ASPERGILLOSIS

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HISTORY OF ASPERGILLOSIS
- 1729 – Fungus Aspergillus first identified and catalogued by Italian biologist/priest Micheli
  - Noticed under microscope the fungi looked like an aspergillum which is used to sprinkle holy water and named the genus after it.
- 1815 – Aspergillus first observed in birds by Mayer
- 1842 – British physician John Hughes Bennett discovered first case of pulmonary aspergillosis in humans.
  - Called aspergilloma which means "fungus ball" in the lungs

- Many early cases of aspergillosis were found in patients with tuberculosis or high risk occupations such as pigeon-crammers and wig combers
  - Some were invasive but most were aspergillomas
- 1953 – Rankin described the ability of Aspergillus to cause opportunistic infection in immunocompromised patients
- 1970 – Histopathology and clinical features of disease described in 98 patients

TAXONOMY
- Kingdom: Fungi
- Phylum: Ascomycota
- Order: Eurotiales
- Family: Trichocomaceae
- Genus: Aspergillus

ETIOLOGY
- Genus Aspergillus includes over 185 species
  - ~20 species reported to cause infections
  - 7 are facultatively pathogenic
- Aspergillus fumigatus most commonly isolated species
  - Found in 90% of infections
  - Widespread in nature
  - Commonly found in soil and compost heaps
  - Can also be found indoors
  - Thermophilic species (Growth at 40° C and above)
  - Angioinvasive


Conidiospores are short, smooth-walled with conical shaped terminal vesicles
**Aspergillus Fumigatus**

- Grown on Czapek dox agar
- Culture has a blue-green surface pigmentation with a suede-like surface consisting of a dense felt of conidiophores

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**Etiology**

- Next most commonly isolated species include:
  - A. flavus
  - A. niger
  - A. clavatus
  - A. glaucus
  - A. nidulans
  - A. oryzae
  - A. terreus
  - A. usuts
  - A. versicolor

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**Epidemiology**

- Aspergillosis affects people with the following:
  - Weakened immune system
  - Low white blood cell levels
  - Lung cavities
  - Long-term corticosteroid therapy
  - A hospital stay
  - Asthma and cystic fibrosis

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**Epidemiology Cont.**

- Invasive aspergillosis affects people who are immunosuppressed such as:
  - People who have had bone marrow transplants or solid organ transplants
  - People who are taking high doses of corticosteroids
  - People who undergo chemotherapy for cancer
  - People who have chronic granulomateous disease
  - People with advanced AIDS
  - Leukemia patients
  - Tuberculosis patients

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**Epidemiology Cont.**

- Aspergillosis is common in the environment and is found worldwide
  - Most people breathe in aspergillus spores everyday
  - It is impossible to completely avoid breathing in aspergillus spores because they are ubiquitous
  - People with compromised immune systems who breathe in the spores acquire infections

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**Epidemiology Cont.**

- Aspergillosis occurs:
  - Soil
  - Air, spores are inhaled
  - Food-spices and ground pepper
  - Compost and decaying vegetation
  - Grains and crops
  - Fire proofing materials
  - Bedding, pillows, carpeting
  - Ventilation and air conditioning systems
  - Dust
MANIFESTATIONS
- Respiratory
- Cranial
- Pathologic
- Clinical
- Thoracic Initial CT

DISEASE SPECTRUM
- Forms of the disease involve:
  - Sinuses
  - Lungs
  - Pre-existing lung cavity
  - Pulmonary aspergillosis
  - CNS aspergillosis
  - Sinonasal aspergillosis
  - Osteomyelitis
  - Endophthalmitis
  - Endocarditis
  - Renal Abscesses
  - Cutaneous (Burns, post surgical wounds, IV insertion sites)
  - Otomycosis
  - Exogenous endophthalmitis
  - Allergic fungal sinusitis
  - Urinary tract fungus balls

HISTOPATHOLOGY
- Tissue reaction in aspergillosis is acute suppurative inflammation with areas of ischemic necrosis
- The fungus proliferates as septate hyphae 2.5-4.5 µm in diameter
- Hyphae can be characterized as branching dichotomously (Approx 45° angle)
- Blood vessel invasion, thrombosis, infarction, and dissemination are common
- The mortality rate for invasive aspergillosis is 50-100% and diagnosis by culture may take as long as 4 weeks.

PATHOGENESIS
- Virulence factors:
  - A. fumigatus has about 4 virulence factors alone:
    - Gliotoxin-inhibits mucociliary system
    - Fumagillin
    - Fumagatin
    - Helvolic acid
  - Since Aspergillus can be found almost everywhere worldwide, it is primarily acquired through the respiratory tract.
  - However, there have been cases of disseminated disease after skin or gastrointestinal infections.

HOST RESPONSE IN NORMAL HOST (NON-IMMUNOSUPPRESSED)
- Normal immune system response:
  - Mucosal barriers – Traps
  - Macrophages – Phagocytosis
  - Neutrophils
    - Kills conidiae and inhibits germination of hyphae

Grocott’s methenamine silver (GMS) stained tissue sections showing Aspergillus fumigatus in lung tissue,
Note: conidial heads forming in an alveolus.
Taken from: http://www.mycology.adelaide.edu.au/gallery/photos/aspergillus08.gif
PATHOGENESIS
- Normal host response can be impaired by a number of factors:
  - Granulocytopenia
  - Impaired macrophages/neutropenia
  - Underlying disease impairing immune system
  - Lung destruction
  - Large numbers/extended exposure to organism
  - Hypersensitivity/allergic response
- In the immunocompromised:
  - Conidia spores colonize lesions or cavities
  - Hyphae begins to form and grow throughout body

PATHOGENESIS
- There are three major ways *Aspergillus* involves the lungs:
  - Mycetoma (non-invasive)
  - IPA
  - Invasive Pumonary Aspergillosis
  - Allergic

DIAGNOSIS
- Clinical Presentations:
  - Fever
  - Cough
  - Dyspnea
    - Difficulty breathing
  - Hemoptysis
    - Coughing up blood
  - Chest Pain

LABORATORY DIAGNOSIS
- Radiographic picture
- Classical
- CT Scan
- Serological testing
- Sputum culture
- Transthoracic needle aspiration

DIAGNOSIS
- The most extreme diagnosis is surgical procedures
  - Tissue examination
  - Transbronchial biopsy (TBB)
  - Open lung biopsy
  - CT guided percutaneous lung biopsy

http://www.isradiology.org/tropical_deseases/meas/chapter6/
diasect123.htm
Courtesy of the Radiology Library, University of Cape Town, South Africa
DISEASE MANAGEMENT

- Allergic Bronchopulmonary Aspergillosis (ABPA)
  - Caused by an allergy to the spores of the *Aspergillus* moulds.
  - Commonly affects people with asthma and cystic fibrosis patients.
  - Steroids by aerosol or mouth
    - Prednisolone
    - Itraconazole
    - An oral antifungal drug

- Aspergillus Sinusitis
  - Disease occurs in the sinuses
  - May be associated with long standing symptoms of runny blocked nose
  - May lead to nasal polyps
  - Surgical drainage, removal of polyps
  - Local steroids
  - Oral Steroids
  - Antifungals

DISEASE MANAGEMENT

- Aspergilloma and Chronic Pulmonary Aspergillosis
  - Fungus caused by the Aspergillus mould
  - Grows in the lung cavity
  - Treatment depends on the symptoms present
    - Itraconazole
    - Voriconazole
    - Surgery
    - Amphotericin B

DISEASE MANAGEMENT

- Invasive Aspergillosis
  - Effects people with poor immune systems
  - Fungus can transfer from the lung through the blood to the brain and other organs
  - Antifungal Drugs
    - Voriconazole
    - Caspofungin
    - Itraconazole
    - Amphotericin B

DISEASE PREVENTION

- This disease commonly affects people with a weak immune system
  - Avoid medications that may further weaken the immune system.
  - Avoid forests, grain stores, rotting vegetation, and piles of dead leaves.
  - Hospitals should have good ventilation
    - Dust control
    - Adequate air flow rate

CASE STUDY – “Sudden death due to pulmonary aspergillosis”

- 35 yr old
- Moderately built and malnourished
- TB patient for a year
- Hemoptysis while traveling in a train.
- Was declared dead upon arrival to the hospital.
- Same day autopsy was performed.
CASE STUDY - SYMPTOMS

External examination
- Blood stains were present over the oral and nasal orifices
- Clubbing of fingers and toes
- No external injuries

Internal examination
- Trachea and bronchi contained blood clots.
- Right sided pleural internal scarring was present.
- Surface of lungs was grayish black with necrotic material.
- Enlarged lymph nodes.
- Pale gastrointestinal organs filled with blood.

CASE STUDY - DIAGNOSIS

- Microscopy
  - Grocott’s methanamine silver stain (GMS)
- Biopsy of the lungs
- Autopsy Findings of the lungs
  - Dilated bronchioles
  - Alveolar septae showed congested vessels.
  - Edema and hemorrhage

CASE STUDY - CONCLUSION

- It was diagnosed to be a case of old fibrocavitatory tuberculosis with Aspergillus colonization.
- No active TB was present.
- Cause of death was as hemorrhage secondary to pulmonary aspergillosis.

REFERENCES


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QUESTIONS

1. What species of Aspergillus most commonly causes infections?
   A) A. fumigatus
   B) A. niger
   C) A. versicolor
   D) A. flavus

2. Aspergillus most commonly affects the:
   A) Heart
   B) Skin
   C) Lungs
   D) GI tract

3. In a normal host, which immune defense mechanism usually inhibits hyphae germination?
   A) Mucosal barriers
   B) Thrombocytes
   C) Neutrophils
   D) All of the Above

4. What type of medications should people affected by Aspergillus avoid?
   A) Amphotericin B
   B) Any that weaken the immune system
   C) Anti-depressants
   D) All above

5. What is a virulence factor for Aspergillus fumigatus?
   A) Fumagillin
   B) Fumagatin
   C) Gliotoxin
   D) All of the above