SEXUALLY TRANSMITTED DISEASES
CASES IN THE CITY
LABORATORY MEDICINE COURSE 2005
CLINICAL MICROBIOLOGY SERVICE
Dr. Phyllis Della-Latta, 52929

STD EPIDEMIC- USA
TIP OF THE ICEBERG

<table>
<thead>
<tr>
<th>CLINICAL SYNDROMES</th>
<th>INCIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISCHARGE</td>
<td></td>
</tr>
<tr>
<td>• Chlamydia - 4 million</td>
<td></td>
</tr>
<tr>
<td>• Gonorrhea - 650,000</td>
<td></td>
</tr>
<tr>
<td>• Trichomoniasis - 180 million</td>
<td></td>
</tr>
<tr>
<td>• BV - Not reportable</td>
<td></td>
</tr>
<tr>
<td>• HPV - 6 million</td>
<td></td>
</tr>
<tr>
<td>• Herpes - 1 million</td>
<td></td>
</tr>
<tr>
<td>• Syphilis - 60,000</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>CLINICAL IMPACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• INFERTILITY</td>
</tr>
<tr>
<td>• ECTOPIC PREGNANCY</td>
</tr>
<tr>
<td>• HIV TRANSMISSION</td>
</tr>
<tr>
<td>• PID, 1 million/yr</td>
</tr>
<tr>
<td>• CERVICAL CA</td>
</tr>
<tr>
<td>• $10 BILLION ANNUAL COST</td>
</tr>
</tbody>
</table>

WOMEN AT RISK
THE “X FACTOR”

<table>
<thead>
<tr>
<th>STDs OFTEN ASYMPTOMATIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 75-90% WOMEN WITH CHLAMYDIA</td>
</tr>
<tr>
<td>• 50-70% MEN WITH CHLAMYDIA</td>
</tr>
<tr>
<td>• PID</td>
</tr>
<tr>
<td>• ≤ 40% UNTREATED CASES GC/CHLAMYDIA</td>
</tr>
<tr>
<td>• INFERTILITY</td>
</tr>
<tr>
<td>• 1 IN 5 UNTREATED</td>
</tr>
<tr>
<td>• CHRONIC PELVIC PAIN</td>
</tr>
<tr>
<td>• HPV CERVICAL CA</td>
</tr>
</tbody>
</table>

| COMPLICATIONS RARE IN MEN......."Y" |

CASE
16-yr old male presented to the ED with 3d painless urethral discharge

<table>
<thead>
<tr>
<th>WHAT IS THE DIFFERENTIAL?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No fever, pain on urination, or inguinal adenopathy</td>
</tr>
<tr>
<td>• Pt sexually active with girlfriend for past 2-3 mths</td>
</tr>
<tr>
<td>• Reported inconsistent condom use</td>
</tr>
<tr>
<td>• He forgets.......</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WHAT TESTS TO ORDER?</th>
</tr>
</thead>
</table>

| HOW IS THE LAB DX MADE? |

DISCHARGE DISEASES

<table>
<thead>
<tr>
<th>MOST COMMON DISCHARGE DISEASE IN U.S.</th>
</tr>
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<tbody>
<tr>
<td>• CHLAMYDIA TRACHOMATIS</td>
</tr>
<tr>
<td>• NEISSERIA GONORRHEAE</td>
</tr>
<tr>
<td>• TRICHOMONAS VAGINALIS</td>
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<td>• 25% SYMPTOMATIC PTS HAVE MIXED GC/CT INFECTIONS</td>
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<td>• SYMPTOMATIC OR ASYMPTOMATIC</td>
</tr>
<tr>
<td>• DYSURIA &amp; FREQUENCY</td>
</tr>
<tr>
<td>• PURULENT DISCHARGE INDIFFERENTIABLE</td>
</tr>
<tr>
<td>• OTHER SITES PHARYNX, RECTUM, EYE</td>
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<td>• BACTEREMIA, ARTHRITIS</td>
</tr>
<tr>
<td>• CERVICITIS</td>
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<td>• URETHRITIS</td>
</tr>
<tr>
<td>• PID</td>
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<table>
<thead>
<tr>
<th>HIV ACQUISITION 5- FOLD</th>
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<table>
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<tr>
<th>HIV ACQUISITION 10- FOLD</th>
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<tr>
<th>ULCERATIVE LESIONS/ GROWTHS</th>
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<th>AT RISK</th>
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<tr>
<td>• SEXUALLY ACTIVE ADOLESCENTS</td>
</tr>
<tr>
<td>• CHECK TWICE A YEAR GC/CT</td>
</tr>
<tr>
<td>• PREVALENCE IS 29%</td>
</tr>
<tr>
<td>• CDC, AMA, AAP GUIDELINES</td>
</tr>
<tr>
<td>• MULTIPLE SEX PARTNERS</td>
</tr>
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<td>• PAST STDs</td>
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**CHLAMYDIA/GC URINE NAAT SCREEN**

- Non-invasive, painless!!!
- Automation
- Turnaround time
  - 4 hrs
- Screening is recommended
  - CDC, AMA, DOH
  - Males & Teens
  - Pregnancy

NAAT = Nucleic Acid Amplification Test

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**& PTs PARTNER(S)?**

**KNOW COLLECTION SITES FOR DISCHARGE DISEASES**

<table>
<thead>
<tr>
<th></th>
<th>Endocervix</th>
<th>Vagina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pH</td>
<td>7.0</td>
<td>&lt;4.5</td>
</tr>
</tbody>
</table>

**Cell Type**

- Columnar epithelial
- Squamous epithelial

**Pathogens**

- Chlamydia trachomatis
- Neisseria gonorrhoeae
- Bacterial vaginosis (BV)
- Trichomonas
- Candida sp

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**LAB DIAGNOSIS C. TRACHOMATIS**

- NA amplification
  - Urine screen
- Direct fluorescent AB
- DNA probes
  - Urethral specimen
- Tissue culture
  - McCoy cells
    - Intracytoplasmic inclusions with iodine
    - Immunofluorescence

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**CDC GUIDELINES CT TESTS IN ASSAULT CASES**

**CHILDREN**

- Cultures
  - Gold standard
  - Anus, vagina
  - Meatal specimen in males if discharge
- Culture pos confirm with direct fluorescent antigen (DFA)
- NAAT not recommended

**ADULTS**

- Cultures from all sites of penetration or
- FDA approved NAAT
- 2 NAATs (different targets)
- Both must be pos
- Assays not approved
- EIA, non-amplified probes, DFA
-Insensitive - false negs

---

**CT/GC DETECTION**

<table>
<thead>
<tr>
<th>Gram Stain</th>
<th>Culture</th>
<th>GC/CT Urine NAAT</th>
</tr>
</thead>
</table>
| GC         | Calcium Alginate Swab (Cotton-tipped) | Sensitivity: 85-98%
            | 85-98% | Specificity: >98%
            | 96%   | TAT: 2-3 Days |
| CT         | McCoy cells | TAT: 4 hrs |
| N/A        |          | TAT: 2-3 Days |

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**BRIEF CASE – FISHY STORY**

**YOUR PATIENT**

- 23 yr old female, married & in 2nd trimester of first pregnancy
- Increased vaginal discharge with “fishy” odor most notable immediately after intercourse
- No urinary urgency or burning
- No vaginal pruritis

**EVALUATION & DIFFERENTIAL**

- Focused history & physical
  - Past STDs
  - Increased risk factors
  - Douche, multiple sex partners, IUD
- Differential
  - Vulvovaginitis
  - STD disease
### CLINICAL SYNDROMES

<table>
<thead>
<tr>
<th>SYNDROME</th>
<th>DISCHARGE</th>
<th>ODOR</th>
<th>PRESENTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>BACTERIAL VAGINOSIS</td>
<td>Watery, gray, homogeneous alkaline</td>
<td>FISHY</td>
<td>Cervix normal, Often asymptomatic</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>Watery, thin, gray, alkaline homogeneous</td>
<td>FISHY</td>
<td>Itching, vaginal erythema, dysuria, vaginal erosions, petechiae strawberry cervix</td>
</tr>
<tr>
<td>CANDIDIASIS</td>
<td>Thick, white, non-homogeneous</td>
<td>SOUR</td>
<td>Same as above but (no petechiae)</td>
</tr>
</tbody>
</table>

### THE FISHY ODOR IN VIVO

- NORMAL VAGINAL FLORA
  - $\text{H}_2\text{O}_2$ Producing Lactobacilli $\Rightarrow$ lactic acid
  - $\hat{\phi}$ pH ($<4.5$)
- BACTERIAL VAGINOSIS
  - Anaerobes increase $\Rightarrow$ Proteolytic enzymes act on vaginal peptides
  - Release of polyamines and trimethylamine
  - Trimethylamine in alkaline pH $\Rightarrow$ fishy odor
  - Polyamines $\Rightarrow$ Exfoliation of epithelial cells (clue cell)
  - Polyamines $\Rightarrow$ Fishy discharge

### BV FACTS

- PREGNANT WOMEN
  - AFFECT 15-20% PREGNANT WOMEN
  - AMNIOTIC FLUID INFECTION
  - POSTPARTUM ENDOMETRITIS
  - PREMATURITY RUPTURE OF MEMBRANES
  - PRETERM DELIVERY
  - LOW BIRTH WEIGHT
- TREAT PREGNANT WOMEN
  - METRONIDAZOLE
  - CLINDAMYCIN

### CONSIDER TRICHOMONAS LAB TESTS

- WET MOUNT
  - URINE OR VAGINAL SECRETION MUST BE VIEWED IMMEDIATELY
  - TRANSPORT INSTABILITY
  - $<50\%$ SENSITIVITY/SPECIFICITY
  - TIME TO RESULTS: 5-10 MINUTES
- IN-POUCH CULTURE
  - NO SPECIMEN TRANSPORT PROBLEM
  - DIRECT INOCULATION INTO POUCH & PARASITE GROWS IN MEDIA
  - $>95\%$ SENSITIVITY/SPECIFICITY
  - TIME TO RESULTS: 18-48 HRS

### BV DIAGNOSED

- VAGINAL SECRETIONS
  - “WET MOUNT” OR GRAM STAIN
  - 10% KOH “WHIFF” TEST
  - ADD KOH
  - AMINE “FISHY ODOR”
  - NO CULTURE !!
  - GARDNERELLA VAGINALIS
  - NORMAL FLORA 30% WOMEN
  - MISCONCEPTION IN OB/GYN

### TRICHOMONAS FACTS

- THIRD MOST COMMON OF THE VAGINITIDES
- PREVALENCE
  - COMMERCIAL SEX WORKERS (TRICKY BUSINESS) - 50-75%
  - STD CLINICS - 32-34%
  - OB CLINICS - 10-26%
- MALES
  - IMPLICATED AS COFACTOR IN HIV TRANSMISSION
  - CAUSES URETHRITIS, PROSTATITIS
- TREATMENT
  - METRONIDAZOLE
  - TINIDAZOLE FOR METRONIDAZOLE-RESISTANCE
### Vulvovaginal Candidiasis

**Etiologic Agent**
- 85-95% *Candida albicans*
- Less susceptible to azoles
- HIV infected

**Frequency**
- 70-75% at least once
- 40-50% recurrence

**Predisposing Factors**
- Antibiotics, diabetes
- Oral contraceptives

**What Tests Should Be Ordered?**
- Culture only when recurrent infections
- Yeast is normal flora
- Susceptibility only with non-albicans if resistance suspected
- What is the TX?
  - Fluconazole or Itraconazole

### Ulcerative Diseases

**Incidence**
- >20 million cases

**Etiologic Agents**
- Herpes simplex virus
- Treponema pallidum
- Human papilloma virus
- Chancroid

**Contribute to HIV Transmission**
- Ulcer is portal of entry

### Primary Syphilis

**Incidence**
- Increase in NYC among men who have sex with men (MSM)
- White men & those in Manhattan
- Largely HIV positive indicating erosion of safe sex

**Stages**
- Primary
  - Chancre lasts 3-6 wks & heals without Tx
- Secondary
  - Serology
- Latent
  - Early
  - Late
- Late/Tertiary

**Primary Syphilis**

- Chancre
  - Appears an average 3 wks (10-90 days) after infection at site where treponemes 1st invaded dermis
  - Usually on or near genitals, can be anywhere on skin or mucous membranes
  - Usually single, painless lesion >0.5 cm in diameter
  - Darkfield for motile spirochetes (if untreated)
  - Persists 2-6 wks, then heals w/o scar
  - Nontender regional LA

**Secondary Syphilis**

- 6 wks – 6 mth after infection (if untreated)
- Rash in ~75% - Extremely variable
- Hepatomegaly, splenomegaly
- Generalized LA in >50%
- Hematogenous dissemination of spirochetes to
  - CSF, Ear, Kidneys
  - Brain, Liver, Skin
  - Eye, Intestines, Endolymph
- Generalized, nonspecific symptoms
  - Fever, Sore throat
  - Malaise, Arthralgias
  - Headache, Anorexia

### STD Brief Case

**Your Patient**

A 51 yr old male presents to the ED with a single, painless penile ulcer & an ulcer in his mouth & on his lip. He denies prior STDs. He frequents prostitutes.

**What is the Differential?**

**What Tests Will You Order?**
LATENT SYphilIS
• No clinical manifestations
• Early = 1st year after secondary syphilis
• Late = > 1 year after secondary syphilis
✓ Lower risk of transmission

LATE/TERTIARY
• Manifests decades after secondary syphilis
• 3 main types of clinical manifestations
✓ Likely due to endarteritis and perarteritis of small and medium-sized vessels
• Cardiovascular
✓ Dilatation of aortic ring
✓ ~10% untreated cases

LATE/TERTIARY
• Manifests decades after secondary syphilis
• 3 main types of clinical manifestations
• Likely due to endarteritis and perarteritis of small and medium-sized vessels
• Cardiovascular
• Dilatation of aortic ring
• ~10% untreated cases

LAB RESULTS
• RPR titer: 1:32
• FTA-ABS: Reactive
• HIV test: Negative

WHAT DO THESE RESULTS INDICATE?
• RPR Neg/FTA Reactive
• RPR Pos/FTA Non Reactive

HERPES SIMPLEX
LAB DX
• DIRECT IMMUNOFluorescence
✓ Scrape cells off base of ulcer & stain
✓ Differentiates Types 1 & 2
• CULTURE
✓ Shell Vial
✓ Cytopathogenic effect
✓ Sensitivity 70-99%, Specificity 99%
• CYTOLOGY & H & E Stain
✓ Multi-nucleated giant cells
✓ Sensitivity & Specificity <60%
• PCR
✓ Investigational
✓ Differentiates Types 1 & 2

LAB DX - syphilis

<table>
<thead>
<tr>
<th>TEST</th>
<th>ANTIGEN</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDRL (CSF) Screen</td>
<td>Cardiolipin, Cholesterol</td>
<td>TRUE POSITIVE ✓ RPR TITER &gt;1:2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ VDRL TITER &gt;1:2 FALSE POSITIVE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Autoimmune Diseases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Infectious mono</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Pregnancy, Old age</td>
</tr>
<tr>
<td>RPR Screen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T. pallidum</td>
<td>+ Fluorescence</td>
</tr>
</tbody>
</table>

SERoLOGICAL TESTS

<table>
<thead>
<tr>
<th>TEST</th>
<th>SENSITIVITY BY STAGE OF syphilis (%)</th>
<th>SPECIFICITY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1&lt;sup&gt;o&lt;/sup&gt;</td>
<td>2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>VDRL</td>
<td>78 (74-87)</td>
<td>100</td>
</tr>
<tr>
<td>RPR</td>
<td>86 (77-100)</td>
<td>100</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>84 (70-100)</td>
<td>100</td>
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</tbody>
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HERPES SIMPLEX VIRUS (HSV)
• Serotypes I AND II
✓ Type I: 5-30% of genital herpes, milder course
• X vs Y
✓ X: 1 out of 4
✓ Y: 1 out of 5
• Differential Diagnosis
✓ Syphilis
✓ Chancroid
• Primary episode—most severe
✓ Cervicitis occurs in 70-90% of 1st episodes
✓ 50% rate of fetal transmission in primary maternal infection
PRIMARY EPISODE

• Appearance
  ▶ Painful, clusters of vesicles on erythematous base that may coalesce
  ▶ Evolve into pustules that erode into ulcers w/scalloped edges
  ▶ Crust over before healing

• Course
  ▶ Incubation: ~2-12 days
  ▶ New lesions until 10th d
  ▶ Lesions shed virus for <10-12 d
  ▶ Re-epithelization occurs after ~15-20 d

RECURRENT EPISODES

• 5-8/yr common
• Triggers
  ▶ Stress, fatigue, menses
• Prodrome (50%)
  ▶ Tingling, itch, burn, or pain at site of eruption 0.5-48 hrs before outbreak
• Compared with primary infection
  ▶ Dysuria less common, symptoms milder
  ▶ Lesions shed virus ~4 days
  ▶ Time to re-epithelization shorter (~10 days)

BRIEF CASE

21 year old sexually active woman presents for routine gynecologic examination. She has had 2 sexual partners in her lifetime & uses condoms 90-95% of the time.

She complained about painful oral lesions.

WHAT'S YOUR DIFFERENTIAL?

HUMAN PAPILLOMA VIRUS

• INCIDENCE
  ▶ U.S. 6 MILLION CASES/YR
  ▶ MOST PREVALENT STD AMONG COLLEGE WOMEN
• CLINICAL IMPRESSION
  ▶ VISIBLE GENITAL WARTS CALLED CONDYLOMA ACUMINATA
  ▶ CONDYLOMA = “KNUCKLES” ACUMINATA = “POINTED”
• EXPOSURE ➔ DETECTION OF WARTS: 3-8 Mth
• > 30 TYPES CAN INFECT ANOGENITAL TRACT
• INVASIVE CANCER
  ▶ 16,18, 31, 33 & 35 TYPES HIGH TO MOD RISK

HPV FACTS

VACCINES

• GARDASIL, MANUFACTURED BY MERCK
  ▶ GENETICALLY ENGINEERED
  ▶ BLOCKS INFECTION WITH HPV 16 & 18
    ▶ ~70% OF CERVICAL CANCERS
  ▶ REDUCES INFECTION WITH HPV 6 & 11
    ▶ ~90% OF GENITAL WARTS
  ▶ 3 DOSES OF VACCINE ADMINISTERED OVER 6 MTHS
    ▶ 97 – 100% EFFICACIOUS IN PREVENTING CERVICAL CANCER WHEN COMPARED TO PLACEBO

THERAPY

REFER TO HANDOUT