Imported mycosis: an update

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Laiko General Hospital, Athens, Greece

Imported systemic mycoses

Factors related to imported mycosis

- Increasing world travelling
- Migration
- Climate changes
- HIV pandemic
### Imported systemic mycoses

**Most common**

- Histoplasmosis
- Coccidioidomycosis
- Paracoccidioidomycosis
- Blastomycosis
- Penicilliosis marneffei

### Histoplasmosis

*Caused by* *Histoplasma capsulatum*

*by inhalation of conidia*
Histoplasmosis

25°C mould
37°C yeast

thermally dimorphic fungus

Phylogenetic studies: 8 clades

The African clade:

H. capsulatum var. duboisi,
H. capsulatum var. capsulatum
(H. capsulatum var. farciminosum)

Distinct clinical picture
**Histoplasmosis**

**Epidemiology**

- Has been reported from all continents
- Is endemic in North, Central and South America, Africa, India and Southeast Asia.
- Fungal growth is promoted by the presence of bird or bat droppings in moist soil
- Outdoor activities like cave exploration carry a high risk
Histoplasmosis

Clinical presentation

Immuno-competent

Healthy

>95% asymptomatic (low inoculum)

50 - 100% symptoms (high inoculum)

acute pulmonary histoplasmosis, “flu-like” illness

pre-existing lung damage

Chronic pulmonary symptoms

with fibrosis and cavitations

Reactivation after up to 50 years

Histoplasmosis

Clinical presentation

Immuno-compromised or extremes of age

Disseminated infection (via the reticulo-endothelial system)

nearly all organs affected

Prevalence in HIV-infected in hyperendemic areas before HAART era:

up to 30%
# Histoplasmosis

## Forms of the Disease

<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>• Occurs in 50–90% of infected individuals</td>
</tr>
<tr>
<td>Acute &amp; symptomatic</td>
<td>• It usually goes unrecognized</td>
</tr>
<tr>
<td>1. Self-limited (Flu-like syndrome)</td>
<td>• Diffuse or localized pneumonitis.</td>
</tr>
<tr>
<td>2. Acute Pulmonary</td>
<td>• &quot;Buckshot&quot; appearance on chest radiograph with subsequent calcification in cases of heavy exposure.</td>
</tr>
<tr>
<td>3. Acute Pericarditis</td>
<td>• It may be severe enough to require ventilatory support</td>
</tr>
<tr>
<td>4. Rheumatologic</td>
<td>• Frequently associated with intrathoracic adenopathy</td>
</tr>
<tr>
<td>manifestations</td>
<td>• Pericardial fluid is usually sterile</td>
</tr>
<tr>
<td></td>
<td>• Arthralgias, arthritis, erythema nodosum, and/or erythema multiforme</td>
</tr>
</tbody>
</table>

## Symptoms

- Fever, headache, malaise, dry cough, chest pain (sec. to mediastinal lymphadenopathy or pericarditis)
- Arthralgias, erythema nodosum, erythema multiforme
- Pneumonitis on imaging
- Skin lesions
- Retinal lesions
- Complication: massive enlargement of mediastinal lymph nodes, fibrosis
Histoplasmosis

Acute primary histoplasmosis

Histoplasmosis
Forms of the disease

Chronic Pulmonary

Radiologic presentations include:

1. a Ghon complex suggestive of tuberculosis,
2. histoplasmoma,
3. and cavitary disease
Histoplasmosis

Chronic histoplasmosis

Histoplasmosis
Forms of the disease

Fibrosing Mediastinitis

• Rare form that produces an intense deposition of fibrotic tissue in the mediastinum encroaching vital structures such as the superior vena cava, esophagus and trachea.
**Disseminated infection**

- In the immunocompromised and extremes of age
- Adrenal insufficiency in 10%

### DISSEMINATED HISTOPLASMOSIS: CLINICAL PRESENTATIONS

<table>
<thead>
<tr>
<th>ORGAN INVOLVED</th>
<th>CLINICAL MANIFESTATION</th>
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</thead>
<tbody>
<tr>
<td>Lymph nodes</td>
<td>Lymphadenitis</td>
</tr>
<tr>
<td>Bone Marrow</td>
<td>Anemia, Leukopenia, Thrombocytopenia</td>
</tr>
<tr>
<td>Heart</td>
<td>Endocarditis</td>
</tr>
<tr>
<td>Adrenal glands</td>
<td>Enlargement without symptoms, Addison's disease</td>
</tr>
</tbody>
</table>
### Disseminated Histoplasmosis: Clinical Presentations

<table>
<thead>
<tr>
<th>System</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Chronic Meningitis, Cerebritis, Mass</td>
</tr>
<tr>
<td>GI tract</td>
<td>Oral ulcers, Small bowel micro and macro ulcers</td>
</tr>
<tr>
<td>Eyes</td>
<td>Uveitis, Choroiditis</td>
</tr>
<tr>
<td>Skin</td>
<td>Papular to nodular rash, Hydronephrosis, Bladder ulcers, Penile ulcers, Prostatitis</td>
</tr>
<tr>
<td>Genitourinary tract</td>
<td></td>
</tr>
</tbody>
</table>

Tongue ulcer in a pt with disseminated histoplasmosis

Histoplasmosis
Histoplasmosis

Skin manifestations of disseminated histoplasmosis in an HIV-positive pt

Histoplasmosis

Histoplasmosis in Europe: Report on an epidemiological survey from the ECMM Working Group

• 118 proven or probable cases, from Jan. 1995 - Dec. 1999

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>disseminated disease</td>
<td>62</td>
</tr>
<tr>
<td>acute pulmonary infection</td>
<td>31</td>
</tr>
<tr>
<td>chronic pulmonary infection</td>
<td>6</td>
</tr>
<tr>
<td>localized disease</td>
<td>2</td>
</tr>
<tr>
<td>Incidental after investigation for lung cancer</td>
<td>17</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Country</th>
<th>Retrospective Jan 95 – Dec 97</th>
<th>Prospective Jan 98 – Dec 99</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>23</td>
<td>23</td>
<td>46</td>
</tr>
<tr>
<td>Italy</td>
<td>14</td>
<td>8</td>
<td>22</td>
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<tr>
<td>UK</td>
<td>10</td>
<td>9</td>
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<tr>
<td>France</td>
<td>8</td>
<td>2</td>
<td>10</td>
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<tr>
<td>Belgium</td>
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<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Sweden</td>
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<td>4</td>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Turkey</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>53</td>
<td>118</td>
</tr>
</tbody>
</table>

Risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traveling endemic area</td>
<td>106</td>
</tr>
<tr>
<td>HIV infection CD4 &lt; 150/µl</td>
<td>45</td>
</tr>
<tr>
<td>Exposure to birds, bats, caves</td>
<td>26</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>7</td>
</tr>
<tr>
<td>malignancy</td>
<td>2</td>
</tr>
<tr>
<td>Recipient infected liver</td>
<td>1</td>
</tr>
<tr>
<td>unknown</td>
<td>12</td>
</tr>
</tbody>
</table>

Most patients had travelled to known endemic areas,
• 8 patients (from Italy, Germany and Turkey) had not been outside their countries of origin and hence these cases appear to be autochthonous.
• The observation of autochthonous cases of disease suggests that the endemic area of histoplasmosis is wider than classically reported and supports continued surveillance of the disease throughout Europe.


### Cases of histoplasmosis in Europe (1998-2006)

<table>
<thead>
<tr>
<th>country</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands</td>
<td>14</td>
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<tr>
<td>Greece</td>
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<tr>
<td>France</td>
<td>4</td>
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<td>Spain</td>
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<tr>
<td>Austria</td>
<td>3</td>
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<td>Italy</td>
<td>5</td>
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<tr>
<td>Belgium</td>
<td>2</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1</td>
</tr>
</tbody>
</table>
**Histoplasmosis**

**Diagnosis**

- Isolation from blood (85% positive), BAL, bone marrow or tissues ("gold standard", disadvantage: time)
- Urine Ag EIA (sens. >92% in dissem.), serum Ag lower sensitivity
- Serology sens. 71% (low sensitivity in immunocompromised)
- Histology (typical budding yeasts in macrophages)
- Pancytopenia and ↑↑↑ LDH → positive predictor
- Real-Time PCR (ITS region of ribosomal DNA), 100% specificity, 77.3% sensitivity → promising
- Histoplasmin skin test: obsolete (insensitive in disseminated Inf.)

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**Histoplasmosis**

**Diagnosis**

- Isolation from sputum
- Urine antigen (low sensitivity in acute infection, high in disseminated infection)
- Serology
- Stains of peripheral blood or sputum
- Histoplasmin skin test: only for epidemiological studies
Histoplasmosis

- Stains of the bronchoalveolar lavage

Evidence-based guidelines for the management of patients with histoplasmosis were prepared by an Expert Panel of the Infectious Diseases Society of America.

Therapy guidelines

Progressive Disseminated Histoplasmosis

**Amphotericin B deoxycholate** (1.0 mg/kg daily for 4–6 weeks) is recommended (AIII).

**Amphotericin B deoxycholate** (1.0 mg/kg daily for 2–4 weeks) followed by **itraconazole** (5.0–10.0 mg/kg daily in 2 divided doses) to complete 3 months of therapy is an alternative (AIII).

• Longer therapy may be needed for patients with severe disease, immunosuppression, or primary immunodeficiency syndromes (AIII).

• Lifelong suppressive therapy with **itraconazole** (5.0 mg/kg daily, up to 200 mg daily) may be required in immunosuppressed patients if immunosuppression cannot be reversed (AII) and in patients who experience relapse despite receipt of appropriate therapy (CIII).
Coccidioidomycosis

History

• 1892: First reported as disease
• 1920-1930
  - Soil recognized as reservoir for agent
• 1987
  - CDC adds coccidioidomycosis to annual survey of HIV-associated diseases
• 1991-1995
  - Incidence increases tenfold in San Joaquin Valley, CA

Coccidioidomycosis

• Dimorphic fungus
  - Saprophytic phase
  - Parasitic phase
• From soil or dust
  - Arthroconidia become airborne, inhaled
  - Transform into spherule and endospore
Human Transmission

- Direct inhalation of *C. immitis* spores
  - Present in contaminated soil and dust
  - Only established mode of transmission
- Not person-to-person
- Not animal-to-person
- Increased incidence after disturbance
Human Transmission

- Natural disturbances
  - Dust storms
  - Earthquakes
- Human disturbances
  - Construction sites
  - Archaeological digs

Coccidioidomycosis

Geographic Distribution

- Endemic areas
  - Southwestern U.S.
    - New Mexico, Texas, California, Arizona
  - Northern Mexico
  - Central America
  - Argentina
- 10-50% skin test positive
Epidemiology

- Endemic in South-Western US, Mexico, S. America
- Inhalation of conidia in arid areas, after sand storms
- In Europe, scattered case reports from pts returning from Arizona, California or Mexico
Coccidioidomycosis

Case reports from Europe (PubMed since 1975)

1) Pulmonary Coccidioides node in a Swiss patient with chronic lymphatic leukemia.
Humbach M, Studt P, Arnold W, Pfiffer GE.

2) Coccidioidomycosis: an imported invasive fungal disease in France.
Chandurini MG, Hot A, Damaoulou E, Bouguenx ME, Vlard JP, Dupont B, Lortholary O.

3) Imported concomitant coccidioidomycosis and histoplasmosis in an asymptomatic Ecuadorian migrant in France.
Chandesris MO, Hot A, Bougnoux ME, Viard JP, Dupont B, Lortholary O.

4) Coccidioidomycosis as an imported lymphoproliferative disease in France.
Chandesris MO, Hot A, Bougnoux ME, Viard JP, Dupont B, Lortholary O.

5) Coccidioidomycosis as an imported pulmonary disease in France.
Chandesris MO, Hot A, Bougnoux ME, Viard JP, Dupont B, Lortholary O.

6) First report of coccidioidomycosis associated with Sweet syndrome.
Holemans X, Loveecke P, Despontin K, Maton JP.

7) Coccidioidomycosis in Hungary. The first import case.
Zalatnai A, Zala J, Sándor G.

8) Bilateral isolated adrenal coccidioidomycosis.
Papadopoulos KI, Castor B, Klingspor L, Dejmek A, Lorén I, Brammert M.

9) Imported pulmonary coccidioidomycosis apropos of an anatomical-clinical study.
Ferrari R.

10) The first two cases of coccidioidomycosis in Finland.
Alakortt K, Kahanpää P, Pätilä E.

Only 7 cases have been reported in Europe from 1998 - 2008, although an increase in incidence has been reported in the USA for reasons not fully understood.

Coccidioidomycosis

- Two forms in humans
  - 60% asymptomatic
    - Only identified with positive skin test
  - 40% mild to severe disease
    - Can be fatal
    - Immuno-compromised persons highly susceptible to serious infection
- Difficult to assess morbidity in animals
**Coccidioidomycosis**

**Clinical Signs: Primary Form**
- Incubation period: 1-4 weeks
- Usually subclinical
- Fever, chills, cough, sore throat
- Chest pain
- Nodular lesions
- Nonspecific respiratory symptoms
- Complications less common
  - Pneumonia, pleural effusion

**Clinical Signs: Disseminate Form**
- Severe form of disease
- Weeks to months to years after primary infection
- Symptoms include
  - Low-grade fever, anorexia, weight loss
  - Muscle aches and stiffness, weakness
  - Excessive sweating
  - Widespread focal lesions
- In HIV-infected persons
  - Mucopurulent or bloody sputum
The multiple skin lesions have resulted from dissemination from the lungs. The rash is an immunologic response to the fungus. Most commonly seen in Caucasian women.

Cavitary Coccidioidomycosis
Severe Coccidioidal pneumonia in HIV-positive pt

Coccidioidomycosis

Direct examination
(helpful but not very sensitive)

Diagnosis

Direct microscopy of skin scrapings from a cutaneous lesion mounted in 10% KOH and Parker ink solution showing characteristic endosporulating spherules (sporangia) of *Coccidioides immitis*. The presence of spherules with endospores is diagnostic.
Coccidioidomycosis

Sampling

• Before collecting or sending any samples, the proper authorities should be contacted

• Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease

Coccidioidomycosis

Diagnosis

• Differentials
  - Tuberculosis

• Clinical
  - Coccidioidomycosis should be considered
    • In endemic areas
    • Following a dust/soil disturbance
    • With characteristic clinical signs
Coccidioidomycosis

Diagnosis

Histological stains

more sensitive:
Grocott- silver

occasionally
Giems, Papanicolaou, mucicarmine

NO GRAM

Culture at 25°C and 37°C

Coccidioidomycosis

Diagnosis

• *C. immitis* spherules visualized in
  - Sputum, pleural fluid, cerebrospinal fluid or exudates from draining lesions

• Complement fixation
  - IgG anticoccidioidal antibodies
    • Titer ≥1:4 = current or recent infection
    • Titer ≥1:32 = increased risk of extrapulmonary dissemination

• Skin test of epidemiological value
Treatment

- **Primary coccidioidomycosis**
  - Treatment generally unnecessary

- **Severe/chronic coccidioidomycosis**
  - Antifungal agents effective
  - Prognosis generally good

- **Disseminate coccidioidomycosis**
  - May require invasive or long-term therapy
  - Prognosis poor to guarded

Coccidioidomycosis

Therapy guidelines

Evidence-based guidelines have been issued by an Expert Panel of the Infectious Diseases Society of America: Galgiani et al, CID 2005;41: 1217-23
Paracoccidioidomycosis

Caused by *Paracoccidioides brasiliensis* (Dimorphic fungus)

Characteristic morphology of budding cells, resembling Mickey mouse

• Paracoccidioidomycosis is a chronic granulomatous disease that characteristically produces a primary pulmonary infection, often inapparent, and then disseminates to form ulcerative granulomata of the buccal, nasal and occasionally the gastrointestinal mucosa.

• The disease in its inception and development is similar to blastomycosis and coccidioidomycosis. The only etiological agent, *Paracoccidioides brasiliensis* is geographically restricted to areas of South and Central America.
Paracoccidioidomycosis

Epidemiology

- Geographically restricted to Latin America.
- In Europe the disease is very rare and only 11 cases have been reported in the literature since 1979, as infections in travelers to Latin America.

<table>
<thead>
<tr>
<th>country</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>6</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1</td>
</tr>
<tr>
<td>Italy</td>
<td>2</td>
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<tr>
<td>Germany</td>
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</tr>
<tr>
<td>Austria</td>
<td>1</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1</td>
</tr>
</tbody>
</table>
Paracoccidioidomycosis

Clinical presentation

- Most common manifestation pulmonary, resembles tuberculosis
- All organs and mucous membranes can be affected by lymphatic dissemination
- Long silent period before symptoms appear (6 months to 40 years)
- Rare in children and young adults (5 – 10%)

Granulomatous lesion involving the nose following dissemination from the lungs.
Paracoccidioidomycosis

Mucocutaneous paracoccidioidomycosis showing extensive destruction of facial features. (Courtesy Dr John Rippon, USA).

Mucocutaneous paracoccidioidomycosis showing an ulcerated lesion on the lips and loss of teeth. (Courtesy Dr John Rippon, USA).
Paracoccidioidomycosis

X-ray of a patient with paracoccidiomycosis

The diagnosis is carried out by direct examination of samples revealing the presence of budding yeasts, as well as culture at 25°C and 37°C.

Diagnosis

- Direct examination of histopathological sections with PAS, H-E and mainly Grocott stains revealing the presence of budding yeasts.

- Culture at 25°C and 37°C
Grocott's methenamine silver (GMS) stained lung tissue section showing multiple, narrow base, budding yeast cells “steering wheels” of *P. brasiliensis*.

Microscopic morphology of *Paracoccidioides brasiliensis* showing multiple, narrow base, budding yeast cells “steering wheels” of *P. brasiliensis*.
Paracoccidioidomycosis

**Therapy**

Azole derivatives. *Itraconazole* the drug of choice (<5% relapse)

Sulfamethoxazole-trimethoprim combination

Amphotericin B

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Blastomycosis

Caused by *Blastomyces dermatitidis*  
*(Dimorphic fungus)*

25°C mould  
Yeast phase KOH preparation
Blastomycosis

Epidemiology

Most often in persons living in midwestern, southeastern, and south central United States and the Canadian provinces that border the Great Lakes and the St. Lawrence Seaway.

Recent reports have shown an increase in the incidence of blastomycosis in some of these regions.

Endemic areas of Blastomycosis
Clinical presentation

- From subclinical infection to acute or chronic pneumonia
- A subset of individuals with acute pulmonary blastomycosis can progress to fulminating multilobar pneumonia and ARDS.
- 25%-40% develop extrapulmonary infection manifested by cutaneous, osteoarticular, genitourinary, or CNS disease.
- Disseminated blastomycosis occurs more frequently in immunosuppressed individuals, such as organ transplant recipients and those infected with HIV.

Case reports from Europe (PubMed since 1976)

1. Histopathologic evidence of North American blastomycosis in the skin: a case of two cases

2. Long-term observation of a case of cutaneous blastomycosis in Poland treated with fluconazole

3. Disseminated blastomycosis occurs more frequently in immunosuppressed individuals, such as organ transplant recipients and those infected with HIV.

4. Blastomycosis in an HIV antibody positive male in the UK

5. Macroscopic and microscopic characteristics of an unusual presentation of blastomycosis

6. Favourable outcome of blastomycosis of the brain associated with Haemophilus and fungi co-infection


9. North American blastomycosis and its possible occurrence in Poland
Clinical classification of Blastomycosis

Clinical presentation

Ulcerated granuloma due to *B. dermatitidis*. (Courtesy of Dr. John Rippon, USA).
Clinical presentation

Large verrucous lesion, typical of Blastomycosis

Osteolytic lesions
Blastomycosis

*Blastomyces* pneumonia

Chronic Blastomycosis, indistinguishable from tuberculosis
Blastomycosis

Therapy

• In the immunocompetent host, acute pulmonary blastomycosis can be mild and self-limited and may not require treatment. However, consideration should be given to treating all infected individuals to prevent extrapulmonary dissemination.

• All persons with moderate to severe pneumonia, disseminated infection, or immunocompromise require antifungal therapy.

Evidence-based guidelines for the management of patients with histoplasmosis were prepared by an Expert Panel of the Infectious Diseases Society of America.

**Penicillnosis marneffei**

Caused by *Penicillium marneffei* (Dimorphic fungus)

Epidemiology

- Endemic in SE Asia
- Incidence rising due to spread of HIV in region. It is the 3rd OI in HIV-infected pts in Northern Thailand
- Presumed association with bamboo rats
- Case reports in Europe of patients from endemic areas (Thailand, China), with HIV co-infection
Temporal emergence of HIV (antenatal data, 1990 to 2000; UNAIDS/WHO working group report, 2003) and P. marneffei-associated penicilliosis (1985 to 2001; Maharaj Hospital, Chiang Mai) for the Chiang Mai region, northern Thailand.


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Case reports of Penicilliosis in Europe

First case of Penicillium marneffei fungemia in Greece and strain susceptibility to five licensed systemic antifungal agents and penicillin.
PmID: 16644342 [PubMed - indexed for MEDLINE]
Related Articles

Disseminated Penicilliosis marneffei infection in an HIV-positive Brazilian patient and a review of cases reported outside endemic regions.
Araujo AM, Garett E, Bonaccorsi C, Pinto AC, Orsce F, Sottra S, Pannavonti C.
PmID: 16706952 [PubMed - indexed for MEDLINE]
Related Articles

Disseminated Penicilliosis marneffei sepsis in a HIV-positive Thai woman in Denmark.
Menis H, Holylng N, Arendrup MC.
PmID: 15307585 [PubMed - indexed for MEDLINE]
Related Articles

Two reported cases of Penicillium marneffei infection in Belgium.
Depraetere K, Collembaurs R, Leen M, De Croygh E, Pelgrom Y, Hauwen E, Van Marck E, Devos C.
PmID: 9791445 [PubMed - indexed for MEDLINE]
Related Articles
Penicilliosis marneffei

Clinical presentation

- Low-grade fever, weight loss
- Skin lesions in 60%, typical, umbilicated, molluscum contagiosum-like
- Fungemia in 50%

Genus: Penicillium
Species: marneffei
Disease(s): Penicilliosis marneffei
Image Type: MacroInfection
Title: Cutaneous lesions
Typical papules often with a central necrotic umbilication "Molluscum contagiosum" like lesions caused by *P. marneffei* in an HIV+ patient. (Courtesy Dr. P. Jones, Sydney, N.S.W.).

Cutaneous lesions resulted from the dissemination of the fungus from the lungs. The patient’s underlying disease is AIDS.
"Molluscum contagiosum" lesions caused by *P. marneffei* in the buccal cavity.

"Molluscum contagiosum" lesions caused by *P. marneffei* below the eye and on the cornea.

**Penicillinosis marneffei**

**Diagnosis**

Methenamine silver (GMS) stained tissue section showing numerous small yeast-like cells of *P. marneffei* that closely resemble those seen in Histoplasmosis.

*Penicillium marneffei* in splenic abscess. Transverse septa are noted.
**Penicillinosis marneffei**

**Diagnosis**

Culture of *P. marneffei* showing distinctive red diffusible pigment.

The mold resembles other penicillium species.

**Penicillinosis marneffei**

**Therapy**

Amphotericin B as induction treatment, followed by oral itraconazole or oral itraconazole only + HAART and oral itraconazole as secondary prophylaxis after treatment of penicilliosis.

The prognosis appeared satisfactory with early diagnosis and administration of appropriate antifungal therapy.
**Penicillinosis marneffei**

**Therapy**

Mycafungin enhances the efficacy of itraconazole or amphotericin B in vitro and might have a potential role in combination therapy. Immunocompromised patients who have been successfully treated should receive oral itraconazole as a maintenance therapy to prevent relapse.

**Imported systemic mycoses**

**Conclusions**

- Given the rarity of imported systemic mycoses, differential diagnosis may be extremely difficult.
- More awareness of these otherwise curable diseases could facilitate diagnosis.
- Early initiation of therapy could prevent considerable morbidity and mortality.
Thank you!
See you in Greece for the 4th Meeting of Trends in Medical Mycology 2009!!!