2015 Update on Sexually Transmitted Infections

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Sneak Peek: What’s New in 2015
- STI screening recommendations summarized
- NGU – new dx criteria, treatment of persistent sx, and role of mycoplasma genitalium
- GC - alternative medication regimens
- Epididymitis in MSM
- Granuloma inguinale: azithromycin preferred
- Genital warts - new imiquimod option, d/c podo
- HIV PrEP
- Hep C screening for HIV+ MSM

Sexually Transmittable Infections
- amebiasis
- chancroid
- chlamydia
- Ebola
- gonorrhea
- granuloma inguinale
- group B strep
- hepatitis A, B, C
- herpes simplex virus
- syphilis
- HIV
- trichomoniasis

Half of New STIs are in adolescents and young adults under age 25

Estimated number of new sexually transmitted infections

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Age 0-24</th>
<th>Age 25-44</th>
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<tbody>
<tr>
<td>Hepatitis B</td>
<td>14,000</td>
<td>5,400</td>
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<tr>
<td>Syphilis</td>
<td>22,000</td>
<td>7,700</td>
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<tr>
<td>Gonorrhea</td>
<td>66,000</td>
<td>32,000</td>
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<tr>
<td>Trichomoniasis</td>
<td>1,200,000</td>
<td>2,000,000</td>
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<tr>
<td>Chlamydia</td>
<td>2,800,000</td>
<td>14,000,000</td>
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</table>

TOTAL: 19,738,800

CDC STD Treatment Guidelines
- Authoritative source of STD treatment and management
- Screening, prevention and vaccination strategies, plus treatment regimens
- Updated q 4-5 years
- Pocket guides, wall charts, slide set, mobile versions
- Download or order at www.cdc.gov/std/treatment


Age-specific STD Rates of Reportable STDs** Wisconsin, 2013

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Rate</th>
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<td>20-24</td>
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<td>25-29</td>
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<td>30-34</td>
<td>48</td>
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<td>35-39</td>
<td>18</td>
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</tbody>
</table>

*Cases per 100,000 population
** Gonorrhea, syphilis, and chlamydia
Chlamydia Screening: Females

- Sexually active females 25 and under: Screened annually
- Repeat testing 3–4 months after treatment due to high rate of re-infection

AAP, USPSTF and CDC Recommendations

Chlamydia Screening: Males

- No guidelines recommending for or against
- Selective screening in high-prevalence populations may be beneficial

see www.cdc.gov/std/chlamydia/ChlamydiaScreening-males.pdf
USPSTF cites "insufficient evidence" to recommend routine screening for ALL males

Chlamydia Testing with NAATs
(Nucleic Acid Amplification Tests)

- Combination test for CT/GC typical
  - can use CT alone, with reflex to GC, for lower risk women
- Self-collected vaginal swab preferred (women)
  - highest sensitivity
- Initial-void urine specimen (men or women)
  - must be a "dirty" catch, first 30ml only
  - no pelvic exam required
- Re-screen @ 3 months if positive
  - test of cure not needed
  - testing too soon may produce a false positive result due to residual chlamydia DNA (allow 4 weeks minimum)

Chlamydia Symptoms

- **Females:** Usually asymptomatic
  - Spotting (esp after intercourse)
  - Dyspareunia
  - Dysuria
  - Vaginal discharge

- **Males:** ~50% develop urethritis
  - Urethral discharge and/or dysuria
  - Often: just urethral "irritation"
  - May be asymptomatic

Chlamydia - Treatment

- **Recommended:**
  - Azithromycin 1g po single dose, $25
  - 500mgtabs are better tolerated than 1g sachet powder
  - Doxycycline 100mg po BID X 7 days, $15
    - doxy was marginally superior to azithro in a meta-analysis
- **Alternatives:**
  - Erythromycin 500mg or 800mg QID X 7 days
  - Levofloxacin 500mg QD po X 7 days
  - Ofloxacin 300mg po BID X 7 days

Collecting a Vaginal Swab
If you have any questions about this procedure, please ask your health care provider.

1. Hold your hands, turn the cap to break the seal. Pull the cap off carefully to avoid damaging the swab. Place it in a test tube or self-test kit.
2. Hold the swab by the ring with one hand and the small cap by the other hand. Place the tip of the swab into the vagina and deep in the fornix (soft part of the cervix) but not too deep.
3. Gently slide the swab up to remove the cells. If the swab does not slide easily, gently move the swab up and down gently. It is very important to get all the cells.
4. Withdraw the swab and immediately place it in the self-test kit or test tube. Do not attempt to continue collecting the sample.
5. Withdraw the swab without touching the air. Place the swab in the tube and test immediately. It will not work well if swab is not screened.
Lymphogranuloma Venereum (LGV)

- A specific serovar (subtype) of chlamydia
- Associated with proctocolitis in MSM
  - test for rectal chlamydia using NAAT
  - additional molecular testing for LGV can be done but is not generally available
- Treat presumptively with doxycycline X 21 days (100mg BID) if LGV is suspected based on clinical presentation (rectal pain + bleeding)

Gonorrhea: overview

- Overall prevalence in 18-26 y.o. is 0.4%; rates in blacks are 13X higher than whites
- Infection more common in specific populations:
  - men who have sex with men (MSM)
  - urban, low income (esp. African American)
- Screen women if increased risk: age < 25, other STI, new/multiple partners, contact, drug use, prior infection, sex workers (USPSTF)
- Screen MSM routinely and use NAATs for all anatomic sites of exposure (pharynx, anal)
- Antimicrobial resistance is a growing problem

Gonorrhea—Rates of Reported Cases by Race/Ethnicity and Sex, United States, 2013

- **Case: Carlos**
  - 22 y.o. gay male, asymptomatic. Reports his partner was diagnosed with urethral gonorrhea.
  - What do you test him for?
  - What anatomic sites get tested?
  - Do you treat him empirically?
  - With which drug?

Gonorrhea

Clinical Presentation

- Urethral infection is usually symptomatic
  - 2-5 day incubation, then purulent urethral discharge
  - Gram-negative intracellular diplococci on Gram stain
- Cervical, rectal and pharyngeal infection is usually asymptomatic
  - rectal pain/discharge/tenesmus suggests GC or CT

Gonorrhea Treatment

**must use dual therapy:**

- **Ceftriaxone 250 mg IM single dose**
- **PLUS Azithromycin 1gm PO single dose**

- include azithromycin regardless of chlamydia test result
- do not use doxycycline
- reconstitute ceftriaxone in 1% lidocaine for patient comfort
- penicillin allergy is not a contraindication to 3rd gen cephalosporins unless documented IgE/anaphylaxis
- allergy to cephalosporin – see guidelines
Gonorrhea Treatment Alternatives
- Cefixime 400mg po + azithromycin 1g po
  - discouraged, use only if ceftriaxone not available
- Gemifloxacin 320mg po + azithromycin 2g po
  - limited availability; poorly tolerated (emesis)
- Gentamicin 240mg IM + azithromycin 2g po
  - poorly tolerated (emesis, multisite injection)
- Suspect treatment failure? Contact local health dept; ID or CDC consult recommended

Chlamydia & Gonorrhea Complications
Epididymitis (men) – cover both GC and chlamydia
- For most young adult males:
  - ceftriaxone 250mg IM single dose + doxycycline 100mg BID X 10 days
- For MSM with history of insertive anal sex:
  - ceftriaxone 250mg + levofloxacin 500mg X 10 days
- For others where CT/GC is not a likely cause:
  - levofloxacin 500mg or ofloxac 300mg X 10 days

Chlamydia & Gonorrhea Complications
Pelvic Inflammatory Disease – PID (women)
- represents ascending infection into upper genital tract
  - abd/pelvic pain plus either adnexal tenderness, cervical motion tenderness, or uterine tenderness
- treat X 14 days to cover gonorrhea, chlamydia, anaerobes:
  - ceftriaxone 250mg IM single dose + doxycycline 100mg BID X 14 days, with or without metronidazole 500mg BID X 14 days
- multiple outpatient and inpatient regimens exist, see STD Treatment Guidelines for discussion and details

Nonspecific Urethritis in Men
- Continuum of symptoms: mild urethral irritation “doesn’t feel right”, to frank dysuria and discharge
- Pearl: dysuria in young men is an STI unless proven otherwise. Always test for CT and GC.
- Primary etiologies are chlamydia and mycoplasma genitalium
- Adenovirus, HSV, Trich, anaerobes, and enteric bacteria are other potential causes
- “Idiopathic urethritis” – urethral symptoms without objective findings. Manage with NSAID.

Urethritis Management
- Diagnostic criteria
  - urethral discharge on exam, and/or
  - Gram stain with >= 2 WBCs/field, or
  - + leukocyte esterase on first void urine, or
  - >10 WBC/field on urine microscopy
- Chlamydia and gonorrhea urine NAAT
- Empiric treatment if objective signs (above) or high risk and unlikely to follow up
  - Azithromycin or doxycycline first
  - Moxifloxacin or metronidazole for recurrence

Urethritis Management
Should you treat for both CT and GC?!
- in most settings, this is common practice
- but in college health, >90% is not GC (unless MSM)

My recommended approach:
- UA to confirm pyuria → empiric treatment with azithromycin single dose
- Cc and Gc NAAT on initial-voided urine
- Gram stain of discharge if available; can r/o GC
- If GC positive, return w/72 hours for IM ceftriaxone
- Treat empirically for GC at visit only if GC is suspected
  - purulent discharge, epi risk, contact to GC
**Mycoplasma genitalium “M-gen”**
an emerging pathogen
- Causes ~25% of NGU; maybe cervicitis, PID
- commercial diagnostic tests not readily available
- azithromycin much more effective than doxycycline (but emerging resistance to azith)
- suspect in persistent or recurrent urethritis; consider in persistent cervicitis or PID
- use moxi for recurrent sx after azithromycin: 400mg p.o. once daily X 7 days

**STI Partner Management**
Recent sexual partners (60 days) of patients diagnosed with these STIs should be treated empirically with the same regimen:
- Chlamydia
- Gonorrhea
- Syphilis (6 months)
- Trichomoniasis
- Pelvic inflammatory disease
- NGU (usually)

**STI Partner Management Strategies**

- **Public Health Referral**
  Partners are contacted by a disease intervention specialist following patient interview

- **Patient Referral**
  Index patient assumes primary responsibility to notify and refer his/her partners at risk

- **Patient Delivered Therapy**
  Providers (1) give patient medication intended for the partners, or (2) write partners’ prescriptions for medication

**Expeditied Partner Therapy**

- Provide extra Rx or meds to your patient to give to their partner(s)
- More effective than simple partner referral
- Use for chlamydia or trich infections
- Legal in most states; including Wisconsin
  - law provides liability protection for provider
  - can label Rx with the phrase “EPT” if no name
  - must provide information handout
  
  www.dhs.wisconsin.gov/communicable/std/ept.htm

**Vaginitis**

- **Vaginal Discharge +/- Dysuria**
  - Trichomoniasis
  - Bacterial Vaginosis
  - Yeast Vaginitis

**Trichomoniasis**

- Vag discharge +/- dysuria, ↑ vag pH, inflammatory
- Diagnostic tests
  - several rapid tests are available, offer improved sensitivity over vaginal wet prep
  - culture is definitive; PCR available in some settings
- Treatment
  - Metronidazole 2 g PO single dose (preferred)
  - Tinidazole 2 g PO single dose (preferred)
  - Metronidazole 500 mg PO BID X 7 days (alternative, HIV+)
  - Metronidazole gel is ineffective and not recommended
  - Treat partners and rescreen women 3 mo post treatment
Bacterial Vaginosis

- Vag discharge with odor, ↑ vag pH, not inflammatory
- Treat all symptomatic women
- Treat all pregnant women (risk of PROM, preterm, etc)
  - insufficient evidence to support routine screening in pregnancy
- Single dose therapy is ineffective
  - Recommended regimens:
    - Metronidazole 500 mg BID X 7 days
    - Metronidazole gel 0.75%, 5g qHS X 5 days
    - Clindamycin cream 2%, 5g qHS X 7 days
  - Alternative regimens:
    - Tinidazole 3g PO qd x 2d, or 1g PO qd x5d
    - Clindamycin 300 mg PO BID X 7 days
    - Clindamycin ovules 100g intravaginally qHS X 3 days
- Do not treat partners

Case: Jenna

- Jenna, age 20, presents with a bump on her genitals
- She has been sexually active for six months with one partner
- She received only one dose of HPV vaccine in high school

Differential Diagnosis

External Genital Warts → Genital Lesion → Folliculitis

Molluscum Contagiosum

Human Papillomavirus (HPV)

- Universal, ubiquitous infection:
  - nearly all adults have had genital HPV infection by age 50
  - 50% of young women have incident HPV infection within 4 years of coitarche; 27% of adults 18-25 have prevalent infection
- Most infections are asymptomatic, benign and self-limited
  - about 10% of infections result in disease (dysplasia or warts)
  - even most of these clear spontaneously
  - persistent infection with high-risk HPV type is the concern
- But: ~1 million people with genital warts, ~1 million with dysplasia, 24,000 people develop HPV-associated cancers annually, and ~20 deaths per day in U.S. due to HPV

HPV Vaccines

- Bivalent (HPV2) protects against HPV 16/18 only
- Quadrivalent (HPV4) protects against HPV 6/11/16/18
- Nine-valent (HPV9): 6/11/16/18/31/33/45/52/58

- All are highly efficacious (>99%) in preventing CIN 2/3;
- HPV4/9 vaccine also prevents genital warts (>99%)
- Protection against vulvar, vaginal, penile and anal cancer and intraepithelial neoplasia
- Very immunogenic (50X natural infection)
- Long duration of protection (10+ years)
- All dosing is 0,1-2, and 6 months

HPV Vaccine Recommendations

<table>
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<th>Population</th>
<th>Recommendation</th>
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<td>Gender</td>
<td>Age</td>
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<td>9-26</td>
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<tr>
<td>All males</td>
<td>9-21</td>
</tr>
<tr>
<td>All males</td>
<td>22-26</td>
</tr>
<tr>
<td>MSM and HIV* males</td>
<td>22-26</td>
</tr>
</tbody>
</table>

- Vaccinate irrespective of sexual history, cytology history, or HPV wart history
- HPV9 may be substituted for any needed dose of HPV4
Cervical Cytology Screening

- Begin screening at age **21**
- Screen with routine Pap every **3 years** for women 21–29 years
- No Pap before age 21 unless immunocompromised
- Add HR-HPV test at age **30**


External Genital Warts: Patient Applied Treatments

- **Imiquimod** cream (Rx)
  - 5%: apply 3 X weekly
  - 3.75%: apply daily

  OR

- **Podofilox 0.5% solution/ gel (Rx)**
  - Apply to visible genital warts twice a day for three days, followed by four days of no therapy

- **Sinecatechins** 15% ointment (Rx)
  - Apply 3 times daily
  - Use no longer than 16 wks
  - Do not wash after use.

External Genital Warts: Provider-Administered Treatments

- **Cryotherapy** with liquid nitrogen or cryoprobe
  - Repeat every 1–2 weeks

- **Trichloroacetic acid (TCA)**
  - Repeat as needed

  OR

- Surgical removal
  - either by scissor excision, shave excision, curettage, or electrosurgery

Case: Justin

Justin is a 19-year-old male who presents with a painful sore “down there.” He noticed it five days ago.

Genital Lesion Differential Dx

- **Herpes**
  - Center of painful (sometimes) sores

- **Genital Sores**
  - Painful ulcer with sharp borders

- **Syphilis**
  - Syphilitic painless ulcer with indurated border

- **Trauma**
  - Usually tender, abrasion or laceration

- **Painful, indurated lesion**
  - Sharp, painful, shallow erosion or ulcer

Genital Herpes - Multiple Ulcers

Diagnostic test of choice: PCR from lesion swab

Source: Cincinnati STD/HRV Prevention Training Center
Genital Herpes Infection

- **HSV-2** is a common cause of first episode genital herpes and causes almost all recurrent genital herpes.
- **HSV-1** is an increasingly important cause of first episode genital herpes but recurrences are infrequent.
  - HSV-1 accounts for as much as 70% of genital herpes infections in adolescent/young adult populations.
  - Most of these are acquired from oral-genital contact.
- Most transmission occurs as a result of asymptomatic viral shedding in the source partner, rather than lesions.
- Important synergism between HIV and HSV.
  - 2-to-5x increased risk of HIV acquisition if HSV2+.

Genital Herpes: 2015 CDC Treatment Recommendations

- Acyclovir, famciclovir, valacyclovir are all therapeutically equivalent.
- Differences in cost, dosing, convenience.
- Treat initial clinical episode for 7-10 days (sometimes need 14-20 days), recurrences for 3-5 days.
- Always offer suppressive therapy for new HSV-2 diagnosis; benefit greatest in first year.
- See treatment guidelines for multiple dosing options.
- Counsel re transmission and prevention (condoms).

Syphilis

STI caused by the bacterium Treponema pallidum.

Includes three stages:
- Primary
- Secondary
- Late and Latent

Primary and Secondary Syphilis—Reported Cases by Sex, Sexual Behavior, and Race/Ethnicity, United States, 2013

- Whites
- Blacks
- Hispanics
- Other
- MSW
- Women
- MSM

Case – Rash on Palms & Soles

Secondary syphilis: there’s nothing else like it!

- Toby, age 23, MSM
- Rash X 1 week
- PMHx: HIV infection

Treatment Options for Genital Herpes

- **Episodic therapy** (preferred for HSV1)
  - Short course of treatment to manage symptoms only.
- **Suppressive therapy** (preferred for HSV2)
  - Daily treatment suppresses viral activity.
    - Initiate at time of diagnosis.
    - Reduce or eliminate recurrent symptoms.
    - Reduce risk of transmission to sexual partners.
- **Episodic suppression**
  - Short term use to cover periods of concern: travel, final exams, etc.
**Syphilis**
- Low incidence; most infections now occur in MSM
- Routine screening of MSM is important; HIV co-infection is common
- Use PCR or dark field for suspicious lesions, if available
- Standard treatment unchanged in decades:
  - Benzathine penicillin G, 2.4 million units IM single dose
  - Repeat x 2 at one-week intervals if latent
- Same tx regimen if HIV+, but monitor with serologic follow up more frequently (q 3 months)
- LP if CNS signs, tertiary syphilis, or serologic treatment failure (not indicated for latent syphilis alone)
- Azithromycin as alternative drug discouraged

**Syphilis: Screening**
- CDC guidelines do not recommend universal screening
  - *Pregnant women*
  - *Sexually active MSM*
  - *Other high risk patients (multiple partners, other STI dx)*

**HIV testing and prevention**
- CDC recommendations for primary care:
  - Screen all adults at least once
  - Screen higher risk patients annually (e.g., MSM)
- Offer post-exposure prophylaxis for significant exposures (occupational or non-occupational)
  - 28 day course of ARV, e.g., Truvada + Isentress
  - See MMWR 2005;54(RR-2) for details
  - Use national PEP hotline 800-448-4911
- Recognize acute HIV/seroconversion illness
  - Unexplained febrile illness in MSM → HIV RNA

**Pre-Exposure Prophylaxis [PrEP]**
- Daily use of an anti-retroviral medication is recommended for persons at substantial risk of HIV infection
- Sustained drug levels provide significant reduction in risk of HIV transmission following exposure (>90%)
- Requires a (very) motivated patient; follow up q3 mo
- Data from the iPrEx study (NEJM 2010 Nov 23):
  - PrEP with TDF/FTC was effective in reducing HIV risk in MSM
  - New infections reduced by 44% overall when compared to placebo
  - Efficacy was correlated with drug adherence (92% if detectable drug)
- CDC has published provider guidance

**Pre-Exposure Prophylaxis [PrEP]**
- PrEP is an important prevention tool that should be available to high risk patients as part of a comprehensive risk reduction strategy
  - Providing PrEP is easier than you think and can (should) be done in college health and other primary care settings
  - Baseline testing: HBV status, HIV status, creatinine (eGFR)
  - Rx: 30 day supply of Truvada with 2 refills
  - Patient must return q90 days for HIV screen and new Rx
  - Cost is ~$1200/month, insurance coverage varies

**Hepatitis C – An Emerging Issue**
- Sexual transmission uncommon, but possible
  - esp in MSM with HIV infection
  - high risk and traumatic sexual practices
  - concurrent ulcerative disease may predispose
- Screen patients at risk:
  - HIV infection (annually)
  - injection or intranasal drug use history
  - long-term hemodialysis or transfusion prior to 1992
  - other percutaneous exposures (incl some tattoos)
  - 1945-1965 birth cohort (screen once)

Other STDs – Skin

- **Molluscum contagiosum**
  - very common, yet not in guidelines
  - umbilicated papules, esp lower abdomen, groin
  - treat with cryo; topicals less effective

- **Scabies**
  - high index of suspicion if systemic itching + rash
  - skin scraping confirms but doesn’t rule out
  - treatment: permethrin 5% cream or ivermectin po
  - treat partners empirically

Transgender Patients & STIs

- Emerging area of research and care
- High prevalence of HIV in trans women (M to F)
  - 28% overall; 56% in African Americans
- STI risk and testing is based on behavioral and sexual practices, independent of gender identity or sexual orientation

MSM: Recommended HIV/STI Screening

- **Urethral** gonorrhea and chlamydia tests in men who have insertive intercourse (with urine NAAT)
- **Rectal** gonorrhea and chlamydia tests in men who have **receptive anal** intercourse
  - single rectal swab, NAAT preferred
- **Pharyngeal** gonorrhea test in men who have **receptive oral** intercourse
  - pharyngeal swab, NAAT preferred
  - pharyngeal screening for chlamydia is not recommended
- **HIV and syphilis** serology
  - 4th gen combo HIV antigen/antibody test preferred
  - RPR,VDRL or EIA screening test for syphilis

Women Who Have Sex with Women (WSW)

- Sexual identity, behaviors, practice and risk behaviors differ.
  - Many self-identified WSW (53%-99%) report having had sex with men.
- Adolescent WSW and females with both male and female partners might be at increased risk for STDs and HIV.
  - Syphilis transmission can occur during oral sex
  - Chlamydia among WSW may be more common; gonorrhea rare
  - HPV transmission can occur from skin to skin or skin to mucosa contact during sex.

Summary – Some Key Things to Remember

- **Chlamydia**
  - screen early, screen often, screen again (after tx)
- **Gonorrhea**
  - use dual therapy (ceftriaxone + azithromycin)
- **HPV**
  - vaccinate all adolescents and young adults, 1+1
- **HSV**
  - genital HSV-1 acquired from oral sex is common
- **MSM patients**
  - screen all exposed sites; include HIV and syphilis