

## Topic 16: Blastomycosis

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### Blastomycosis

A chronic granulomatous and often suppurative disease having a primary pulmonary stage that is frequently\* followed by dissemination to other body sites, particularly skin and bones.

**Causative Agent:**

teleomorph - *Ajellomyces dermatitidis*

anamorph - *Blastomyces dermatitidis*

**Synonymy:**

North American Blastomycosis

Gilchrist's Disease

Chicago Disease

\*much more so than in histoplasmosis (as far as is known). More like chronic histoplasmosis with some dissemination to other body sites. Traditionally not considered opportunistic. Sporadic AIDS association.

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### Blastomycosis vs Histoplasmosis

**Similarities:**

1. both have approximately the same endemic U.S location
2. both caused by a single species of genus *Ajellomyces*, which are closely related and heterothallic
3. both are initiated most often as primary pulmonary infections brought about by inhalation of conidia
4. both caused by fungi whose dimorphism is regulated similarly by temperature
5. both thought to be generally fatal before pulmonary forms discovered and before use of Amphotericin B

**Differences:**

1. caused by different species
2. although former is not opportunistic, it does not appear that many infections are self-limiting
3. induction of specific immunity after exposure and resolution may be uncommon (maybe even non-existent)
4. the propensity of the disease is to progress to production of active skin lesions and bone lesions (like hybrid disease among histoplasmosis, sporotrichosis and cryptococcosis)?
5. does not involve intracellular pathogen
6. resolution, when it occurs, does not leave residual lesions (e.g. calcified lesions)

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## History

Gilchrist\* - 1894 - new skin disease by unknown yeast in tissue\*\*

Gilchrist & Stokes\* - 1896 - 2nd case

- long-term study of disease
- isolated & studied fungus
- recognition of dimorphism
- 1898 named fungus *Blastomyces dermatitidis*

Ricketts\* ~ 1900's - studied Chicago Disease (15 cases)

1. used X-ray for treatment
2. began to define endemic area
3. experimented with KI therapy
4. began to distinguish from cryptococcosis

Pre-1950's - mainly thought that only 2 clinical forms of blastomycosis existed

1. Cutaneous form initiated by traumatic implantation of fungus into skin and subcutaneous tissue (e.g. like sporotrichosis and chromoblastomycosis)
2. Systemic form initiated in lungs and then disseminated to internal organs

Schwarz and Baum, etc. 1950s → 1970s virtually all cases of blastomycosis (except very rare primary cutaneous) originate in lungs

1. is an erroneous concept

\*All Americans; Ricketts better known for studies of Rocky Mountain Spotted Fever and Typhoid Fever (*Rickettsia rickettsii* named in his honor and therefore *Rickettsia typhi* too.).

\*\*a formalin-killed autopsy specimen

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## Taxonomy

*Ajellomyces dermatitidis*\*^

*A. capsulatus*\*

Ascomycota

Euascomycotina

Plectomycetes

Onygenales (blastoconidia/gymnothecia)

Gymnoascaceae (Sessile spiral-forming cleistothecia)

\* heterothallic, dimictic teleomorphs\*\*

\* holoblastic, hyphomycete anamorphs

^ varietal differences uncertain; African form may be a variety or species

Teleomorphs discovered

Dermatophytes 1960 -->1970's

*Blastomyces* 1968\*\*\*

*Histoplasma* 1972

*Cryptococcus* 1975

\*\* 1 contrasting "set" of mating-type genes (idiomorphs) at the same locus of homologous chromosomes of self-sterile mating strains.

\*\*\* McDonald & Lewis - 1968.. 1st of the "endemic" pathogens induced to sex

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### Blastomycosis - Clinical Forms

1. Primary pulmonary
2. Chronic cutaneous\*
3. Generalized systemic\*
4. Single organ systemic\*
5. Inoculation blastomycosis

\*pre-1950s recognized main forms.

#### Primary Pulmonary (resolve spontaneously or disseminate)

1. Inhalation of spores
2. Alveolitis with M invasion
3. Inflammatory reaction involving PMNs & granuloma formation
4.
  - a. often lung disease resolves, but lesions appear at other sites
  - b. less often resolution in lungs and no progression
  - c. severe progressive pulmonary form

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### Distribution

1. originally thought to be more common in whites, however today thought to be equal distribution among races
2. most cases traditionally among older individuals (30->60 age group); exception with AIDS cases
3. male/female ratio of 6-9/1
  - since same in dogs may not be occupational only
  - some thoughts about hormonal relationship (no direct evidence)

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**Signs of cutaneous involvement in blastomycosis**

1. **formation of subcutaneous nodules or ulcerating lesions**
  2. **usually occur singly or in groups on exposed areas (face, hands, wrists, arms, lower leg and infrequently mucocutaneous regions; e.g. larynx, tongue, mouth surfaces)**
  3. **25 - 50% of these cases with cutaneous lesions may show bone involvement (sometimes only presenting symptom; occult osteolytic lesion, pain in joints, mostly lesions in nonjoint bone; ribs, skull, long and short bone)\***
1. **Amphotericin B drug of choice**
  2. **hydroxystilbamidine (in children) (not used today except rarely)**
  3. **Itraconazole (current or near future drug of choice); compliance problems w/ oral drugs apply here too.**

**Mortality rate ~78% in untreated; Ampho treatment in life-threatening; 90% effective  
keto 90 . 95% effective, but w/ side effects  
itra only -> 8% relapse, 90% > effective**

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**Serodiagnosis**

1. **Compliment fixation test**
2. **Immunodiffusion test**

**C.F - uses broken yeast cells as antigen**

- many false negatives & some false positives ~ 50% undetected
- newer tests with antigen A\* better. -- Titer of 1:8 positive

**ID - uses antigen A\***

- positive band of identity basis for immediate treatment, ~ 80% reliable

**\* culture filtrate antigen from yeast form**

**-selective labs & CDC have very good records of detection by serodiagnosis today.**

**-positive sputum culture also often leads to diagnosis; characteristic yeast cells in pus or biopsy tissue; ID also by gene-probe technology (AccuProbe™)**