

## Funguses Among Us

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## Reportable Fungal Diseases in Michigan

- *Coccidioidomyces immitis*
  - Nationally notifiable
  - CSTE Case definition
- *Histoplasma capsulatum*
  - State-level reporting
  - Michigan Case Definition
- *Blastomyces dermatiditis*
  - State-level reporting
  - Michigan Case Definition (**NEW!**)

## Mycoses of Public Health Importance

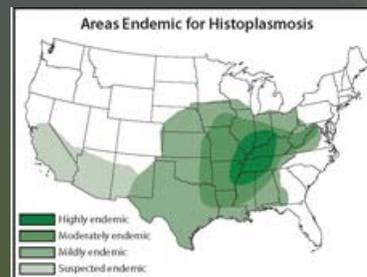
- Dimorphic fungi (exist in two forms)
  - Mold in the environment (at atmospheric temps; 25°C)
  - Yeast/endospore in humans and animals (at body temps; 37°C)
- Infection occurs following disturbance of mycelial cells existing in the soil, leading to inhalation of microconidia or arthrospores, which convert to parasitic yeast forms on the pulmonary alveoli
- Cause serious and life-threatening infections in immune-suppressed patients
- Environmental pathogens, occasionally associated with **outbreaks** due to common environmental exposure
- Immune response may not eliminate infection, **reactivation** is possible for these infections



## Histoplasmosis

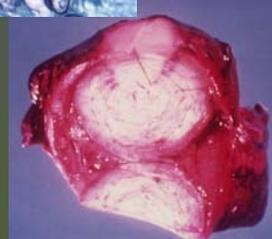
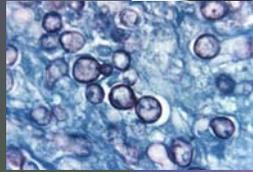
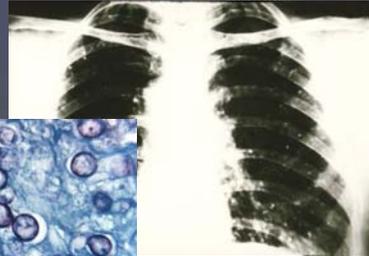
- *Histoplasma capsulatum*
- Associated with accumulations of bird and bat droppings (likes the nitrogen)
- 50-80% of people from endemic areas will show evidence of exposure to this fungus in their lifetime\*
- 10-25% of HIV patients in endemic areas will develop disseminated disease
- No national reporting requirement
- Michigan is "mildly" endemic

\*Makes interpretation of serologic tests difficult



## Diagnostic Testing-Histoplasma

- Fungal Culture
  - BAL, blood, sputum
  - Biopsy
- Molecular evidence (+ PCR or DNA "probe")
- Histopathology
- Antigen Test
  - Urine
- Serology (detects antibody only)
  - Immunodiffusion
  - Complement fixation



## Immunodiffusion Test



Texas Dept of State Health Services

### Coccidioidomycosis

Well 1, 4 = Positive Controls

Well 3 = + Coccidioidomycosis

### Histoplasma

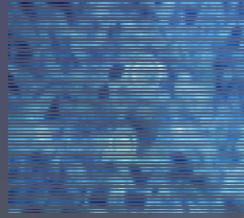
Well 1, 4 = positive control

Well 2 = + H and M band

Well 3 = + M band only

# Blastomycosis

- Found in areas of the U.S. and Canada that border large river valleys and the Great Lakes
- Favors moist soil rich in organic matter in wooded sites and along waterways
- Dogs are uniquely sensitive to infection, and are good sentinels for the presence of the fungus in endemic areas
- Spreads lympho-hematogenously to extra-pulmonary sites



Incidence of Reported Blastomycosis in Michigan 2002-2011

Legend

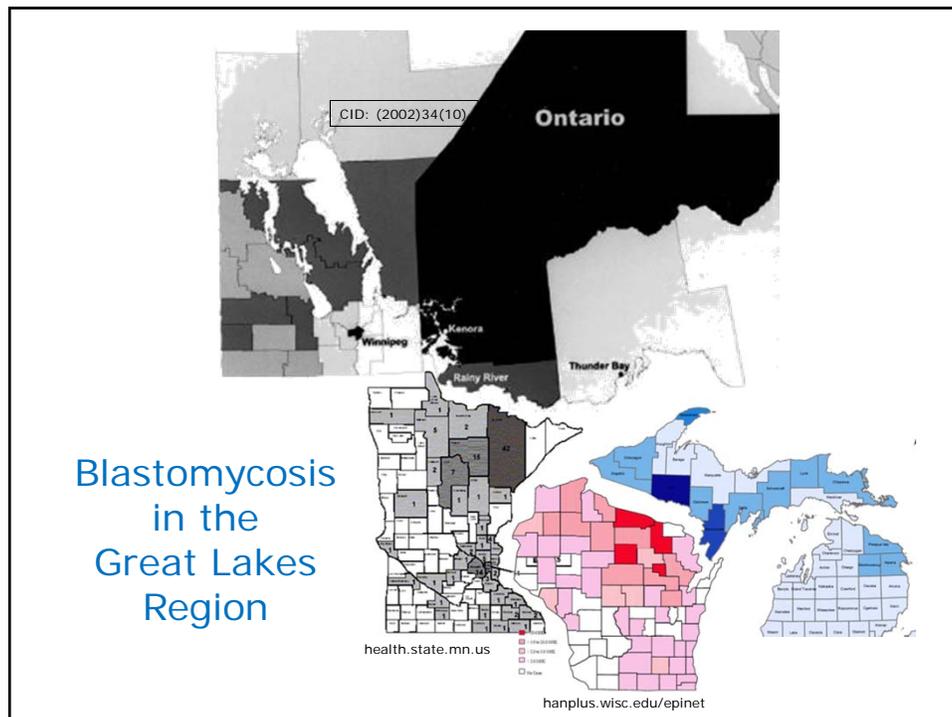
| Blastomycosis Incidence: 2002 - 2011 |                                       |
|--------------------------------------|---------------------------------------|
| Lightest Blue                        | 0 - 20 Cases per 100,000 Population   |
| Light Blue                           | 20 - 40 Cases per 100,000 Population  |
| Medium Blue                          | 40 - 60 Cases per 100,000 Population  |
| Dark Blue                            | 60 - 80 Cases per 100,000 Population  |
| Darkest Blue                         | 80 - 102 Cases per 100,000 Population |

Michigan Department of Community Health



Zoonotic Disease and Special Projects Section  
Division of Communicable Disease  
May, 2012





## Diagnostic Testing\* -Blastomycosis

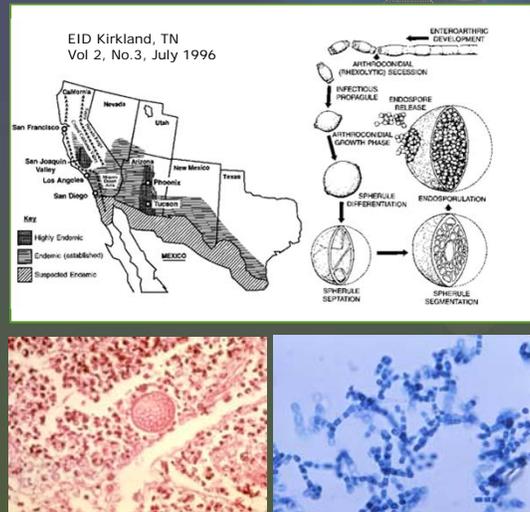
- Isolation of *B. dermatitidis* from sputum, bronchial wash, or skin lesion
- Molecular evidence of infection (+ DNA probe performed on culture isolate)
- Visualization of the organism in cytologic or histologic specimens (characteristic thick-walled, broad-based budding yeast)

\*Serologic tests (EIA, CF, ID) lack specificity and sensitivity and should not be used alone to diagnose blastomycosis.

Urine antigen tests are likewise non-specific for Blastomyces, frequently cross-reacting with histoplasma, paracoccidioidomyces and penicillium.

## Coccidioidomycosis

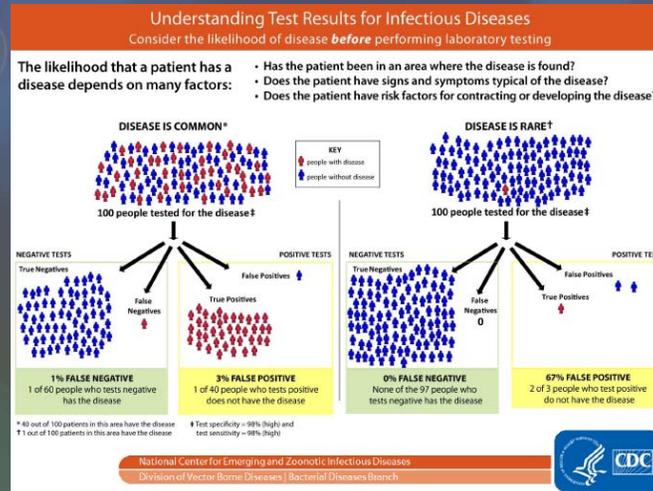
- Endemic in the Southwest U.S.
- Two genetically distinct species; *C. immitis* and *C. posadasii* ("non-California")
- NOT FOUND IN MICHIGAN but
- Cases occur in travelers to endemic areas (particularly "snow birds")



## Diagnostic Testing- Coccidioidomycosis

- Culture
- Histopathology
- Molecular testing (+ DNA probe)
- Positive serologic test for coccidioidal antibodies in serum, CSF, or other body fluid
  - Detection of IgM by ID, EIA, latex agglutination or tube precipitin
  - Detection of IgG by ID, EIA, or CF
- Skin test conversion from negative to positive after onset of clinical signs and symptoms

## Limitations of Serologic Testing



- In populations where disease is rare or unlikely, testing is likely to lead to false positives more frequently than true positives.

## Case Classification

Confirmed or probable cases include patients with:

**CLINICALLY COMPATIBLE ILLNESS**

and

**LABORATORY EVIDENCE OF RECENT INFECTION**

(as described in the Case Definition for each disease)

[www.michigan.gov/cdinfo](http://www.michigan.gov/cdinfo)

## Fungal Case Classification Key Components

- Presence of a **clinically compatible illness**
  - Generally respiratory (pneumonia) with a fever
  - Can involve other tissues such as bone, skin, lymph nodes, etc.
- Clinical correlation (Does treating physician feel this is an acute illness vs previous exposure?)
- Exposure to an endemic area
  - For Coccidioidomycosis, need to have traveled to the southwest U.S.
  - For Blastomycosis, important to ask about travel or other risk factors

## Steps in Case Investigation

1. Receive laboratory report (paper or electronic through MDSS)

### Methodology?

Culture/histopath/PCR

Urine Ag

Serology/antibody detection

Methodology (EIA, CF, ID, IFA)

What was the titer or index?

Meets laboratory criteria for a potential case?

## Laboratory Criteria for Case Classification\*

### Histoplasma

- Culture (molecular) or histopathology
- Urine Ag
- Serology
  - H band
  - CF titer  $\geq$  1:32

### Blastomyces

- Culture (molecular) or histopathology

### Coccidioidomyces

- Culture (molecular) or histopathology
- Serology
  - Detect IgM or IgG
- Skin-test conversion following clinical signs and symptoms

\*If above laboratory criteria are not met, close as NOT A CASE

## Steps in Case Investigation

### 2. Clinically compatible illness?

Determine why patient was tested for disease  
(**contact healthcare provider**).

Is this an **incidental finding**?

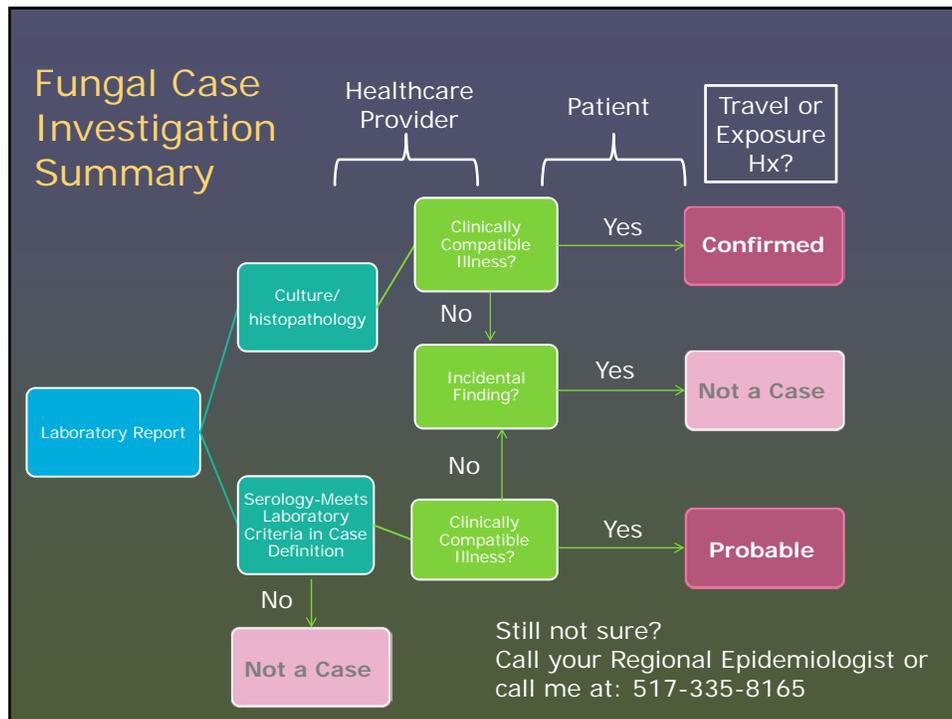
Old granuloma? (no acute disease, not causing symptoms)

Rule out Malignancy? (biopsy of mass)

Previous exposure? (low or background titer)

Was the patient treated for this disease  
(prescribed antifungal medication)?

If at this point, case does not meet either probable or confirmed criteria, no further investigation is needed.  
Close these as "NOT A CASE"



## Co-infection?? Or what to do when a patient has antibodies to more than one fungal agent?

- While possible, particularly in immune-suppressed patients, co-infection is rare.
- The **dimorphic fungi** share antigens and this can cause cross-reactions on antibody tests
- For this reason, serologic testing must be supported with clinical correlation.
- In general, the titer with the highest value probably represents the infecting organism.
- If there is other supportive laboratory evidence, such as a culture or histopathologic diagnosis of a fungal agent, then the titer to a second fungal agent likely reflects cross-reaction rather than co-infection.

Questions?

