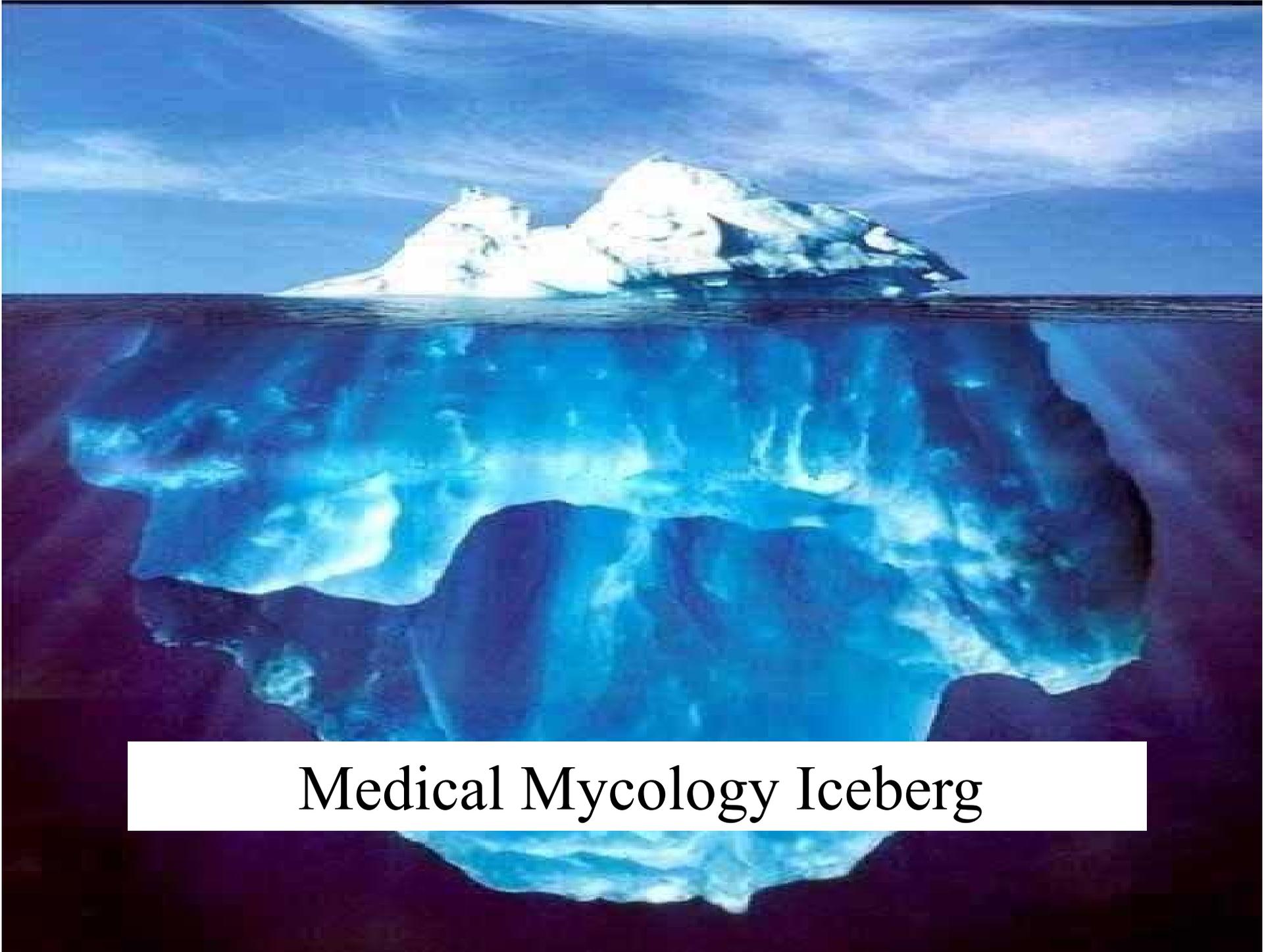


Opportunistic Mycoses

Ordinary fungi causing extraordinary
disease

Opportunistic Mycoses

Infections due to fungi of low virulence in patients who are immunologically compromised



Medical Mycology Iceberg

PATHOGENIC FUNGI

- **NORMAL HOST**

- Systemic pathogens - 25 species
- Cutaneous pathogens - 33 species
- Subcutaneous pathogens - 10 species

- **IMMUNOCOMPROMISED HOST**

Opportunistic fungi - 300 species

Opportunistic Fungi

1. Saprophytic - from the environment
2. Endogenous – a commensal organism

Opportunistic Fungi

Include many species from:

A (Aspergillus)

To

Z (Zygomycetes)

MOST SERIOUS OPPORTUNISTIC INFECTIONS

- CANDIDA SPECIES
- ASPERGILLUS SPECIES
- MUCOR SPECIES (ZYGOMYCES)

Upward Trend In Opportunistic Mycoses

1. Increased clinical awareness
2. Improved clinical diagnostic tools
3. Improved laboratory diagnostic techniques
4. An increase in susceptible hosts.
5. More invasive diagnostic and therapeutic procedures

Must distinguish between

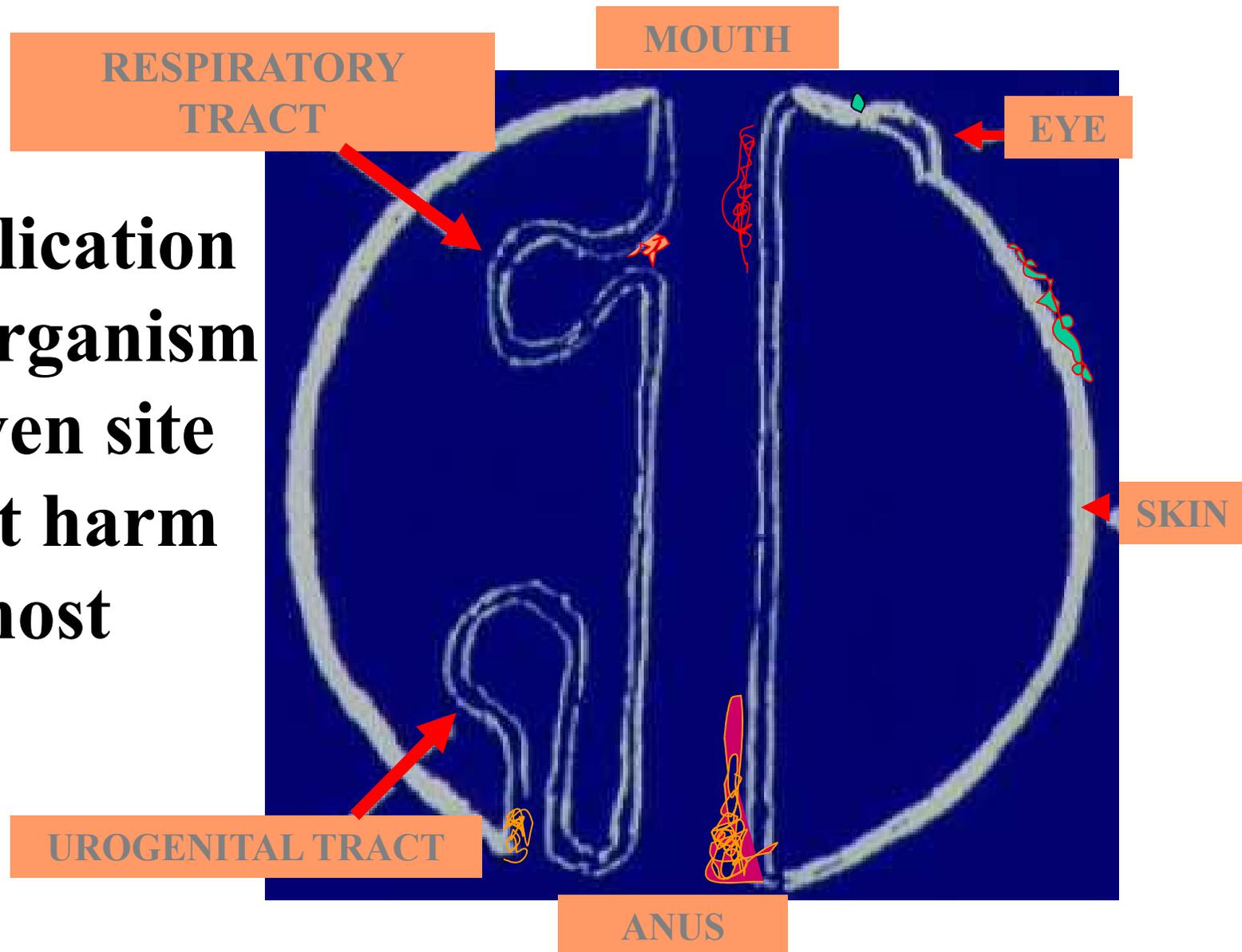
1. Transient fungemia
2. Colonization
3. Infection

Transient fungemia

The fortuitous isolation of a commensal or environmental organism

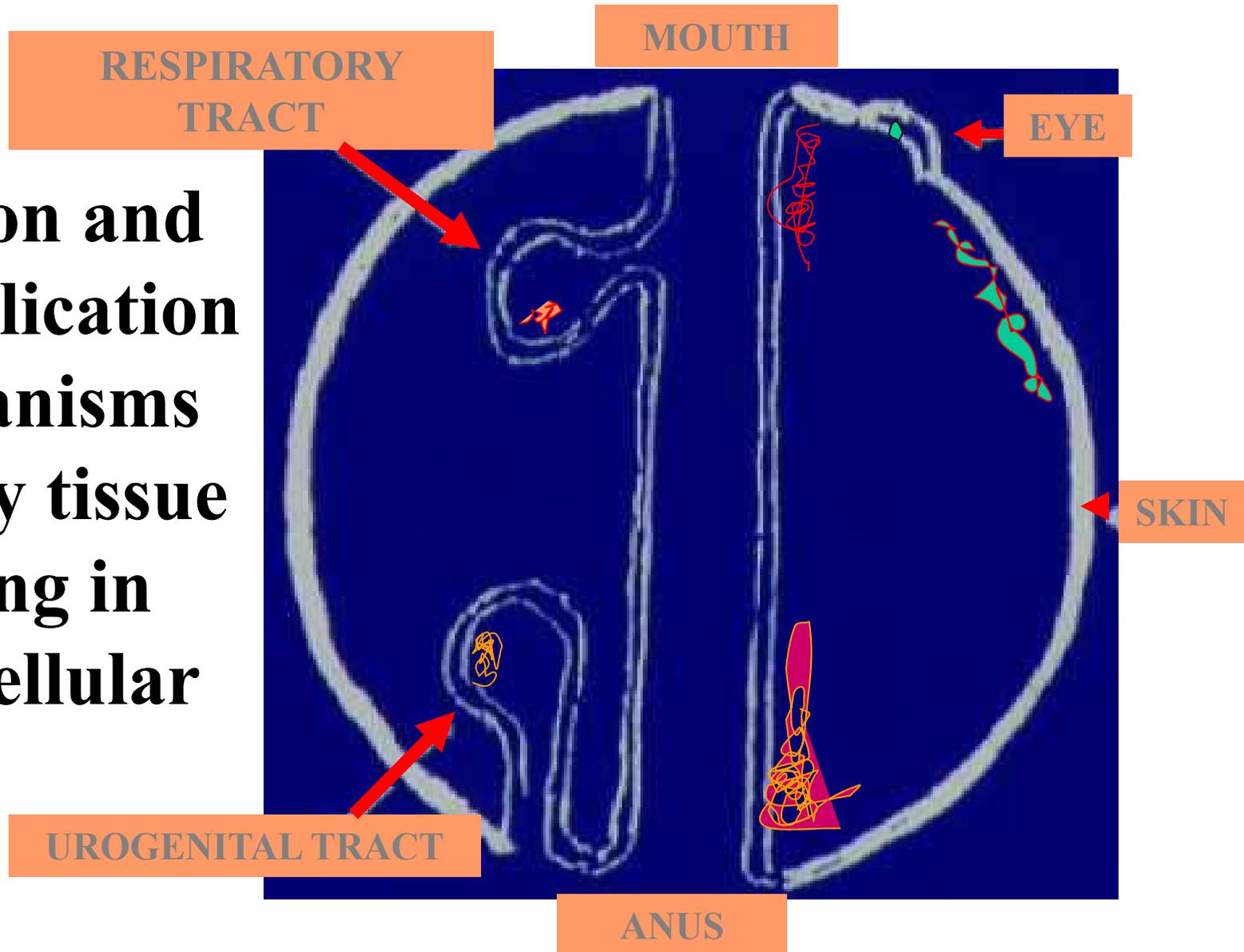
COLONIZATION

**Multiplication
of an organism
at a given site
without harm
to the host**



INFECTION

Invasion and multiplication of organisms in body tissue resulting in local cellular injury.



Predisposing Factors

Malignancies

- Leukemias
- Lymphomas
- Hodgkins Disease

Predisposing Factors

Drug therapies

- Anti-neoplastics
- Steroids
- Immunosuppressive drugs

Predisposing Factors

Antibiotics

Over-use or inappropriate use of antibiotics alter the normal flora allowing fungal overgrowth

Predisposing Factors

Therapeutic procedures

- Solid organ or bone marrow transplant
- Open heart surgery
- Indwelling catheters
- Artificial heart valves
- Radiation therapy

Predisposing Factors

Other Factors

- Severe burns
- Diabetes
- Tuberculosis
- IV Drug use

BIOFILMS

A POLYSACCHARIDE SLIME
WHICH IS A MICROCOLONY OF
ORGANISMS CONTAINING
CHANNELS TO BRING IN
NUTRIENTS AND CARRY OFF
WASTE



Diagnosis of opportunistic infections requires a high index of suspicion

1. Atypical signs or symptoms
2. Unusual organ affinity
3. Outside the endemic area
4. Unusual Histopathology
5. Etiologic agent may be a “saprophyte”
6. Serological response may be suppressed

CLINICAL PRESENTATION

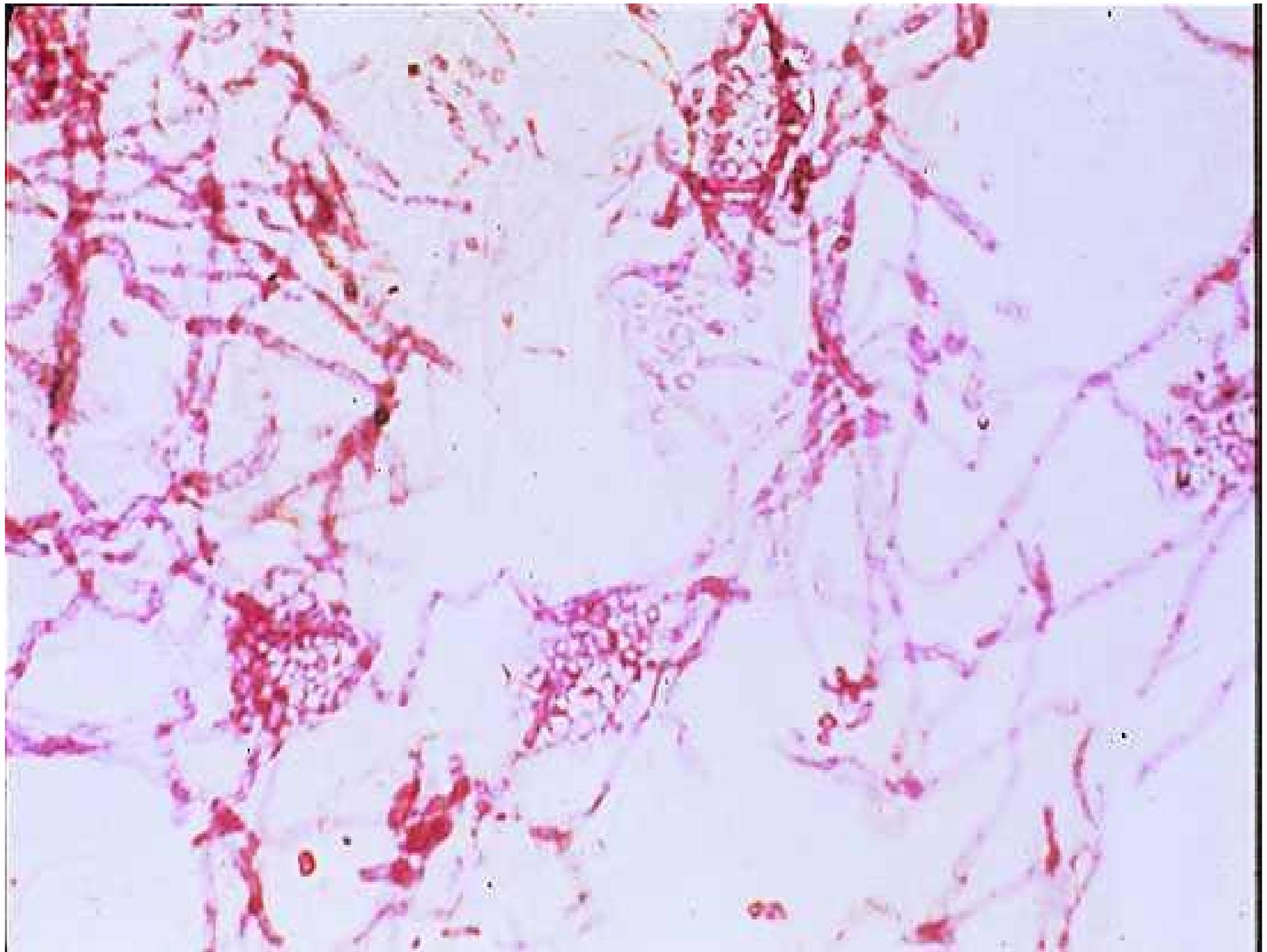
1. *Atypical Signs and Symptoms*
2. Unusual Organ Affinity
3. Outside Endemic Area
4. Unusual histopathology
5. Unusual Pathogens
6. Depressed serological response

NORMAL PATIENT

Malassezia furfur

Tinea versicolor
(mild disease)





COMPROMISED PATIENTS

Malassezia furfur can cause disseminated infection-----Particularly in patients receiving hyperalimentation.

CLINICAL PRESENTATION

1. Atypical Signs and Symptoms
2. Unusual Organ Affinity
3. Outside Endemic Area
4. Unusual histopathology
5. Unusual Pathogens
6. Depressed serological response

Candida species

Endogenous

Normal Flora

The population of microorganisms that may be found residing in or on the human body without causing disease.



Candida albicans

NORMAL HOST: Oral candidiasis

COMPROMISED: Esophageal
candidiasis

IMMUNOCOMPROMISED PATIENTS

**CAN DEVELOP HEPATIC
CANDIDIASIS**



Candida species

In the previous lecture I only mentioned Candida albicans. There are several Candida species that infect the compromised host.

Candida species

- *C. glabrata*
- *C. krusei*
- *C. torulopsis*
- *C. parapsilosis*
- *C. lusitaniae*
- *C. dubliniensis*

Cryptococcosis

A sub-acute or chronic infection which may affect the lungs or skin but most commonly manifests as a meningitis

Ecological Niche

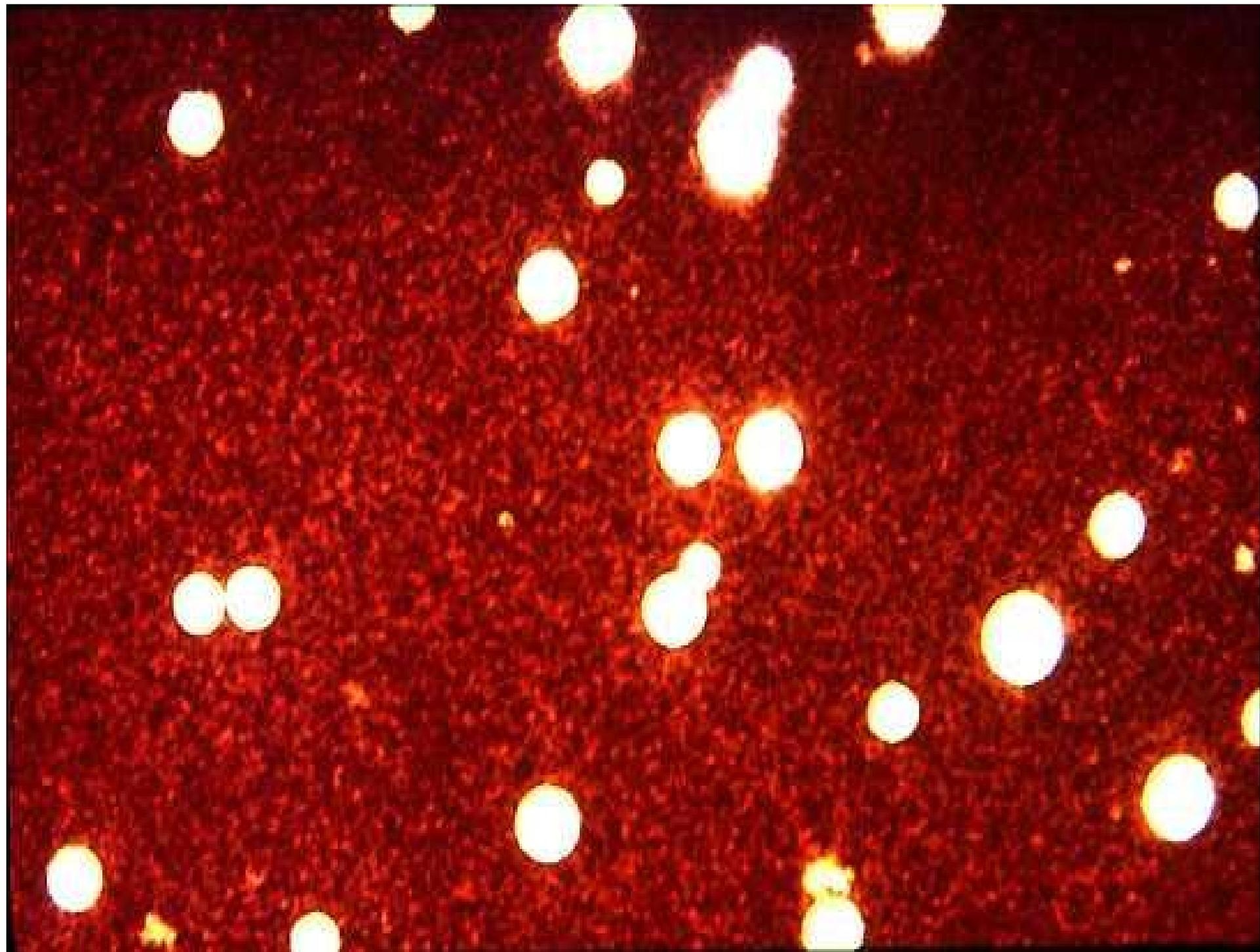
Cryptococcus neoformans

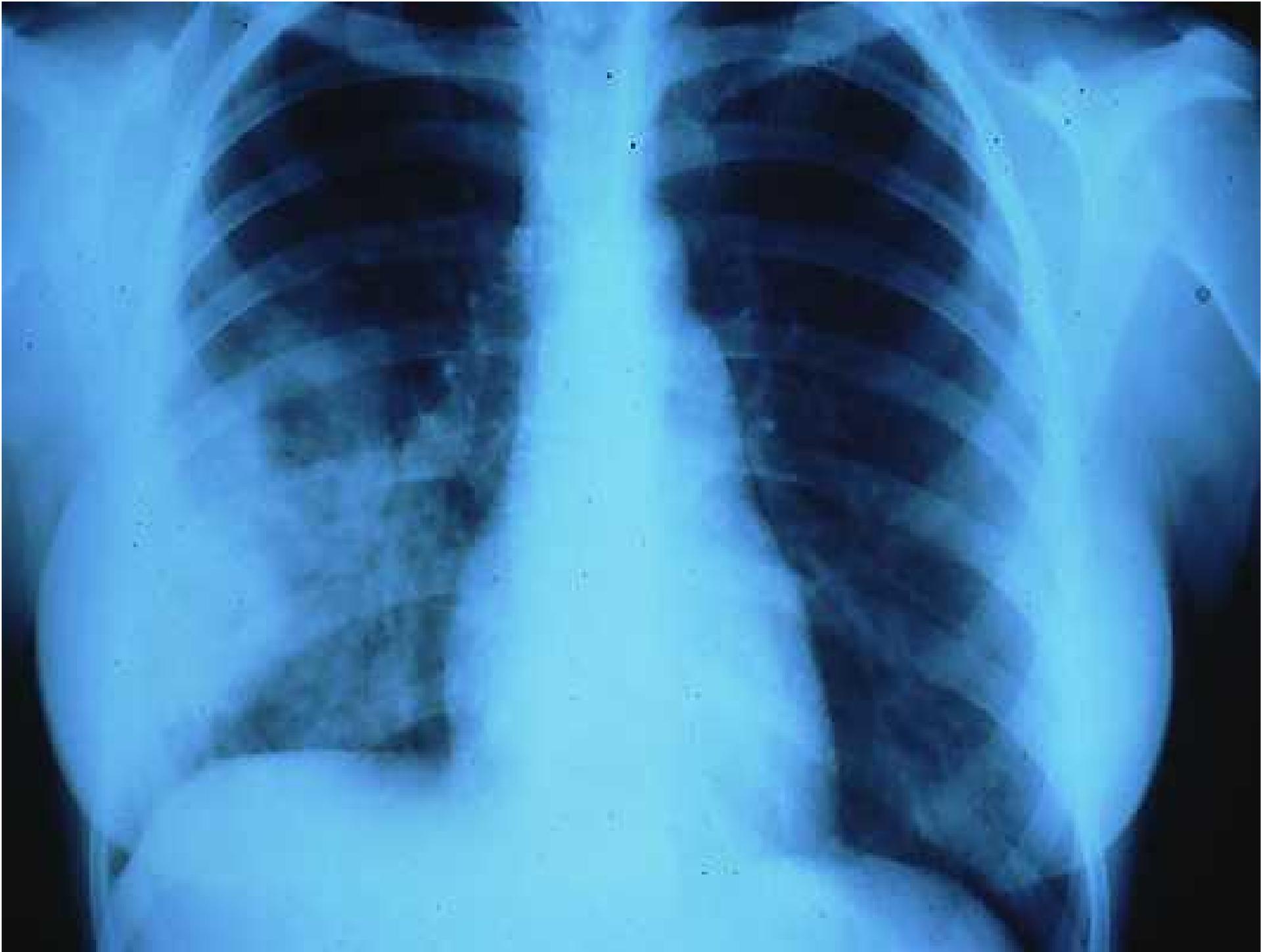
- pigeon droppings
- Chicken droppings

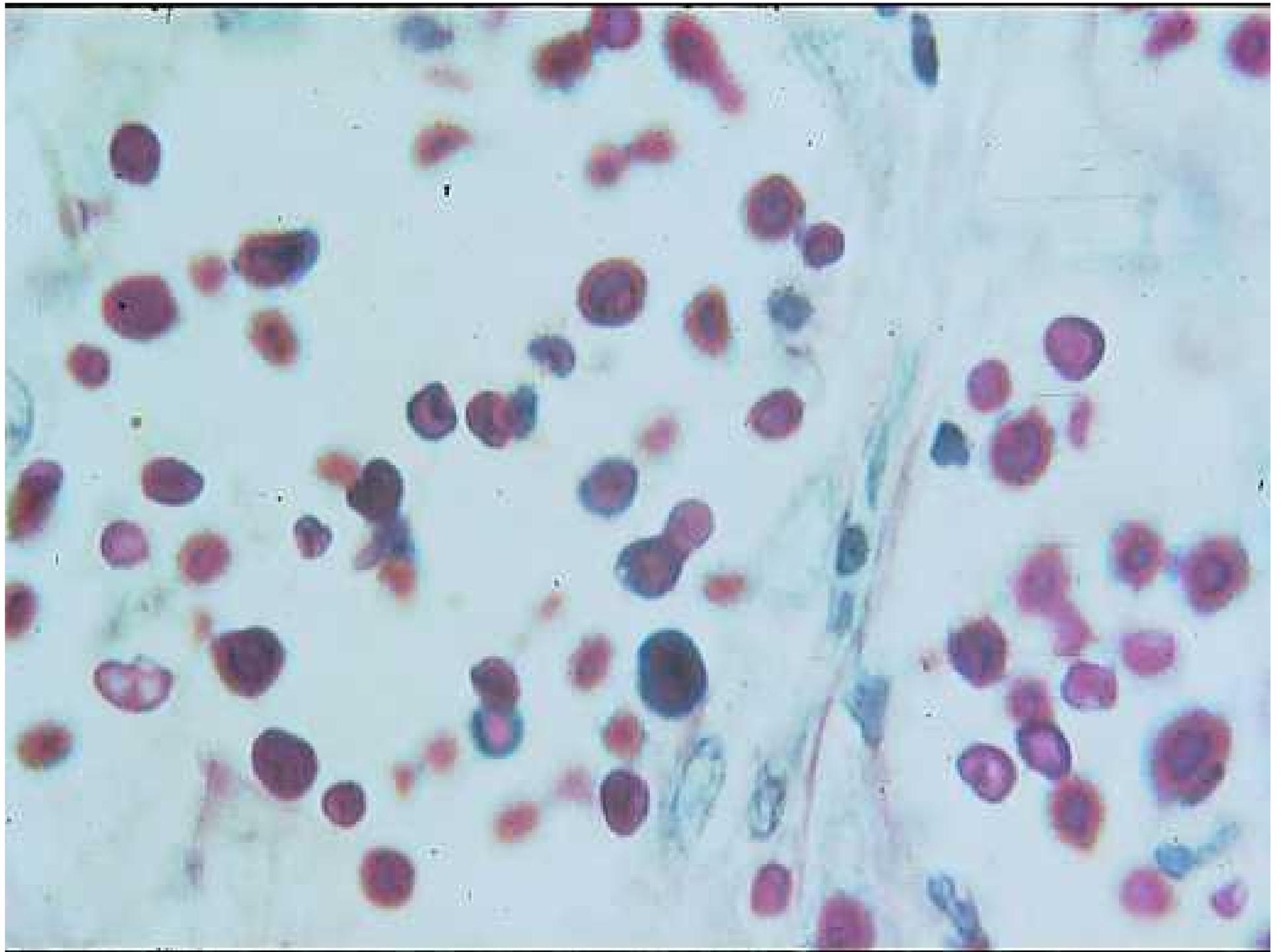
Cryptococcus neoformans
PORTAL OF ENTRY

- INHALATION
- INOCULATION

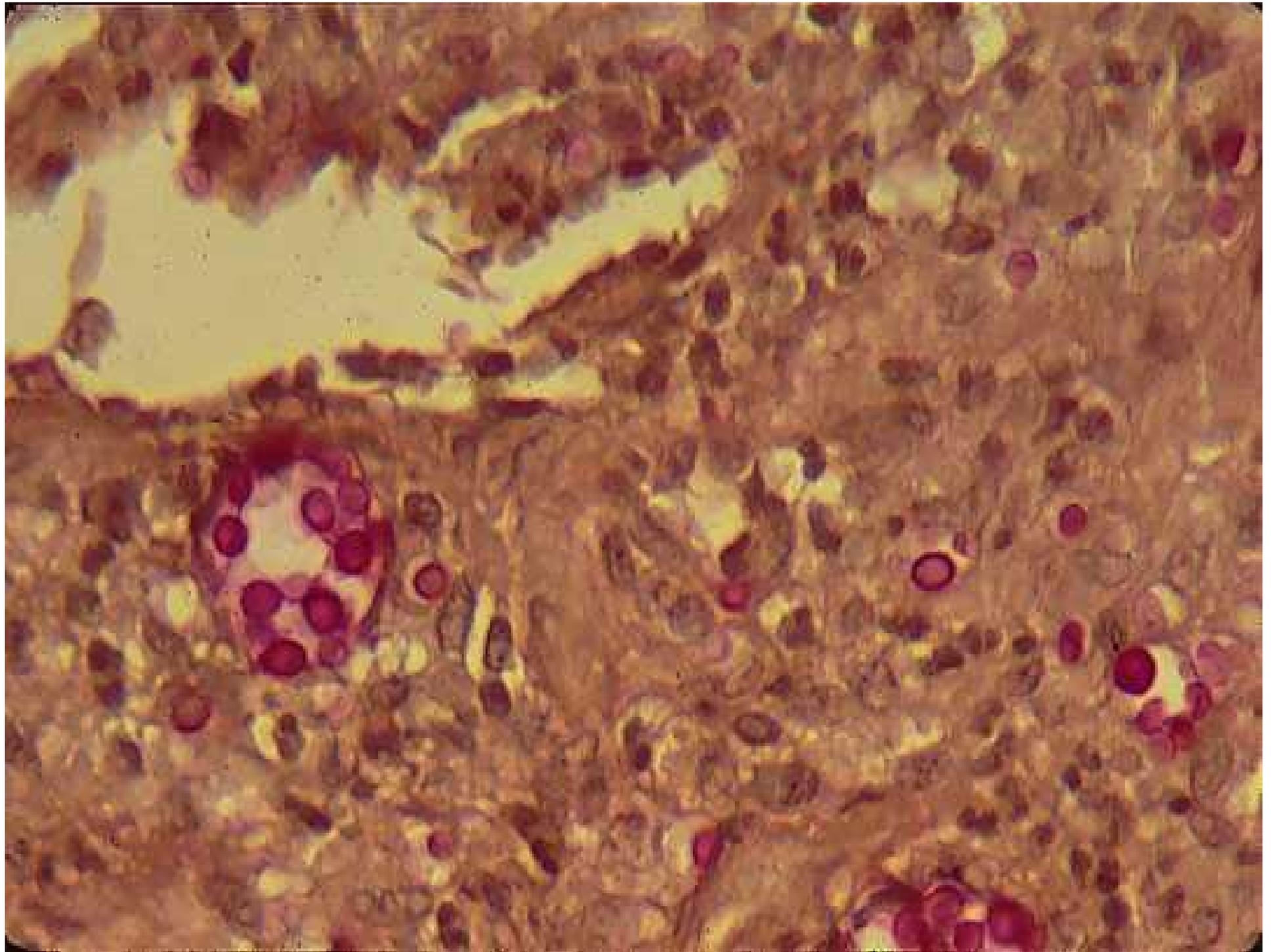


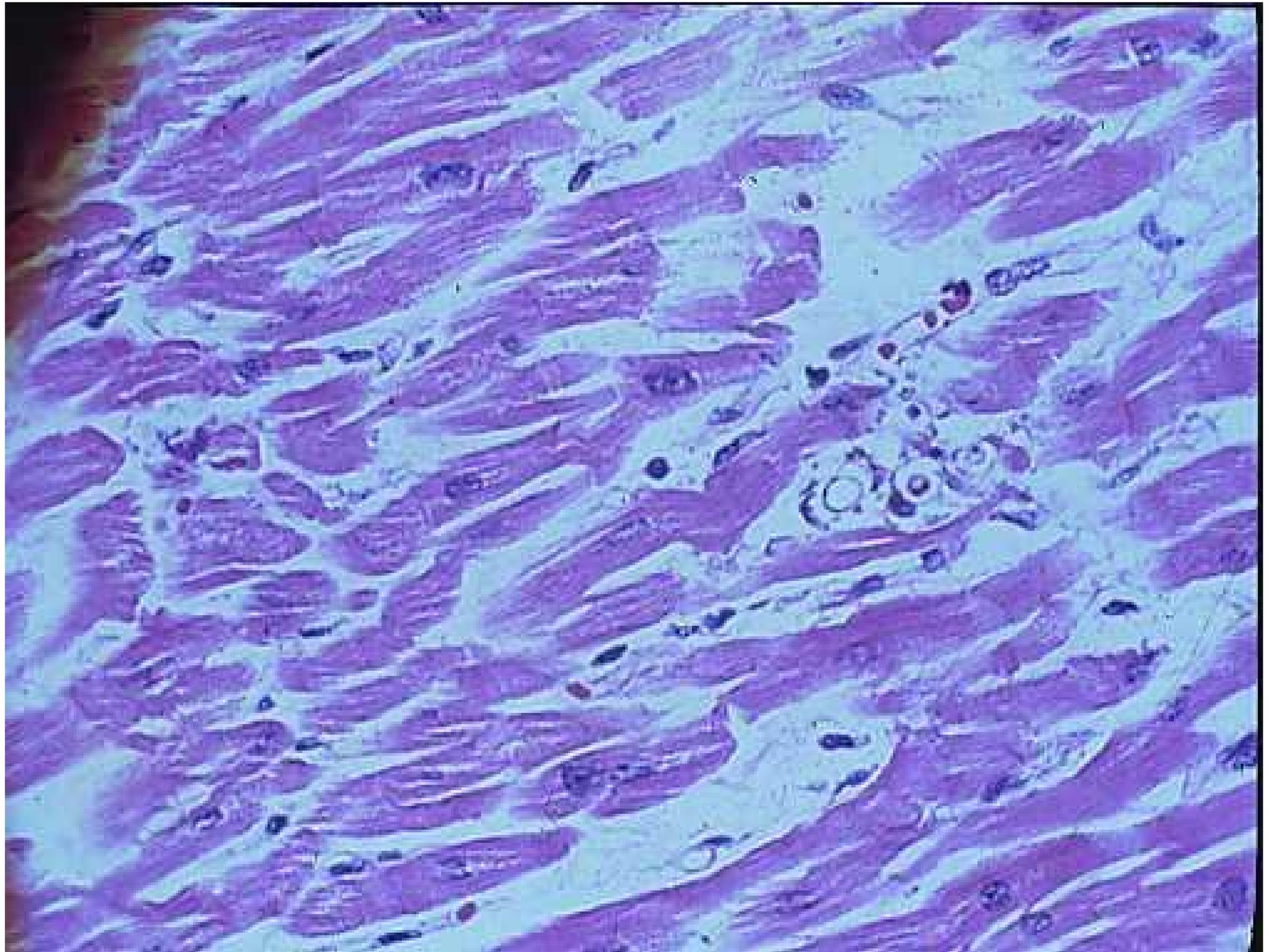












Cryptococcosis

In the Compromised patient:

- Amphotericin B
- 5 FC

Then Fluconazole the remainder of their life.

Fluconazole penetrates the CSF

Cryptococcosis

Relapse Rate

- Non AIDS patient: 15 - 20 %
- AIDS patient: 50 %

With relapse there is a 60 % mortality

cryptococcosis

Mortality

- Without treatment - 100 %
- With treatment - 20 %

SPOROTRICHOSIS

Primarily a disease of the cutaneous tissue and lymph nodes. Recently, pulmonary disease.

PORTALS OF ENTRY

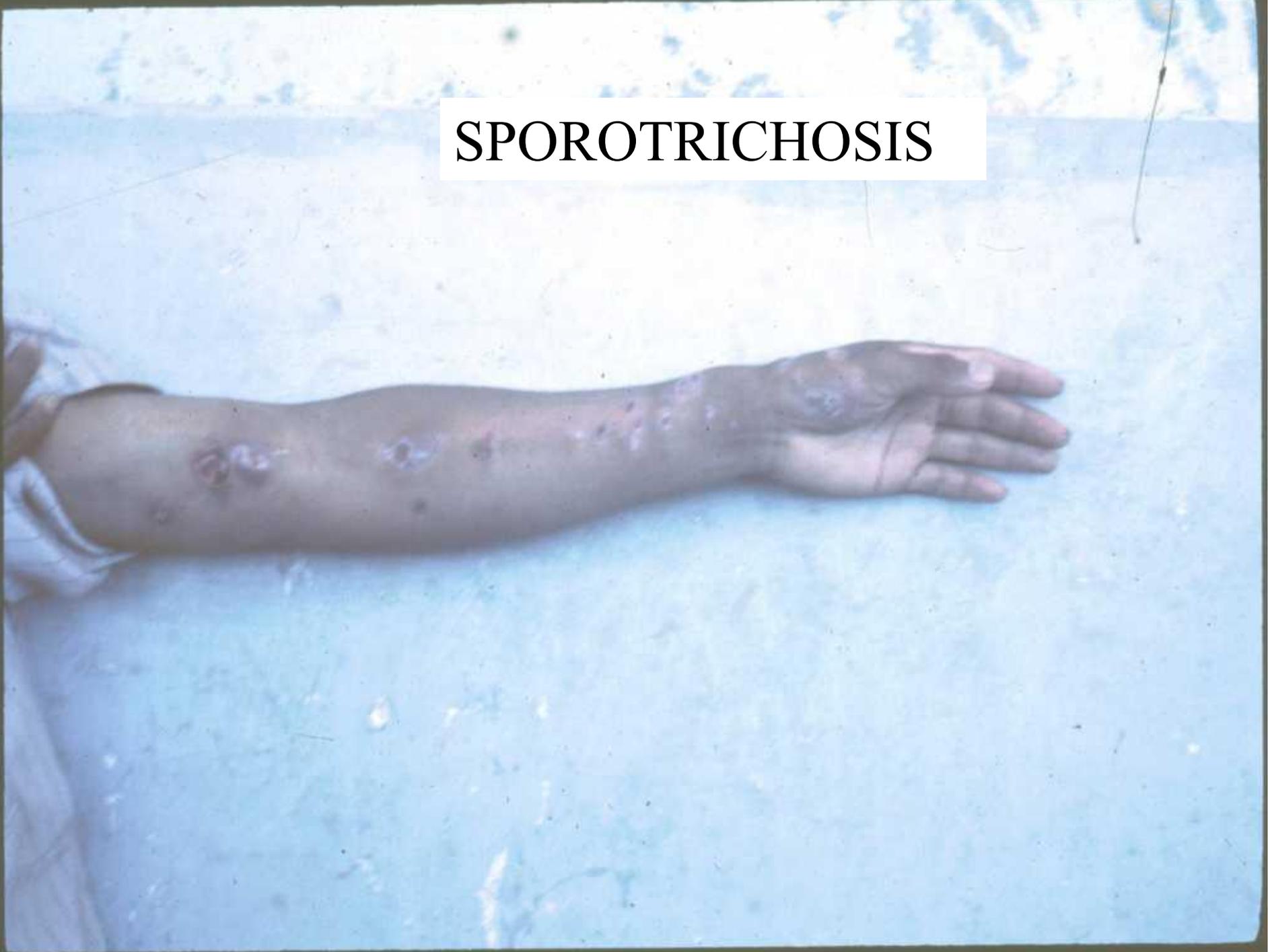
- Inhalation
- Inoculation

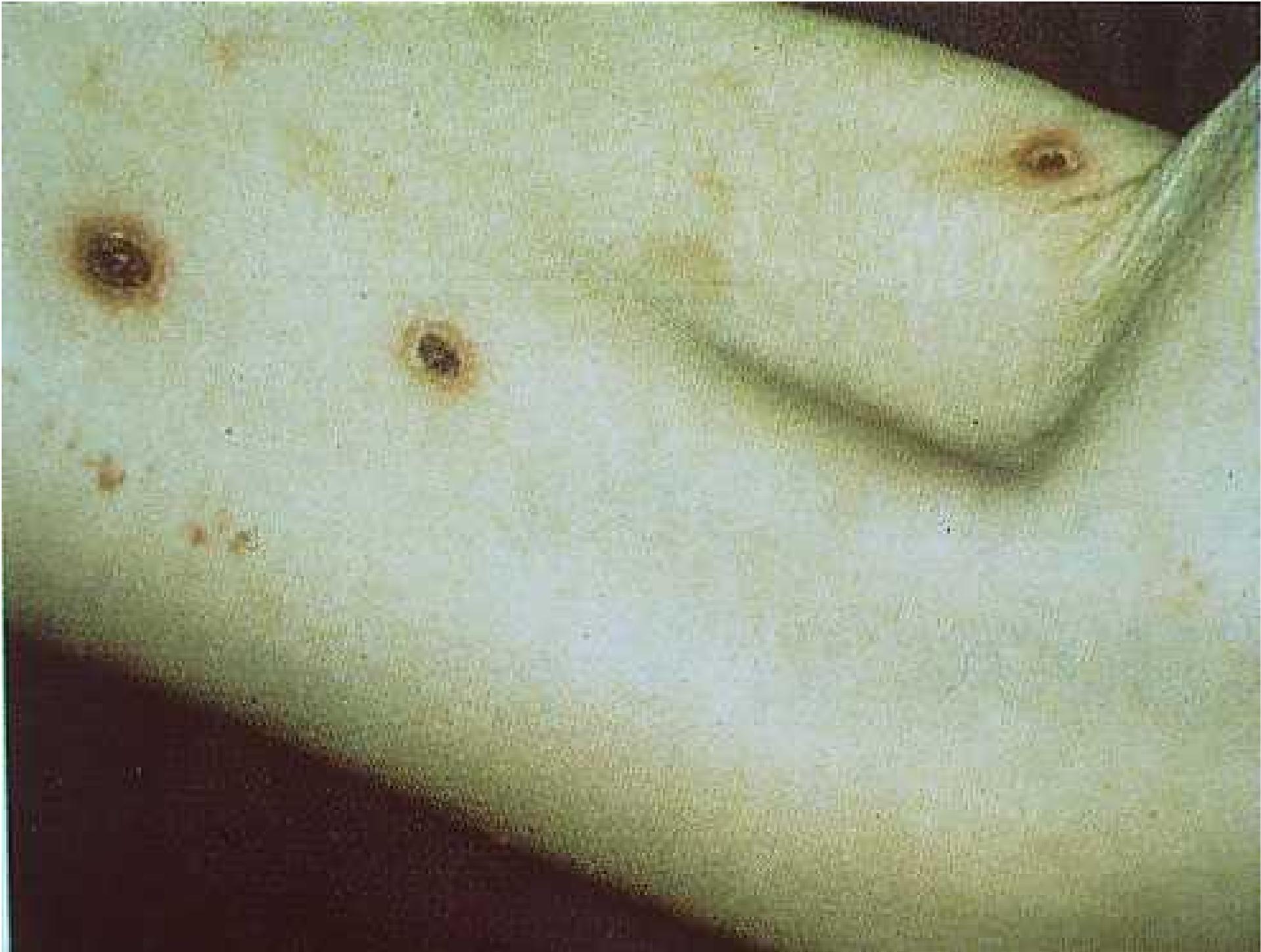


ECOLOGICAL ASSOCIATIONS

- Rose thorns
- Sphagnum moss
- Timbers
- Soil

SPOROTRICHOSIS





Aspergillus species

HIGH NUMBER X LOW VIRULENCE = NO DISEASE
NORMAL HOST

Aspergillus species

LOW NUMBER X LOW VIRULENCE = INFECTION
COMPROMISED HOST



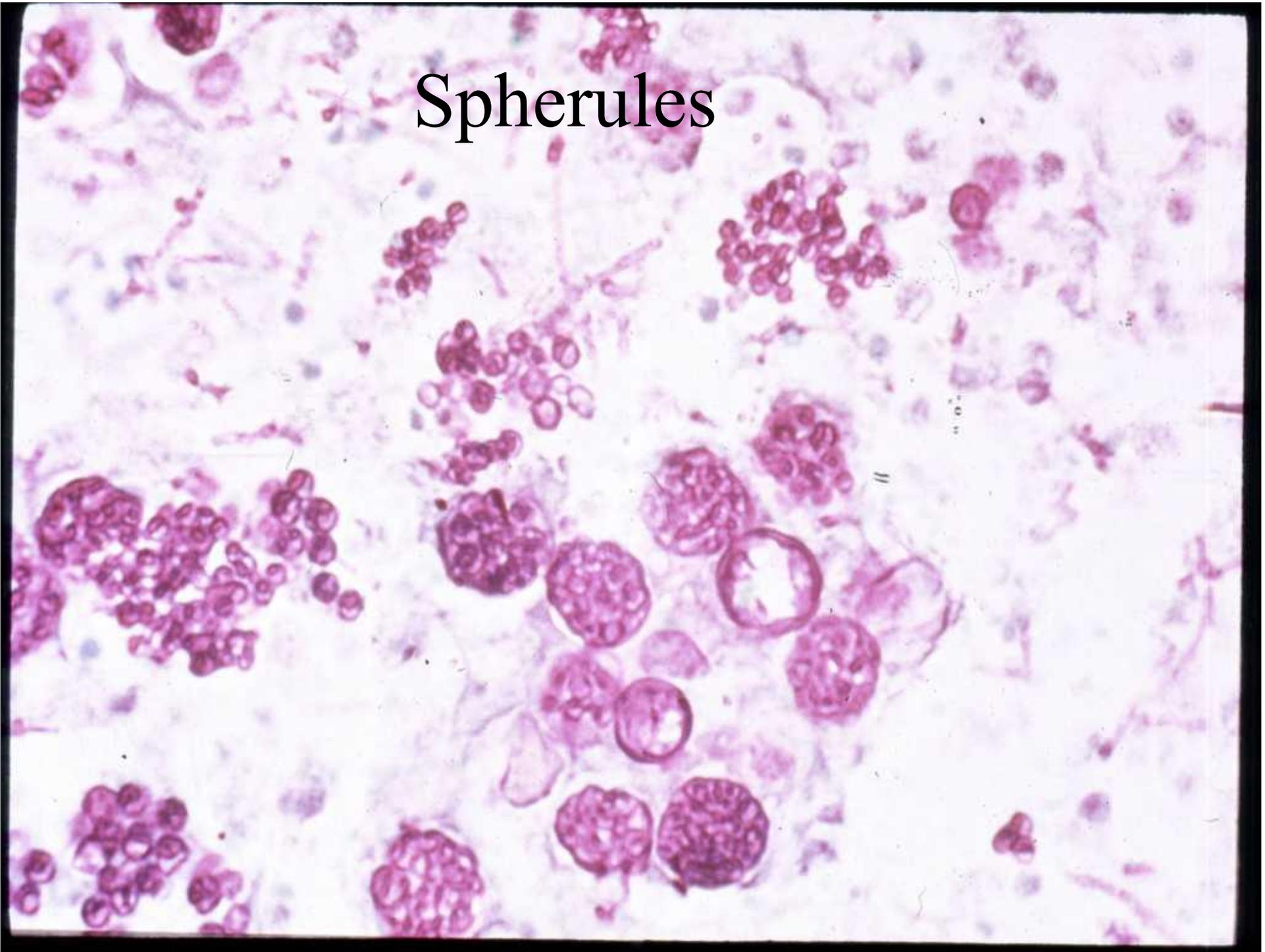
CLINICAL PRESENTATION

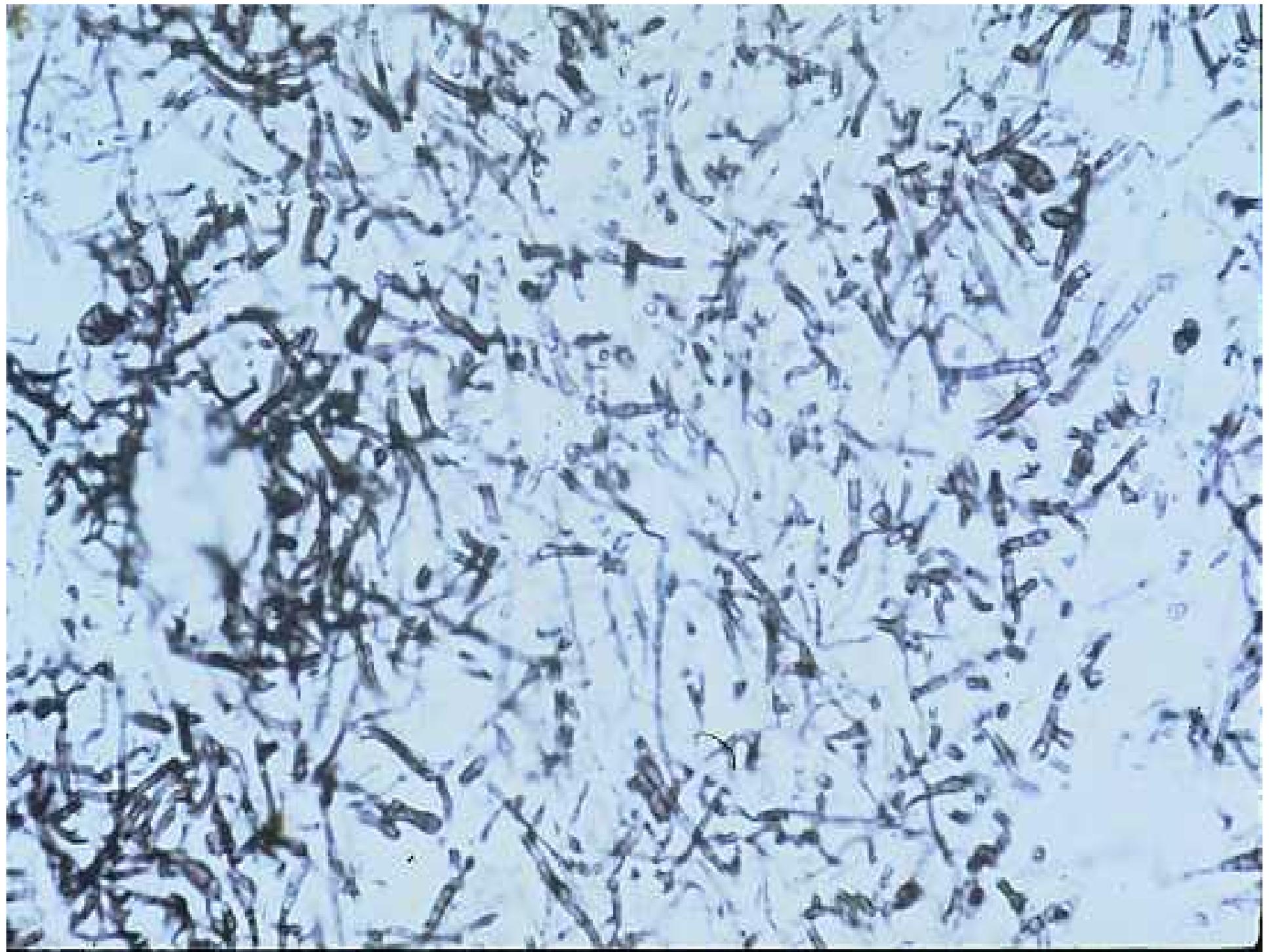
1. Atypical Signs and Symptoms
2. Unusual Organ Affinity
3. Outside Endemic Area
4. Unusual histopathology
5. Unusual Pathogens
6. Depressed serological response

AIDS Patient

- Pneumocystis pneumonia
- Disseminated coccidioidomycosis
(not pulmonary)
- Mycelial forms in abscesses
(not spherules)
- Outside the endemic area
(St. Louis, MO)

Spherules





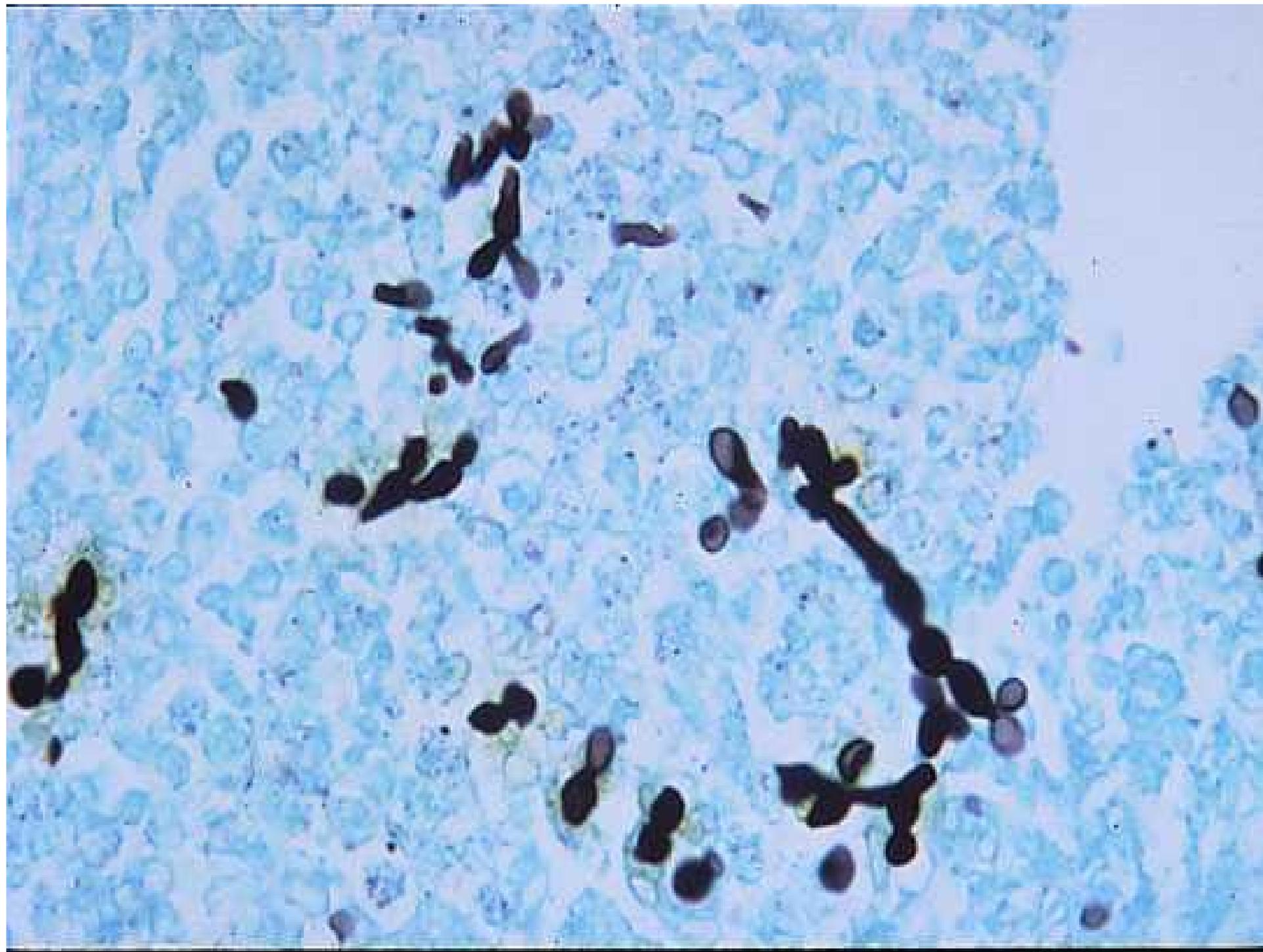
HISTOPLASMOSIS IN AIDS PATIENTS

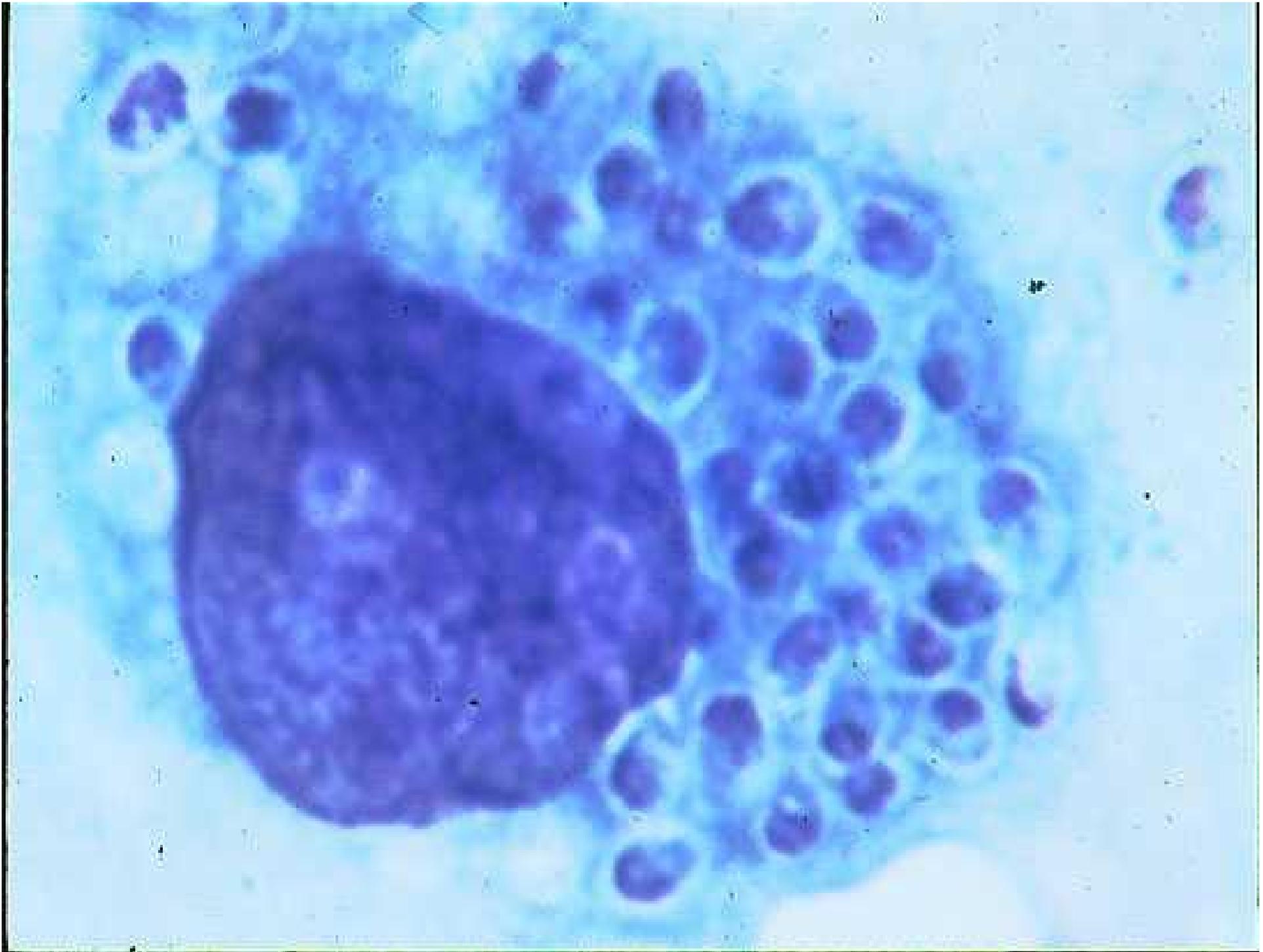
- ALL CASES ARE DISSEMINATED
- RELAPSES ARE GREATER THAN 50 %
- RAPIDLY FATAL IN 10 %

AIDS Patients

- **Disseminated histoplasmosis**
(not pulmonary disease)
- **New York City**
(outside the endemic region)







CLINICAL PRESENTATION

1. Atypical Signs and Symptoms
2. Unusual Organ Affinity
3. Outside Endemic Area
4. Unusual Histopathology
5. Unusual Pathogens
6. Depressed serological response

INFLAMMATORY REACTION

- NORMAL HOST
 - PYOGENIC
 - GRANULOMATOUS
- IMMUNODEFICIENT HOST
 - NECROTIC

CLINICAL PRESENTATION

1. Atypical Signs and Symptoms
2. Unusual Organ Affinity
3. Outside Endemic Area
4. Unusual histopathology
5. Unusual Pathogens
6. Depressed serological response

Opportunistic Fungi

Include many species from:

A (Aspergillus)

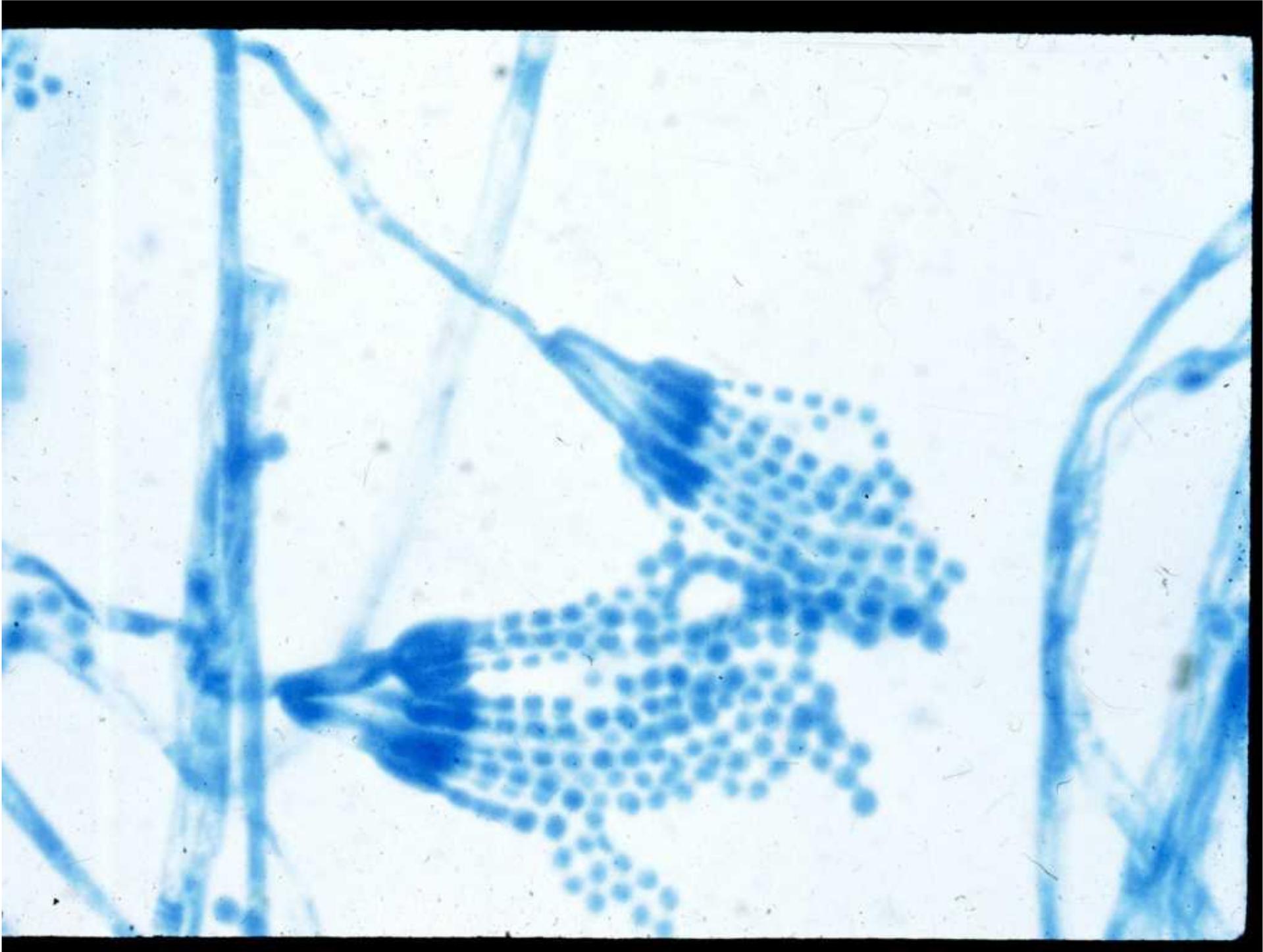
To

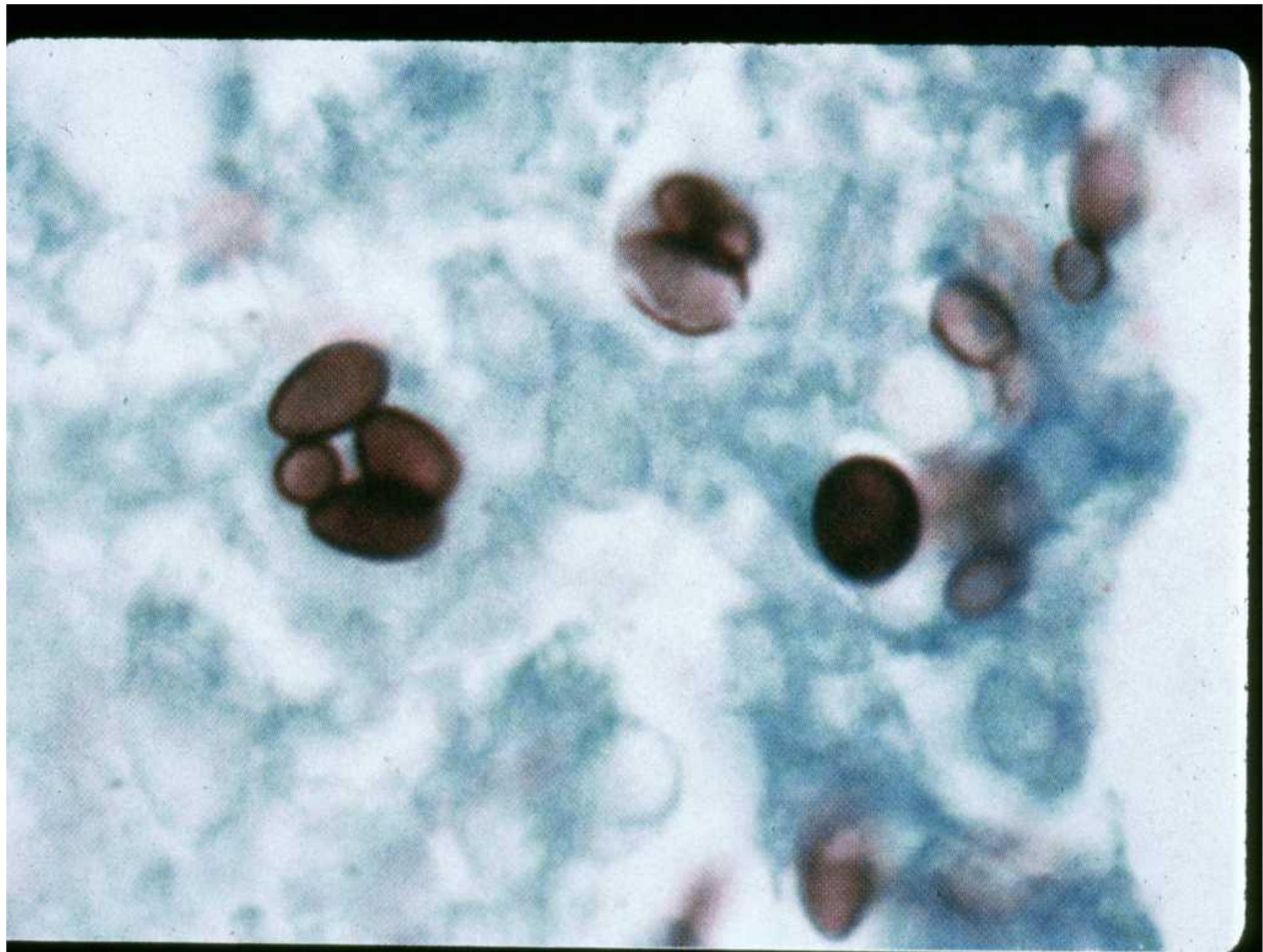
Z (Zygomycetes)

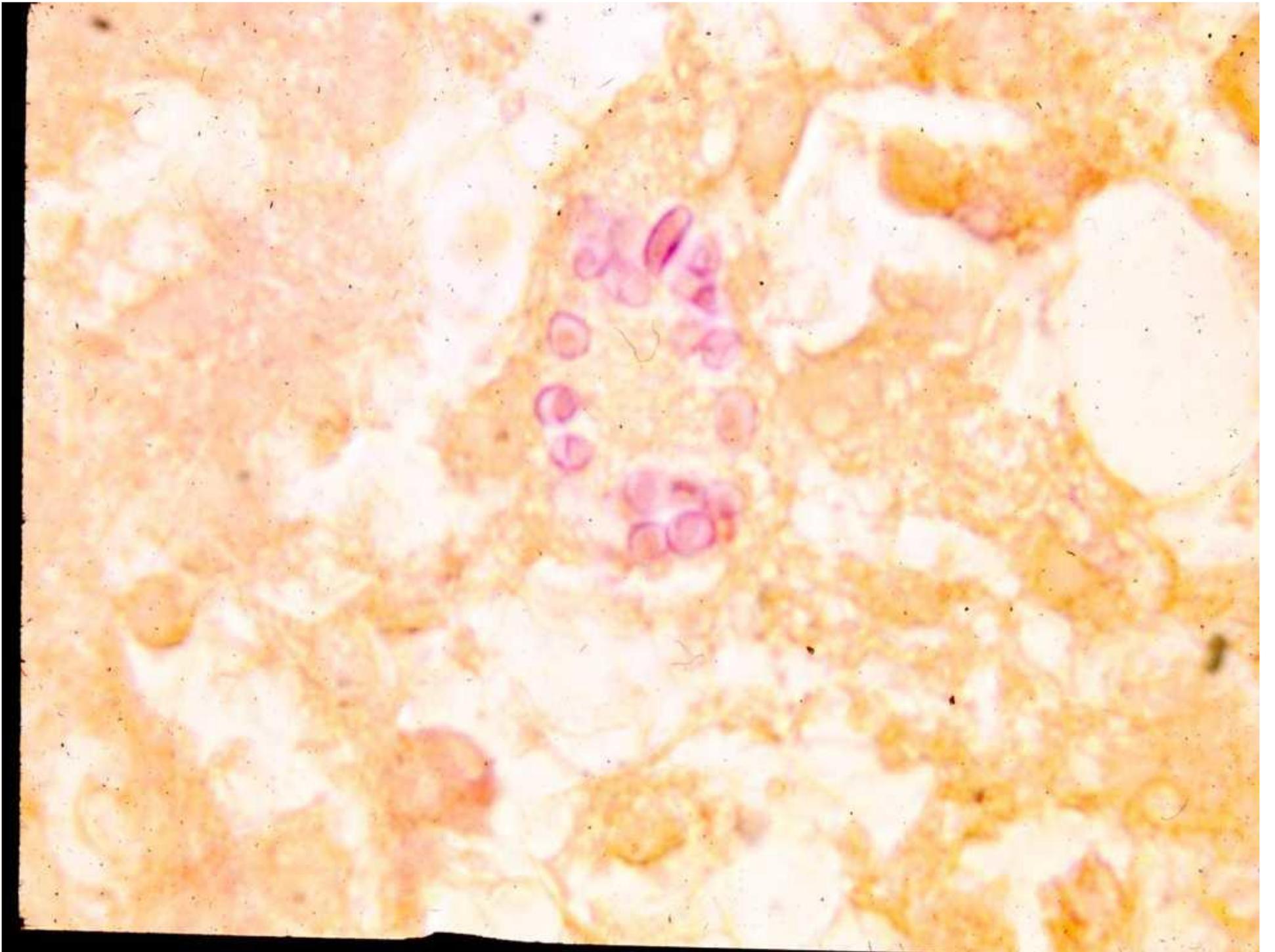
Penicillium marneffeii

1. Usually not a pathogen
2. The only dimorphic penicillium
3. Produces a red pigment
4. Endemic in the Far East



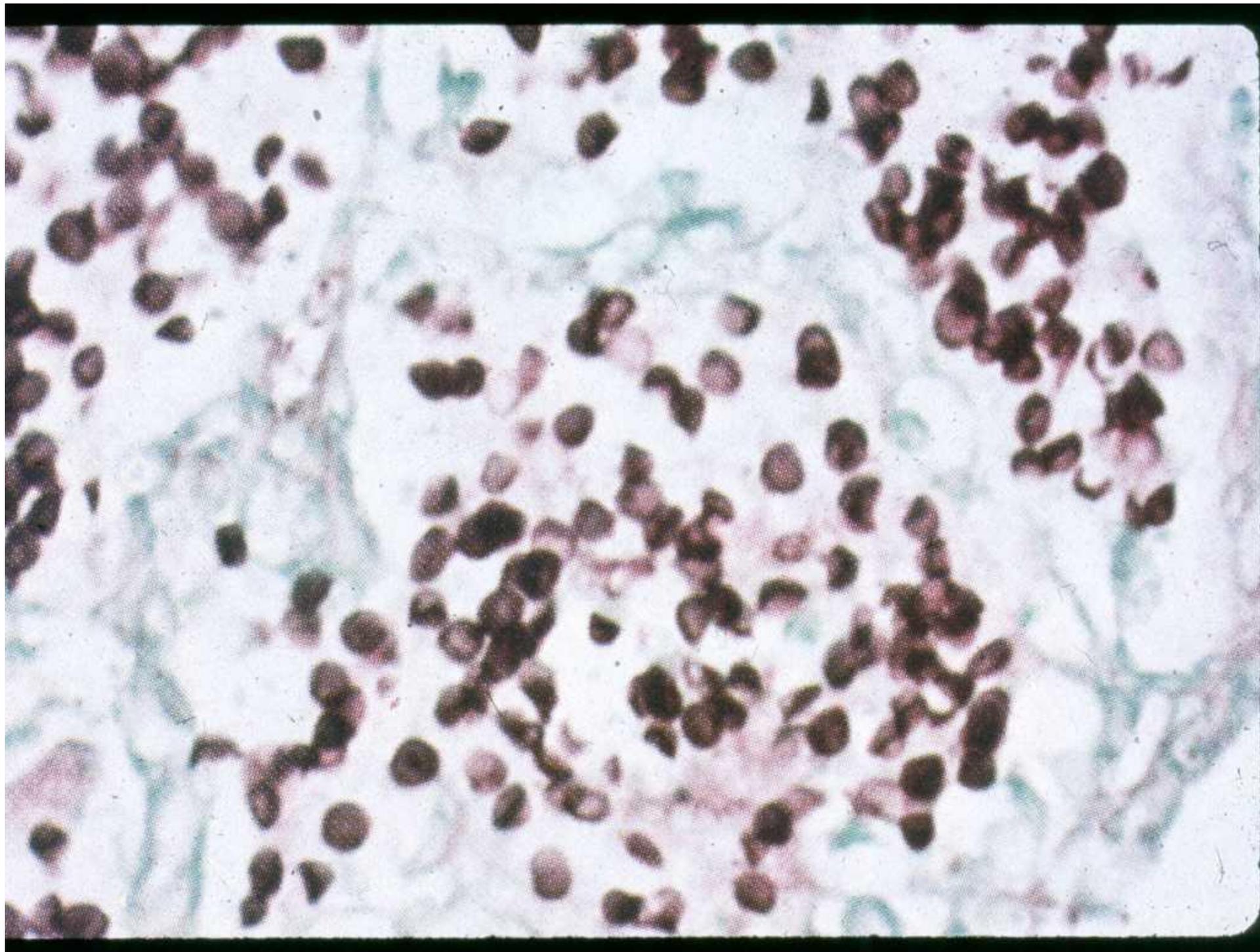






Pneumocystis jiroveci (P. carinii)

Recently confirmed as a member of Kingdom Fungi. Formerly thought to be a protozoan.



Cryptococcus neoformans

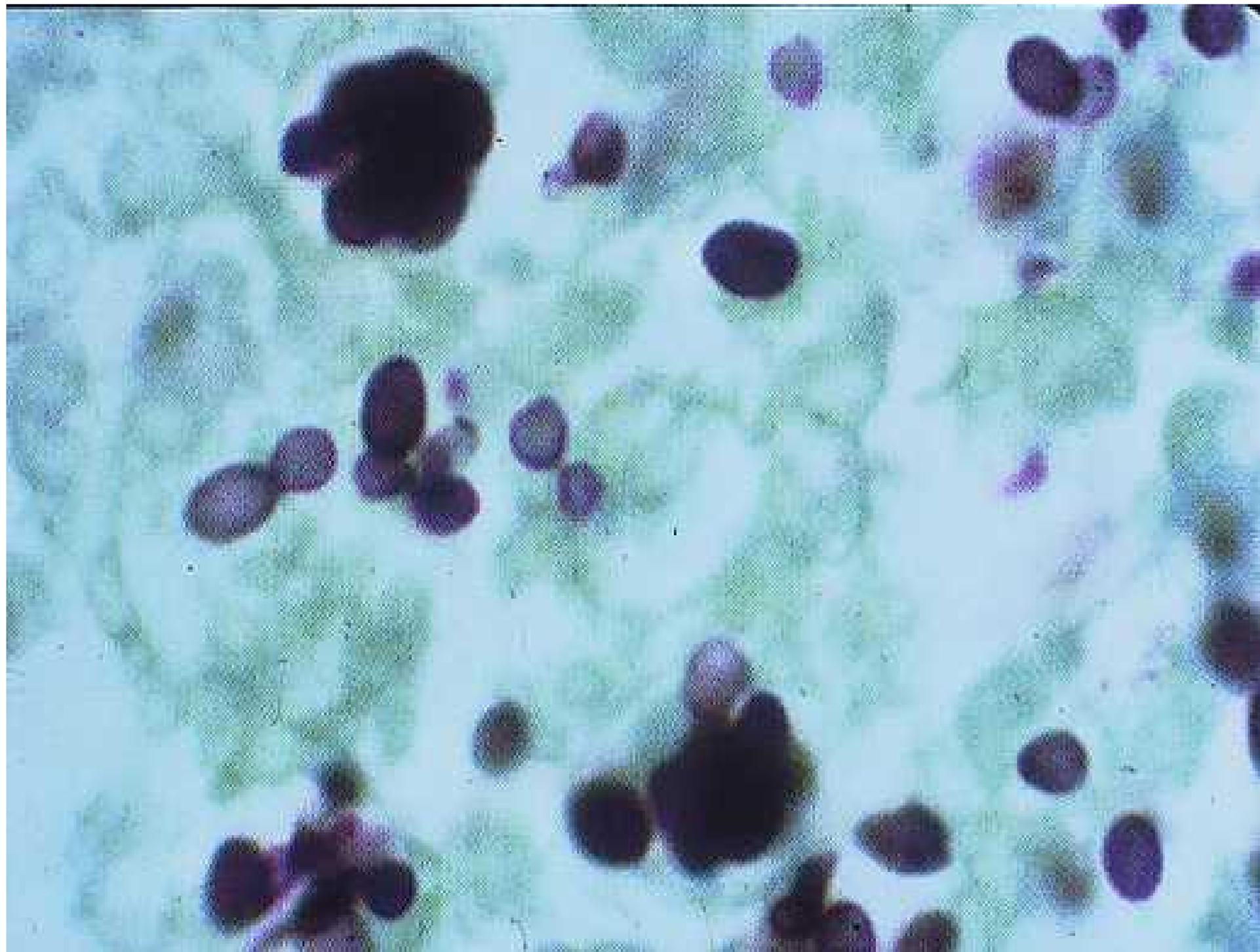
- Diabetes mellitus
- Tuberculosis
- Lymphoma
- Hodgkin's disease
- Corticosteroid therapy
- Immunosuppression

Candida albicans

- Prolonged antibiotic therapy
- Prolonged intravenous therapy
- Prolonged urinary catheters
- Corticosteroid therapy
- Diabetes mellitus
- Hyperalimentation
- Immunosuppression

Torulopsis (Candida) glabrata

- Cytotoxic drugs
- Immunosuppression
- Diabetes mellitus
- Hyperalimentation
- Intravenous catheters



Mucormycetes

- Diabetes mellitus
- Leukemias
- Corticosteroid therapy
- Intravenous therapy
- Severe burns

Aspergillus species

- Leukemias
- Corticosteroid therapy
- Tuberculosis
- Immunosuppression
- Intravenous drug abuse

IMPROVING TREATMENT

1. New Drugs
2. New therapeutic regimen
3. Aggressive therapy
4. Conjunctive therapy

IMPROVING TREATMENT

New Drugs

Lipid Amphotericin B

Third generation azoles

(Posaconazole, Voriconazole)

New classes of antifungal agents

(Echinocandins)

IMPROVING TREATMENT

CONJUNJUNCTIVE THERAPY

Antifungal agent plus a recombinant monoclonal antibody.

IMPROVING TREATMENT

CONJUNCTIVE THERAPY FOR IMMUNOCOMPROMISED PATIENTS

The use of anti-fungal agents with
immunotherapy.

Immunotherapy

- Interferons
- Colony stimulating factors
- Interleukins