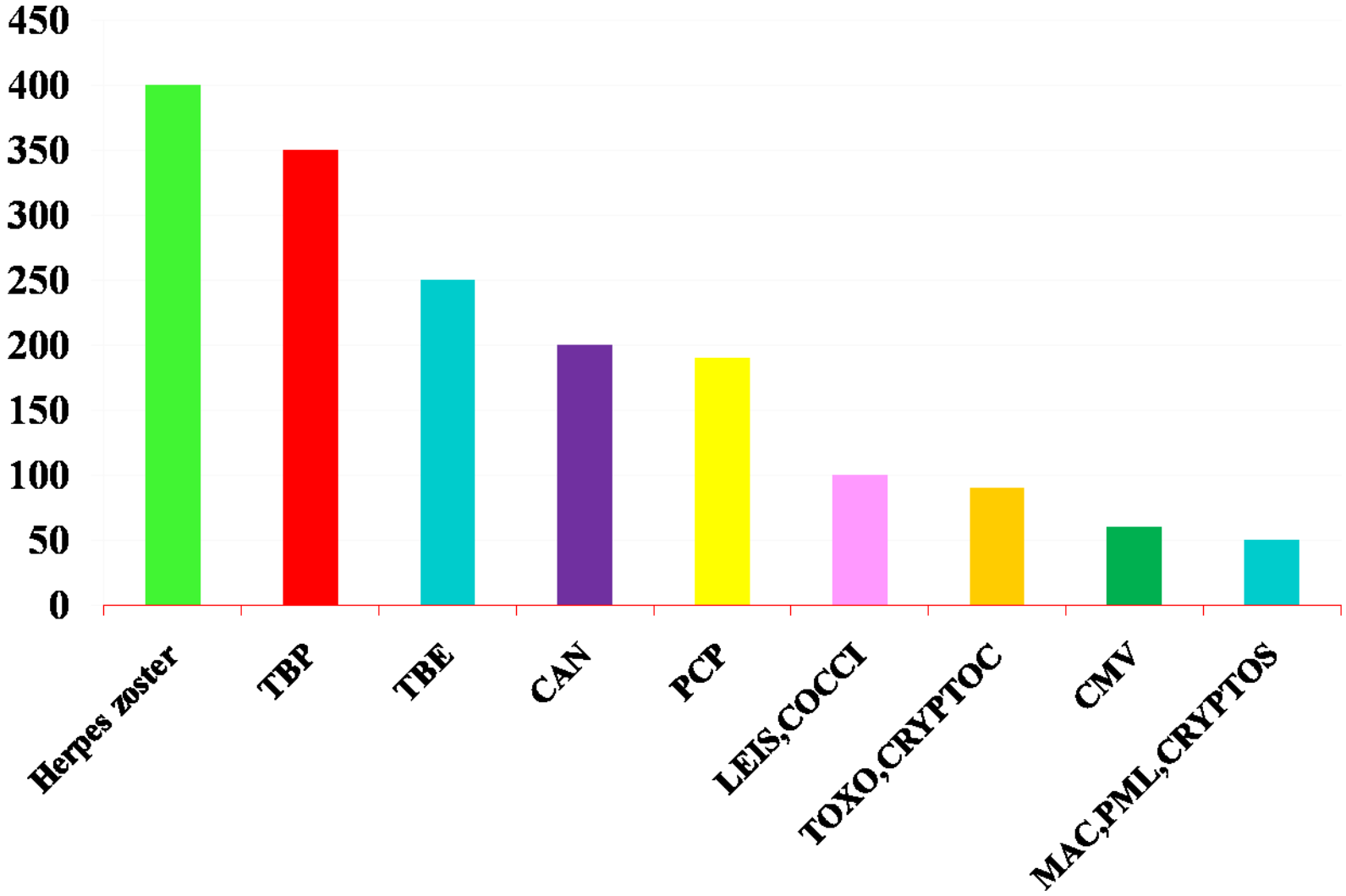
Opportunistic infections

Opportunistic infections

- **Decrease in number of CD4 lymphocytes** is condition for development of opportunistic infections
- Risk is started, when number of CD4 lymphocytes drops to number **500 of CD4 lymphocytes/mm^3**

CD4 count and opportunistic infection



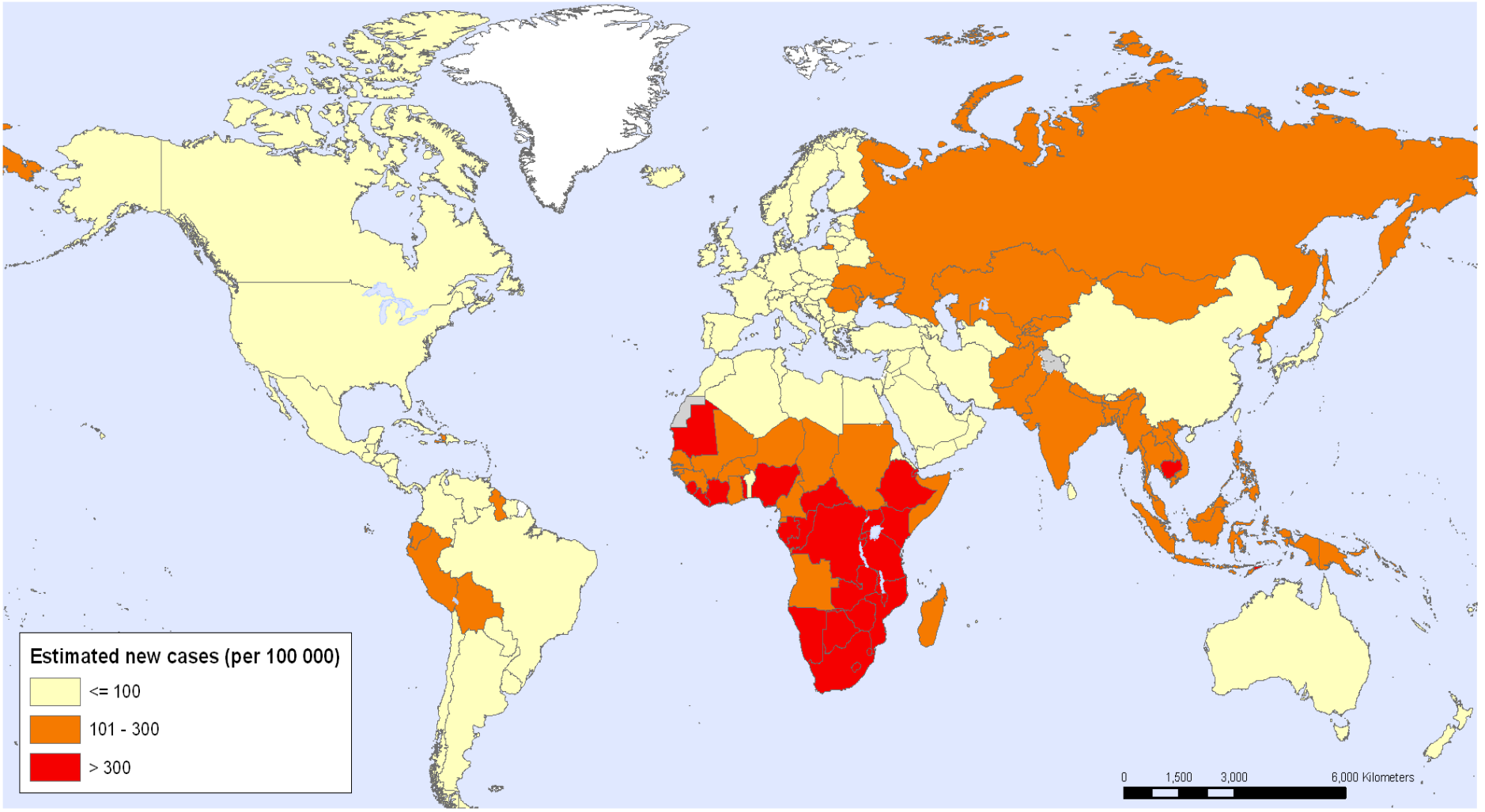
TUBERCULOSIS

- the most important
- the most common OI

Epidemiology

- **One-third** of the world´s population is infected with TB
- **HIV infection** has had **a big impact** in increasing the numbers of patients affected with disease caused by TB
- TB is **the most important** severe **opportunistic infection** among patients with HIV in developing countries

TB – estimated new cases (per 100 000)



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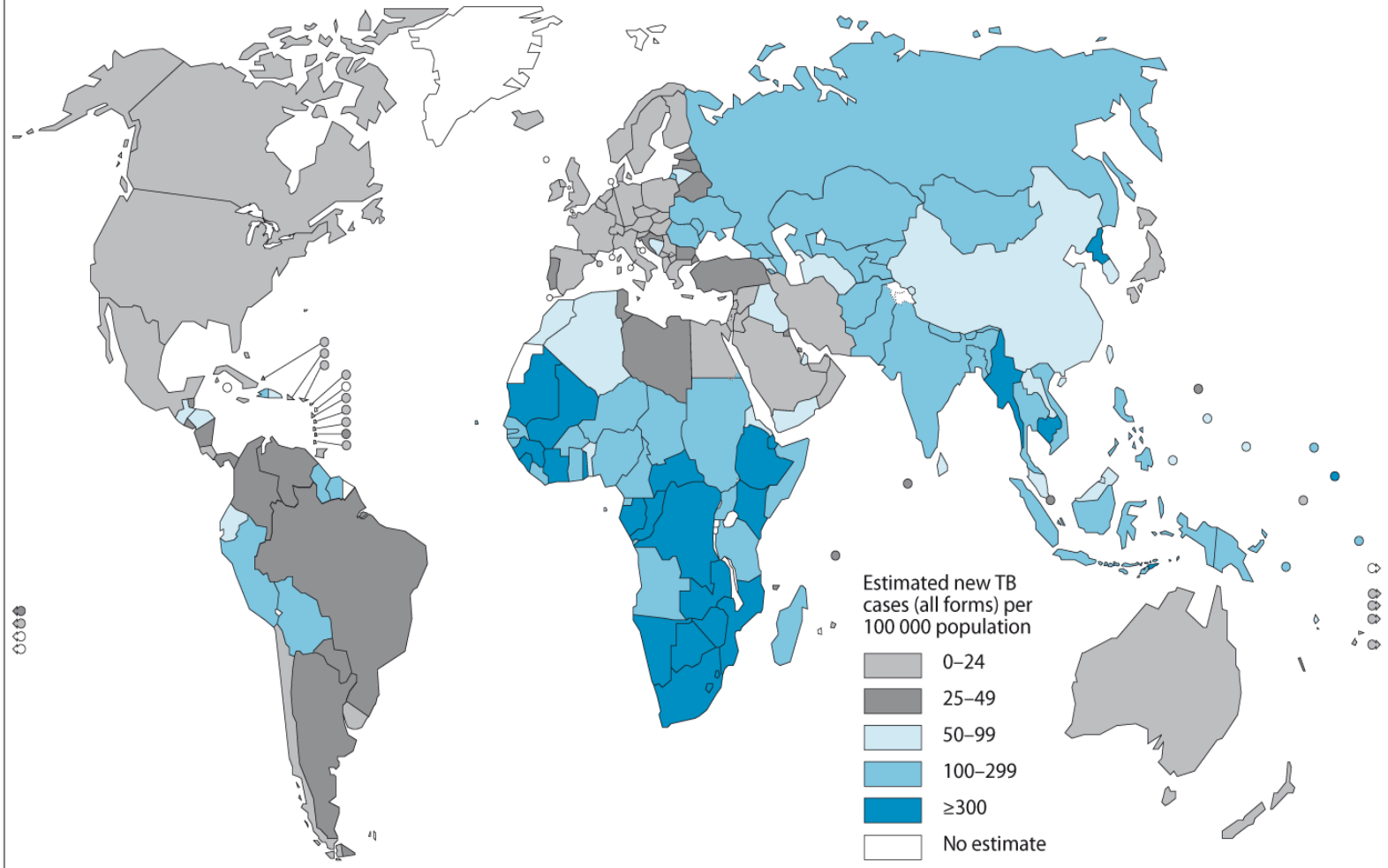
Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Tuberculosis

- Is **a leading cause of HIV-related deaths** worldwide
- In some countries with higher HIV preavalence, up to **80% of people with TB test positive for HIV**
- Globally approximately **30% of HIV** infected persons are estimated to have **latent TB infection**

Estimated TB incidence rates, by country,



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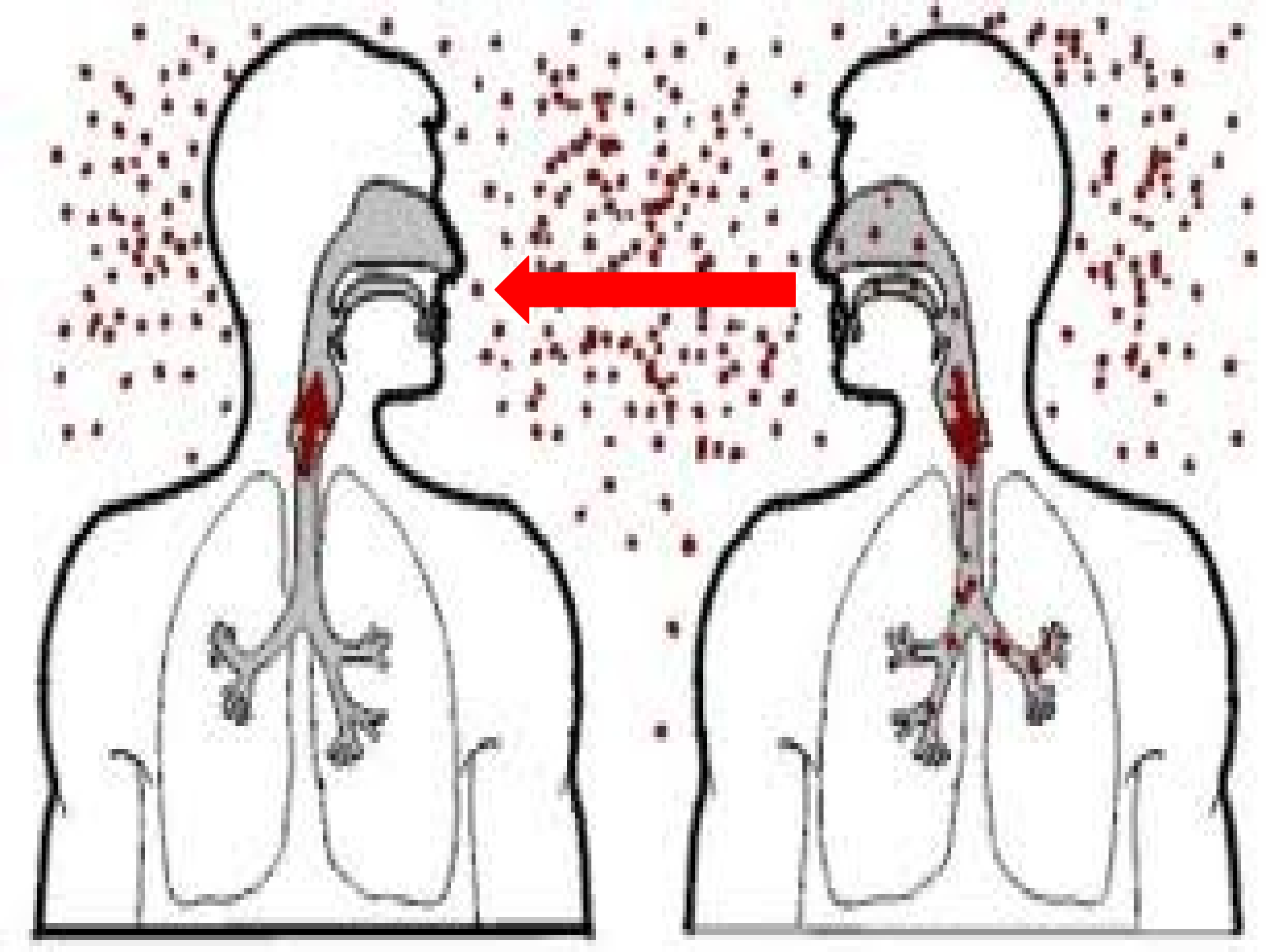
Source: *Global Tuberculosis Control 2010.* WHO, 2010.

World Health Organization

- **TB is transmissible to both people**
  - **with HIV infection**
  - **uninfected persons**

can be treated and can be prevented

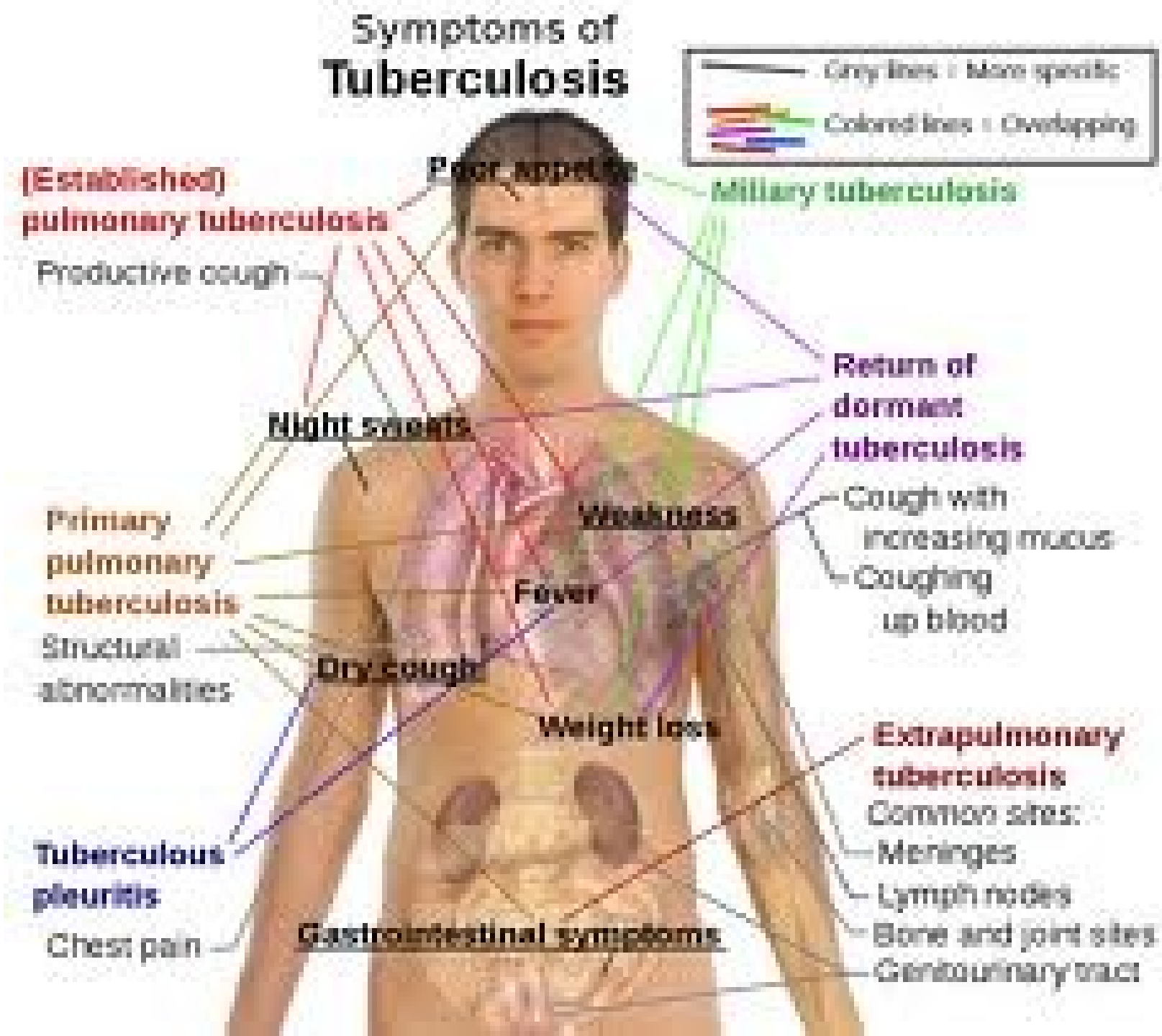


Clinical Manifestations

Myco TB

- Is highly contagious
- Leads to a number of serious medical syndromes affecting, at time,

  most of the organ systems


Symptoms of
Tuberculosis
Grey lines = More specific
Colored lines = Overlapping
(Established)
pulmonary tuberculosis
Productive cough
Poor appetite
Military tuberculosis
Return of
dormant
tuberculosis
Night sweats
Weakness
Cough with
increasing mucus
Coughing
up blood
Primary
pulmonary
tuberculosis
Fever
Structural
abnormalities
Dry cough
Weight loss
Extrapulmonary
tuberculosis
Common sites:
Meninges
Lymph nodes
Bone and joint sites
Genitourinary tract
Tuberculous
pleuritis
Chest pain
Gastrointestinal symptoms

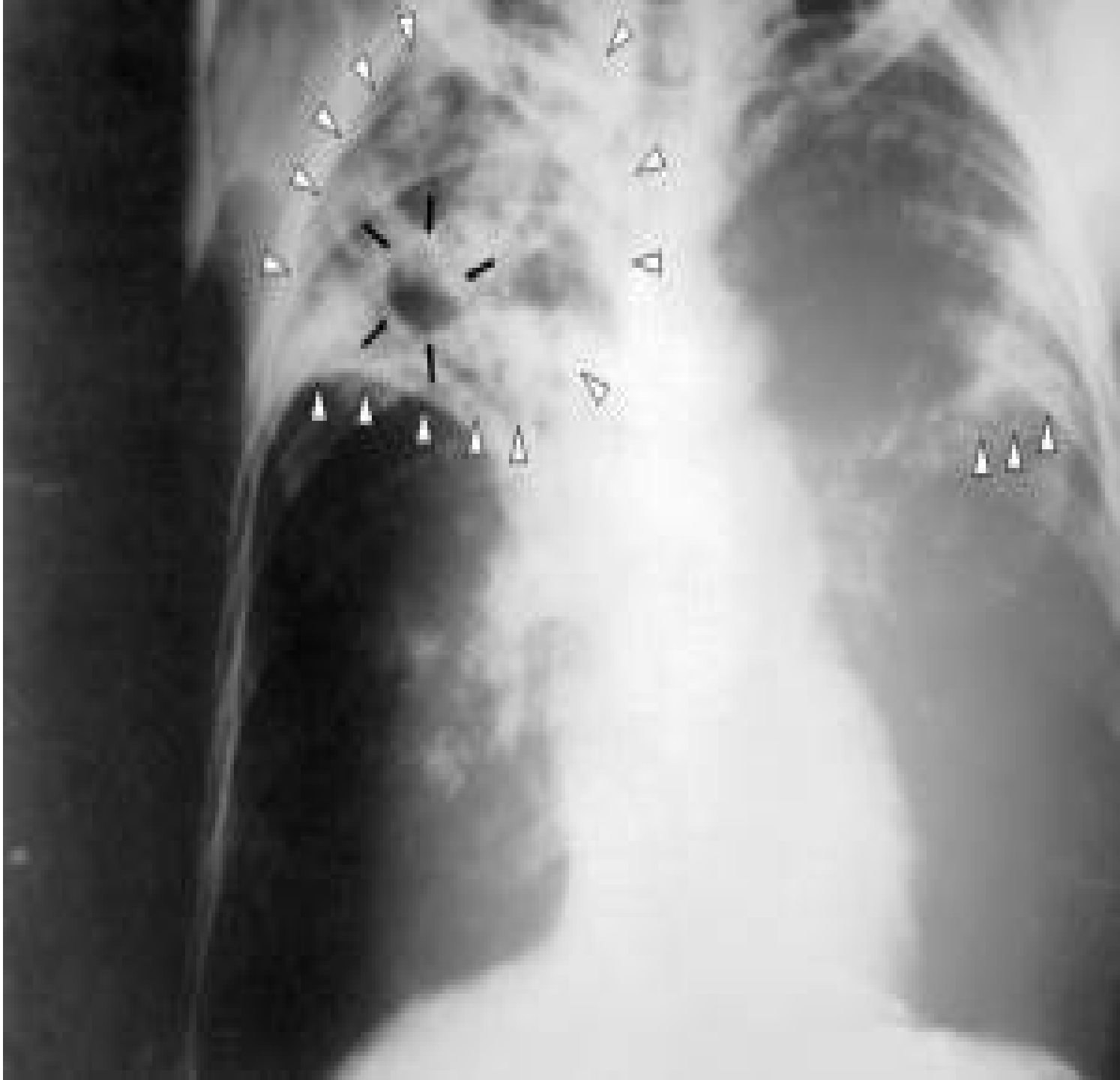
***Myco TB* can causes:**

1. **Pulmonary disease**

    - **Pneumonia**
    - **Cavitary disease**

Cavities in the lungs

(X-ray of thorax)

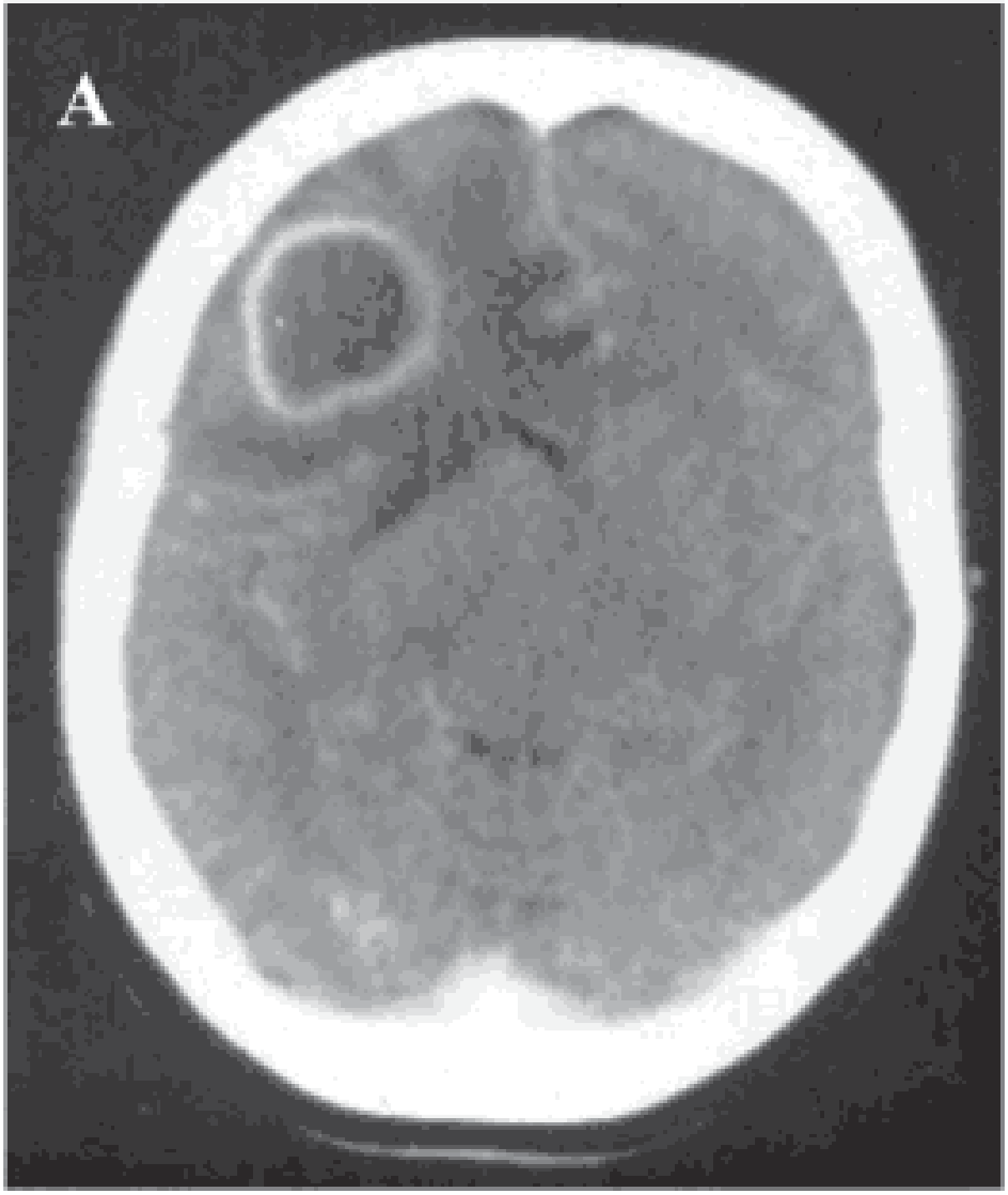


2. Extrapulmonary disease

- **Adenitis („scrofula“)**
- **Otitis media**
- **Laryngitis**
- **Miliary TB**
- **Meningitis**
- **Skeletal TB**
- **Gastrointestinal TB**
- **Renal TB…**

scrofula

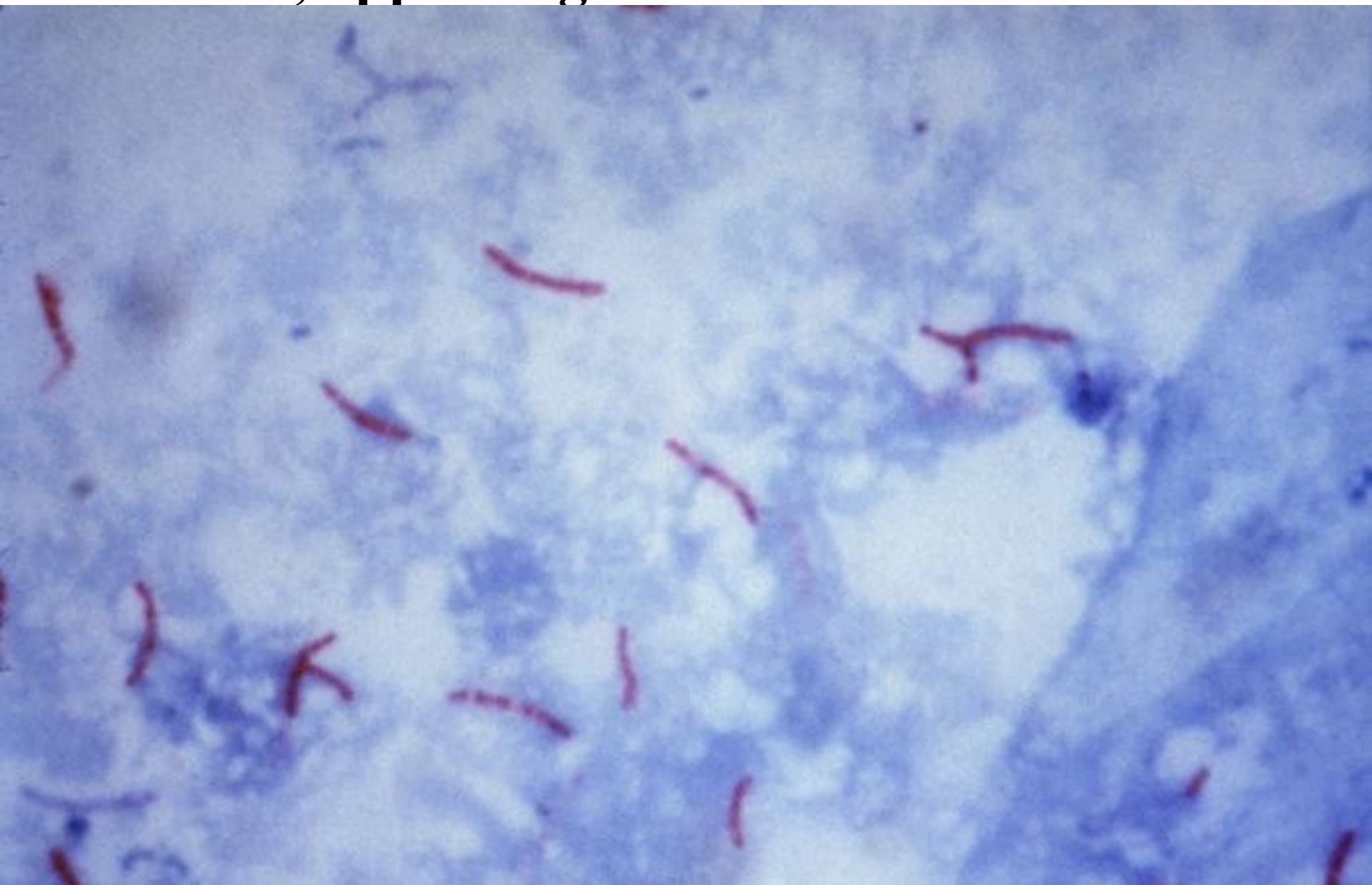
TB absces in brain



Skeletal TB

- destruction of the lumbar vertebrae
- skeleton of the Great Moravian Empire

***Mycobacterium tuberculosis* bacteria (G+)**
is acid-fast, appearing red on a Ziehl-Neelsen stain



Primary prophylaxis

conditions	pathogen	drug
CD4+ any + TB exposure (when HIV+ individual is in exposure of TB we must start primary prophylaxis)	***M. tuberculosis***	**isoniazid (+pyridoxin), rifampicin, pyrazinamid, ethambutol**

Myco TB is highly contagious !!!

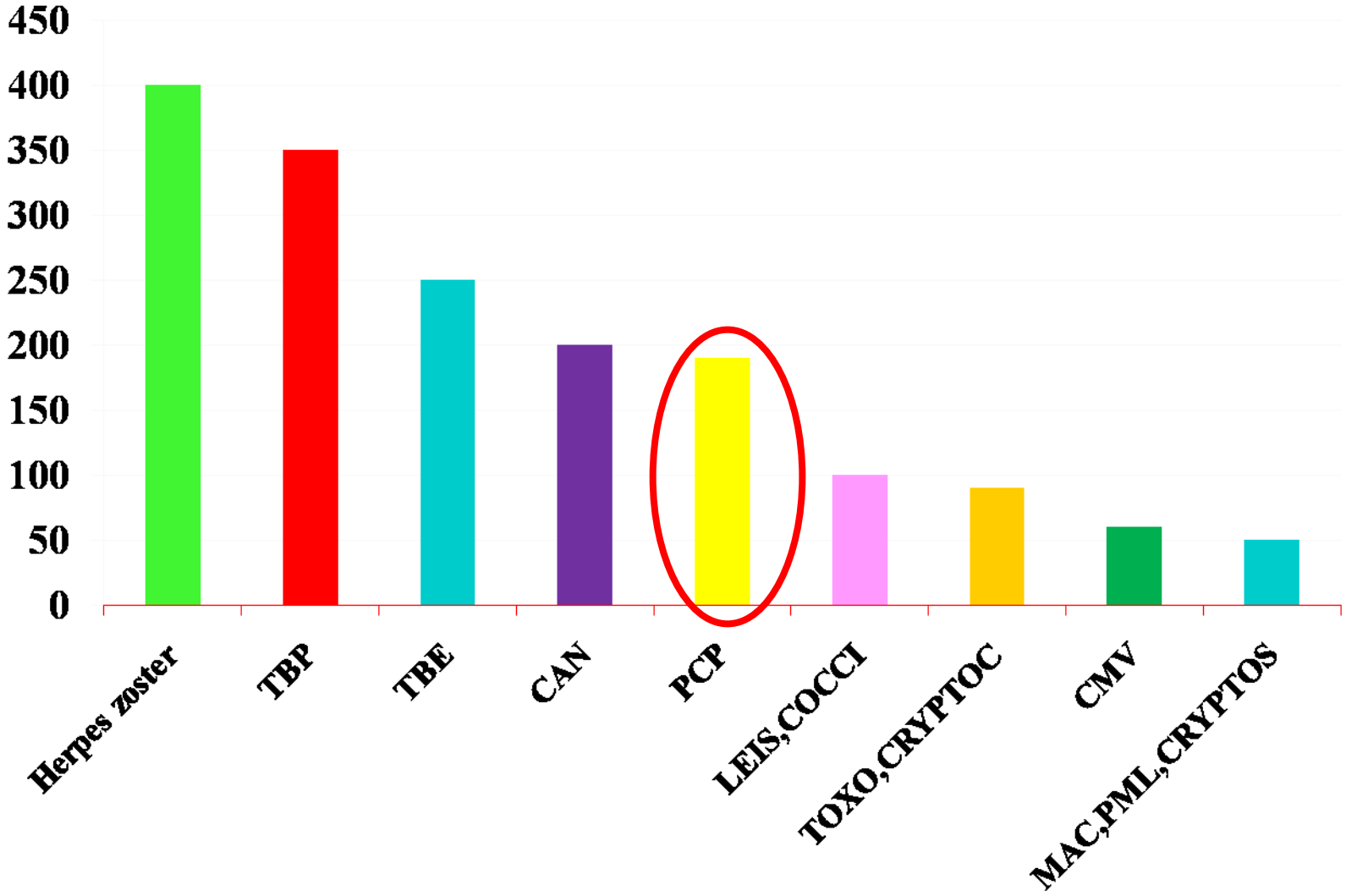
Pneumocystis carinii jiroveci

Infection

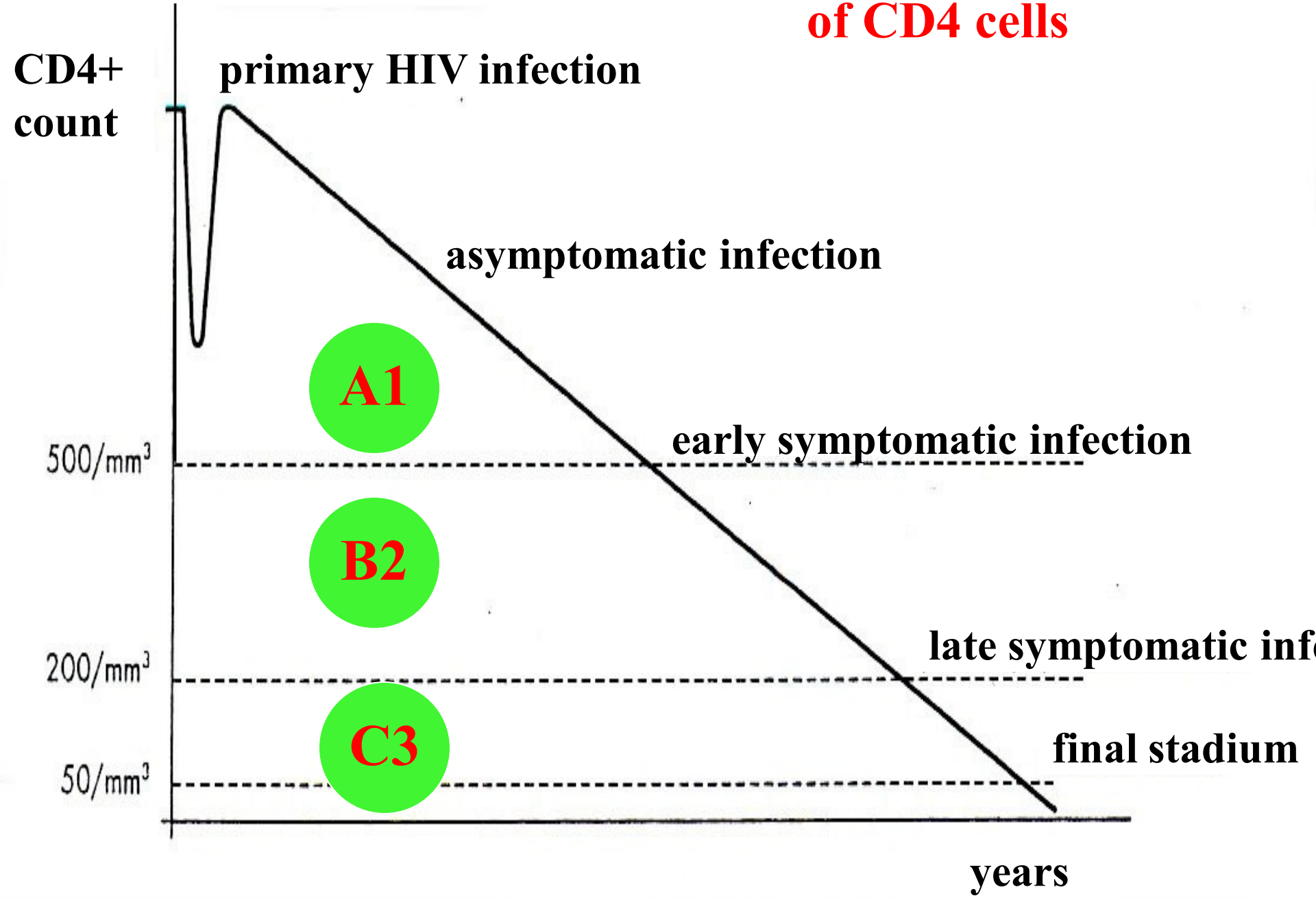
Pneumocystis carinii jiroveci

- **Is an opportunistic pathogen, the natural habitant of which is the lung**
- **The organism is an important cause of pneumonia in the compromised host**
- **The organism can be found in other organs and tissues**

CD4 count and opportunistic infection



CD4+ lymphocytes depletion – gradual loss of number of CD4 cells



Pneumocystis carinii jiroveci

- **Has a worldwide distribution**
- **Serologic serveys indicate that already most healthy children have been esposed to the organism**
- **It means that we meet with this organism in early childhood**
- **Taxonomy – the fungal kingdom**

Incidence

- **PCP accounted for 42% of all AIDS-indicator diseases before ART**
- **Incidence of PCP in this population is declining (with ART and prophylaxis)**
- **But incidence of extrapulmonary *Pn. carinii jiroveci* is increasing**

Extrapulmonary *Pn.carinii jiroveci* infection

involves in fewer than 3% of cases.

- **Lymph nodes** (in up to 50% of cases)
- **Spleen**
- **Liver**
- **Bone marrow**
- **GI and genitourinary tracts**
- **Adrenal and thyroid glands**
- **Heart, pancreas, eyes, ears, skin…**

Incubation Period

- **On the basis of animal studies, the incubation period is thought to be**

from 4 to 8 weeks

Typical Symptoms

- **Patients with PCP usually develop the following:**
  - **Dyspnea**
  - **Mild fever**
  - **Nonproductive cough**

The late signs

- **Physical findings of PCP include the following:**
  - **Tachypnea**
  - **Tachycardia**
  - **Cyanosis**
- **Lung auscultation is usually unremarkable**

Differential Diagnosis

The differential diagnosis of PCP is very broad and includes

- **infectious diseases**

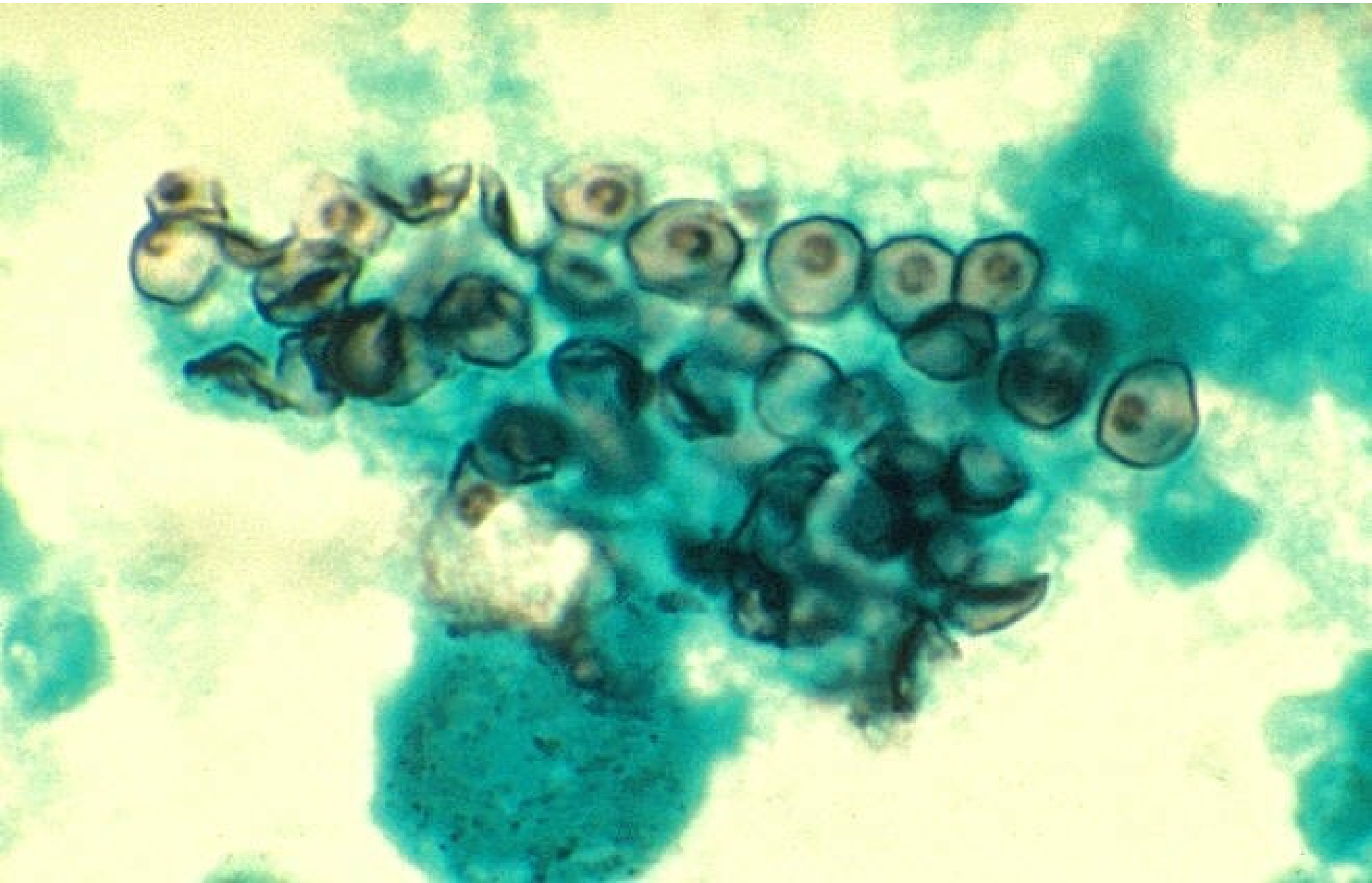
and also can mimic

- **noninfectious diseases**

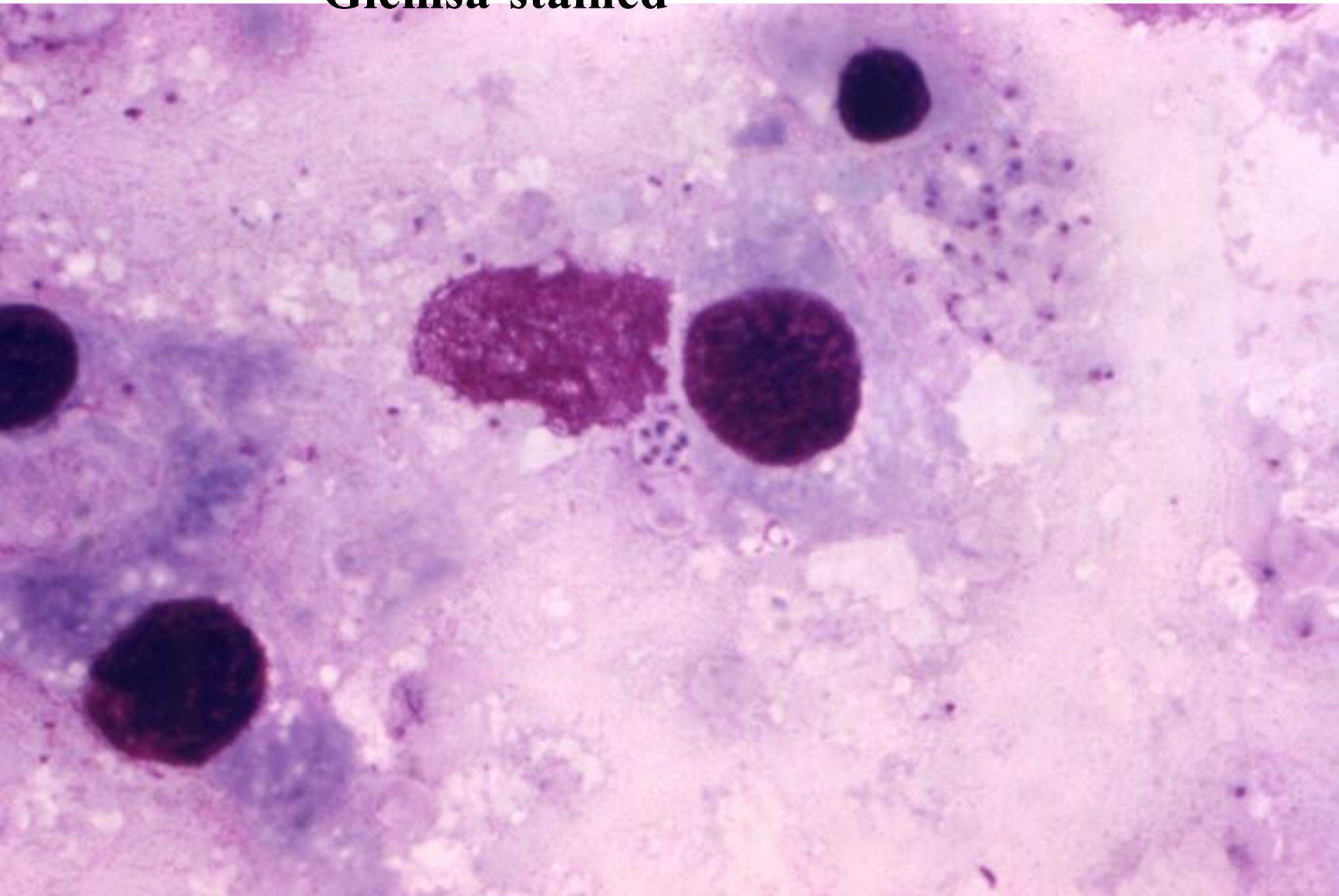
Laboratory

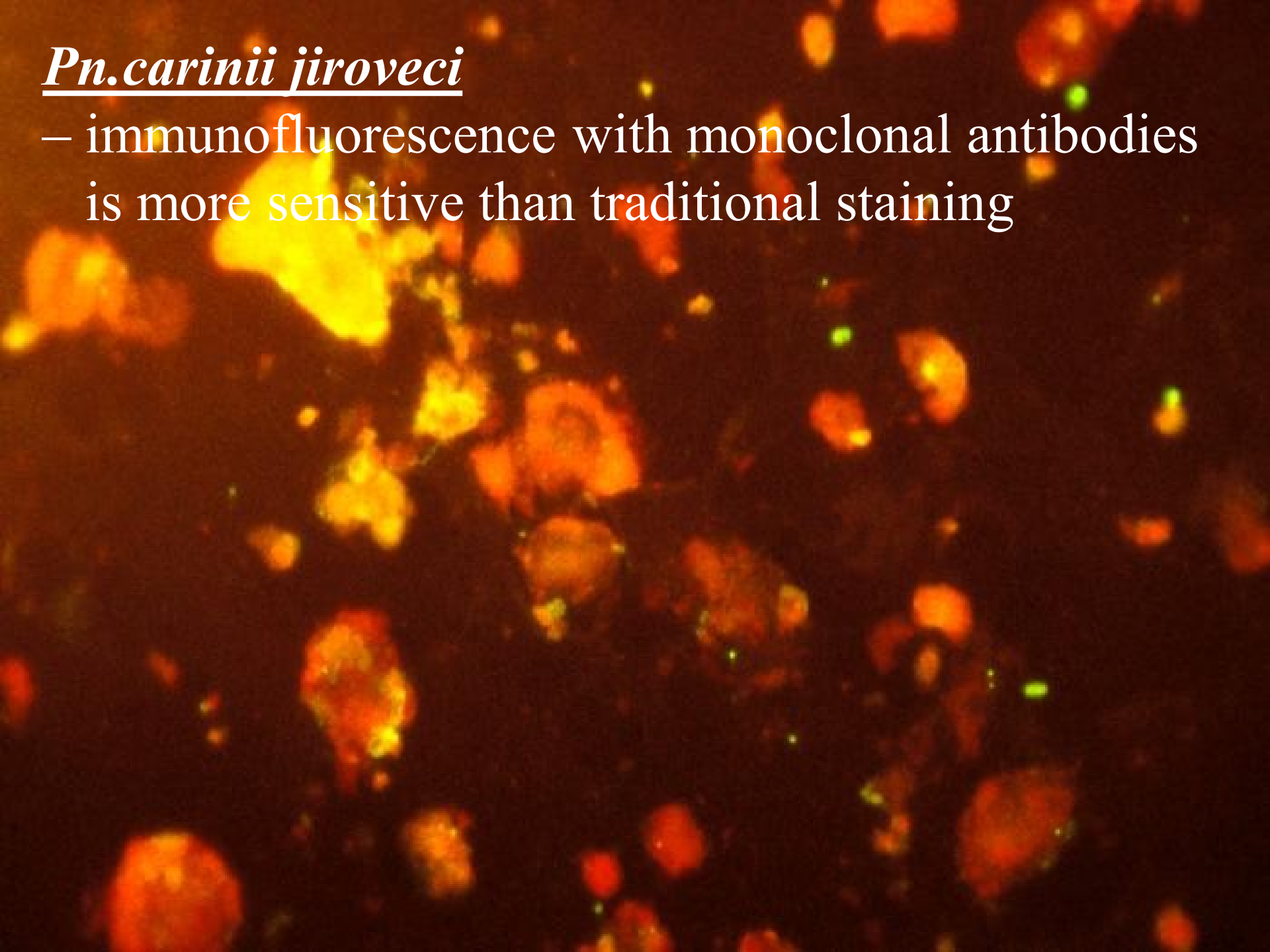
- There is no reliable way to cultivate the organism *in vitro*
- A definitive is made by histopathologic staining, which selectively stain the wall of *Pn. carinii jiroveci,* cysts or nuclei
- PCR technique which demonstrate nuclei acid

Cysts of *Pn. carinii jir*. Methenamine silver stain.
In smear from bronchoalveolar lavage.



Pn. carinii **– trophozoites** (growth stage)**,**
Giemsa-stained





Pn.carinii jiroveci

– immunofluorescence with monoclonal antibodies is more sensitive than traditional staining

Laboratory

LDH

- Elevated serum concentrations of lactate dehydrogenase have been reported but are not specific to *Pn. Carinii* infection

Leucocytes

- The white blood cell count is low

Oxygen saturation is very low

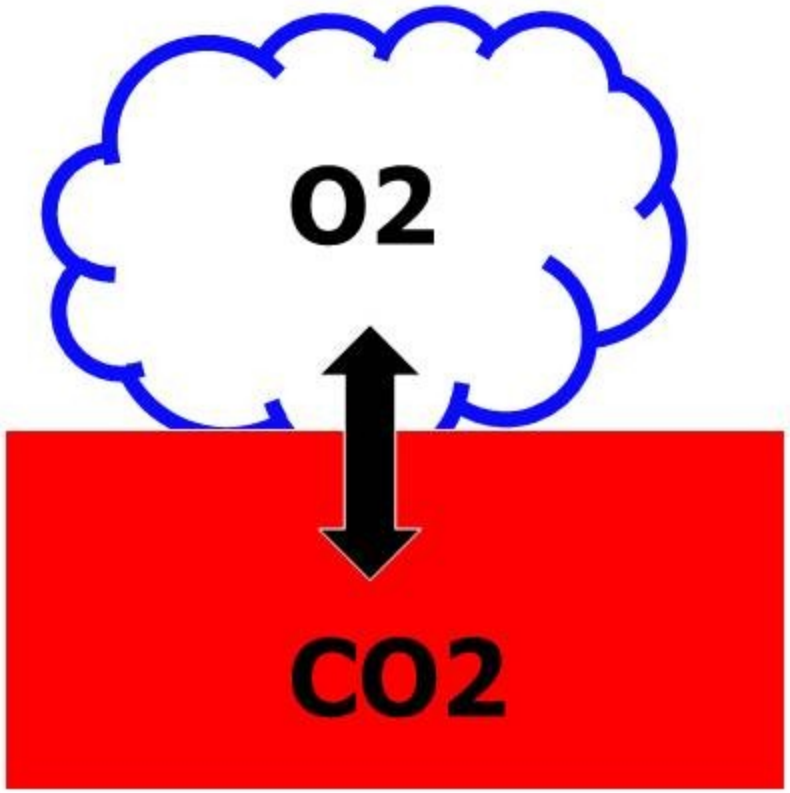
- Is probably the most sensitive noninvasive test for dg. PCP

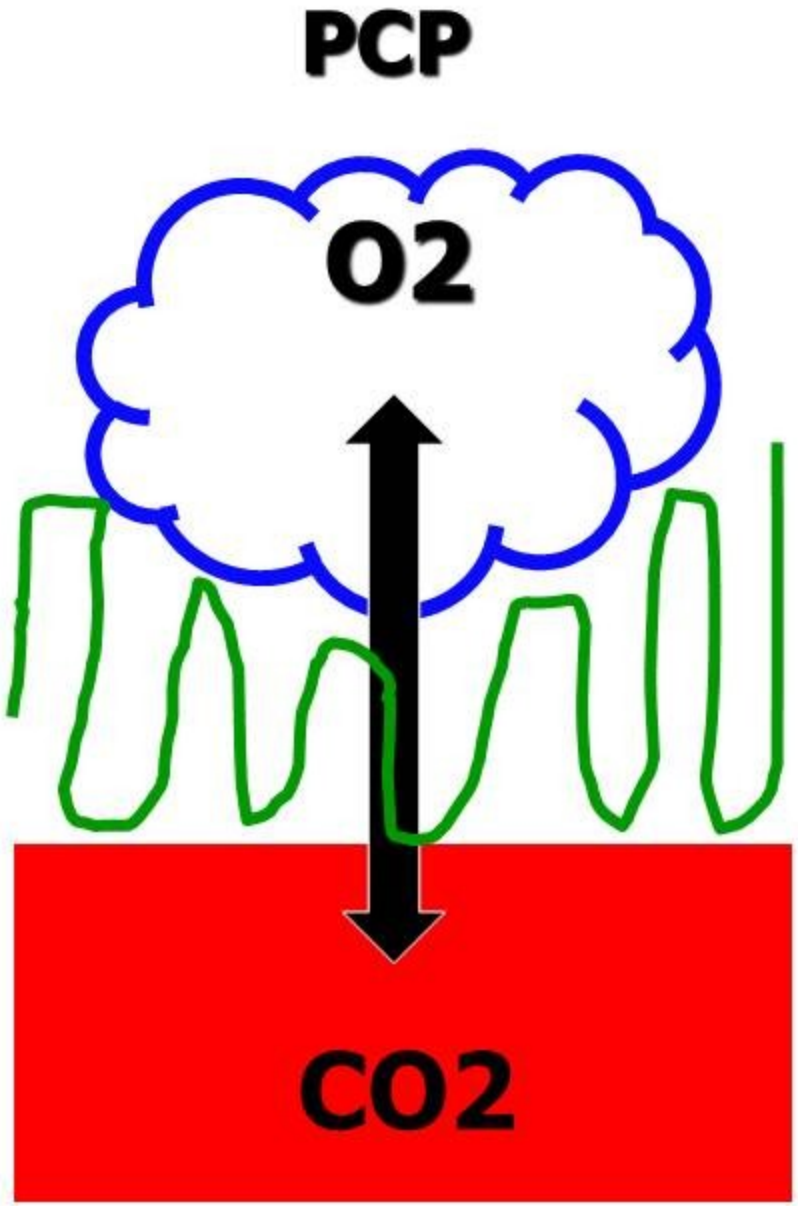
Arterial blood gases demonstrated

- **Hypoxia**
- **An increased alveolar-arterial oxygen gradient**

Alveolocapillary membrane

- characteristic exudate
  is in the inter alveolar space





Imaging

- The classic findings on chest radiography consist of bilateral diffuse infiltrates involving the perihilar regions.
- Atypical manifestations also have been reported.
- Early in the course of pneumocystosis, the chest radiograph may be normal.

Imaging – HR CT

- The most important imaging method shows
- **White glass picture**

CT -White glass picture

Diagnostic/testing procedures

Fiberoptic bronchoscopy

- With bronchoalveolar lavage remains the mainstay of *Pn. Carinii* diagnosis

Sputum

- is a simple, noninvasive technique, but its sensitivity has extremely low

Transbronchial biopsy and open lung biopsy

- are the most invasive, are reserved for situations in which a diagnosis cannot be made by lavage

Main treatment

Trimethoprim-sulfamethoxazol

- **Is the drug of the first choice for all forms of *Pn. Carinii* infection**
- **It is administered intravenously (orally) at a dosage 120 mg of TSX/kg/d in four divide doses**

Glucocorticoids

- Administration of glucocorticoids to HIV-infected patients with moderate to severe pneumocystosis can improve the rate of survival
- The recommended regimen:

  40 mg prednisone PO twice daily, with tapering to a dose of 20 mg/d over a 3-week period

Duration of treatment

non-HIV-infected patients

- Treatment of pneumocystosis should be continued for 14 days (better 21 days)

HIV-infected patients

- Treatment of pneumocystosis should be continued for 21 days

Alternative treatment

- **Pentamidine**

  4 mg/kg/d by slow intravenous infusion
- **Clindamycin**
- **Primaquine**

  avoided in patients with glucose-6-phosphate dehydrogenase deficiency
- **Trimethoprim + dapson**
- **Atovaquone**

Complications

- In the typical case of untreated PCP, progressive respiratory compromise leads to death.
- Therapy is most effective when instituted early in the course of the disease, before there is extensive alveolar damage.

Primary prophylaxis

- Is indicated for HIV-infected patients at high risk of developing pneumocystosis

CD4+ lymphocyte count < 200/mm^3

Secondary prophylaxis

Is indicated for all patients

who have recovered from PCP

Prophylactic regimen

- **Trimethoprim-sulfamethoxazol**

  (160mg of trimethoprim) per day

Alternative regimens

- **Dapsone (50mg daily), pyrimethamine (50mg once per week), and folinic acid (24mg once per week)**
- **Dapsone (100mg daily)**
- **Nebulized pentamidine**

  (300mg once per month via nebulizer)

Primary prophylaxis

conditions	pathogen	drug
CD4+ any + TB exposure	*M. tuberculosis*	isoniazid (+pyridoxin), rifampicin, pyrazinamid, ethambutol
CD4+ < 200/mm3	*Pn. carinii jiroveci*	co-trimoxazol, pentamidine (aerosol), dapson

TOXOPLASMOSIS

DEFINITION

- An acute or chronic infection caused by the obligate intracellular protozoan ***Toxoplasma gongii***
- Infection in human is usually **asymptomatic**
- When symptoms occur, they range from a mild, self-limited **to a fulminant disseminated disease**

SYMPTOMS

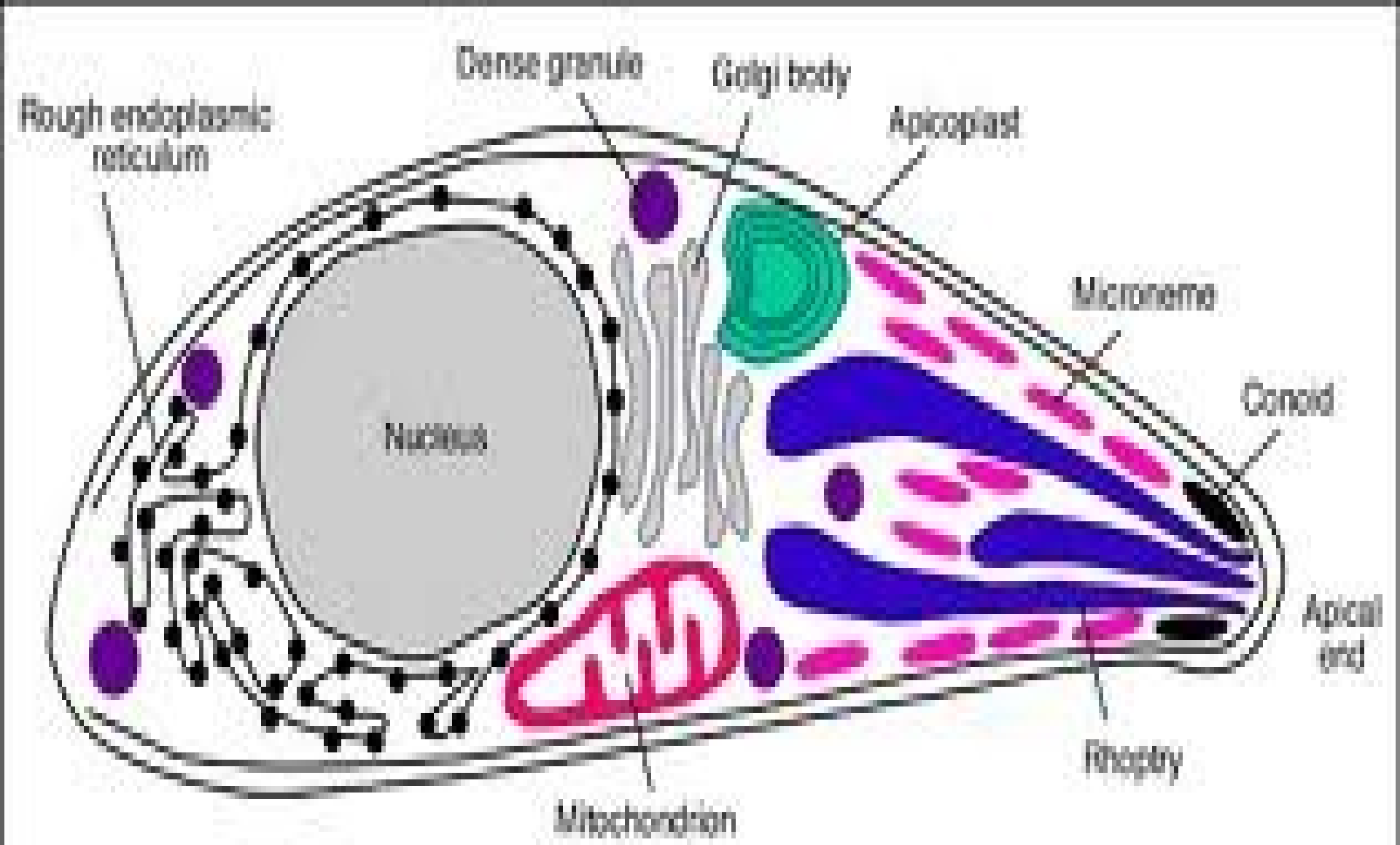
Usually involve the following:

- Central nervous system
- Eyes
- Skeletal or cardiac muscles
- Lymph nodes
- Liver
- Lungs

DISEMINATED DISEASE

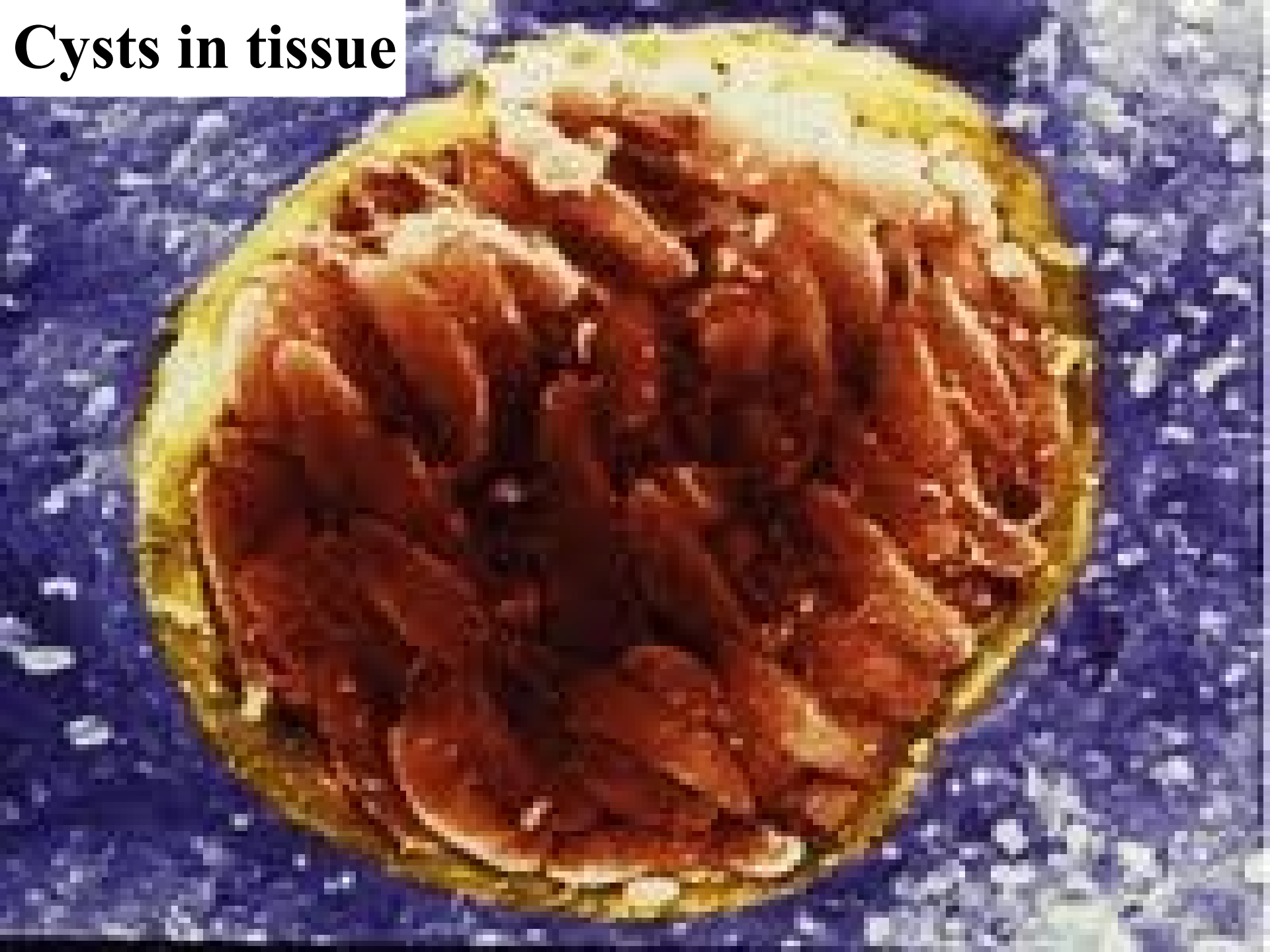
Severe infections usually occur

- In an **immunocompromised patient**
- By the transplacental passage of parasites **from an infected mother to the fetus** (congenital toxoplasmosis)



Ultrastructure of a *Toxoplasma gondii* tachyzoite

Cysts in tissue



EPIDEMIOLOGY

Cases are caused by:

- **Eating undercooked meat**
- **Contaminated vegetables**
- Ingestion of oocysts

  from **contaminated soil**

The seroprevalence depends on geografic location: US – between 3-67%

tropical countries – up to 90%

SYMPTOMS AND SIGNS

- Immune responses are able to eliminate most of the tachyzoites

- **80 – 90%** of cases in immunocompetent persons are **asymptomatic**

CEREBRAL TOXO

Clinical manifestations of CNS infection include the following:

- Headache, seizures,weakness
- Cranial nerve abnormalities
- Visual field defects
- Mental status changes
- Cerebellar signs

CEREBRAL TOXO

- Speech abnormalities
- Meningism
- Sensory or motor disorders
- Disorientation
- Hemiparesis
- Convulsions
- Coma and death

EXTRACEREBRAL TOXO

- Less common among patients with HIV inf.
- The prevalence is estimated

  at 1,5% to 2,0%

  - **lungs** (pneumonitis)
  - **eye** (chorioretinitis)
  - **heart**

Cases of gastrointestinal, liver, skin, or multiorgan involvement also have been reported

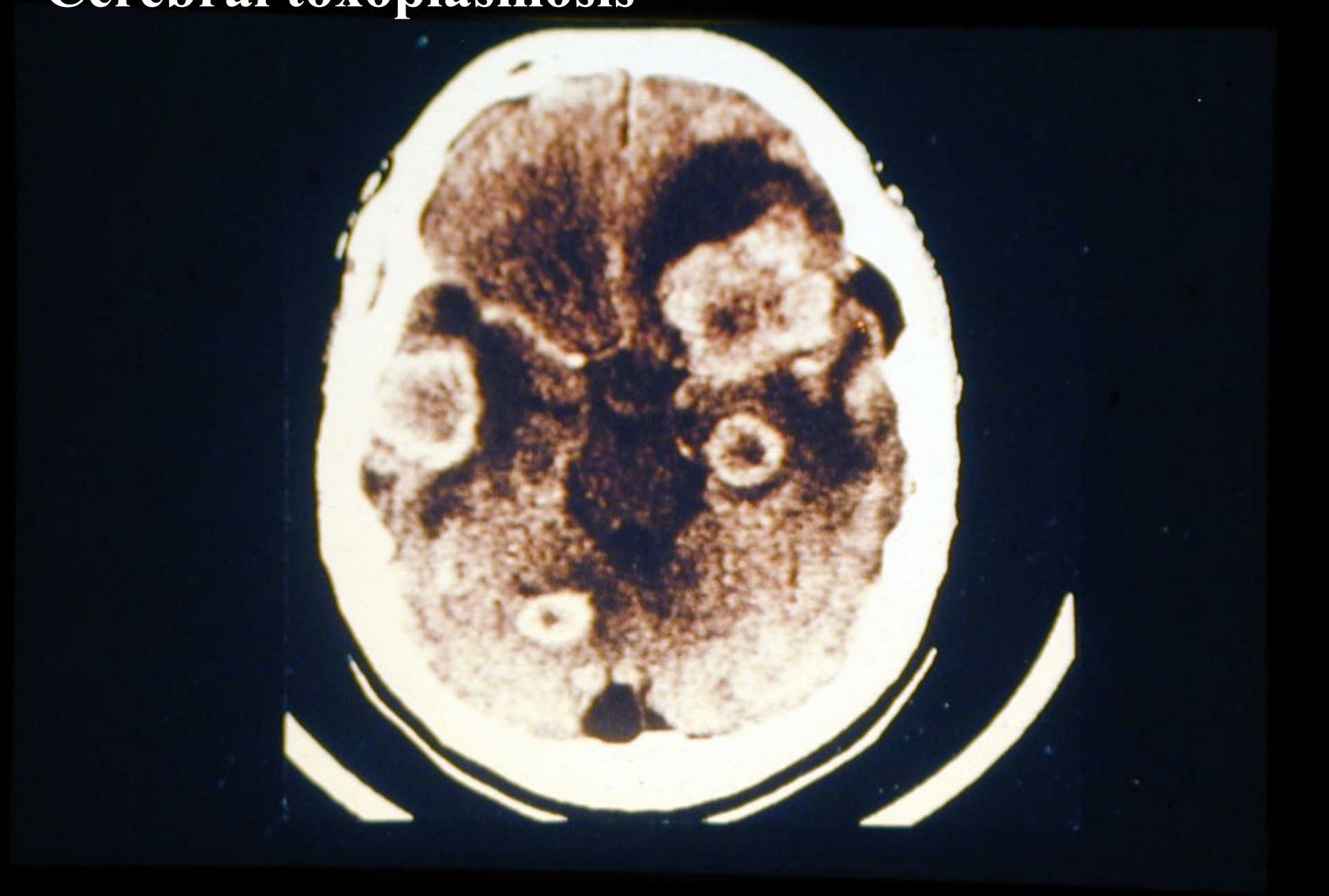
IMAGING

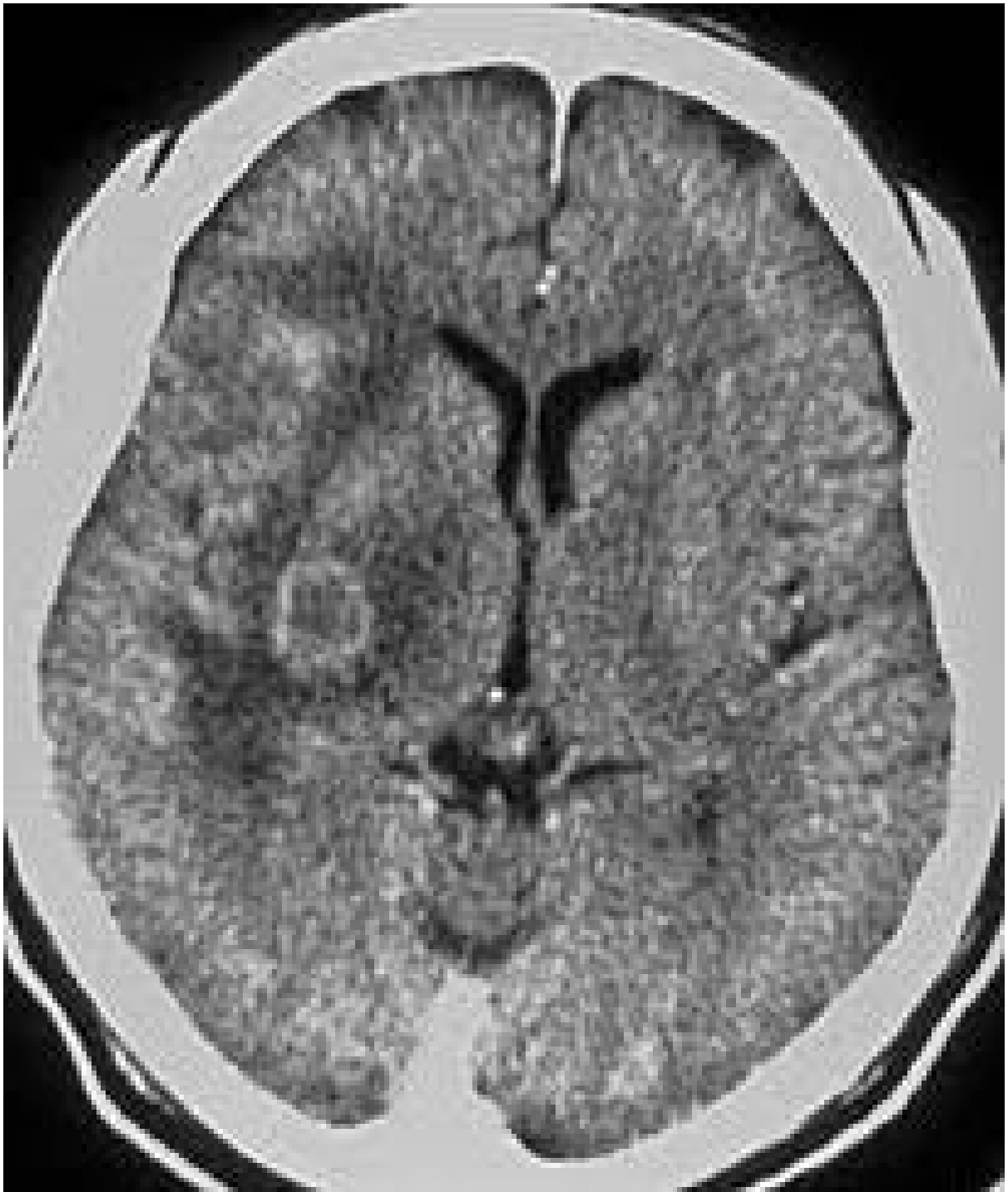
On neuroimaging (CT, MRI)

The **abscesses** of cerebral toxoplasmosis are typically

- Multiple
- Located in the cortex or deep nuclei (thalamus and basal ganglia)
- Surrounded by edema
- Enhance in a ringlike pattern with contrast

Cerebral toxoplasmosis





SEROLOGY

- Approx. **20%** of patients

  have no detectable antibodies
- Titer of antibodies does not always rise during infection
- Negative serology does not rule out infection
- But a rising titer may be of diagnostic significance

OTHER LABORATORY METHODS

PCR (polymerase chain reaction)

in blood samples suggest that

- This modality has limited diagnostic value in cases of cerebral toxoplasmosis

CSF (cerebrospinal fluid)

- Is also nonpathognomonic and reveals **elevated protein** and **mild pleocytosis**

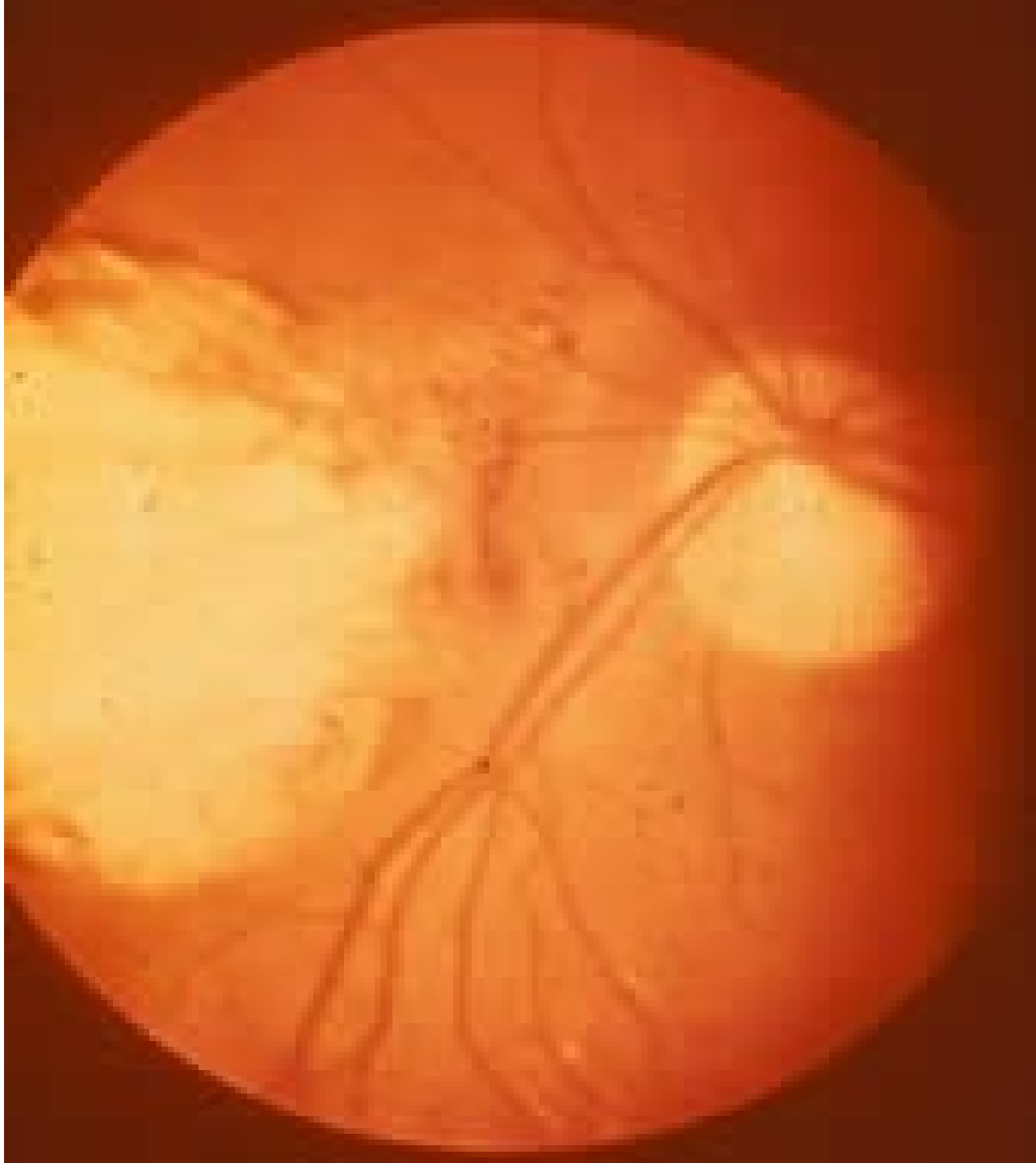
EXTRACEREBRAL TOXOPLASMOSIS

- Involving other organs among HIV-infected patients is rare
- Dg. is usually based on biopsy

OCULAR TOXOPLASMOSIS

- Is usually based on a suggestive **ophthalmoscopic picture**
- Histopathologic identification of *T.gondii* in the eye can establish the diagnosis

retinochoroiditis



MAIN TREATMENT

The regimen of choice for acute therapy

- **Pyrimethamine** 50 to 75 mg/d

  \+ **sulfadiazine** 4 to 8 g/d

- Leucovorin – coadministtered to prevent the folinic acid deficiency and ameliorate the hematologic toxicity of pyrimethamine
- Duration of treatment

  – usually **for 6 to 8 weeks**

PATIENT FOLLOW-UP

After induction treatmen

- HIV-infected patients schould receive lifelong **suppression therapy**

  pyrimethamine 25-50 mg/d

  + sulfadiazine 2-4 g/d

- The doses of TMP/SMX recommended for *P. carinii* pneumonia appear to be effective

PREVENTION
FOR INDIVIDUALS AT RISK

- Not to eat raw or undercooked („pink“) meat
- Wash fruits and vegetables
- Wash hands after contact with raw meat
  and after contact with soil
- Wash hands after changing a cat litter box

PRIMARY PROPHYLAXIS

conditions	pathogen	drug
CD4+ any + TB exposure	*M. tuberculosis*	isoniazid (+pyridoxin), rifampicin, pyrazinamid, ethambutol
CD4+ < 200/mm3	*Pn. carinii jiroveci*	co-trimoxazol, pentamidine (aerosol), dapson
CD4+ < 150/mm3 + antibody to *Toxoplasma* positive	*Toxoplasma gondii*	co-trimoxazol, dapson, pyrimethamin(+folinat)

CONGENITAL TOXOPLASMOSIS

- Clinical findings are variable
- There may be **no sequelae**, or sequelae may develop at various times after birth
- **Premature infants** may present with CNS or ocular disease
- **Full-term infants** usually develop milder disease, with hepatosplenomegaly and lyfadenopathy

CONGENITAL TOXOPLASMOSIS

Sabin tetrade (classic tetrade of signs)

1. Retinochoroiditis
2. Hydrocephalus
3. Convulsions
4. Intracerebral calcifications