HISTOPATHOLOGY AND LABORATORY FEATURES OF SEXUALLY TRANSMITTED DISEASES

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LEARNING OBJECTIVES:

- Identify the etiologic agents causing pelvic inflammatory disease and the pathologic changes they produce.
- Discuss the characteristic clinical and pathologic findings caused by herpes simplex virus (HSV) infections:
    a. fever blisters
    b. genital herpes simplex virus infection
    c. disseminated neonatal HSV
- Describe the pathologic changes produced by *Treponema pallidum.*
- Describe the clinical features and pathologic changes produced by *Chlamydia trachomatis*and *Neisseria gonorrhoeae*
- Describe the clinical and laboratory features of vaginal infections including: *Trichomonas, Candida,* and bacterial vaginosis.
- Describe the clinical and laboratory features of ectoparasite infections

PURPOSE OF THE LECTURE:

1. To describe the various agents of sexually transmitted diseases and their disease manifestations

2. To describe the pathologic features associated with STDs

3. To introduce some of the laboratory aspects of STDs

TERMS INTRODUCED IN LECTURE:

Condyloma lata
Disseminated gonococcal infection
Gummatous syphilis
Lymphogranuloma venereum
Pelvic inflammatory disease
Rapid Plasma Reagin (RPR)
Salpingitis
Syphilis/endarteritis obliterans
Venereal Disease Research Laboratory (VDRL)
Treponema pallidum particle agglutination (TPPA)

MAJOR CONCEPTS EMPHASIZED IN LECTURE

I. **Syphilis** (Will be covered by Dr. Norgard in later lecture).

II. **Gonorrhea**

A. Causative agent: *Neisseria gonorrhoeae*, a Gram negative diplococcus. Humans are the only natural reservoir. Infection is acquired via direct contact with the mucosa of an infected person. The incubation period averages 2-5 days with a range of 1-14 days. The organism preferentially invades columnar and transitional epithelium but rapidly dies outside the host and is not transmissible via fomites.

B. Virulence factors:
1. Pili: Surface proteins that promote adherence to host cells.
2. Outer membrane porin proteins (PorA and PorB): Promote invasion into epithelial cells.
3. Opa (opacity) proteins: outer membrane proteins that promote adherence and invasion into epithelial cells.

C. Genital infection in males
1. Urethritis with dysuria and a purulent urethral discharge.
   a. 1-5% of men may be asymptomatic
   b. If untreated, most infections resolve spontaneously in several weeks
   c. Complications: epididymitis, prostatitis, seminal vesiculitis, orchitis, urethral stricture, and sterility.

D. Genital infection in females; can be localized to the cervix or spread to adjacent structures: pelvic inflammatory disease (PID)
1. Often asymptomatic (50%)
2. Cervicitis/urethritis: dysuria, lower pelvic pain, vaginal discharge
3. PID
   a. 10-20% of infected women develop PID
   b. Salpingitis, endometritis, pyosalpinx, tubal/ovarian/tuboovarian abscess, peritonitis
   c. Fitz-Hugh-Curtis Syndrome: peritoneal exudate tracks around dome of liver causing perihepatitis. Develops in 15-30% of women with PID.
   d. Complications of PID: ectopic pregnancy, ovarian torsion, sterility

E. Anorectal infection
1. About 40% of women and men who have sex with men (MSM) with uncomplicated gonorrhea will have positive rectal cultures for GC.
2. In 40% of MSM and 5% of women with GC, the rectum is the only site found to be infected.
3. Most patients are asymptomatic but may have tenesmus, anal pruritus and purulent rectal discharge or bleeding.

F. Pharyngeal infection
1. Majority of patients are asymptomatic
2. Some may have purulent pharyngitis and cervical lymphadenitis
3. 10-20% of women and 10-25% of MSM, 3-7% of heterosexual men may develop gonococcal pharyngitis

G. Disseminated disease
1. Seen in about 0.5-3% of patients and is more common in females.
2. Manifestations: tenosynovitis, arthritis, pustular or hemorrhagic skin lesions, migratory arthralgias (usually knees, elbows, distal joints).
3. Patients may be deficient in the late complement components and are unable to clear the organisms.

H. Infants
1. Infection acquired during passage through the birth canal of an infected mother.
2. Ophthalmia neonatorum: conjunctivitis
3. Antibiotic ointment at delivery has dramatically decreased neonatal infection

I. Laboratory testing
1. Direct Methods
a. Molecular tests have virtually replaced conventional methods but only for genital sources and are not admissible in court in cases of abuse. Amplified tests may also be performed on first catch urine in addition to genital sources.
b. Males: urethral Gram stain with intracellular Gram negative diplococci is diagnostic
c. Females: backup with culture
2. Culture
a. Non sterile sites: Thayer-Martin (TM), Modified TM, Martin-Lewis, NYC, JEMBEC
1) Media have antibiotics to inhibit overgrowth by normal flora
b. Sterile sites: blood culture, blood agar/chocolate agar
c. Identification
1) Genital sources: presumptive GC: growth on TM of oxidase-positive Gram-negative diplococci
2) All other sources, children, medicolegal: 2 identification methods required
d. Susceptibility testing not routinely performed

III. ***Chlamydia trachomatis***

A. #1 bacterial STD in the US with clinical features similar to GC
B. Major cause of PID, nongonococcal urethritis (NGU)/cervicitis
1. Other causes of NGU include: *Trichomonas vaginalis, Ureaplasma urealyticum, Mycoplasma genitalium.*
C. Most women asymptomatic
D. Perinatal infections: conjunctivitis, pneumonia
E. Primary syndromes
1. Trachoma (A, B, Ba, C)
2. Lymphogranuloma venereum (L1, L2, L3)
3. Conjunctivitis, common STDs, pneumonia (D-K)
F. Obligate intracellular pathogen of columnar/cuboidal epithelial cells that form distinct cytoplasmic inclusions depending on phase in life cycle.
1. Elementary body: infective form, metabolically inactive
2. Reticulate body: active form
G. Diagnosis
1. Culture on McCoy cells (epithelial cell line). Low sensitivity. Useful for medical legal
2. Molecular tests: high sensitivity and specificity
a. Amplified tests may be performed on first catch urine in addition to genital sources but not approved for non-genital sources.
3. Serology: not useful
H. Lymphogranuloma venereum (LGV)
1. Chronic, ulcerative disease
2. Sporadic cases in US but endemic in parts of Asia, Africa, Caribbean, South America.
3. Incubation 5-20 days
4. First stage: transient vesicle involving genitalia that later ulcerates
5. Second stage: 2-6 weeks later with inguinal lymphadenopathy/buboes

6. Lymphatic obstruction secondary to inflammation and extensive fibrosis can lead to elephantiasis and rectal strictures
7. Diagnosis
   a. Culture 25-30% sensitive (not recommended)
   b. Serology
   c. Molecular
   d. Histology: stellate, suppurating granulomas in the ulcerating lesions and involved lymph nodes

IV. **Trichomoniasis**
A. *Trichomonas vaginalis* (a flagellated protozoan)
B. Malodorous yellow-green vaginal discharge
C. Males: NGU or asymptomatic
D. Erythematous cervical mucosa
E. Diagnosis
   1. Saline wet mount
   2. Pap smear
   3. Antigen tests
   4. Culture
   5. Molecular tests

V. **Vaginal candidiasis**
A. Usually *Candida albicans* but other *Candida* species also
B. Risk factors: DM, OCPs, pregnancy, antibiotic therapy
C. Thick white discharge with pruritis
D. Diagnosis
   1. Wet mount/KOH
   2. Gram stain
   3. Pap smear

VI. **Bacterial vaginosis**
A. Secondary to a shift in the normal vaginal flora
B. *Gardnerella vaginalis* and anaerobes
C. Thin, gray discharge
D. Diagnosis
   1. Wet mount for “clue cells”
   2. Whiff test with 10% KOH
   3. Pap smear/Gram stain

VII. **Herpes simplex virus (HSV) infection**
A. Life cycle:
   1. Acute primary infection
   2. Latent infection
   3. Reactivation
   4. Clinically: clusters of vesicles on an erythematous base
B. HSV-1
   1. Primary: orolabial
   2. Recurrent: lips

C. HSV-2
1. Usually genital
D. Lab diagnosis
1. Culture
a. HSV is the easiest virus to grow in culture and grows quickly
b. Most useful for fresh vesicular lesions
c. Sensitivity lower on healing lesions
2. Direct
a. Tzanck smear (multinucleated cells with characteristic intranuclear inclusions)
b. FA (fluorescent antibody)/EIA (enzyme immunoassay)
c. Cytology (Pap)

d. Molecular (PCR)
1. Most sensitive detection method
2. Better on older lesions than culture
3. Serology
a. May be useful in the following scenarios
1. Recurrent genital symptoms or atypical symptoms with negative HSV PCR or culture
2. Clinical diagnosis of genital herpes without laboratory confirmation
3. A patient whose partner has genital herpes
b. IgG testing for HSV-specific glycoprotein G2 (HSV-2) and glycoprotein G1 (HSV-1) is recommended
c. IgM testing is not recommended as it is not type specific and can be positive in recurrent episodes

VIII. **Scabies**
a. *Sarcoptes scabiei* (mite)
b. More associated with poverty, overcrowding and poor hygiene
c. Sexual transmission is usually incidental
d. Patients present with pruritis
e. reddish burrows and papules
f. Burrows usually appear in the folds of hands and wrists, or on nipples, penis, scrotum, and lower buttocks
g. Diagnosis: Scrapings of skin from affected areas can be treated with 10% potassium hydroxide or mineral oil as clearing agents and examined microscopically for mites
h. Crusted scabies (i.e., Norwegian scabies) is an aggressive form seen in immunodeficient, debilitated, or malnourished patients

IX. **Pediculosis pubis (pubic lice)**
a. *Phthirus pubis*
b. Patients present with pruritis or notice lice and/or nits on their pubic hair
c. Usually sexually transmitted
d. Diagnosis: hair and lice can submitted to the lab for microscopic confirmation