The Non-Reportable STDs: Questions and Answers

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Disclosures

• None
Objectives

• By the end of the presentation, participants should be able to:
  – Describe the epidemiology, common clinical manifestations, and management of:
    • HSV
    • HPV
    • Trichomoniasis
Probability of Asymptomatic STDs

<table>
<thead>
<tr>
<th>Location</th>
<th>Gonorrhea</th>
<th>Chlamydia</th>
<th>Trich</th>
<th>Herpes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethra/Cervix</td>
<td>70%</td>
<td>80%</td>
<td>60%</td>
<td>90%</td>
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<tr>
<td>Rectum</td>
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<td>Pharynx</td>
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<td>90%</td>
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<tr>
<td>Urethra/Vagina</td>
<td>70%</td>
<td>80%</td>
<td>60%</td>
<td>90%</td>
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<tr>
<td>Any</td>
<td>80%</td>
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<td>70%</td>
<td>90%</td>
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</tbody>
</table>

Men, Women
Part I

HERPES SIMPLEX VIRUSES (HSV)
What is the Epidemiology of HSV-1 & 2?

• Both HSV-1 and HSV-2 cause genital herpes
• HSV-2 mainly causes genital herpes
• HSV-1 also causes herpetic stomatitis (fever blisters) and can be transmitted in childhood via oral secretions
• NHANES Study of Adult U.S. Population:
  – Seroprevalence of HSV-2: 17% *MMWR.* 2010;59(15):456-9
• NHANES Study of U.S. Children:
• When an adult acquires HSV-1, it is 3X more likely that it was acquired sexually
If Infected with One Virus can you Become Infected with the Other?

- Previous HSV-1 infection did not reduce the rate of HSV-2 infection, but it did increase the likelihood of asymptomatic seroconversion 2.6 fold as compared with symptomatic seroconversion.  

- Acquisition of HSV-1 infections in persons with prior HSV-2 infections is rare.  

- Prior orolabial HSV-1 infection appears to protect against HSV-1 genital infection.  
What about Recurrences of HSV-1 & 2?

- Recurrences are less severe than primary infection and of shorter duration.
- Recurrences of HSV-2 tend to be more frequent and more severe than recurrences of HSV-1.
  - 90% of symptomatic persons with primary HSV-2 had a recurrence in subsequent 12 months; 38% had at least 6 recurrences; a longer duration of primary infection increases risk of recurrences.
  - 57% of symptomatic persons with primary HSV-1 had a recurrence in subsequent 12 months and <4% will have 4 or more recurrences.

How Frequently does Viral Shedding Occur?

• Shedding occurs even in the absence of symptoms
• The number of viral copies in subclinical shedding is similar to the number of viral copies with recurrent lesions
• Shedding tends to precede symptoms
• Shedding occurs on 30% of days during the first year following primary infection

Corey L and Wald A. Sexually Transmitted Diseases 4th edition, Chapter 24
How Well do Condoms Work to Prevent Transmission of HSV?

• **Per coital act:**
  - 3.6% increased odds of acquisition without condoms vs. 0.8% odds of acquisition with 100% condom use (i.e. 78% reduction in odds of acquisition per coital act when condoms are used)
    • Limited data on MSM
    • Small sample size

• **Over time:**
  - Consistent condom users (used 100% of the time) had a 30% lower risk of HSV-2 acquisition compared with those who never used condoms

How well does the combination of antiviral suppression and condoms work for preventing transmission?

Consistent condom use and viral suppressive therapy decreased the risk of HSV acquisition by about 55%
How do we Diagnose HSV?

- **Symptomatic Patient**
  - Tzanck smear (only 40% sensitive)
  - Culture (sensitivity 30-70%)
  - Antigen detection (~70% sensitive)
  - PCR (FDA cleared, >90% sensitive)

- **Asymptomatic Patient**
  - Use Glycoprotein G-based type-specific assays (gG1 & gG2)
  - If gG2 is positive, pt has genital herpes
  - If gG1 is positive, patient either has oral herpes or genital herpes
  - Do **NOT** use crude antigen-based serological assays
  - **NEVER** order or try to interpret IgM serologies

**REMEMBER:**
- Antibodies may be negative in early primary infection
- The specificity of these tests is high but not perfect. As such, if the pre-test probability of having herpes is low, a positive test result has a high likelihood of being a false positive
Who Should Have Serological Testing for HSV?

- Type-specific HSV serologic assays may be performed in the following patients:
  - Patients with recurrent genital symptoms, or atypical symptoms in whom HSV cultures have been negative
  - Patients who have been given a clinical diagnosis of genital herpes without laboratory confirmation
  - Patients who have a partner with genital herpes
  - Consider in persons presenting for an STD evaluation, persons HIV+, and MSM
Part II

HUMAN PAPILLOMAVIRUSES
What are Papillomaviruses?

• Papillomaviruses are DS DNA viruses.
• >100 different HPV types which infect the cutaneous or the mucosal epithelium; ~30 are sexually transmissible
• Anogenital and oral HPV is largely transmitted by sexual activity and the vast majority of infections are self-limiting with no clinical consequences.
• Approximately 12–14 HPV types are carcinogenic to humans (HR HPV), causing cancers of the anogenital tract and oral cavity in both men and women. Carcinogenicity of HPV is highest in the female cervix.
What is the Prevalence of HPV in the US?

• ~50% of sexually active men and women acquire genital HPV at some point in their lives.
• Up to 80% of women will have acquired genital HPV by the age of 50.
How Easily is HPV Transmissible?

What are the Diseases Most Commonly Associated With Low Risk HPV Types?

- 1 million new cases of genital warts occur every year in the United States.
- HPV 6 and 11 are responsible for >90% of genital warts cases.
- In the US, an estimated 1.1 million to 1.6 million Pap tests are diagnosed as CIN1 annually. ~10% are associated with HPV 6 & 11.
- HPV 6 and 11 cause ~100% of both juvenile- and adult-onset recurrent respiratory papillomatosis (RRP).
What are the Diseases Most Commonly Associated With High Risk HPV Types?

- Essentially all cervical carcinomas are associated with HPV infection
- HPV-16 and 18, account for 70% of invasive cervical carcinomas
- These infections are common, asymptomatic and most are “cleared” within months

<table>
<thead>
<tr>
<th>Cancer</th>
<th>HPV types 16/18</th>
<th>HPV types 31/33/35/52/58</th>
<th>Other HPV types</th>
<th>HPV-negative*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>10,000</td>
<td>4,000</td>
<td>2,000</td>
<td>3,000</td>
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<tr>
<td>Vagina</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
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<tr>
<td>Vulva</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
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<tr>
<td>Anus</td>
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<td>Rectum</td>
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<tr>
<td>Oropharynx</td>
<td>1,000</td>
<td>1,000</td>
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</tbody>
</table>

*Can be prevented by bivalent and quadrivalent vaccines

**Note:** Data represents average number of cases per year.
What is the Natural History of HPV Infection and how does it Progress to Cervical Cancer?
What are the Clinical Manifestations and Symptoms?

- In most cases, genital HPV infection is transient and asymptomatic.
- Vulvar, vaginal warts--dyspareunia, pruritus, burning discomfort, rarely bleeding
- Urethral meatal warts--occasional hematuria or impairment of urinary stream
- Penile warts—asymptomatic, pruritus (rare)
How do We Diagnose HPV-Related Precancerous and Cancerous Changes?

• **Cytology (Pap test)**
  – Useful screening test to detect cervical dysplasia
  – Detects squamous epithelial cell changes due to HPV

• **HPV testing for high-risk women >25yo.**

• Anal cytology for adults with HIV infection
  – No national recommendations
  – Some HIV specialists offer testing
  – NYS guidelines at:
How do we Treat Warts?

• Cryotherapy with liquid nitrogen or cryoprobe
  – Repeat applications every 1-2 weeks, OR

• Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%
  – Apply small amount only to warts and allow to dry
  – Treatment may be repeated weekly if needed, OR

• Surgical removal--tangential scissor excision, tangential shave excision, curettage, or electrosurgery
Can we Prevent HPV?

- Consist of VIRUS-LIKE PARTICLES (noninfectious; NO DNA) but use different adjuvants
- Efficacy: >97% against CIN 2/3, vulvar, and vaginal lesions; >98% against genital warts (quadrivalent)
- Formulations: Bivalent (16 & 18), Quadrivalent (6,11, 16,18), and nonavalent (16, 18, 31, 33, 45, 52 and 58) cause approximately 90% of cervical cancers & 80% high-grade cervical lesions worldwide. These seven HPV types also cause 85-90% of HPV-related vulvar cancers, 80-85% of HPV-related vaginal cancers, and 90-95% of HPV-related anal cancers. HPV types 6 and 11 cause approximately 90 percent of genital warts cases. In addition, approximately 50 percent of cases of low-grade cervical lesions (CIN 1) are caused by the nine HPV types included in the vaccine.
- Vaccines recommended for routine use in 9 to 26 year old women (even those who have a history of abnormal Pap smears); routine use of quadrivalent HPV vaccine in boys ages 11-12 years, a catch-up dose for males ages 13-21, and permissive use of the vaccine in men ages 22-26.
Part III

TRICHOMONIASIS
What is the Epidemiology of Trichomoniasis?

• Most common non-viral STI
• Women are the main disease carriers; may persist for years in women
• ~2/3 of male partners have urethral colonization; men rapidly clear the organism (<10 days, on average)
• 2.3% prevalence in adolescents and 3.1% among women 14-49 years old
  – Rates in AA women 10 X higher
• Transmission via fomites is possible
What are the Clinical Manifestations of Trichomoniasis?

• **85% of women are asymptomatic**
  – 30% of those may become symptomatic within 6 months
  – Symptoms: Vaginal discharge, dysuria, itching, vulvar irritation, abdominal pain
  – Sequelae: HIV and other STD acquisition, PID, low birth weight, pre-term delivery, and premature rupture of membranes
  – Perinatal transmission possible

• **77% of men are asymptomatic**
  – Symptoms: Urethral discharge and dysuria; rarely, epididymitis and prostatitis

How do We Diagnose Trichomoniasis?

• **Wet mount** is only 50-70% sensitive  
  – Must be read within 10 minutes

• **Culture** is more sensitive but time consuming and expensive  
  – Not sensitive in men

• **NAATs**: Sensitivity 95-100%; specificity 95-100%  
  – Urine; vaginal swab; ThinPrep Pap medium; endocervical swabs  
  – 15% false positive NAATs testing at 3 weeks following Rx

• **POC Tests**: OSOM Trich Rapid Test & Affirm VP III  
  – Sensitivity ~80% and specificity >95%

How do we Treat Trichomoniasis?

• Metronidazole 2g PO X1 OR tinidazole 2g PO X1 OR metronidazole 500mg PO BID X 7 days [do NOT use topical gel formulations]
• Preferred Rx for HIV+ women: 7 days of metronidazole
• Resistance: ~5% of strains have low-level resistance to metronidazole; <1% have high level resistance
• Partners in the preceding 60 days must be treated

Curr Infect Dis Rep 2011;13(2):188-95
How do we Treat Pregnant Women with Trichomoniasis?

- No benefit to treating asymptomatic trichomoniasis during pregnancy
- Treat symptomatic pregnant women with 2 g metronidazole. No teratogenic or mutagenic effects in infants

Who do we Screen for Trichomoniasis?

- Screen all HIV+ women annually
Part IV

BONUS
Patient 1

- 36 year old gay man with sudden onset of fluctuating bilateral hearing loss and tinnitus
  - Sensorineural with poor word discrimination
  - Diffuse maculopapular rash on trunk sparing palms and soles
  - Serum CIA reactive; RPR 1:2048
  - CSF examination negative
  - IV aqueous crystalline penicillin G 4,000,000 units IV q 4 hours + steroids X 10 days
  - JH reaction after 1\textsuperscript{st} dose of penicillin
  - Complete resolution of symptoms 1 month after therapy
Otosyphilis

• **Diagnostic criteria**: cochleovestibular dysfunction and syphilis infection without an alternate diagnosis; ~50% bilateral
  – Diagnosis is presumptive; CSF examination is normal in 90% of cases
• **Therapy**: IV penicillin (+ corticosteroids)
• **Prognosis**: 23% experience improvement in hearing; up to 80% experience improvement in tinnitus and vertigo
  – Absence of hearing fluctuations, longer duration of symptoms, and age >60 years are bad prognostic indicators
Patient 2

- 48 year old man with a history of Hepatitis C infection and alcohol abuse presents to ED with a pustular rash, decreased PO intake, and nausea
  - Pustular rash on arms, back, and abdomen; no stigmata of chronic liver disease
  - AST 52 U/L; ALT 58 U/L; AP 1260 U/L; t-bili 1.2 mg/dl
  - Serum CIA reactive; RPR 1:128
  - BPG 2.4 MU IM X1
  - Sent to ultrasound for HCC screening and discharged after PCN therapy
Syphilitic Hepatitis

• Involvement of the liver in late stages of the disease as fibrosis, gumma, and hepar lobatum well documented in the pre-antibiotic era

• Early stage asymptomatic involvement usually as a disproportionately elevated alkaline phosphatase in the setting of secondary syphilis is a more recent observation- but is not universal
  – Clinical: ? Association with rash and anorectal lesions
  – Histology: pericholangiolar inflammation; mild (proliferation of sinus endothelial cells and Kupffer cells, eosinophils, and lymphocytes) to severe (diffuse necrosis especially in periportal region and central vein)
  – In half of the cases spirochetes were found in the necrotic foci, walls of sinusoids, and in the endothelial cells

• Incidence of LFT abnormalities in both immunocompetent and HIV-infected persons in secondary syphilis noted in up to 38% -but majority are asymptomatic

• Treatment: 2.4 MU of BPG IM X1

West J Med. 1978;128(1):64-7  Int J STD AIDS. 2012;23(8):e4-6
Patient 2 continued

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  - Serum CIA reactive; RPR 1:128
  - BPG 2.4 MU IM X1
  - Sent to ultrasound for HCC screening and discharged after PCN therapy
    - 12 cm mass in liver consistent with HCC
    - Follow-up appointment with IR scheduled 1 week later for CT-guided biopsy
    - At follow-up with IR, mass had disappeared
# Liver Abscesses and ‘Tumors’

<table>
<thead>
<tr>
<th>Radiologic Findings</th>
<th>Mass Lesion</th>
<th>Background Liver Adjacent to Mass Lesions</th>
<th>Immunohistochemistry for <em>T. pallidum</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1 Two lesions in the liver with</td>
<td>Variously cellular fibrotic area with entrapped portal areas.</td>
<td>Portal expansion and edema. Neutrophils surrounding and within bile duct epithelium.</td>
<td>Positive</td>
</tr>
<tr>
<td>surrounding edema, 1.4 and 1.6 cm</td>
<td>Cellular storiform spindle cell proliferation with plasma cells, neutrophils,</td>
<td>Patchy mild to moderate mixed inflammatory cell infiltrate within the sinusoids and lobules with rare acidophil bodies</td>
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<tr>
<td></td>
<td>eosinophils, and histiocytes. Focal small abscess</td>
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</tr>
<tr>
<td>Case 2 Biopsy 1 Multiple enhancing lesions</td>
<td>Variously cellular fibrotic areas with storiform spindle cell proliferation</td>
<td>Portal expansion and edema. Neutrophils surrounding and within bile duct epithelium.</td>
<td>Positive</td>
</tr>
<tr>
<td>in the liver, up to 5.7 cm. Multiple</td>
<td>with reactive atypia, incorporating portal areas at the edges. Patchy</td>
<td>Patchy dense mixed inflammatory cell infiltrate within sinusoids with rare acidophil bodies.</td>
<td></td>
</tr>
<tr>
<td>enhancing lesions in the spleen</td>
<td>inflammation focally obscuring background spindle cells, comprising</td>
<td></td>
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<td>numerous neutrophils, focally coalescing into microabscesses, admixed with</td>
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<tr>
<td></td>
<td>eosinophils, lymphocytes, histiocytes, and rare plasma cells</td>
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</tr>
<tr>
<td>Biopsy 2</td>
<td>Variously cellular plump storiform and short fascicular spindle cell</td>
<td>Not represented</td>
<td>Positive</td>
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<td></td>
<td>proliferation with entrapped inflamed bile ducts at the edges. Mixed</td>
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<td>inflammation with numerous neutrophils, histiocytes, foamy histiocytes,</td>
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<tr>
<td></td>
<td>and lymphocytes. Necrotizing abscesses</td>
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<td>Case 3 Greater than 50 rim-enhancing</td>
<td>Not represented</td>
<td>Rare granulomas with focal subtle necrosis. Portal expansion and edema with neutrophils surrounding and within duct epithelium. Patchy dense mixed inflammatory cell infiltrate within sinusoids with increased hepatocyte cytoplasmic pigment</td>
<td>Negative</td>
</tr>
<tr>
<td>lesions in the liver, up to 2.6 cm. Bilateral lung nodules 0.2-1.0 cm</td>
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</tbody>
</table>
Patient 3

• 58 y/o man R eye pain and redness X 4 days
  – No medical care X 20 years
  – Right eye: Panuveitis
  – Serum CIA reactive; RPR 1:128
  – CSF Examination: 46 WBCs (mononuclear cells); VDRL 1:4;
  – IV aqueous crystalline penicillin G 4,000,000 units IV q 4 hours + topical steroids
THANK YOU!