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</td>
<td>4 million</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>650,000</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>180 million</td>
</tr>
<tr>
<td>BV</td>
<td>Not reportable</td>
</tr>
<tr>
<td>ULCERATIVE</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>6 million</td>
</tr>
<tr>
<td>Herpes</td>
<td>1 million</td>
</tr>
<tr>
<td>Syphilis</td>
<td>60,000</td>
</tr>
</tbody>
</table>

<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>
STDs
THE HIDDEN EPIDEMIC

DISCHARGE DISEASES
✓ HIV ACQUISITION ↑ 5- FOLD
ULCERATIVE LESIONS/ GROWTHS
✓ HIV ACQUISITION ↑ 10- FOLD

AT RISK
✓ SEXUALLY ACTIVE ADOLESCENTS
  • CHECK TWICE A YEAR GC/CT
  • PREVALENCE IS 29%
  • CDC, AMA, AAP GUIDELINES
✓ MULTIPLE SEX PARTNERS
✓ PAST STDs

WOMEN AT RISK
THE “X FACTOR”

• STDs OFTEN ASYMPTOMATIC
  ✓ 75-90% WOMEN WITH CHLAMYDIA
  ✓ 50-70% MEN WITH CHLAMYDIA
• PID
  ✓ ≤ 40% UNTREATED CASES GC/CHLAMYDIA
  ✓ INFERTILITY
    • 1 IN 5 UNTREATED
  ✓ CHRONIC PELVIC PAIN
• HPV CERVICAL CA

• PREMATURE LABOR & DELIVERY
  ✓ LARGEST RATE OF INFANT MORTALITY
• PREMATURE RUPTURE OF MEMBRANES
• ECTOPIC PREGNANCIES
• NEONATES
  ✓ CONJUNCTIVITIS
  ✓ PNEUMONIA

COMPLICATIONS RARE IN MEN……”Y”
CASE

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

✓ No fever, pain on urination, or inguinal adenopathy
✓ Pt sexually active with girlfriend for past 2-3 mths
✓ Reported inconsistent condom use
  ✓ He forgets……..

• WHAT IS THE DIFFERENTIAL?
• WHAT TESTS TO ORDER?
• HOW IS THE LAB DX MADE?

DISCHARGE DISEASES

• MOST COMMON DISCHARGE DISEASE IN U.S.
  ✓ CHLAMYDIA TRACHOMATIS
  ✓ NEISSERIA GONORRHAEEAE
  ✓ TRICHOMONAS VAGINALIS
• 25% SYMPTOMATIC PTS HAVE MIXED GC/CT INFECTIONS

• CLINICAL SYNDROME
  ✓ SYMPTOMATIC OR ASYMPTOMATIC
  ✓ DYSURIA & FREQUENCY
  ✓ PURULENT DISCHARGE INDISTINGUISHABLE
  ✓ OTHER SITES PHARYNX, RECTUM, EYE
  ✓ BACTEREMIA, ARTHRITIS
  ✓ CERVICITIS
  ✓ URETHRITIS
  ✓ PID
**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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**LAB DIAGNOSIS**

**C. TRACHOMATIS**

- **NA AMPLIFICATION**
  - ✓ URINE SCREEN
- **DIRECT FLUORESCENT AB**
- **DNA PROBES**
  - ✓ URETHRAL SPECIMEN
- **TISSUE CULTURE**
  - ✓ McCoy CELLS
    - ✓ INTRACYTOPLASMIC INCLUSIONS WITH IODINE
    - ✓ IMMUNOFLUORESCENCE
CT/GC DETECTION

<table>
<thead>
<tr>
<th>GRAM STAIN</th>
<th>CULTURE</th>
<th>GC/CT URINE NAAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC</td>
<td>GRAM – DIPLOCOCCI (bean-shaped)</td>
<td>CALCULUM ALGINATE Swab (Cotton-toxic)</td>
</tr>
<tr>
<td></td>
<td>SENSITIVITY - MALES  ✓ 95-99%  ✓ 69% Symptomatic ✓ 45-65% Asymptomatic</td>
<td>CHOCOLATE AGAR CO₂ TAT- 2 Days</td>
</tr>
<tr>
<td></td>
<td>SENSITIVITY - FEMALES  ✓ 95-99%  ✓ 69% Symptomatic ✓ 45-65% Asymptomatic</td>
<td>SENSITIVITY 85-98%</td>
</tr>
<tr>
<td>CT</td>
<td>N/A</td>
<td>McCoy Cells TAT- 2-3 Days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SPECIFICITY &gt;98% TAT- 4 hrs</td>
</tr>
</tbody>
</table>

& PTs PARTNER(S)?
KNOW COLLECTION SITES FOR DISCHARGE DISEASES

<table>
<thead>
<tr>
<th>ENDOCERVIX</th>
<th>VAGINA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pH</td>
<td>7.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>COLUMNSAR EPITHELIAL</th>
<th>SQUAMOUS EPITHELIAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogens</td>
<td>Chlamydia trachomatis, Neisseria gonorrhoeae</td>
<td>Bacterial Vaginosis (BV), Trichomonas, Candida sp</td>
</tr>
</tbody>
</table>
CDC GUIDELINES
CT TESTS IN ASSAULT CASES

CHILDREN
• CULTURES
  ✓ GOLD STANDARD
  ✓ ANUS, VAGINA
  ✓ MEATAL SPECIMEN IN MALES IF DISCHARGE
• CULTURE POS CONFIRM WITH DIRECT FUORESCENT 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

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
  ✓ Douching, 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><strong>BACTERIAL VAGINOSIS</strong></td>
<td>Watery, gray, homogeneous alkali</td>
<td>FISHY</td>
<td>Cervix normal, Often asymptomatic</td>
</tr>
<tr>
<td>Trichomonas</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><strong>CANDIDIASIS</strong></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
  - $\downarrow$ 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 DIAGNOSED

SPECIMENS TO ORDER
• 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

MICRO REPORT
• GRAM STAIN SHOWS “CLUE CELLS”
  ✓ EPITHELIAL CELLS & GNR
  ✓ NUGENT SCORE
  ✓ FEW GRAM- POS LACTOBACILLI
  ✓ ANAEROBES 10-100 X NORMAL
  • NOT VAGINITIS - NO WBCs

BV FACTS

• PREGNANT WOMEN
  ✓ AFFECT 15-20% PREGNANT WOMEN
  ✓ AMNIOTIC FLUID INFECTION
  ✓ POSTPARTUM ENDOMETRITIS
  ✓ PREMATURERUPTUREOFMEMBRANES
  ✓ PRETERM DELIVERY
  ✓ LOW BIRTH WEIGHT

• TREAT PREGNANT WOMEN
  ✓ METRONIDAZOLE
  ✓ CLINDAMYCIN

BV ASSOCIATED WITH
RECURRENT UTI
PID
POST-OP GYN
INFECTIONS
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

TRICHOMONAS FACTS

• THIRD MOST COMMON OF THE VAGINITIDES

• PREVALENCE
  ✓ COMMERCIAL SEX WORKERS (TRICKY BUSINESS) - 50-75%
  ✓ STD CLINICS - 32-54%
  ✓ OB CLINICS - 10-26%

• MALES
  ✓ IMPLICATED AS COFACTOR IN HIV TRANSMISSION
  ✓ CAUSES URETHRITIS, PROSTATITIS

• TREATMENT
  ✓ METRONIDAZOLE
    • TINIDAZOLE FOR METRONIDAZOLE-RESISTANCE
FUN GAL INFECTION
VULVOVAGINAL CANDIDASIS

- ETIOLOGIC AGENT
  - 85-95% Candida albicans
  - Candida glabrata
    - 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 suspect

- 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
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?

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
- HIGHER IN THE SOUTH
  - HETEROSEXUAL BLACK MEN
- INCUBATION UP TO 6 MTHS

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 Lymph Nodes**

**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
  - Malaise
  - Headache
  - Sore throat
  - Arthralgias
  - Anorexia
**LATENT SYPHILIS**
- No clinical manifestations
- Early = 1\textsuperscript{st} 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

---

**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</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ RPR TITER &gt;1:2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ VDRL TITER &gt;1:2</td>
</tr>
<tr>
<td>RPR Screen</td>
<td></td>
<td>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>FTA-AB confirmatory</td>
<td>T. pallidum</td>
<td>+ FLUORESCENCE</td>
</tr>
</tbody>
</table>
SEROLOGICAL TESTS

<table>
<thead>
<tr>
<th>TEST</th>
<th>1&lt;sup&gt;st&lt;/sup&gt;</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt;</th>
<th>LATENT</th>
<th>LATE</th>
<th>SPECIFICITY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDRL</td>
<td>78 (74-87)</td>
<td>100</td>
<td>95 (88-100)</td>
<td>71 (37-94)</td>
<td>98 (96-99)</td>
</tr>
<tr>
<td>RPR</td>
<td>86 (77-100)</td>
<td>100</td>
<td>98 (95-100)</td>
<td>73</td>
<td>98 (93-99)</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>84 (70-100)</td>
<td>100</td>
<td>100</td>
<td>96</td>
<td>97 (94-100)</td>
</tr>
</tbody>
</table>

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

**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 10\textsuperscript{th} d
  - Lesions shed virus for \leq 10-12 d
  - Re-epithelization occurs after \sim 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)

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**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