

HIV, TUBERCULOSIS, LYME DISEASE

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OBJECTIVES: Upon completion of this presentation each participant should be able to:

1. Recognize the clinical signs and symptoms of infections produced by the following pathogens.
 - a. Human immunodeficiency virus (HIV)
 - b. Tuberculosis
 - c. Lyme disease
2. Describe the usual clinical course, including significant sequelae for each of these diseases.
3. Describe the appropriate screening and diagnostic tests for each of these diseases.
4. Describe pharmacological and palliative management of these diseases.

CONTENT:

I. HIV

A. Incidence

Approximately 40 million people in the world are infected with HIV. In the US, women and children are the fastest growing segment of AIDS patients, comprising more than 12% of new cases.

1. HIV Risk Assessment from History

High-risk history includes history of STDs, multiple sex partners, intravenous drug use (IVDU), IVDU partners, partner of bisexual male, recipient of blood product (1/1/79 - 6/1/85), donor inseminated women, women from geographic areas where AIDS is endemic (Africa and Haiti), and health care workers.

2. High Risk Assessment from Clinical Presentation

Clinical presentation of the following may indicate compromised immune functioning: multi-dermatomal herpes zoster, oral candidiasis, perianal herpes or candidiasis, oral hairy leukoplakia, chronic vaginitis, persistent unexplained fatigue, fever, diarrhea, unexplained weight loss, night sweats, enlarged liver or spleen, and various other dermatologic disorders.

3. Characteristic Laboratory Results

The following laboratory results are characteristic of HIV: low WBC (<3000), anemia, elevated sedimentation rate, depressed cholesterol, elevated LDH, and

thrombocytopenia. Tests that indicate rapid disease progression include a low or dropping CD4, low percentage of CD4 cells, and elevated serum B2 microglobulin levels.

B. Etiology

- HIV is a retrovirus. The retrovirus stores genetic information in the form of ribonucleic acid (RNA) rather than deoxyribonucleic acid (DNA).
- The retrovirus which causes HIV has an affinity for the CD4 molecule on the surface of human lymphocytes (usually T-lymphocytes) or monocytes.
- The viral RNA, through the action of an enzyme, reverse transcriptinase, creates viral DNA from the host cell DNA.
- Eventually host cells are destroyed, damaging cell-mediated immunity.
- Opportunistic infections overcome the resistance of the damaged immune system, killing the human host.
- This entire disease process, from latent infection to symptomatology to death, usually takes years.
- HIV levels vary markedly because of the life cycle of the virus. These levels are highest with the initial onset of infection and at the end of the disease process, when the CD4 count is low.
- This is when the vertical transmission rate of the virus from the pregnant woman to the fetus is the highest.
- There are two viral types. HIV-1 has a higher transmission rate and is associated with the worldwide epidemic of AIDS. HIV-2 has a longer incubation period and a slower progression to AIDS. This viral type is found primarily in West Africa.
- The HIV virus is also found in some apes, and this viral type is called simian HIV.

C. Progression of HIV Infection

- During the early years after infection, the annual progression to AIDS low. The HIV viral burden is low.
- By 8 to 9 years after infection, 12% of those women infected with the virus who are untreated will develop AIDS each year.
- By year 11, 50% of those who are untreated will have AIDS.
- The CDC criteria for AIDS diagnosis changed in 1992 to include cervical cancer. This diagnosis in an HIV infected woman means that this woman means the woman has progressed to AIDS.

D. Transmission

Transmission of the virus is through body fluids, with the following modes of transmission:

- Sexual intercourse (vaginal, anal or oral). Transmission of the virus through sexual contact may be facilitated by any coexisting infection which disrupts mucus membranes.
- Blood transfusion or sharing of needles.
- Maternal-fetal-infant by vertical transmission during pregnancy and labor.
- Maternal-infant through lactation

E. Symptoms

1. Clinical Symptoms

- Night sweats and fever
- Anorexia and unexplained weight loss
- Extreme fatigue
- Lymph node enlargement persisting longer than one month
- Cough
- Shortness of breath
- Colds that persist longer and are more severe than usual
- Severe watery diarrhea
- Neurological dysfunction

2. Diseases Associated with AIDS

- Kaposi's sarcoma
- Pneumocystis carinii pneumonia (PCP)
- Oral candidiasis
- Hairy leukoplakia
- Cervical cancer

F. Diagnosis

1. ELISA

The ELISA examination tests for the presence of antibodies against HIV and is the most commonly used screening test. This test is highly sensitive (93-100%) and specific. Concerns about false positives may be relieved by repeating the test and performing a confirmatory test. Concerns about false negatives may occur with very early HIV infection and late-stage AIDS. A window of time exists, during which the HIV antibody cannot be detected but virus is present.

2. Western Blot Test

This is the most commonly used confirmatory test. This test detects specific antigens against which antibodies are directed. The CDC criteria require the presence of at least two bands of antigens (p24, gp41, or gp160/120) for HIV to be diagnosed. This test is highly specific.

3. Polymerase Chain Reaction (PCR)

PCR is a direct viral test. This technique amplifies a specific segment of DNA or RNA approximately 1,000,000 times.

4. Viral Culture

Viral culture is expensive, slow, and of unknown sensitivity, and is not currently being used in the routine care of HIV patients.

5. HIV Antigen Detection - p24 and gp41

These tests are used to detect the presence of core antigens in serum specimens. The sensitivity varies with the stage of illness, although modifications have improved sensitivity.

6. Other Lab Tests

CBC with differential, T-cell counts, Hepatitis B screen, PPD with Candida skin test as control), toxoplasmosis titer, stool specimens, indicated bacterial, viral or fungal testing, and other antepartum testing as indicated.

7. Screening Tests with Quick Results and Home Testing

The FDA has approved 2 screening tests with quick results. These tests must be confirmed with a confirmatory test, such as the Western Blot. Testing is available over through internet sources. Anonymous testing is available.

G. Complications

1. Pregnancy

- The HIV patient should always be referred to a physician for care.
- Pregnancy does not seem to affect the progression of HIV to AIDS. However, vertical transmission can occur in pregnancy or during labor (approximately 30%).
- AZT prophylaxis, as stated in treatment, is thought to reduce this transmission to around 8%, and should be started as soon as possible.
- Many states mandate that HIV testing must be offered at the initial antepartal visit and again at birth. The patient may refuse this test. Anonymous testing may then be offered.
- HIV status is confidential.
- Do not tell a patient that she is HIV positive over the phone. Arrange for trained counseling on a person-to-person basis in these circumstances.
- Avoid invasive procedures such as cordocentesis, scalp pH, electric scalp monitors or amniocentesis with the HIV positive patient.
- Wear gloves when handling newborn until the infant is washed.
- Counsel against breast feeding.
- Advise her that ACOG recommends cesarean section at 38 weeks gestation in HIV positive women, unless their viral levels are very low.

2. Women

- Early identification and referral of women with HIV is imperative.
- New combinations of therapies and initiation of therapy prior to AIDS diagnosis may prolong life and well-being.
- Women should be offered effective contraception and counseling about transmission of disease.
- Women should begin regular Pap screens, as well as screening for other opportunistic infections.

3. Newborn

- HIV can be diagnosed in 30-50% of infected infants at birth and in nearly 100% of infected neonates by 4-6 months of age with combinations of viral culture, PCR, and p24 antigen testing.
- Few neonates show signs of infection in the first weeks after birth.
- Pneumocystis carinii pneumonia is the most common opportunistic infection in HIV infected children.
- Antiretroviral therapy during pregnancy decreases vertical transmission from the mother to the fetus.

H. Treatment

1. Treatment in Pregnancy

a. HIV-infected pregnant women who have not received prior antiretroviral therapy

- Pregnant women with HIV infection must receive standard clinical, immunologic, and virologic evaluation.
- Recommendations for initiation and choice of antiretroviral therapy should be based on the same parameters used for persons who are not pregnant, although the known and unknown risks and benefits of such therapy during pregnancy must be considered and discussed.
- The 3-part ZDV chemoprophylaxis regimen, initiated after the first trimester, should be recommended for all pregnant women with HIV infection regardless of antenatal HIV RNA copy number to reduce the risk for perinatal transmission.
- The combination of ZDV chemoprophylaxis with additional antiretroviral drugs for treatment of HIV infection is recommended for infected women, who's clinical, immunologic, or virologic status requires treatment or who have HIV RNA viral particles numbering over 1,000 copies/mL regardless of clinical or immunologic status.
- Women who are in the first trimester of pregnancy may consider delaying initiation of therapy until after 10-12 weeks gestation.

b. HIV-infected woman receiving antiretroviral therapy during the current pregnancy.

- HIV-1 infected women receiving antiretroviral therapy whose pregnancy is identified after the first trimester should continue therapy. ZDV should be a component of the antenatal antiretroviral treatment regimen after the first trimester whenever possible, although this may not always be feasible.
 - For women receiving antiretroviral therapy whose pregnancy is recognized during the first trimester, the woman should be counseled regarding the benefits and risks of antiretroviral administration during this period, and continuation of therapy should be considered.
 - If therapy is discontinued during the 1st trimester, all drugs should be stopped and reintroduced simultaneously to avoid the development of drug resistance.
 - Regardless of the antepartum antiretroviral regimen, ZDV administration is recommended during the intrapartum period and for the newborn.
- c. HIV-infected women in labor who have had no prior therapy**
- Several effective regimens are available. These include:
 1. Single dose nevirapine at the onset of labor followed by a single dose of nevirapine for the newborn at the age of 48 hours.
 2. Oral ZDV and 3TC during labor, followed by one week of oral ZDV/3TC for the newborn.
 3. Intrapartum intravenous ZDV followed by 6 weeks of ZDV for the newborn and option #4.
 4. The 2-dose nevirapine regimen combined with intrapartum intravenous ZDV and 6 weeks ZDV for the newborn.
 5. In the immediate postpartum period, the woman should have appropriate assessments (e.g., CD4+ count and HIV-1 RNA copy number) to determine whether antiretroviral therapy is recommended for her own health.
- d. Infants born to mothers who have received no antiretroviral therapy during pregnancy or intrapartum**
- The 6-week neonatal ZDV component of the ZDV chemoprophylactic regimen should be discussed with the mother and offered for the newborn.
 - ZDV should be initiated as soon as possible after delivery---preferably within 6-12 hours after birth.
 - Some clinicians may choose to use ZDV in combination with other antiretroviral drugs, particularly if the mother is known or suspected to have ZDV-resistant virus. However, the efficacy of this approach for prevention of transmission is unknown, and appropriate dosing regimens for neonates are incompletely defined.
 - In the immediate postpartum period, the woman should undergo appropriate assessments (e.g., CD4+ count and HIV-1 RNA copy number) to determine if antiretroviral therapy is required for her own

health. The infant should undergo early diagnostic testing so that if HIV-infected, treatment can be initiated as soon as possible.

(Source: Recommendations for Use of Antiretroviral Drugs in Pregnancy HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.)

I. Education

- Sexual partners should be contacted and screened for HIV.
- Measures to decrease transmission of disease should be taught: proper disposal of all substances contaminated by body fluids, abstinence or condom use, and formula feeding instead of breast feeding.
- The woman should be referred for medical care and for social work/psychiatric support.
- The Public Health Department should be notified of the diagnosis per the laws of the state.

II. Tuberculosis (TB)

A. Incidence

- Approximately 20 to 43% of the world's population is infected with the *Mycobacterium tuberculosis*.
- In the United States, approximately 15 million people are infected, and the number of reported TB cases increased 18% from 1985 to 1991.
- TB occurs disproportionately among disadvantaged populations.
- There is an increase occurrence of TB among HIV positive individuals.

B. Etiology

- *Mycobacterium tuberculosis* is an acid-fast bacilli transmitted through the air via droplets. The pathogen must be inhaled in order to produce infection.
- With initial exposure, macrophages engulf the pathogen, and it is encapsulated into tubercles. The TB bacilli can remain in a dormant stage within these tubercles indefinitely. The infection is contained, but not eradicated. People with latent tuberculosis infection do not have active disease and cannot transmit the organism to others.
- Approximately 10% of the individuals with latent tuberculosis who do not receive treatment will develop the disease sometime during their lifetime. Reactivation may occur when host immune systems are compromised.
- If the infected person has HIV, the chances of developing active tuberculosis within 2 years after infection increase to 50%.
- If the initial immune response is inadequate (5%), the individual will develop progressive primary tuberculosis with pulmonary and constitutional symptoms.
- *Mycobacterium tuberculosis* is now developing resistant strains to first-line antituberculous drugs.
- Although *Mycobacterium tuberculosis* generally infects the lungs, this pathogen may cause infection in almost any body tissue.

C. Symptoms of Active Pulmonary Infection

- Chronic cough
- Malaise
- Anorexia and weight loss
- Fever and night sweats
- Blood-streaked sputum

D. Screening

- The Mantoux test method is preferred with 0.1 ml of purified protein derivative (PPD) containing 5 tuberculin units is injected intradermally with a 27-gauge needle on a tuberculin syringe.

- A tuberculin skin conversion is an increase of 10 mm of induration within a 2-year period, regardless of patient age. (See the following table for interpretation of skin results.)
- BCG vaccine recipients may have a + test. These individuals may be from third world countries, and they may have a scar on their shoulder. Any person with a positive PPD should have a chest x-ray, even with a history of BCG vaccine.
- Women with known positive reactions should be excluded from testing.
- Testing should be delayed in those who have received the MMR within the last 10 days.
- Generally, the higher the risk of the individual, the less induration is required for a positive test result. Individuals with lowered immune responses require less induration for a positive test result.
- The test is generally positive 2 to 20 weeks after exposure.

Positive TB Skin Reaction by Group

Induration	Risk Group
≥ 5mm	Highest Risk <ul style="list-style-type: none"> • HIV + individuals • Individuals with recent contact with active TB • Individuals with fibrotic changes on chest x-rays, consistent with prior TB • People who have had organ transplants or other immunosuppressed people (> 15 mg prednisone per day for 1 month or more)
≥ 10 mm	Moderate Risk <ul style="list-style-type: none"> • Recent immigrants from countries with a high prevalence of TB (Asia, Africa, Latin America) • Injection drug users who are HIV negative • Health care workers or laboratory personnel with higher risk of exposure • People with gastrectomy, weight 10% below ideal weight, jejunioleal bypass, diabetes mellitus, silicosis, chronic renal failure, leukemia, or certain other malignancies • Family members or children of high-risk groups • Residents of long-term care facilities (jail, nursing homes, mental institutions, homeless shelters) • Medically underserved, low-income, racial or ethnic minorities
≥ 15 mm	Lowest Risk <ul style="list-style-type: none"> • Positive for anyone regardless of risk factors for TB

E. Treatment

- All suspected and confirmed cases should be reported to the Public Health Department.
- Refer patients to physicians skilled in TB management.
- Drugs used to treat TB include isoniazid (INH), rifampin, ethambutol, pyrazinamide, rifapentine, and streptomycin.
- Latent TB should be treated, and several regimens may be used. Generally 6 to 12 months of pharmacological treatment is recommended.
- Generally active TB in pregnancy is treated with isoniazid, rifampin, and ethambutol. Streptomycin is contraindicated in pregnancy. Pregnant women taking INH should receive 10-25 mg pyridoxine daily. Breast feeding is not contraindicated.
- Antitubercular medication may decrease the effectiveness of hormonal contraception.

VI. Lyme Disease

A. Etiology

- The spirochete, *Borrelia burgdorferi*, is a tick-borne pathogen that is generally transmitted in the United States by white-tail deer and some rodents.
- Incubation is generally from 3 to 32 days after tick exposure.
- There is no evidence that the disease is spread from person to person.

B. Symptoms and Treatment

- The disease usually has 3 stages, although prompt identification and treatment may minimize complications.
- The first stage is characterized by erythema chronicum migrans (ECM), a circular erythemas rash with a whitened center, between 5 and 20 inches in diameter. Some people (approximately 1/3) do not develop the rash.
- Symptoms concurrent with ECM include headache, chills, nausea, fever, aching joints, and fatigue.
- The second stage includes complications involving the heart and nervous system, including heart blockage, meningitis, encephalitis, Bell's palsy, and arthralgias.
- The third stage is characterized by arthritis, with the large joints being most commonly affected.
- Diagnostic testing indicates a rise in spirochete-specific antibodies, with a titer of more than 1:128 indicating recent or current infection. Cross reactivity may occur with individuals with syphilis, although this is less likely to occur with the RPR.
- Treatment usually includes penicillin for children and tetracycline for adults.

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