OBJECTIVES

- Sharpen Differential DX
- Importance of Lab Tests for the STD Detection
- Know what specimens to collect
- Learn optimal micro tests to order

HISTORY (5 “P”s)
1. Partners
   - MEN, WOMEN, BOTH
   - NUMBER
2. Protect vs STD
3. Practices
   - VAGINAL, ANAL, ORAL
   - CONDOM USE?
4. Past Hx STD
   - EVER HAVE STD, E.G.
     PENILE SORE/SCAB
   - PARTNERS WITH STD
5. Prevent Pregnancy

EXAM
- Discharge?
  - URETHRITIS
  - PROSTATITIS
  - VAGINITIS
  - CERVICITIS
- Ulcer?
  - TYPE OF LESION
  - NUMBER
- Look at other Sites
  - PHARYNX, EYE, RECTUM

BACKGROUND

STD DISEASES

DISCHARGE
1. Trichomoniasis
2. *Chlamydia
3. *Gonorrhea

HIV ACQUISITION
- 5- FOLD

*REPORTABLE DISEASES

ULCERATIVE
1. Herpes Simplex virus
2. Human Papilloma Virus
3. *Treponema pallidum
4. *Chancroid
   (Hemophilus ducreyi)

HIV ACQUISITION
- 10- FOLD

*REPORTABLE DISEASES

STD EPIDEMIC- USA

TIP OF THE ICEBERG

CLINICAL SYNDROMES

INOCENCE
- Chlamydia - 4 million
- Gonorrhea - 650,000
- 25% symptomatic pts mixed
  CT/GC infections
- Trichomoniasis - 180 million
- BV - Not reportable

ULCERATIVE
- HPV - 6 million
- Herpes - 1 million
- Syphilis - 60,000

INFERTILITY
ECTOPIC PREGNANCY
HIV TRANSMISSION
PID, 1 million/yr
CERVICAL CA
~$10 BILLION ANNUAL COST

CASES ARE OFTEN ASYMPOTOMIC
CASE

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

- CLINICAL EXAM
  - No fever, no dysuria
  - No inguinal adenopathy
- HISTORY
  - Pt sexually active with girlfriend for past 2-3 mths
  - Girlfriend asymptomatic
  - Reported inconsistent condom use
    - He forgets when he parties

DIFFERENTIAL & MICRO TESTS

- DIFFERENTIAL
  - Discharge STD
    - Chlamydia trachomatis (CT) or Neisseria gonorrhoea (GC)
    - Purulent discharge is indistinguishable
- WHAT TEST TO ORDER?
  - Nucleic acid amplification test (NAAT)
    - Can test GC & CT at same time – one test
    - 4 hrs (same day results)
  - Gram stain & culture
    - Swab purulent discharge
    - Results gram stain: same day
    - Culture 2 days
  - Other STD tests should be ordered
    - HIV, Syphilis

TEST COMPARISONS FOR GC

<table>
<thead>
<tr>
<th>TEST</th>
<th>GC - MALES</th>
<th>GC - FEMALES</th>
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<tbody>
<tr>
<td>SENSITIVITY</td>
<td>95-99% Symptomatic</td>
<td>45-65%</td>
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<tr>
<td>SPECIFICITY</td>
<td>98%</td>
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</table>

<table>
<thead>
<tr>
<th>TEST</th>
<th>GC - URINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSITIVITY</td>
<td>85-98%</td>
</tr>
<tr>
<td>SPECIFICITY</td>
<td>&gt;98%</td>
</tr>
</tbody>
</table>

PT TEST RESULTS

- NAAT – DAY ONE
  - Positive for GC
  - Negative for CT
- GRAM STAIN – DAY ONE
  - Positive for GN diplococci
- CULTURE – DAY TWO
  - Neisseria gonorrhoea

WHAT ABOUT THE PTs PARTNER?

PARTNER NOTIFICATION

- “contact tracing”
- Public health authorities arrange evaluation & treatment
- Reduce risk of reinfecting index case
- Reduce STD transmission

PT WAS SEEN IN EYE CLINIC 1 DAY BEFORE

DX: Ophthalmitis

TESTS ORDERED

BEFORE CONTACT NOTIFICATION

- Gram stain & culture of eye exudate
- PT discharged
- Gram stain – day one
- GN diplococci
- Presumptive GC opthalmia
- PT called for appt

AFTER CONTACT NOTIFICATION

- PT no complaints of discharge, dysuria
- NAAT screen ordered for GC/CT
- Urine specimen obtained
- Test positive for GC
- Practiced vaginal & rectal intercourse
- NAAT not FDA cleared for rectal specimen
- Pelvic exam
- Cervicitis
- Other STD tests
  - HIV, syphilis
  - Results negative
WOMEN AT RISK
THE “X FACTOR”

- STDs OFTEN ASYMMPTOMATIC
  75-90% WOMEN WITH GC/CT
  50-70% MEN WITH CHLAMYDIA
- PT PELVIC EXAM
- ECTOPIC PREGNANCIES
- NEONATES
- CONJUNCTIVITIS
- PNEUMONIA
- PID
  UP TO 40% UNTREATED CASES GC/CHLAMYDIA
  1 IN 5 UNTREATED
- CHRONIC PELVIC PAIN
- PREMATURE LABOR & DELIVERY
- LARGEST RATE OF INFANT MORTALITY

COMPILATIONS RARE IN MEN……."Y"

CHLAMYDIA/GC
URINE NAAT SCREEN

- URINE
- NON-INVASIVE, PAINLESS!!!
- SCREENING IS RECOMMENDED
  - CDC, AMA, DOH
  - PREGNANCY
  - ANNUAL IN SEXUALLY ACTIVE TEENS & YOUNG ADULTS
- EVEN IF ASYMMPTOMATIC

TEEN SEX

“OOPS I DID IT AGAIN…. I’M NOT THAT INNOCENT !!”
The Britney Influence

- 9-12 GRADES
  50% HAVE HAD SEXUAL INTERCOURSE
- 58% USED CONDOMS
- 3 MILLION TEENS INFECTED
- SEX <13 YRS OLD – 8%
- SEX 15-17 YR OLD
  31% “MET THE RIGHT PERSON”
  16% “THE OTHER PERSON WANTED TO”
  15% “JUST CURIOUS!”
- CONCEPT OF RECURRING INFECTIONS
  THEY DON’T GET IT!

TEENS & SEX
STD ADOLESCENT CLINICS

- AT-RISK GROUP
  - MULTIPLE SEX PARTNERS
  - UNPROTECTED SEX
  - INJECTING DRUG USERS
  - PAST STDs
- THE X FACTOR: FEMALES
  - GC HIGHEST IN 15-19 YRS
  - 5-10% TEENS – CHLAMYDIA
  - 28-46% <25 YRS – HPV
  - SEX PARTNERS WITH OLDER MEN
  - PREVALENCE UP TO 29%
  - RECOMMEND SCREENING AT LEAST ANNUALLY < 25 YRS

CDC GUIDELINES
CT TESTS IN ASSAULT CASES

CHILDREN
- GC, CT & SYPHILIS ACQUIRED AFTER NEONATAL PERIOD
  100% INDICATIVE OF SEXUAL CONTACT
- CULTURE
  GOLD STANDARD
- ANUS, VAGINA, URETHRAL
- 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

THE VAGINA MONOLOGUES
WOMEN AT RISK
YOUR PATIENT
• 23 yr old female, married & in 2nd trimester of first pregnancy
• Increased watery vaginal discharge with “fishy” odor most notable immediately after intercourse
• No dysuria
• No vaginal pruritis

EVALUATION & DIFFERENTIAL
• HISTORY EXAM
  ✓ Past STDs
  ✓ Douching
  ✓ Multiple sex partners, IUD
• PELVIC EXAM
  ✓ No cervicitis
  ✓ DIFFERENTIAL
    ✓ Vulvovaginitis
    ✓ STD disease

SYNDROME | DISCHARGE | ODOR | PRESENTATION
----------|-----------|------|------------------
BACTERIAL VAGINOSIS | Watery, gray, homogeneous alkaline | FISHY | Cervix normal, Often asymptomatic
Trichomonas | Watery, thin, gray, alkaline homogeneous | FISHY | Itching, vaginal erythema, dysuria, vaginal erosions, petechiae strawberry cervix
CANDIDIASIS | Thick, white, non-homogeneous | SOUR | Same as above but (no petechiae)

KNOW COLLECTION SITES TO SAMPLE FOR CULTURE

<table>
<thead>
<tr>
<th>ENDOCERVIX</th>
<th>VAGINA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pH</td>
<td>7.0</td>
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<tr>
<td>Cell Type</td>
<td>COLUMNAR EPITHELIAL</td>
</tr>
<tr>
<td>Pathogens</td>
<td>Chlamydia trachomatis</td>
</tr>
<tr>
<td></td>
<td>Bacterial Vaginosis (BV)</td>
</tr>
<tr>
<td></td>
<td>Candida sp</td>
</tr>
</tbody>
</table>

THE FISHY ODOR IN VIVO

• NORMAL VAGINAL FLORA
  ✓ \(H_2O_2\) Producing Lactobacilli \(\Rightarrow\) LACTIC ACID
  ✓ \(\downarrow\) pH (<4.5)
• BACTERIAL VAGINOSIS
  ✓ ANAEROBES INCREASE \(\Rightarrow\) Proteolytic enzymes act on vaginal peptides
  ✓ RELEASE OF POLYAMINES & TRIMETHYLAMINE
  ✓ TRIMETHYLAMINE IN ALKALINE pH \(\Rightarrow\) FISHY ODOR
  ✓ POLYAMINES \(\Rightarrow\) EXFOLIATION OF EPITHELIAL CELLS
    (CLUE CELL)
  ✓ POLYAMINES \(\Rightarrow\) FISHY DISCHARGE

LAB DX BV

Micro Report
- Gram Stain shows “CLUE CELLS”
- Epithelial cells & GNR
- Few Gram-pos Lactobacilli
- Anaerobes 10-100 x normal
- IMBALANCE of normal flora

Specimens to Order
- VAGINAL SECRETIONS
  ✓ “WET MOUNT”
  ✓ SWAB FOR GRAM STAIN
  ✓ 10% KOH “WHIFF” TEST
  ✓ ADD KOH
  ✓ AMINE “FISHY ODOR”
- NO CULTURE!!
  ✓ GARDNERELLA VAGINALIS
  ✓ NORMAL FLORA 30% WOMEN

NORMAL VAGINAL FLORA
CLUE CELLS

BV FACTS

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

Bacterial Vaginosis (BV) not vaginitis - no WBCs

BV ASSOCIATED WITH RECURRENT UTI
PID
POST-OP GYN INFECTIONS

THE FISHY STORY

CLINICAL SYNDROMES

Itching, vaginal erythema, dysuria, vaginal erosions, petechiae strawberry cervix

CLINICAL SYNDROMES

Itching, vaginal erythema, dysuria, vaginal erosions, petechiae strawberry cervix
WHAT IF.....

- REPORT BACK FROM LAB THAT PT WAS "CLUELESS"
- WHAT IS YOUR DIFFERENTIAL?
  - TRICKY QUESTION

CONSIDER TRICHOMONAS

LAB TESTS
- WET MOUNT
  - URINE OR VAGINAL SECRETION MUST BE VIEWED IMMEDIATELY
  - <50% SENSITIVITY/SPECIFICITY
- IN-POUCH CULTURE
  - 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 GALL INFECTION VULVOVAGINAL CANDIDIASIS

- ETIOLOGIC AGENT
  - 85-95% Candida albicans
  - Candida glabrata
  - Less suscept 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
  - HAEMOPHILUS DUCREYI
- CONTRIBUTE TO HIV TRANSMISSION
  - ULCER IS PORTAL OF ENTRY

STD BRIEF CASE

YOUR PATIENT

EXAM
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.

PHYSICAL EXAM

PENILE ULCER

WHAT IS THE DIFFERENTIAL?

WHAT TESTS WILL YOU ORDER?
STD CASE
YOUR PATIENT
Upon further questioning, you learn that he had had anonymous sex with men at bathhouses.

DIFFERENTIAL?
CHANCRE (primary syphilis) OR CHANCROID (H. ducreyi)

PHYSICAL EXAM

LAB TESTS
• PRIMARY SYPHILIS
  ✓ DARK FIELD POSITIVE FOR TREPONEMA PALLIDUM
• SPECIMEN
  ✓ ULCER (NOT ORAL)
  ✓ SCRAP AT BASE OF LESION
• SEROLOGY (secondary)
  ✓ INSENSITIVE
• R/O OTHER STDS
  ✓ HIV, HERPES

SYphilis facts
CHANCRE
• Appears average 3 wks (10-90 days) after infection site where treponemes 1st invade dermis
• Usually near genitals, or other skin & mucous membrane areas
• Usually single, painless, indurated lesion >0.5 cm in diameter
• Persists 2-6 wks, then heals w/o scar

INCIDENCE
• INCREASE IN NYC AMONG MEN WHO HAVE SEX WITH MEN (MSM)
  ✓ WHITE MEN & THOSE IN MANHATTAN
  ✓ LARGELY HIV + INDICATING EROSION OF SAFE SEX
• HIGHER IN THE SOUTH
  ✓ HETEROSEXUAL BLACK MEN

INCIDENCE
6 WKS – 6 MTH AFTER INFECTION
✓ If untreated
• RASH IN ~75%
• HEPATOMEGALY, SPLENOMEGALY
• GENERALIZED LA IN >50%
• HEMATOGENOUS DISSEMIN
• SEROLOGY TESTS ARE SENSITIVE
  ✓ RPR (rapid plasma reagin)
  ✓ FTA (fluorescent treponemal Ab)
  ✓ Confirmatory test
  ✓ VDRL - CSF

LAB DX - SYphilis

<table>
<thead>
<tr>
<th>TEST</th>
<th>ANTIGEN</th>
<th>INTERPRETATION</th>
</tr>
</thead>
</table>
| VDRL (CSF) Screen | CARDIOLIPIN           | TRUE POSITIVE
|               | CHOLESTEROL           | ✓ RPR TITER >1:2
|               |                       | ✓ VDRL TITER >1:2
|               |                       | FALSE POSITIVE
|               |                       | ✓ Autoimmune Diseases
|               |                       | ✓ Infectious mono
|               |                       | ✓ Pregnancy, Old age
| RPR Screen    |                       | + FLUORESCENCE
| FTA-ABS confirmatory | T. pallidum          | + FLUORESCENCE

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>1º</td>
<td>2º</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>
</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

STD CASE

HISTORY
- 35 y.o. male with HIV+, dx 2001
- Sexual intercourse with men & women
- FTA reactive, RPR NR
- Tx for GC/Chlamydia
- HSV2 – 1 outbk/mth
- +Groin LAD

STD CASE HISTORY

BEEFY GRANULAR BASE, RED MARGIN, LIKE HSV, PAINFUL RAGGED EDGES, LARGER AND < 50% TENDER INGUINAL LA

CASE

DIFFERENTIAL
- 1st - Genital herpes most common in U.S.
- 2nd - primary syphilis
- 3rd - chancroid - fewer than 1,000 cases reported each year

CASE DIFFERENTIAL

SYphilis chancre
- Painless, indurated, clean-based ulcer
- Sensitivity 31%, Specificity 98%

Chancroid
- Painful, deep, undetermined, purulent ulcer surrounded by erythematous ring
- Sensitivity 34%, Specificity 94%

Genital Herpes
- Multiple, shallow, tender ulcers
- Sensitivity 35%, Specificity 94%

SPECIMEN COLLECTION & MICRO TESTS

Chancroid- Culture & PCR
- Smear of lesion from serous exudate from the ulcer base or border or aspiration
- Roll the swab over the slide in one direction or prepare a touch preparation
- Gram stain
- Inoculate selective chocolate agar with vancomycin at the “bedside” or hand deliver swab to the Micro lab
- Multiplex PCR
- Sensitivity 95-98%
- Specificity 99.6% (New Orleans)

Chancroid- Dark Field

OTHER STD TESTS (HERPES, HIV)

H.ducreyi

DIFFICULT TO CULTURE
- Cultures must be hand delivered to lab
- Chocolate agar with vancomycin
- Incubate 35 C in high humidity with CO2 enrichment or up to 3 days
- Cultures often contaminated

H. ducreyi

Small, fastidious, GNR
Short Chains “schools of fish”
Treatment Azithromycin

BRIEF CASE

20 yr old sexually active female presents with 4 day history of fever, chills, myalgia & painful genital lesions.

Pelvic exam revealed extensive vesicular & ulcerative lesions with marked edema.

Brief Case

Multiple lesions vesicle & ragged ulcers, Tender, LA

Mucosa macerated, Edematous, Erythematous, Copious yellow-green discharge
**DIFFERENTIAL & LAB TESTS**

- **DIFFERENTIAL**
  - Herpes, Syphilis, Chancroid

- **LAB TESTS FOR HERPES**
  - **DIRECT IMMUNOFLUORESCENCE +**
    - Scrape cells off base of ulcer & stain
    - Sensitivity highest with vesicular lesions
  - **CULTURE**
    - Sensitivity 70-99%, specificity 99%
  - **CYTOLOGY & H & E STAIN**
    - Multi-nucleated giant cells
    - Sensitivity & specificity <60%
  - **PCR TEST +**
    - Differentiates types 1 & 2
    - >95% sensitivity & specificity

**HERPES SIMPLEX VIRUS (HSV)**

- **SEROTYPES I AND II**
  - Type I: 5-30% of genital herpes, milder course

- **Appearance**
  - Painful, clusters of vesicles on erythematous base that may coalesce
  - Highest test sensitivity
  - Evolve into pustules that erode into ulcers that crust over before healing
  - Lowest test sensitivity

- **PRIMARY EPISODE: MOST SEVERE**
  - Cervicitis occurs in 70-90% of 1st episodes
  - 50% rate of fetal transmission in primary maternal infection

- **HSV & Pregnancy**
  - Prophylactic C-section not indicated for women who do NOT have active genital lesions at delivery

- **TREATMENT**
  - Acyclovir

**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?**

**LAB DX - HPV**

- ThinPrep Pap Test
  - Liquid based pap test with fluid transport medium that eliminates mucous, blood from cervical specimens
  - Increased accuracy, easier reading

- Digene HYBRID CAPTURE DNA TEST
  - Uses residual fluid from Thin Prep Pap vials
  - Detects 13 high-risk HPV types
  - Triage test for women with inconclusive/ASC-US Pap test abnormalities

**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 TYPES**
  - 16, 18, 31, 33 & 35 high to moderate 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
STDs IN UNLIKELY PLACES
BEAUTY IS IN THE EYE OF THE BEHOLDER

SHIP TO SHORE
- Skipper was 3 mths at sea & had urethral discharge of 2 wks
  - Gram stain showed intracellular gram negative diplococci
  - Culture positive for N. gonorrhoeae
- No woman onboard the ship
- Denies homosexual contacts
- Onset of symptoms was >2 mths after leaving the port

GUYS & DOLLS
- A few days before onset of symptoms, he awakened the engineer in his cabin during the night because of engine trouble.
- After the engineer left his cabin, the skipper found an inflatable doll with artificial vagina in his bed
- The skipper admitted to having “intercourse” with the doll.

THE ENGINEER’S STORY
- Admitted intercourse with a girl in a town some days before going to sea.
- Observed mild urethral discharge since he left port but did not see the ship’s doc & was not tx with antibiotics.
- Admits to sleeping with his “doll”.
- Engineer had GC.
- THIS IS THE ONLY REPORTED CASE OF GC TRANSMISSION THROUGH AN INFLATABLE DOLL

AM Renton, CA Ison, L Whisker, K Kirkland, E Kupak, and JR Harris
Neisseria gonorrhoeae isolated at St. Mary’s Hospital London, 1980-91