice insertive anal sex): Ceftriaxone IM X1 + levofloxacin X 10 days
  - For acute epididymitis most likely caused by enteric organisms: Levofloxacin 500mg PO X10 days

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## Question #4

A 30-year-old man with HIV presents with severe pain on defecation and bloody anal discharge. He had unprotected anal sex one week ago. He experiences pain with DRE. There are no visible anal ulcers, but a bloody mucoid anal discharge is noted. No diagnostic tests are available.

Which of the following empiric antibiotic regimens is most appropriate?

- A. Ceftriaxone 500mg IM + Azithromycin 1g PO X1
- B. Ceftriaxone 500mg IM + Doxycycline 100mg PO BID X 7d
- C. Ceftriaxone 500mg IM + Azithromycin 1g PO weekly X 3wks
- D. Ceftriaxone 500mg IM + Doxycycline 100mg PO BID X 21d
- E. Ceftriaxone 500mg IM + Doxycycline 100mg PO BID X 7d + oral valacyclovir

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## Proctitis/Proctocolitis

### COMMON

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis* D-K
- *Chlamydia trachomatis* L1-L3 (LGV)
- *T. pallidum*
- HSV (severe especially among HIV+)
- Mpox

### OTHER CAUSES

- *Campylobacter*
- *Shigella*
- *Entamoeba*
- CMV
- *Giardia lamblia*\* (mainly enteritis; especially among MSM)

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## Proctitis Therapy

- **Ceftriaxone 500mg IM X1 + Doxycycline 100mg PO BID X 7-21 days depending on extent of symptoms**
- **Treat for 21d:** Moderate to severe symptoms- (e.g., pain, bloody discharge +/- ulcers)
- **Treat for HSV:** Painful perianal ulcers or mucosal ulcers are detected on anoscopy
- Azithromycin is less effective than doxycycline when treating proctitis due to *C. trachomatis*.

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## HPV

- >30 types cause genital infections
- High risk (e.g., 16, 18) and low-risk (e.g., 6 & 11)
- 16 & 18 cause ~70% of cervical cancers in addition to significant proportion of vulvar, vaginal, anal, and upper airway cancers
- Low-risk types can cause genital warts and low-grade dysplasia (CIN I)
- Low-risk types cause recurrent respiratory papillomatosis
- Single biggest risk factor for dysplasia is PERSISTENCE of infection
- Risk factors for persistence: older age; immunosuppression; smoking; concurrent infection with multiple types



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## Genital Warts

- 90% of warts caused by HPV 6 & 11; concomitant infection with types 16, 18, 31, 33, and 35 increases risk of HSIL
- Genital warts may develop months or years after infection
- Up to 60% of warts will recur within 3 months after therapy. Many will clear spontaneously after 12 months
- Available therapies do not completely eradicate infectivity
- Hypopigmentation or hyperpigmentation can occur with ablative modalities (cryotherapy and electrocautery) and with immune modulating therapies (imiquimod).
- No c-section in pregnant women with visible warts
  - C-section only if the warts are obstructing the birth canal or if vaginal delivery may lead to increased risk of bleeding

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## HPV Vaccines

- **Nonavalent (6, 11, 16, 18, 31, 33, 45, 52, 58);** 2-3 doses given over 6-12 months (2 doses induce good immunity if age ≤ 14 years)
- Consists of VIRUS-LIKE PARTICLES (**noninfectious**; NO DNA)
- Efficacy: >97% against CIN 2/3, vulvar, and vaginal lesions; >98% against genital warts\*
- Recommended for routine use in 9- to 26-year-old women (even those who have a history of abnormal Pap smears); routine use in boys ages 11-12 years, catch-up for males ages 13-21, and permissive use of the vaccine in men ages 22-26; vaccine FDA cleared for women up to age of 45 (but ACIP has not recommended it in women age > 26)

\*FDA approved a supplemental biologics licensure application in 6/2020: prevention of oropharyngeal and other head and neck cancers caused by HPV types targeted by the vaccine

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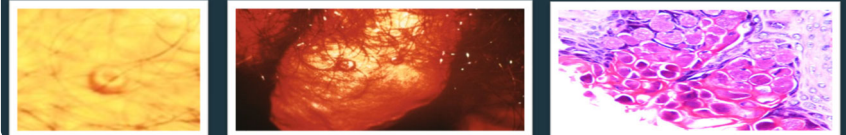
## HPV Vaccines (Cont.)

- Do not give during pregnancy; no need to restart schedule for patients who don't follow-up on time: **JUST PICK UP WHERE YOU LEFT OFF**
- Continue routine Pap smears on all women who get the vaccine
- Side effects: vasovagal response; local reactions
- Not a therapeutic vaccine

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## Molluscum Contagiosum

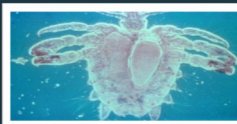
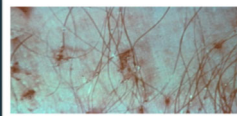
- Poxvirus
- 1 to 5mm lesions; painless papules; **CENTRAL UMBILICATION**
- Not necessarily sexually transmitted
- Molluscum bodies: intracytoplasmic inclusions
- Rx: curettage; cryotherapy; topical cidofovir



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## Pediculosis Pubis

- Pediculosis pubis= pubic lice= crabs (*Pthirus pubis*)
  - Nits confined to upper shaft=old infection (no need for retreatment)
  - Maculae ceruleae (blue gray macules)
  - Permethrin 1% cream OR Pyrethrins with piperonyl butoxide (topical)
  - Resistance increasing; consider malathion 0.5% lotion or Ivermectin in case of treatment failure
  - Do NOT use Lindane; toxicities include seizures and aplastic anemia
  - Treat sex partners within previous 30 days



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## Scabies

- *Sarcoptes scabiei*
- Severe pruritus; especially at night or after bathing; burrows; the diagnosis is usually a clinical one
  - Permethrin cream 5% (wash off after 8 hours) OR
  - Ivermectin 200 mcg/kg PO day 1 and 14
  - Only use Lindane as an alternative
- **Crusted scabies or 'Norwegian scabies'**
  - Mainly occurs in immunodeficient patients (HIV)
  - May NOT cause pruritus or burrows
  - Contagious and aggressive
  - Ivermectin 250mcg/kg on days 1, 15, and 29
- Rash and pruritus of scabies may persist for up to 2 weeks after successful therapy\*\*\*



Arch Dermatol. 2007;143(5):626

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## Prevention: Doxy-PEP

- Doxycycline 200 mg within 72 hours of a sexual exposure in MSM and transgender women with  $\geq 1$  STI in prior 12 months
  - Data in cis-gender women do not yet suggest benefit (additional studies are in progress)
  - Significant protection against syphilis and chlamydia; data on gonorrhea are less clear
  - In addition to known doxycycline toxicities, questions about emergence of antimicrobial resistance, impact on microbiome, and impact on syphilis management remain unanswered

MMWR Recomm Rep 2024;73(No. RR-2):1–8. DOI: <http://dx.doi.org/10.15585/mmwr.r7302a1>  
Clinical Infectious Diseases, 2024;, ciae062, <https://doi.org/10.1093/cid/ciae062>

## The End

**Thank you and good luck!**

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