Lecture 9: lect. Dr. Ahmed Yaseen Abed

Systematic mycosis : Histoplasmosis

Histoplasmosis: -

is an infection caused by breathing in spores of a fungus often found in bird and bat droppings. Histoplasmosis is most commonly transmitted when these spores become airborne, often during cleanup or demolition projects.

1. Introduction and Epidemiology

- **Causative Agent:** Histoplasmosis is caused by the dimorphic fungus ***Histoplasma capsulatum*.**
- **Geographical Distribution:** Endemic in the Ohio and Mississippi River valleys in the United States, as well as parts of Central and South America, Africa, Asia, and Australia.
- **Environmental Reservoirs:** Found in soil contaminated with bird or bat droppings. Explain how activities like construction, farming, or spelunking can disturb these areas and release spores. Although most people who breathe in the spores don't get sick, those who do may have a fever, cough, and fatigue. Many people who get histoplasmosis will get better on their own without medication, but in some people, such as those who have weakened immune systems, the infection can become severe.

2. Pathogenesis

- **Mode of Infection**: Inhalation of microconidia (spores) from the environment.
- **Lifecycle**: Once inhaled, the spores convert to the yeast form in the lungs. They can survive and replicate within macrophages.
- **Dissemination**: Although primarily a pulmonary infection, it can spread to other organs, particularly in immunocompromised individuals.

3. Clinical Manifestations

- **Acute Pulmonary Histoplasmosis**: Flu-like symptoms including fever, chest pain, cough, and fatigue.
- **Chronic Pulmonary Histoplasmosis**: Resembles tuberculosis, with symptoms such as chronic cough, weight loss, and night sweats.
- **Disseminated Histoplasmosis**: Severe form that can affect multiple organs. Symptoms include fever, weight loss, hepatosplenomegaly, and anemia. More common in immunocompromised individuals (e.g., those with HIV/AIDS).

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Symptoms of histoplasmosis may appear between 3 and 17 days after a person breathes in the fungal spores.

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4. LABORATORY DIAGNOSIS

Serological test ,culture , stain, antigen detection , biopsy and histopathology and cytological analysis When to Use Each Method

- **Mild Infections:** Serologic tests for antibodies are typically sufficient.
- **Severe or Disseminated Disease:** Cultures, antigen detection, and histopathology are more useful.
- **Immediate Diagnosis:** Biopsy of involved organs and cytological analysis may be required, especially when initial tests are negative and rapid diagnosis is crucial.

➢ Serologic Tests for Histoplasmosis

1- **Immunodiffusion and Complement Fixation Tests**:

- **Immunodiffusion**: This test detects antibodies to *Histoplasma capsulatum* by allowing them to diffuse through a gel and form a visible precipitate (bands) when they encounter antigens.
- **Complement Fixation**: This test measures the presence of antibodies by their ability to fix complement, a part of the immune system, in the presence of specific antigens.

2- **H and M Bands**:

- **H Bands**: These are antibodies that react with the histoplasmin antigen. They can be detected in less than 25% of patients and usually clear within the first 6 months following exposure to the fungus.
- **M Bands**: These antibodies react with the M antigen and are found in over three-quarters of patients with histoplasmosis. M bands can persist for years in some patients, indicating a past or ongoing infection.

3- **Complement Fixation Titers**:

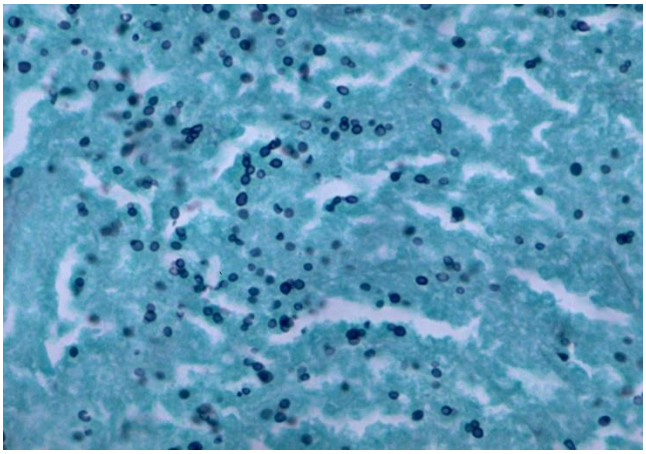
- **Titers of 1:8 or More**: Found in most patients with histoplasmosis, indicating exposure to the fungus.
- **Titers of 1:32 or Higher**: More suggestive of active infection, as higher titers indicate a stronger immune response, which is often seen in active or recent infections.

➢ Cultures in Histoplasmosis Diagnosis

1. **Specimens**: Blood, bone marrow, respiratory secretions (sputum, bronchoscopy samples).
2. **Use**: Highly reliable for disseminated histoplasmosis, especially in HIV/AIDS patients (75% yield from blood/bone marrow). Also useful for chronic pulmonary cases (60-85% yield from cavitary lesions).
3. **Sensitivity**: Low in mild forms of histoplasmosis (10-15%).
4. **Time Requirement**: Cultures can take 2-4 weeks to grow, making them less suitable for rapid diagnosis in severe cases.
5. **Confirmation**: Gold standard for definitive diagnosis despite time constraints.

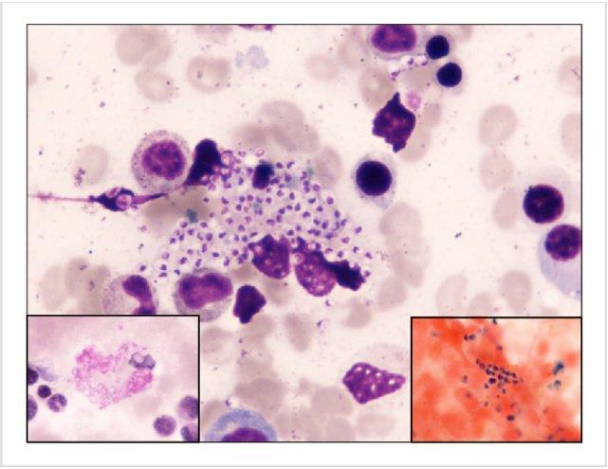
➢ Staining Techniques for Rapid Diagnosis

1- **Silver Stain (GMS)**:



- **Use**: Commonly used for detecting fungi in tissue sections.
- **Sensitivity**: Lower than culture or antigen detection, but useful for rapid identification.
- **Appearance**: Fungal elements stain black against a light background.
- **Limitations**: Positive in about 50% of cases of disseminated histoplasmosis.

2- **Wright Stain**:



- **Use**: Primarily used for peripheral blood smears.
- **Sensitivity**: Lower compared to culture or antigen detection, but allows quick screening.
- **Appearance**: Stains various blood cell components; less specific for fungi.
- **Limitations**: Not as reliable for detecting fungi as more specific fungal stains.

3- **Potential Misidentifications**

Various organisms and artifacts can sometimes be mistaken for *Histoplasma capsulatum* in stained specimens:

- **Candida glabrata**
- **Cryptococcus neoformans**
- **Blastomyces dermatitidis**
- **Penicillium marneffei**
- **Pneumocystis carinii (jirovecii)**

- **Toxoplasma gondii**
- **Leishmania**
- **Staining Artifacts**

➢ **Antigen Detection in Histoplasmosis**

1- **Antigen Detection**: Essential for the rapid and sensitive diagnosis of severe or epidemic forms of histoplasmosis.

2- **Comparison with Other Methods**: More reliable than quick but insensitive fungal stains and faster than time-consuming cultures, making it ideal for urgent cases.

3- **Applications**:

- **Epidemic Acute Pulmonary Histoplasmosis**: Useful in diagnosing patients who experience heavy exposure and develop diffuse infiltrates within a week or two.
- **Disseminated Histoplasmosis**: Valuable in detecting antigen in patients with widespread infection, especially those with weakened immune systems.

4- **Specimens for Antigen Detection**:

- **Urine**: Commonly tested due to ease of collection and high sensitivity.
- **Serum**: Blood samples are also used for antigen testing.
- **Other Body Fluids**: CSF or bronchoalveolar lavage fluid may be tested in severe or disseminated cases.

➢ **Biopsy and Histopathology**

- **Specimens**: Involved organs, such as lungs, liver, or lymph nodes.
- **Techniques**: Use of GMS or PAS stains to identify intracellular yeast forms.
- **Use**: Essential when serologic and antigen tests are negative, or immediate diagnosis is necessary for severely ill patients.

➢ **Cytological Analysis**

- **Specimens**: Respiratory secretions, tissue aspirates, or fluids.
- **Techniques**: Microscopic examination to identify characteristic yeast forms within macrophages.
- **Use**: Supplementary to histopathology and cultures, particularly in invasive procedures.