**Aspergillus**
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**History of Aspergillus**
- First case of *Aspergillus* disease in humans was reported in the mid 1800s
- In 1960, aflatoxins literally exploded onto the scene when over 100,000 turkeys died after consuming contaminated peanut meal
- 20 people with 100% mortality rate was investigated in 1974 in India
- consumption of maize (corn) heavily infested with the fungus *Aspergillus flavus*

**Etiology/Causative of Aspergillus**
- *Aspergillus niger*
- *Aspergillus fumigatus*
- *Aspergillus flavus*

**Taxonomy of Aspergillus flavus**
- Kingdom: Fungi (Mycota)
- Phylum: Ascomycota
- Sub-phylum: Deuteromycota (Fungi imperfecti)
- Family: Trichocomaceae
- Genus: Aspergillus

**Biology of Aspergillus flavus**
- Fungus
- Saprophyte
- Haploid filamentous fungi
- Mycelium secretes enzymes
  - Hyphae (branching filamentous)
  - Fuel fungal growth
- Asexual, non motile spores (conidia)
- No Ascospores
Predominately a saprophyte
- Grows on dead plant and animal tissue
- Nutrient recycler

Temperature
- Optimum growth is 37°C (98.6°F)
- Grows from 12-48°C (54-118°F)

Environmental defense
- Either mycelium or as sclerotia,
- Stored nutrients

**Ecology of Aspergillus flavus**

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Fungus
- Haploid
- Produces spores inside asci
- Mycelial
  - Many units of hyphae
  - White to yellow mat later bearing black conidia
- Asexual spores only (conidia)
- Cell wall is mostly chitin, and glucan

**Biology of Aspergillus niger**

- Growth
  - Aerobically on organics
  - Soil, waste, and decayed plants
- Temperature & pH
  - 6 to 47°C with a preferred optimum temperature at 35-37°C
  - 1.4 to 9.8 pH
- Environmental defense

**Ecology of Aspergillus niger**

- Makes aflatoxin can be seen on crops as yellow green mold

- Symptoms for humans (aflatoxicosis)
  - Vomiting
  - Abdominal pain hemorrhage
  - Pulmonary edema
  - Acute liver damage including fatty change
  - Loss of function of the digestive tract
  - Convulsions
  - Cerebral edema and even death.

**Disease manifestation (A. flavus)**

- Black mold, not (*Stachybotrys*), to appear on some fruit and vegetables

**Disease manifestation (A. niger)**
Disease manifestation (A. niger)
- Disease in humans
  - Lung disease
  - Fungal ear infection (otomycosis) M
  - Most common
  - Ear pain
  - Impaired hearing
  - Ear inflammation
  - Tinnitus
  - Impaired lung function
- Through inhalation and fungal spores

Disease prevention for Aspergillus
- Plant and animal life
  - Caspofungin, anidulafungin and micafungin
  - Target 1,3-β-glucan synthase
  - Disrupt hyphal growth at tips and branch points

Disease prevention Aspergillus
- Human
  - No major prevention for humans
  - Check and clean food products
    - Live stock
    - Produce

Cites used
- http://www.aspergillusflavus.org/aflavus/
- http://mic.sgmjournals.org/cgi/content/full/153/6/1677
- http://en.citizendium.org/wiki/Aspergillus_niger
- http://en.citizendium.org/wiki/Aspergillus_flavus
- http://microbewiki.kenyon.edu/index.php/Aspergillus_niger
- http://ats.ctsnetjournals.org/cgi/content/full/80/1/359

Epidemiology
- Differs depending on the host species.
- Usually attacks people who are immunocompromised.
  - HIV/AIDS
  - Leukemia
  - Chronic obstructive pulmonary disease (COPD)

Risk Factors
- Asthma
- Cystic Fibrosis
- Patients with preexisting structural lung disease
Diagnosis of Aspergillus flavus
- Can take as long as 4 weeks if done by culture
- Mortality rate is high, so slow diagnosis is a problem.
- Recent discovery
  - The detection of galactomannan antigen is very useful in early diagnosis.
    - 5-8 days before clinical signs begin to show.

Diagnosis of Aspergillus fumigatus
- Chest computed tomography scans
- Antigen detection
- Polymerase chain reaction
  - The most common species of Aspergillus to cause disease in humans.

Diagnosis of Aspergillus niger
- High mortality rate
- Diagnosis is very difficult
  - Except if there were prior imaging
  - Lung histiopathy
  - Sperm culture
  - Needle biopsy

Treatment for Aspergillus flavus
- Until recently, few drugs were available for treatment.
  - Amphotericin B
  - Itraconazole
  - New drugs are now available.
    - Voriconazole
    - Posaconazole
  - Resistance is beginning to become a concern.

Treatment for Aspergillus niger
- Much like treatment for Aspergillus flavus.
  - Same drugs prescribed.
  - Combination of drugs is only recommended in extreme cases.
Treatment for Aspergillus fumigatus
- Itraconazole is the drug most commonly used
- Drugs also used:
  - Voriconazole
  - Posaconazole
- Amphotericin B can not be used because it caused nephrotoxicity.

CASE REPORT: Invasive Aspergillosis After H1N1
- Immunocompromised individuals at risk of invasive aspergillosis
  - Prolonged neutropenia, inherited immunodeficiency, immunosuppressive agents, COPD
- Invasive aspergillosis major cause of life-threatening infections after H1N1
- Influenza strains can cause cell-mediated defects, disruption of normal ciliary clearance, leukopenia
  - These abnormalities with corticosteroids forms unique group of risk factors

Patient 1: 28-year-old man, 18.1 BMI, normal medical history
- Admitted for shortness of breath 1-1.5 weeks, respiratory failure upon admission → H1N1
- High dose antibiotics for one month
- Poor improvement, underwent bronchoscopy
- Necrosis of airway walls and cartilage
- Tissue cultures showed A. fumigatus

Patient 1 continued:
- IV voriconazole initiated, clinical condition steadily worsened
- Voriconazole best known treatment for invasive aspergillosis
- New tests done: lymphopenia, renal failure, respiratory failure
- A. fumigatus isolated from sputum
- Treated with amphotericin B, azoles, vancomycin
- Died after 70 days of cardiopulmonary arrest

Patient 2: 51-year-old man, 24.5 BMI, normal medical history
- Hospitalized for fever and fatigue
- CT scan showed diffuse alveolar consolidation
- Broad-spectrum antimicrobial drugs given
  - Vancomycin, azithromycin, fluconazole
- Patient’s respiratory status still worsened
- Diagnosed with H1N1
Patient 2 continued:
- Lung biopsy showed alveolar hemorrhage but no fungal elements
- Fever went away when given prednisone, returned when dose tapered
- Bronchoscopy showed bleeding and closer examination showed fungal hyphae
- Lab tests confirmed A. fumigatus

Patient 2 continued:
- Given IV voriconazole 3 days, then given broad-spectrum antimicrobial agents
- Condition deteriorated, care withdrawn and death occurred on day 21
- Autopsy showed severe pulmonary congestion, hemorrhage, acute necrotizing bronchopneumonia
- Many fungal abscesses involving Aspergillus spp. found in lung, thyroid, liver

Invasive aspergillosis after influenza rare complication but many at risk due to H1N1
- Previous studies of influenza-associated aspergillosis looked at by author have 100% mortality rate
- Bronchoscopy common for intubated patients, but negative test results do not necessarily indicate absence of invasive aspergillosis

Invasive diagnostic testing impractical in event of hypototoxicity or thrombocytopenia
- Assays for detection of 1,3-β-glucan useful
- Appropriate antifungal therapy can be initiated

Assorted Videos
- [http://www.youtube.com/watch?v=X77ag6shK3s](http://www.youtube.com/watch?v=X77ag6shK3s)
- [http://www.youtube.com/watch?v=JW2V7pvVEV8](http://www.youtube.com/watch?v=JW2V7pvVEV8)

Bibliography
Resources

- http://www.aspergillusflavus.org/aflavus/
- http://mic.sgmjournals.org/cgi/content/full/153/6/1677
- http://en.citizendium.org/wiki/Aspergillus_niger
- http://en.citizendium.org/wiki/Aspergillus_flavus
- http://microbewiki.kenyon.edu/index.php/Aspergillus_niger

Questions

1.) What is the most common symptom of A. niger?
   a.) otomycosis
   b.) otitis
   c.) tinnitus
   d.) lung disease

2.) Amphotericin B can be used with all of the following except:
   a.) A. flavus
   b.) A. fumigatus
   c.) A. niger
   d.) A. flavescens

3.) Which of the following is not a symptom of A. flavus?
   a.) ear pain
   b.) vomiting
   c.) pulmonary edema
   d.) ear pain

4.) Which strain has the highest occurrence rate (approximately 85%)?
   a.) A. niger
   b.) A. flavescens
   c.) A. fumigatus
   d.) A. flavus

Resources

- www.aspergillus.org.uk/pdfs/18365992.pdf
- http://ajrccm.atsjournals.org/cgi/content/full/173/7/1727
- http://www.springerlink.com/content/t7pspsun53p7pp2/
- http://radiographics.rsna.org/content/21/4/825.full
5.) Which of the following is the best known treatment for invasive aspergillosis?
   a.) Amphotericin B
   b.) azithromycin
   c.) voriconazole
   d.) gentamicin