SEXUALLY TRANSMITTED DISEASES
CASES IN THE CITY

LABORATORY MEDICINE COURSE
2005

CLINICAL MICROBIOLOGY SERVICE
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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

COMPLICATIONS RARE IN MEN……"Y"

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

STD EPIDEMIC- USA
TIP OF THE ICEBERG

CLINICAL SYNDROMES INCIDENCE

DISCHARGE
- *Chlamydia* - 4 million
- Gonorrhea - 650,000
- Trichomoniasis - 180 million
- BV - Not reportable

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

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

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 ?

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

DISCHARGE DISEASES

- MOST COMMON DISCHARGE DISEASE IN U.S.
  - ✓ *CHLAMYDIA TRACHOMATIS*
  - ✓ *NEISSERIA GONORRHAEAE*
  - ✓ *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

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

	ENDOCERVIX	VAGINA
Normal pH	7.0	<4.5
Cell Type	COLUMNAR EPITHELIAL	SQUAMOUS EPITHELIAL
Pathogens	*Chlamydia trachomatis* *Neisseria gonorrhoeae*	Bacterial Vaginosis (BV) *Trichomonas* *Candida* sp

LAB DIAGNOSIS *C. TRACHOMATIS*

- NA AMPLIFICATION
  - ✓URINE SCREEN
- DIRECT FLUORESCENT AB
- DNA PROBES
  - ✓URETHRAL SPECIMEN
- TISSUE CULTURE
  - ✓McCOY CELLS
    - INTRACYTOPLASMIC INCLUSIONS WITH IODINE
    - IMMUNOFLUORESCENCE

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

CT/GC DETECTION

	GRAM STAIN	CULTURE	GC/CT URINE NAAT
GC	GRAM – DIPLOCOCCI (bean-shaped) SENSITIVITY - MALES ✓ 95-99% Symptomatic ✓ 69% Asymptomatic SENSITIVITY - FEMALES ✓ 45-65%	CALCIUM ALGINATE Swab (Cotton-toxic) CHOCOLATE AGAR CO_2 TAT- 2 Days	SENSITIVITY 85-98% SPECIFICITY >98% TAT- 4 hrs
CT	N/A	McCoy Cells TAT- 2-3 Days	

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

SYNDROME	DISCHARGE	ODOR	PRESENTATION
BACTERIAL VAGINOSIS	Watery, gray, homogeneous alkaline	FISHY	Cervix normal, Often asymptomatic
Trichomonasis	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)

BV FACTS

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

BV ASSOCIATED WITH
RECURRENT UTI
PID
POST-OP GYN
INFECTIONS

THE FISHY ODOR IN VIVO

- NORMAL VAGINAL FLORA
  - ✓ H_2O_2 Producing Lactobacilli ⇒ lactic acid
  - ✓ ⇓ pH (<4.5)
- BACTERIAL VAGINOSIS
  - ✓ Anaerobes Increase ⇒ Proteolytic enzymes act on vaginal peptides
  - ✓ Release of polyamines and trimethylamine
  - ✓ Trimethylamine in alkaline pH ⇒ fishy odor
  - ✓ Polyamines ⇒ Exfoliation of epithelial cells (clue cell)
  - ✓ Polyamines ⇒ Fishy discharge

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

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
  - ✓ IMBALANCE OF NORMAL FLORA
- NOT VAGINITIS - NO WBCs

NORMAL EPITHELIAL CELL

CLUE CELL

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 suscep 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

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

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

- 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

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?

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

LATENT SYPHILIS

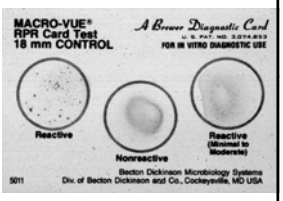
- **No clinical manifestations**
- **Early = 1st year after secondary syphilis**
- **Late = > 1 year after secondary syphilis**
  - ✓ **Lower risk of transmission**

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**

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

LAB DX - SYPHILIS

TEST	ANTIGEN	INTERPRETATION
VDRL (CSF) Screen	CARDIOLIPIN CHOLESTEROL	TRUE POSITIVE ✓RPR TITER >1:2 ✓VDRL TITER >1:2 FALSE POSITIVE ✓Autoimmune Diseases ✓Infectious mono ✓Pregnancy, Old age
RPR Screen		
FTA-AB confirmatory	*T. pallidum*	+ FLUORESCENCE

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**

SEROLOGICAL TESTS

	SENSITIVITY BY STAGE OF SYPHILIS (%)				SPECIFICITY (%))
TEST	1^0	2^0	LATENT	LATE	
VDRL	78 (74-87)	100	95 (88-100)	71 (37-94)	98 (96-99)
RPR	86 (77-100)	100	98 (95-100)	73	98 (93-99)
FTA-ABS	84 (70-100)	100	100	96	97 (94-100)

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)**

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

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**