Clinical Manifestations of the most common STDs

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Most Common STDs

- Neisseria gonorrhoea
- Chlamydia trachomatis
- Trichomonas vaginalis
- Acute HIV infection
Objectives

- Understand the critical role of health care providers in preventing and treating STDs
- Identify clinical signs and symptoms of most common STDs
- Update on the diagnosis and treatment

**STD Screening:** Requires asking

“Whoa—way too much information.”

www.nnptc.org/online_training/asi
Persons Aged 50 and older

- Prevalence of HIV infection and AIDS continues to grow

- Older HIV-infected persons are living longer due to highly active therapy

- New infections of individuals unaware of their risk

CDC

Estimated Numbers of Cases of HIV/AIDS, by Age - 2005

No. = 37,351

Based on data from 33 states with long-term, confidential name based HIV reporting

CDC
Underestimation of Risk by Health Care providers (HCPs)

- Influenced by stereotype that older patients are not sexually active and don’t use drugs

- Uncomfortable about asking sexual activity questions with patients older than them

- In one study only 38% men and 22% women discussed sex with their HCPs after age 50

Lack of Knowledge about HIV/AIDS (CDC)

- 60% of older single women who had been sexually active during the past 10yrs had sex without a condom

- Only 13% of women in one study said that condoms were effective prevention

- Several studies revealed older persons believe HIV can be transmitted only by blood transfusions and Intravenous drug use
Distribution of GC by anatomical site in MSM attending STI clinics

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>% of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal only</td>
<td>21%</td>
</tr>
<tr>
<td>Urethral only</td>
<td>15%</td>
</tr>
<tr>
<td>Pharyngeal only</td>
<td>36%</td>
</tr>
<tr>
<td>Rectal and urethral</td>
<td>6%</td>
</tr>
<tr>
<td>Rectal and pharyngeal</td>
<td>12%</td>
</tr>
<tr>
<td>Urethral and pharyngeal</td>
<td>5%</td>
</tr>
<tr>
<td>All 3 sites</td>
<td>5%</td>
</tr>
</tbody>
</table>

- 90% of urethral infections were symptomatic
- Only 16% of rectal infections were symptomatic

Kent C, Chaw J, Wong W et al., Clinical Inf Dis 2005; 41:67-74

Case 1

- 63 y/o male presents with 3 day h/o penile discharge. Involved in a monogamous relationship. HIV negative. Recently attended a party where he used Crystal Meth
- PE: No rash, fever or adenopathy
Case 1

- RPR negative

- NAAT of urethral discharge positive for gonorrhea
Neisseria Gonorrhea and Chlamydia Trachomatis

- Most common causes of STDs
- Lead to costly acute illnesses
- Asymptomatic
- Neonatal complications
- Co-infection occurs in 40% men, 30-50% of women
- Increased risk of HIV infection

Rates of Infection (USA)

- Number of cases of GC has decreased, declining slower in minorities
- Sexually active adolescents have highest rates of infection (15-24y/o)
- C. Trachomatis has steadily increased
- Large disparities by race
- Increase in Lymphogranuloma venereum infections (LGV) cases in MSMs

CDC
STD Surveillance Network—(SSuN)—Proportion of MSM,* MSW,* and Women Among Interviewed† Gonorrhea Cases by Site, 2010

* MSM = men who have sex with men; MSW = men who have sex with women only.
† SSuN interviews conducted from a randomly selected patient population with gonorrhea (n = 3,446).
‡ California data excludes San Francisco.

Neisseria Gonorrhea

- May be symptomatic or asymptomatic
- Genital, anorectal, pharyngeal sites
- Symptoms occur within 2-5 days
- 80% of women no symptoms
- Complications include: epididymitis, PID, urethral stricture, infertility
Diagnostic Testing for Gonorrhea

- Culture: Thayer Martin 80-90% sensitivity
- Gram stain: urethral 90% sensitivity, cervical 50-70% sensitivity
- Nucleic acid amplification tests (NAATs): 98-94% sensitivity and specificity

Decreased Cephalosporin Susceptibility

- 1999: Japan: 0% isolates have MICs to cefixime ≥ 0.5 µg/ml
- 2001: Japan: Possible treatment failure with cefdinir
- 2002: Japan: 30% isolates have MICs to cefixime ≥ 0.5 µg/ml
- 2003: Japan: 8 (12%) of men with GC in study unsuccessfully treated with cefixime
- 2007: Hong Kong: 4 treatment failures with cefixime
- 2008-2009: Increasing MICs to cephalosporins reported in Australia, Europe, and US
  - Japan: isolate with Ceftriaxone MIC of 2 µg/ml (female CSW)
- 2010: Norway: 2 treatment failures with cefixime
  - Sweden: 1 pharyngeal GC treatment failure with ceftriaxone 250 mg
GISP QRNG isolates

- 2005: 9.4%, 29% MSM, 3.8% heterosexual men (HM)

- 2006: 13.3%, 38% MSM, 6.7% HM excluding Hawaii, CA: 5.1% HM

CID 2006

Gonococcal Isolate Surveillance Project (GISP)—Distribution of Minimum Inhibitory Concentrations (MICs) to Cefixime Among GISP Isolates, 2006 and 2009–2010

NOTE: Isolates were not tested for cefixime susceptibility in 2007 and 2008.
Percentage of gonorrhea isolates with cefixime MICs $\geq 0.25$ µg/mL and ceftriaxone MICs $\geq 0.125$ µg/mL, by sex of sex partner --- Gonococcal Isolate Surveillance Project, United States, 2000--2010

"On May 17, 2011, a *Neisseria gonorrhoeae* isolate from a young women in Hawaii was found to exhibit high-level resistance to azithromycin as demonstrated by a high minimal inhibitory concentration (MIC $\geq 1024$ mcg/ml). To CDC’s knowledge, the patient and her partner were infected in Hawaii. She was successfully treated with ceftriazone and azithromycin...

This is the first case of an isolate with high-level resistance to azithromycin to be detected in the United States, reminding us of the growing threat of multidrug resistant *N. gonorrhoea*.
Treatment (uncomplicated)

- Ceftriaxone 250mg IM x 1
  PLUS
  Azithromycin 1g po x 1
  OR
  Doxycycline 100mg po BID x 7 d
- Co Infection with Chlamydia: Azithromycin
  Doxycycline or Emecin 500mg po qid x 7d
- FLOUROQUINOLONES AND ORAL
  CEFIXIME (Suprax) NO LONGER
  RECOMMENDED

Treatment (complicated)

- Disseminated GC (DGI): Ceftrixaone 1gm
  IV until 24-48hrs improved, then oral
  cefixime 400mg QD total 7 days.
- Epididymitis:
  - GC/CT: Ceftriaxone1gm plus doxycycline
    100mg BID 10 days
  - Enteric Gm neg: Ceftriaxone 1gm plus
    levofloxacin 500mg QD or ofloxacin 300mg
    BID 10days
Follow up

• Test of cure for all

• Test of cure on those treated with alternative regimens

• Perform culture and sensitivity or NAAT in one week

Case 2

• 24y/o MSM presents with 1 week H/O malaise, low grade fever and painful inguinal adenopathy

• HIV positive with Viral load undetectable on HAART and CD4 count 500

• Sexually active and uses condoms with his partner but not with anonymous contacts
Case 2

• Perirectal area without lesions

• Urethral gram stain has rare polyps. No organisms seen. RPR negative. Urine NAAT for GC/Chlamydia negative

Lymphogranuloma Venereum (LGV)

• LAD is unilateral in 2/3 pts
• Diagnosis by serology: C. trachomatis serovars L1, L2, L3 (>1:64)
• Treatment Doxycycline 100mg po BID or Emycin 500mg po QID for 21 days
• Untreated: Colorectal fistulas, strictures, proctocolitis
Lymphogranuloma Venereum (LGV)

- Primary stage: *C. Trachomatis* enters through breaks in skin

- Secondary stage: days to weeks later develop lymphadenopathy and systemic symptoms

Chlamydia Trachomatis

- Serologic classification:
- Trachoma: A, B, Ba, C
- Genitourinary and ocular infections: D-K
- LGV: L1-L3
**Chlamydia Trachomatis**

- 70% of females are without symptoms
- Vaginal discharge, mild abdominal pain, or dysuria
- Mucopurulent cervicitis
- Pelvic inflammatory disease (PID)
- Nongonococcal urethritis (NGU)

Chlamydia—Rates by Region, United States, 2001–2010

![Graph showing rates by region](chart.png)
Diagnostic testing for Chlamydia

- Culture: 70% sensitivity
- Direct fluorescent antibody DFA 85%
- **Gold Standard**: NAATs
  - FDA cleared on endocervical, urethral, urine and vaginal swabs. Not FDA cleared for rectal or pharyngeal specimens but CDC recommends their use
  - Does not distinguish between D-K, L1-L3 serotypes

Complications of *Chlamydia*:

- Acute urethral syndrome
- Bartholinitis
- Endometritis, salpingitis
- Infertility, ectopic pregnancy
- Spontaneous abortions
- Neonatal infections
- Males: NGU, proctitis, proctocolitis, epididymitis, prostatitis
Chlamydia Trachomatis treatment

- Azithromycin 1g po X 1 or doxycycline 100mg po BID for 7 days
- LGV: Doxycycline 100mg po BID for 21 days or Azithromycin 1 gm po q week for 3 weeks
- Azithromycin is safe in pregnancy

Chlamydia

- Annually screen all sexually active women under age 26
- Repeat testing q 3-4 months
- Screening for GC/chlamydia in all sexually active young MSMs
- Drug resistance is uncommon but has been reported
- Rectal LGV has made a resurgence
Case 3

- 30y/o female presents to STD clinic with her new partner of 3 months with 1 week h/o vaginal discharge and itching
- HIV + on HAART. CD4 count 200, VL 3000c/ml
- Monogamous relationship
- Partner is without symptoms
Case 3

- Treated with Metronidazole 2 gms X1
- Partner is treated
- Symptoms persist after one week
- Her and her partner have not had other partners or had sex in one week
- Repeat Wet prep positive for motile trichomonads

Trichomonas Vaginitis

- Parasitic infection spread through sexual contact
- Causes diffuse malodorous yellow green discharge in women
- Majority of men asymptomatic
Objective Findings *T. Vaginalis*

- Erythema of vagina and cervix, “strawberry cervix”
- Motile trichomonads on wet mount
- KOH whiff test positive
- Vaginal Ph will be high

### Trichomoniasis and Other Vaginal Infections—Women—Initial Visits to Physicians’ Offices, United States, 1966–2010

**Visits (in thousands)**

<table>
<thead>
<tr>
<th>Year</th>
<th>Trichomoniasis</th>
<th>Other Vaginitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1966</td>
<td>900</td>
<td>400</td>
</tr>
<tr>
<td>1969</td>
<td>1,800</td>
<td>2,700</td>
</tr>
<tr>
<td>1972</td>
<td>3,600</td>
<td>3,600</td>
</tr>
<tr>
<td>1975</td>
<td>4,500</td>
<td>3,600</td>
</tr>
</tbody>
</table>

**NOTE:** The relative standard errors for trichomoniasis estimates range from 16% to 27% and for other vaginitis estimates range from 8% to 13%.

Diagnostic testing for Trichomonas

- Wet mount microscopy: 36-60% sensitivity
- Culture (TV pouch) more sensitive, 3-7 days
- PCR: 97% sensitivity, 98% specificity, 2-3 days. Can be performed on urine.

NAAT for Trich

- APTIMA TMA (Gen-Probe) (ATV)
  - Same technology, specimen as APTIMA Combo 2 (for CT/GC)
  - FDA approval May 2010

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet mount</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td>Culture</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>ATV vaginal swab</td>
<td>97</td>
<td>100</td>
</tr>
<tr>
<td>ATV cervical swab</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td>ATV urine</td>
<td>88</td>
<td>100</td>
</tr>
</tbody>
</table>

Nye, AJOG 2009
Trichomoniasis Treatment 2010

**Recommended regimen:**
- Metronidazole 2 g PO x 1
- Tinidazole 2 g PO x 1

**Alternative regimen:**
- Metronidazole 500 mg PO BID x 7d*
  - Preferred in HIV+; 17% cure vs. 9% for single dose

* A Randomized Treatment Trial: Single Versus 7-Day Dose of Metronidazole for The Treatment of *Trichomonas Vaginalis* Among HIV-Infected Women

- Vaginal therapy is ineffective
- Treat sex partner(s): male and female
- Consider retesting women for TV in 3 months

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**Case 4**

- A 20 yo male, college student presents to the ER with 1 week H/O fever 101 F, sore throat, painful cervical adenopathy and a rash. He denies headache, photophobia. He denies nausea, vomiting and abdominal pain
- On exam BP 120/70, he has pharyngitis with scant white exudates, neck is supple.
- The rash is maculopapular located on his chest. It does not itch.
Case 4

- WBC count: 3.3, HGB 11, HCT 33, Plt 90,000 with 80% polys, 10 Lymphs, 5 monocytes, 3 Atypical lymphs, 2 eos
- ALT 89, AST 95, Throat swab rapid test negative for Group A strep
- RPR is negative. Mono spot is negative
- Rapid HIV antibody test is negative

Primary HIV Infection: Signs & Symptoms

- 40-90% of patients will be symptomatic
- A mononucleosis-like illness of non-specific signs and symptoms
- Signs and symptoms typically begin 1-4 weeks post-exposure
- High index of suspicion is critical

Primary HIV Infection: Common Signs & Symptoms

- Fever: 96%
- Lethargy: 74%
- Myalgia: 69%
- Rash: 57%
- Headache: 55%
- Pharyngitis: 44%
- Adenopathy: 42%

N = 160 patients with PHI in Geneva, Seattle, and Sydney

Vanhems P et al. AIDS 2000; 14:0375-0381

Primary HIV Infection: Other Signs & Symptoms

- Aseptic meningitis: 24%
- Oral ulcer: 15%
- Genital ulcer: 10%
- Thrombocytopenia: 45%
- Leukopenia: 40%
- Transaminitis: 21%

Gynecological Manifestations

- Recurrent yeast infections
- PID
- Cervical dysplasia
- Genital warts

Algorithm for AHI Screening

**FEVER**

- Cough or nasal congestion
  - yes
  - no

- Presence of:
  - rash
  - pharyngitis
  - LAN
  - arthralgias/myalgias
  - mucocutaneous ulcers
  - H/A/meningitis
  - yes
  - no

- Consider Screening for AHI
  - yes
  - no

- Treat underlying infection
  - yes
  - no

Screen for AHI
Detection of HIV by Diagnostic Tests

Symptoms
p24 Antigen
HIV RNA
HIV EIA*
Western blot

0 1 2 3 4 5 6 7 8 9 10

Weeks Since Infection

*3rd generation, IgM-sensitive EIA
*2nd generation EIA
*viral lysate EIA

After Fiebig et al, AIDS 2003; 17(13):1871-9

AHI and Hyperinfectiousness

Persons with AHI are very infectious

- High-titer viremia in plasma and genital fluids\(^1,2\)
- Absence of immune factors that may neutralize infectivity\(^2\)

Awareness of Serostatus Among People with HIV and Estimates of Transmission

~25% Unaware of Infection
~75% Aware of Infection

accounting for:
~54% of New Infections
~46% of New Infections

People Living with HIV/AIDS: 1,039,000-1,185,000
New Sexual Infections Each Year: ~32,000

Early Identification

Early identification is important to:

- Establish appropriate medical care
- Decrease HIV-related morbidity & mortality
- Provide opportunity to counsel regarding risk behaviors
- Help prevent transmission to others
Behavior Change After Diagnosis

- Multi-Site Acute HIV Infection Study
  - 27 participants (most of them MSM) completed assessments of their sexual behavior before and after diagnosis of AHI
- Results
  - Significant drop in the # of sexual partners after diagnosis (p=0.05)
  - After diagnosis, more than 95% of sex acts were with people who were also HIV-positive (sero-sorting)
  - No significant change in the number of sex acts, but a significant increase in sex using condoms. (p=.001)

Steward WT, et al. NIMH Multi-Site Acute HIV Infection Study 2007

Treatment & Care

Linkage to effective treatment for HIV-positive individuals:
- Prolongs life
- Delays progression to AIDS
- Reduces:
  - Hospitalizations
  - Opportunistic infections
  - Drug resistance
- Greatly reduces the transmission of HIV
Why so few AHI diagnoses?

1. Treatment and diagnosis of HIV infection has been relegated to specialists
   • Lack of education of how to diagnose AHI
   • Discomfort related to difficult issues surrounding HIV and the testing for HIV

2. Clinicians inability to spend the additional time


AHI Summary

1. Acute HIV infection should be considered in the differential diagnosis of patients presenting with a mono-like illness.

2. Acute HIV can be diagnosed with an HIV viral load (RNA) assay, obtained at the same time as the HIV Ab test, after the patient has consented to the HIV test.
AHI Summary

3. Knowledge of HIV serostatus *does* impact sexual behavior in the majority of patients who are diagnosed with HIV infection.

Prevention Methods

- Most reliable: abstinence or monogamous relationship with uninfected partner
- Preexposure vaccinations (Hepatitis B, A, HPV)
- Male / Female condoms
- Post exposure prophylaxis (PEP) with TDF/FTC for HIV discordant couples
Newer Topical agents

- Topical gel (tenofovir): Use during sexual intercourse reduced rate of HIV acquisition by 39% (South African Women)

- Reduced acquisition of HSV by 51%

Science 2010: 329: 1168-74

Summary

- Physicians and healthcare providers play a critical role in preventing and treating STDs
- Consider Preexposure vaccination of persons at risk for vaccine preventable STD
- FQs and cefixime are no longer recommended for the treatment of Gonorrhea
- Test of cure should be performed on all but especially those treated with alternative regimens
- Health care providers should routinely obtain sexual histories from their patients and address management of risk reduction
Take-Home Messages

• Screen, screen, screen
  – Baseline then annually for all; at 3-6 month intervals if at ↑ risk
• Be aware of antibiotic-resistant gonorrhea
• Recognize and treat LGV in MSMs
• Recognize and treat trichomoniasis in women, with a longer course in HIV+


STD Resources

• Seattle STD/HIV Prevention Training Center
  – www.seattlestdhivtraining.org
• National Network of STD/HIV Prevention Training Centers
  – www.stdhivpreventiontraining.org
• CDC Treatment Guidelines
  – www.cdc.gov/std/treatment
• American Social Health Association (ASHA) booklets, books, handouts, the Helper www.ashastd.org (800) 230-6039
• ASHA patient herpes hotline (919) 361-8488
References

- [www.cdc.gov](http://www.cdc.gov): STD Guidelines


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