Paracoccidioidomycosis

- Paracoccidioidomycosis refers to the infectious, endemic disease caused by the fungi pathogen, *Paracoccidioides brasiliensis*
  
  Phylum: Ascomycota  
  Genus: *Paracoccidioides*

- Wide spectrum of disease severity depending on strain  
- Healthy individuals are affected

- Infections may include:  
  - lungs  
  - skin  
  - buccal mucosa  
  - nose  
  - spleen/liver  
  - GI tract

- Dimorphic fungi
  
  - 25°C mold  
  - 37°C yeast  
  - mold form has no known sexual form (Fungi Imperfecti)

**Species: Paracoccidioides brasiliensis**

- **GEOGRAPHICAL DISTRIBUTION**
  - Central and South America  
  - 23° north of Mexico down to Argentina  
  - NOT in Chile or the Caribbean  
  - most frequent in:  
    - Brazil  
    - Venezuela  
    - Colombia

- **ECOLOGICAL NICHE**
  - unknown!  
  - isolated 4 times in soil  
  - has been found in wood, fruit bats, armadillos
• **DIMORPHIC COMPARISON**
  
  25°C Mold Form: slow growing  
  flat, wrinkled  
  yellowish brown  
  septate hyphae (sterile)  
  aleuriconidia  
  do not sporulate

  37°C Yeast Form: folded, wrinkled  
  white  
  multiple buds around mother yeast cell "steering wheel"  
  buds form short chains

• Conversion occurs on enriched medium (brain heart agar)
• Needs 10-20 days of incubation to occur

• Observed conversion into yeast form is critical for diagnosis  
  - DNA confirmation confuses w/ *Blastomyces dermatitidis*  
  - Conidia formation similar and confuses w/ genus Chrysosporium

• **KEY CHARACTERISTIC**  
  * exo-cellular serine-thiol proteinase enzyme  
    - enables the fungus to invade tissue better

• Strains vary geographically and exhibit varied severity of infection

**Paracoccidioidomycosis: The Disease**

• Can lay dormant for years within the lymph nodes and appear later with relation to an immunodeficiency.

• **Risk factors**  
  • Agricultural workers  
  • Farmer/ hunter  
  • Smoker/ Alcoholism  
  • Immunocompromised conditions

• But effects healthy individuals as well  
• Presumably acquired via inhalation of conidia
• **Histopathology**
  - Areas of granulomatous inflammation
    - Central caseation
    - Pyogenic abscesses
  - Giant cells are present in granulomata (contain yeast)
    - fungus occurs as budding yeast with cells 12-14 µm
  - Central cell surrounded by numerous blastoconidia varying in size, attached by narrow necks

• **Epididimology**
  - Very common among men
  - Women less commonly affected
  - Mean male to women ratio is 15:1
  - Rare in children and teens
  - Most patients are 30 years or older
  - Person to person transmission does not occur

• **Two major categories:**
  - Chronic adult form
    - 80-90% of cases
  - Acute or subacute juvenile form

• **Forms of disease:**
  - Asymptomatic
    - Occurs in most cases
  - Mucosal lesions
    - Ulcerative lesions of mouth and nose areas
  - Pulmonary
    - Affect central and basal zones of lungs
  - Skin
    - Ulcerative, crusty lesions

• **Diagnosis**

• Direct examination of:
  - Skin scraping
  - Sputum
  - Pleural fluid
  - Bone marrow
  - Material biopsies
  - Pus draining from lymph

• **Skin**
  - 10% KOH and Parker Ink
  - Or Calcofluor white mount
• **Tissue**
  - PAS
  - GMS
  - Gram stain

• **Exudates and Body Fluid**
  - 10% KOH and Parker Ink

• Chest X-ray used for key characteristics, BUT not diagnosis

• **Serology Test**
  - Western blot
  - ELISA
  - Immunodiffusion

• **Prognosis**
  - Good if treated
  - High mortality rate in acute juvenile type if not treated quickly

• **Antifungal Treatment**
  - Very long time
  - Frequent relapse

  - Azoles
    - Fluconazole
    - Ketoconazole
    - Itraconazole

  - Sulfas (5 years)
    - Sulfadiazine
    - Sulfamethoxypyridazine
    - Sulfadimethoxine

  - Amphotericin B
    - Not effective alone
    - Needed along with azoles or sulfas

**Case Report 1**

• Pellegrino et al., The American journal of tropical medicine and hygiene, 68(3), 301-303.

• A 34 year old man, had a history of hepatitis C and he was a heavy smoker & drinker.
• **Complaints:**
  - Fever
  - Asthemia
  - Weight loss
  - Coughing
  - Abdominal Pain

• **Physical Examination**
  - Fever
  - No lesions
  - Right eye showed hemorrhage of the fundus with a white center

• **Lab Work**
  - Bone Marrow biopsy
    - Stained with H&E, showed abundant yeasts, similar to *P. brasiliensis*
  - Liver Biopsy
    - Stained with H&E and GMS, tissue showed reaction compatible to *P. brasiliensis*

• **Histopathology**
  - Double immunodiffusion test performed in serum was positive for *P. brasiliensis*
  - Isolated & cultured in Sabourad’s glucose agar at 37°C for 18 days, showing budding yeast

• **Treatment**
  - 50 mg/day amphotericin B (AMB)
  - Then anemia and severe hypokalemia occurred
  - Amphotericin was decreased to 25 mg/day
  - Health worsened and thoracotomy and tube drainage was performed
  - Pleural liquid showed *P. brasiliensis*
  - So AMB was increased to 50 mg/day and 400 mg/day of intraconazol
  - 2 grams of AMB for the following six months
  - No recurrence of disease after one-year check up

**Case Report 2**


• In October 1998, a 60 year old Dutch man presented at the Department of Oral and Cranio-Maxillofacial Surgery

• **Complaints**
  - Painful ulceration on right side of face in the buccal vestibular mucosa
• **History**
  – Past 3 months lesion persisted
  – Dentist prescribed Corsodyl (mouth rinse), and Daktarin (oral gel)
  – Heavy Smoker
  – Worked as a carpenter with in third world aid programs in the jungles of Peru and Equador
    • 1967-1991

  Lived in:
  – Tocahe (12 years)
  – Cuzco (5 years)
  – West Ecuador (5 years)

• Check-up in Germany revealed in 1998 that he had an increase erythrocyte sedimentation rate

• Diagnosed with coughing and wheezing

• **Lab Work**
  – Radiography of chest reveals a pattern of radiodensities
  – CT scan of lungs showed sarcoidosis or bronchoilitis obliterans organizing pneumonia
  – Lung tests and biopsies revealed pneumonia with restricted lung function
    * NO EVIDENCE OF TUBERCULOSIS
  – Diagnosed with endstage sarcoidosis

  **5 months later**
  showed no improvement
  – Dentist noticed: irregular mucosa and gingiva on the right side of face
    teeth were loose
    showed signs of periodontitis

  **1 week later**
  no improvement; referred to oral surgeon
  – Weight loss, fatigue, fever, and night sweats
  – Sample from mouth showed:
    pseudo-epithelial hyperplasia
    inflamed cells
    many large budding yeast cells
  – A 2nd biopsy used direct fluorescence microscopy of a wet preparation stained with calcoflour white mount
  – Finally, showed multiple peripheral buds characteristic of Paracoccidioides brasiliensis
  – Complained of prostate pain – urine taken for cultures

• **Histopathology**
  **Oral Culture**
  – Mold grew after 3 weeks at 28°C
  – Unicellular yeast grew at 37°C
• **Diagnosis**
  * Chronic multifocal paracoccidioidomycosis

• **Treatment**
  – Itraconazole oral solution initially
  – After 1 week peri-oral symptoms improved
  – After 3 weeks lung function improved
  – 5 years later was slightly dyspnic, but otherwise free of symptoms

**References**

• [www.mycolgy.adelaide.edu](http://www.mycolgy.adelaide.edu) (accessed June 14, 2007)
• [www.doctorfungus.com](http://www.doctorfungus.com) (accessed June 14, 2007)