Histoplasmosis is an intracellular mycotic infection of the reticuloendothelial system. Type of chronic respiratory infection. It is introduced in the body via the inhalation of conidia of the fungus *Histoplasma capsulatum*.

May primarily affect lungs, but may spread to other organs and tissues in the body. The spectrum of the disease is wide.

Histoplasmosis is caused by the fungus *Histoplasma capsulatum* (*H. capsulatum*).

**Taxonomy**

- **Kingdom:** Fungi
- **Phylum:** Ascomycota
- **Subphylum:** Ascomycotina
- **Class:** Ascomycetes
- **Order:** Onygenales
- **Family:** Onygenaceae
- **Genus:** Ajellomyces (Histoplasma)
Etiological agent of histoplasmosis.

Is an ascomycete that exhibits clinically relevant dimorphism.

Macroscopic features:
- Grows as a mold form first at 25°C
  - Colonies are slow growing and granular to cottony in appearance.
- Then grows into a yeast form at 37°C
  - Creamy, slow growing, moist yeast-like colonies formed.

Microscopic features:
- At 25°C
  - Hyphae are septate and hyaline
- At 37°C
  - Narrow-based, budding yeast cells are formed.

There are 3 variances of *H. capsulatum*
- *H. capsulatum var. capsulatum*
- *H. capsulatum var. duboisii*
- *H. capsulatum var. farciminosum*
  (Found in horses)

The teleomorphic (sexual) state of the 3 variances is called *Ajellomyces capsulatus*.

Commonly infects the lungs where chronic pulmonary disease may occur.

Rarely involve the thyroid glands and may be isolated in fungemia.

Have small narrow yeast cells.
**A mycotic infection primarily involving cutaneous, liver, lung, lymphatic, subcutaneous, and bony tissues.**

- **A dimorphic fungus**
- **Skin and bone are the most frequently invaded sites.**
- **Characteristics:**
  - Nodular, ulcerative cutaneous, and osteolytic lesions of the bone that can disseminate or remain localized.

**The etiologic agent grows as a large yeast within giant cells.**

**The people down there will probably get infected.**

**Ecology of H.capsulatum**

- Found worldwide in regions known for humidity and moderate temps
- Var. *capsulatum* is endemic in North America- Ohio Mississippi River Valleys, Asia, Australia, Africa and South America
- Var. *duboisii* is endemic in Africa.
  - Mostly in central Africa

**Ecology of H.capsulatum**

- Mainly found in soil with bird or bat droppings.
- The people down there will probably get infected.
**Epidemiology**
- Occurs in healthy individuals
- Occurs in immunocompromised/debilitated people
  - Aids and HIV
- People you have traveled to endemic areas
- 500,000 new infections each year in U.S.
- Outdoor activities

**Risk Factors**

**Var. Capsulatum**
- Acquired from inhalation of microconidia or fragments of mycelia from soil
- No evidence of being contagious
- Causes a chronic respiratory infection in lungs

**Var. Capsulatum (cont.)**
- Manifestation depends upon:
  - Size of inoculum/exposure
  - Underlying health of patient
  - Immunity status to organism
- Asymptomatic to disseminated
- Symptoms similar to tuberculosis

**Var. Capsulatum (cont..)**
- Asymptomatic:
  - Low level exposure
  - Usually in healthy individuals
  - Hilar or mediastinal lymphadenopathy with focal or patchy pulmonary infiltrates
  - Lesions may evolve into nodules representing areas of granuloma formation
  - Nodules and lymph nodes undergo calcification

**Var. Capsulatum (cont..)**
- Acute
  - Heavy exposure
  - Presents as diffuse pulmonary infiltrates with some degree of respiratory difficulty
  - Symptoms are flu-like
- Sub acute
  - Similar to acute form
**Chronic**
- Flu-like symptoms
- Calcified lung lesions or lymph nodes
- Leads to gradual progression with destruction of lung tissue

**Disseminated**
- Occurs before cellular immunity starts
- PDH (Progressive Disseminated Histoplasmosis)
- If lesions expand, parenchymal necrosis develops usually followed by granuloma formation and encapsulation

**Virulence Factors**
- Thermally Dimorphic
  - Mold to yeast in human tissue
  - Melanin
  - Heat shock protein 60
  - Alpha (1,3) glucan
    - Alpha (1,3) glucan synthase and alpha (1,4) amylase
  - Calcium Binding Protein
  - YPS3 (Yeast Phase Specific Protein 3)

**Virulence Factors (cont..)**
- Ability to modify environment
  - 6-6.5 PH
  - M Antigen
  - Catalase B
  - H Antigen
  - Secreted beta glucosidases
  - Ability to survive in phago-lysosomes of macrophages

**Host Response**
- With sub acute form
  - Pericarditis and Rheumatologic inflammatory response
  - Induce a neutrophilic inflammatory response
  - Initial reaction is histiocytic
  - Innate cellular response
  - Leads to recovery
**Var. Duboisii**

- Inhalation of microconidia
- Affinity for bones and skin
- Pulmonary lesion are rare
- 2 forms present:
  - Localized
  - Disseminated

**Virulence**

- Similar to Var. Capsulatum
  - Dimorphic
  - Melanin

- Possible for Proteinase and collagenase
  - Breaks down proteinaceous components of host tissue leading to typical necrosis observed in lesions caused by the fungus.

**Host Response**

- For both localized and disseminated form
  - A dispersed granulomatous inflammatory reaction
  - Enormous number of yeast like cells are clustered within the cytoplasm of giant cells.

**Diagnosis**

- Sample taken form sputum, lung tissue, blood, CSF, or bone marrow is then cultured and incubated.
- Only positive test result 60% of the time for chronic patients
- 15% of the time for acute patients
- Fungus may take from 2 to 12 weeks before the fungus can be identified.
Diagnosis (Cont..)
- Skin tests
- Serum tests can be conducted with blood, urine, and CSF through radioimmunoassay
- Highly sensitive in disseminated cases
- Tests for antigens and antibodies
- Potentially high rate of false positive results.
- ASPERGILLUS BLASTOMYCES AND COCCIDIOIDES

Diagnosis (Cont..)
- Stains
- Giemsa stain
- Methenamine silver stain
- Tested on blood sputum, bone marrow, and lymph node aspirates

Diagnosis (Cont..)
- XRAYS or CT scans of chest region
- Observe lungs and or lymph nodes of chest

Disease Management
- Antifungal drugs
  - Itraconazole, ketoconazole, amphotericin B, avastin, ketoconazole, fluconazole, acetaminophen
- Length vary depending on each case
- Surgery is not typical
  - Pericardiocentesis or a pericardial window procedure
    - Removes fluid that would otherwise compress the heart

Disease Prevention
- Immunosuppressed individuals should avoid “high risk” areas such as caves, bridges, construction sites, chicken coops large avian gathering places
- Wear a Part 84 particulate mask

Case Study 1
- 56 year old male
- Normally healthy
- Symptoms of fever, cough, respiratory distress, disorientation, hypotension
- Positive ID with Histoplasma capsulatum in bone marrow aspirate
Case Study 1 (Cont..)

- Patient started on Amphotericin B
- Condition steadily improved until patient developed aspiration pneumonia on day 3 of treatment and died one week later
- Possible source of entry was a visit to a Bangladesh chicken farm

Case Study 2

- 32 year old male with advanced HIV
- Multiple face lesions
- Initial hospital symptoms included fever, extensive oral thrush, multiple mouth ulcers and an enlarged lymph node.
- Blood culture returned negative results

Case Study 2 (Cont..)

- Lymph node biopsy performed
- Positive Histoplasma capsulatum identified.
- Given Amphotericin B intravenously for 7 days followed by a twice daily oral dose for 21 days
- Followed up with oral itraconazole 200mg twice daily

Citations

- Atlas of Fungal Infections
- Journal of Chinese Clinical Medicine
- Microbes and Infection Journal
- Pathologic Diagnosis of Fungal Infections
- Infectious Disease journal
- Histoplasmosis a review article
- Medical Mycology Journal
1. Which variance is mostly found in Central Africa?
   A. *H. capsulatum* var. *duboisii*
   B. *H. capsulatum* var. *capsulatum*
   C. *H. capsulatum* var. *farciminosum*
   D. All of the above

2. Which variance grows small and narrow yeast cells?
   A. *H. capsulatum* var. *duboisii*
   B. *H. capsulatum* var. *farciminosum*
   C. *H. capsulatum* var. *capsulatum*
   D. All of the above

3. *Histoplasmosis* *capsulatum* mainly infects what part of the body?
   A. Lungs
   B. Hair
   C. Nails
   D. Bones

4. One of the virulence factors for *H. Capsulatum* is?
   A. No melanin
   B. Mold form in human tissue
   C. Proteinase
   D. Heat shock protein 60

5. One possible explanation for disseminated cases of *histoplasmosis* in otherwise healthy patients can include a dysfunction of the following?
   A. Alpha/beta transducing pathway
   B. Interferon alpha/ interleukin-12 pathway
   C. Beta epoxidase
   D. Beta-1,6 glucophosphate pathway