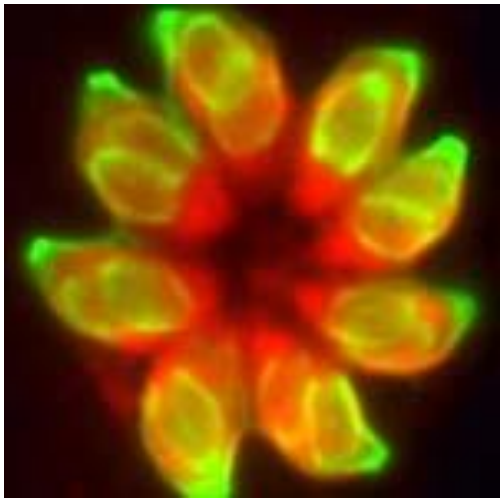
Toxoplasma gondii



Jarmila Kliescikova, MD
1. LF UK

Toxoplasma gondii

Apicomplexa, Koccidia

Obligate intracellular parasite

Distribution: **cosmopolite**

Transmission:

alimentary

transplacentary

(transfusions, transplantations…)

Very **low host specifity**

Final host:

Felidae

discharging

Intermediate host:

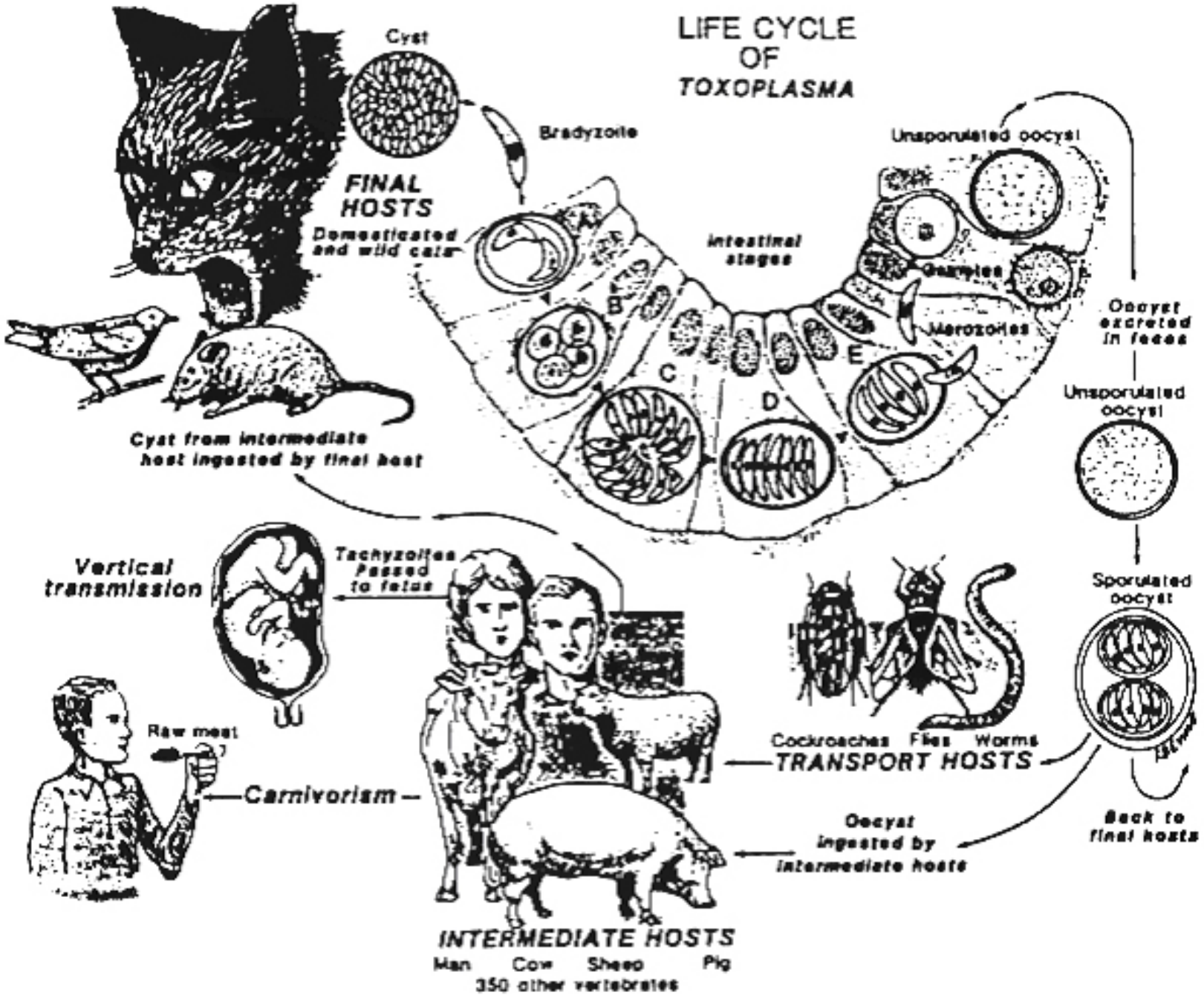
350 types of birds and mammals creating

Oocysts

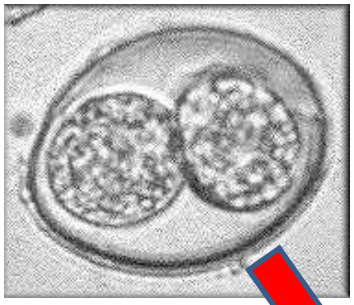
(5-20 days)

Tissue cysts

rabbit, pork, lamb

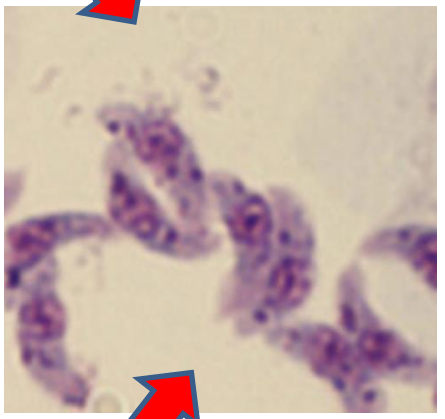

LIFE CYCLE
OF
TOXOPLASMA
Cyst
Bradyzoite
FINAL
HOSTS
Domesticated
and wild cats
Cyst from intermediate
host ingested by final host
Unsporulated oocyst
Intestinal
stages
Gamètes
Merozoites
Oocyst
excreted
in feces
Unsporulated
oocyst
Sporulated
oocyst
Vertical
transmission
Tachyzoites
Passed
to fetus
Raw meat
Carnivorism
Cockroaches Flies Worms
TRANSPORT HOSTS
Oocyst
ingested by
intermediate hosts
Back to
final hosts
INTERMEDIATE HOSTS
Man Cow Sheep Pig
350 other vertebrates

GIT: Oocyst: sporozoites



Trophozoites:

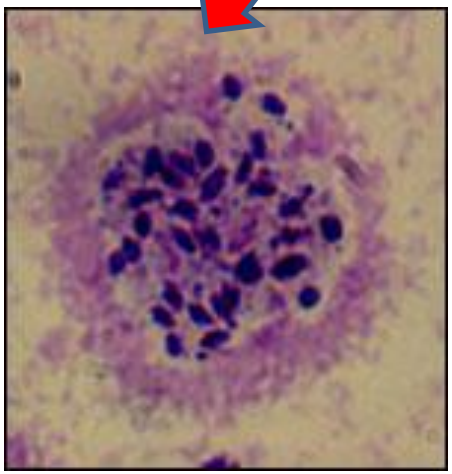
Tachyzoites: **acute infection**



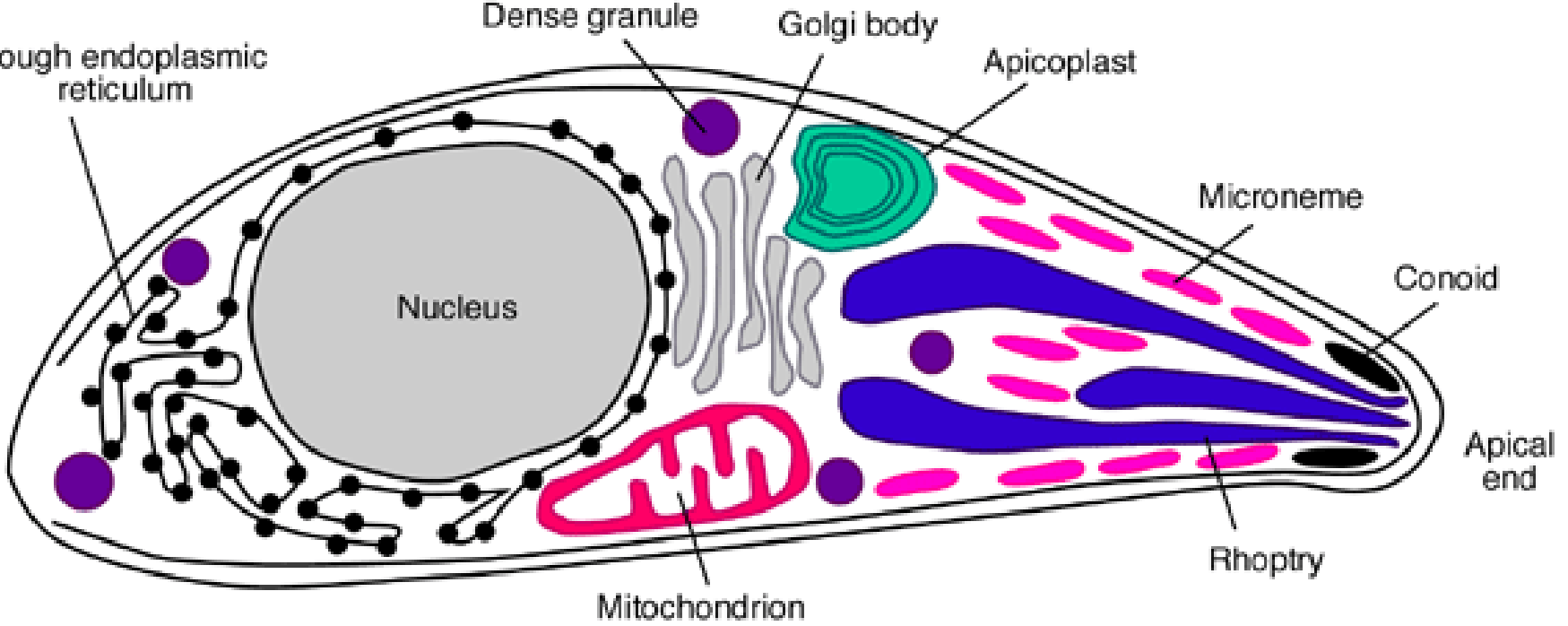
Trophozoites:

Bradyzoites : **latent infection**

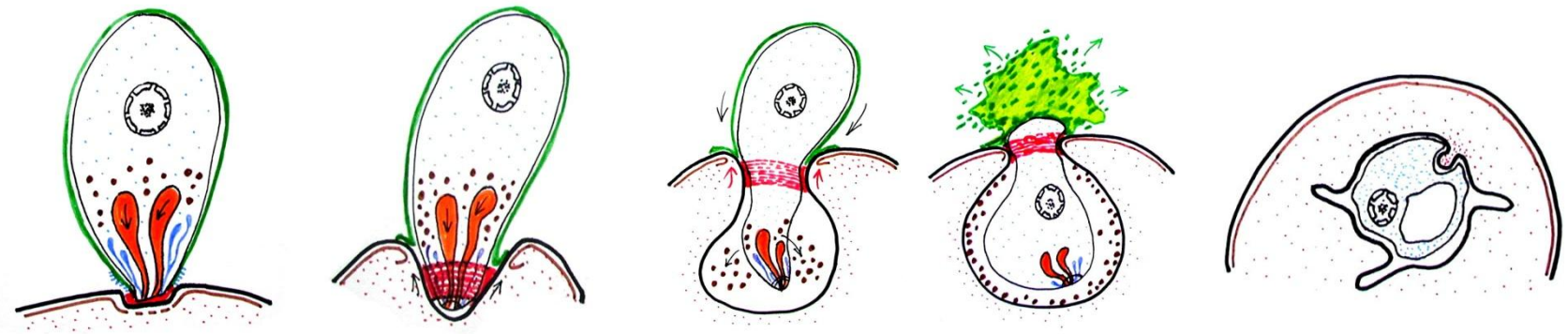
Tissue cyst



Toxoplasma is highly specialized for invasion of the host cell



Ultrastructure of a *Toxoplasma gondii* tachyzoite



Contact (healthy cell; K+ ionts)

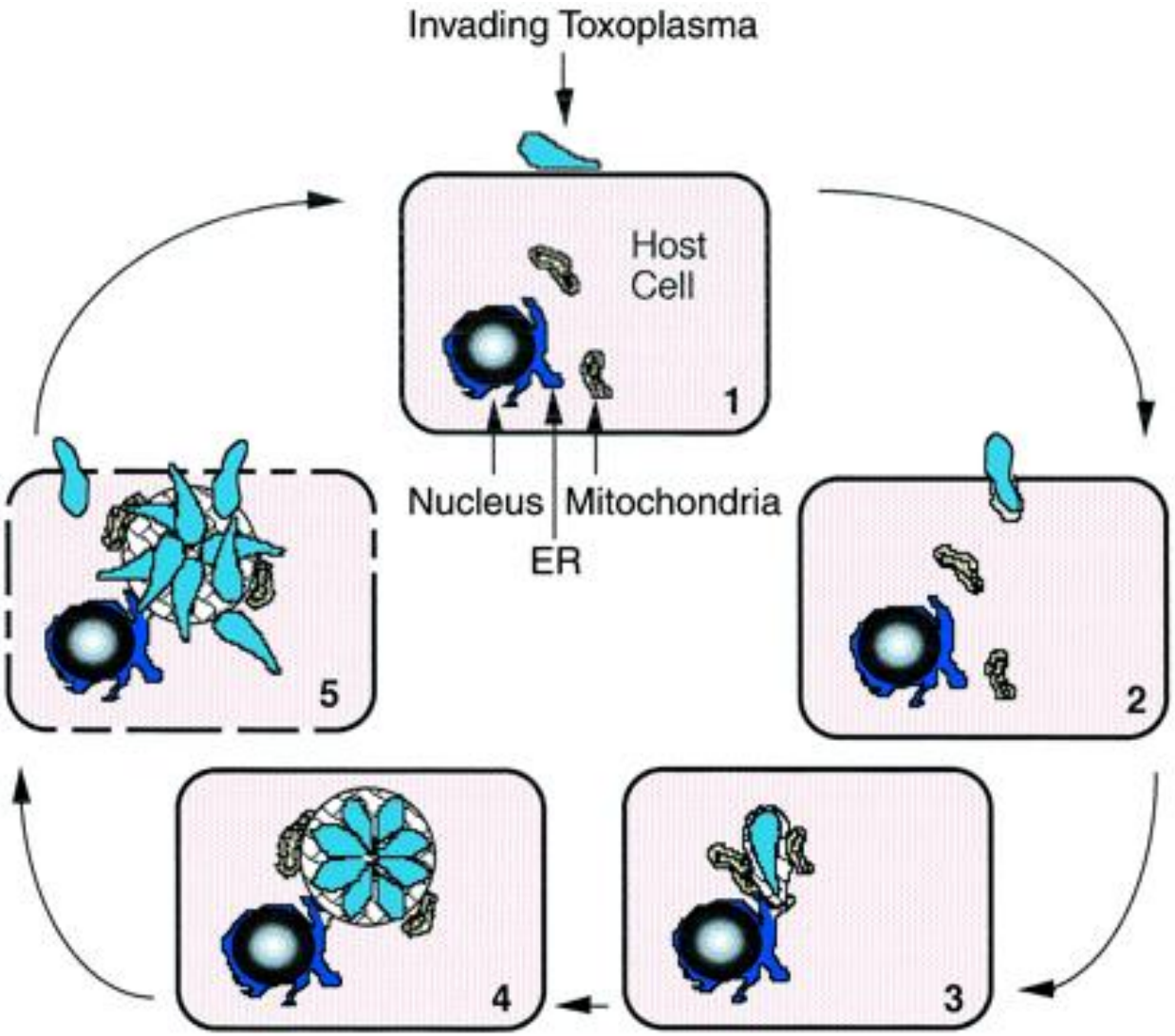
Orientation

Invasion

Formation of parasitophorous vacuole

Whole process: 30 s

Toxoplasma is modificating the host cell



Tissue cyst destruction

+ 67°C

- 20°C

radiation γ

Infective stages

Oocyst

not infectious immediately

development: 2-3 days (air, sun)

remains infectious if favourable conditions for about

1 year

Dissemination

hematogenous/lymphatic system

Immunity can control infection however is not able to eradicate it – tissue cysts

Infecting different types of cells

Preference:

neurons (brain)

muscles

cells of retina

Epidemiology

USA: about 20-40% seropositive

Europe: 20-80% seropositive

HIV: 40% develop toxoplasmosis

Mortality: immunocompromised and not treated always fatal

Development of the infection depends on the **immune status** of the host

Immunocompetent is usually asymptomatic

Symptomatic disease

glandular form: general lymphadenopathy

ocular form: chorioretinitis

Toxoplasma is capable invade thru placentar barrier and infect the fetus

TORCH syndrome

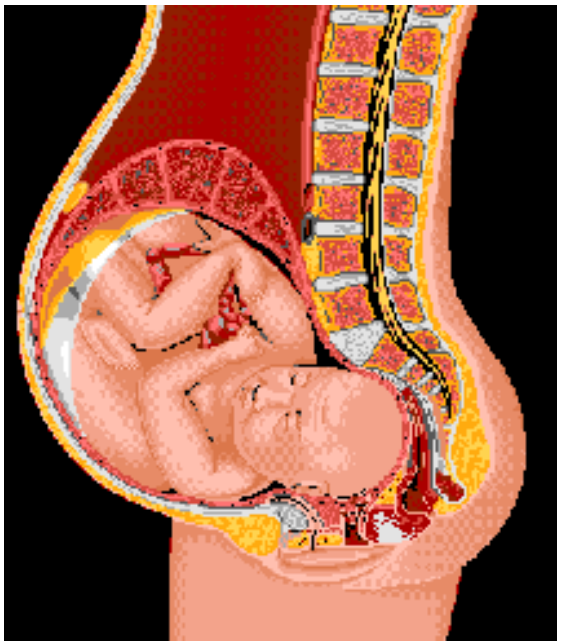
Asymptomatic infection vs

Symptomatic infection:

abortus

brain

retina



Congenital toxoplasmosis

- Mild disease: **slightly diminished vision**

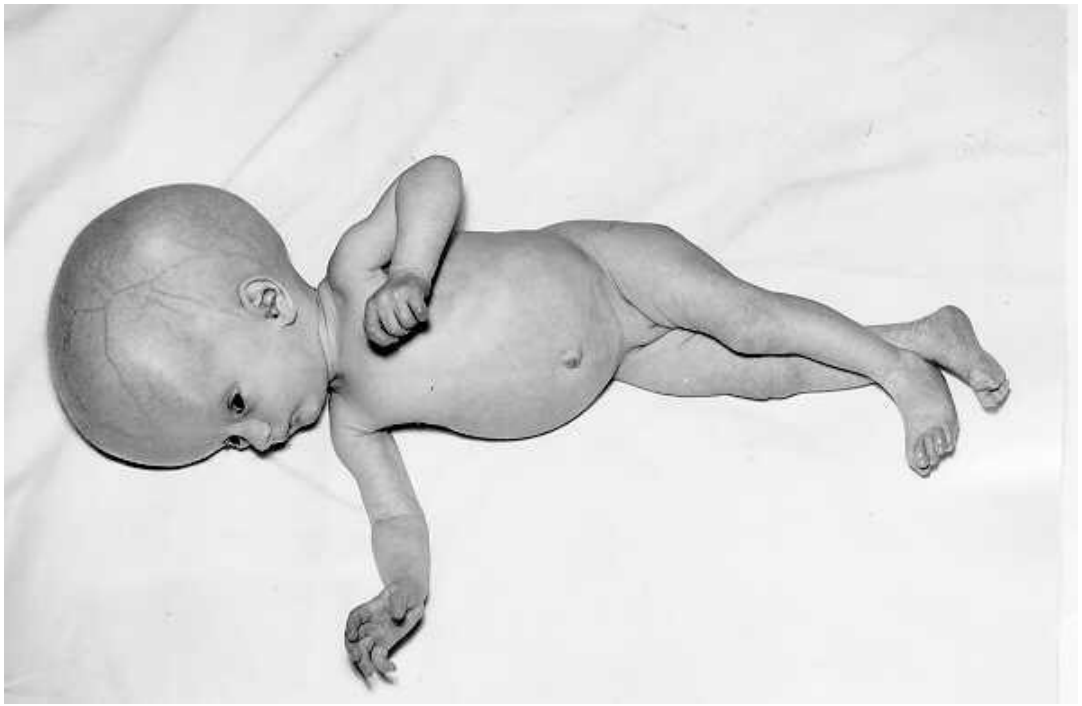
- Severe disease:

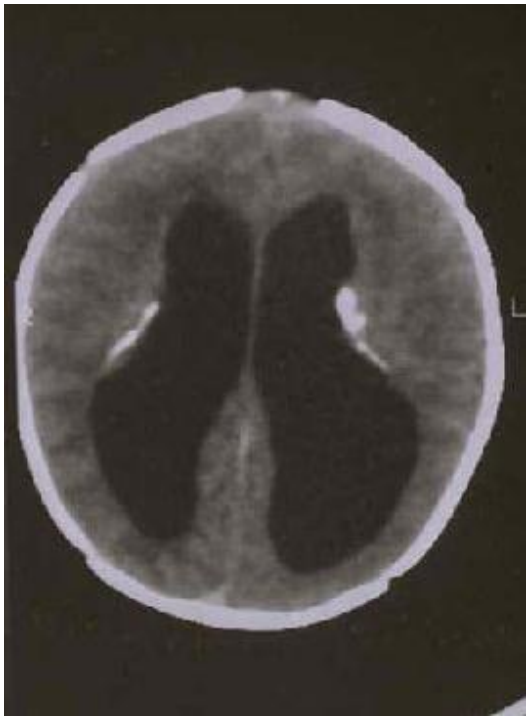
  chorioretinitis

  hydrocephalus

  convulsions

  intracerebral calcifications

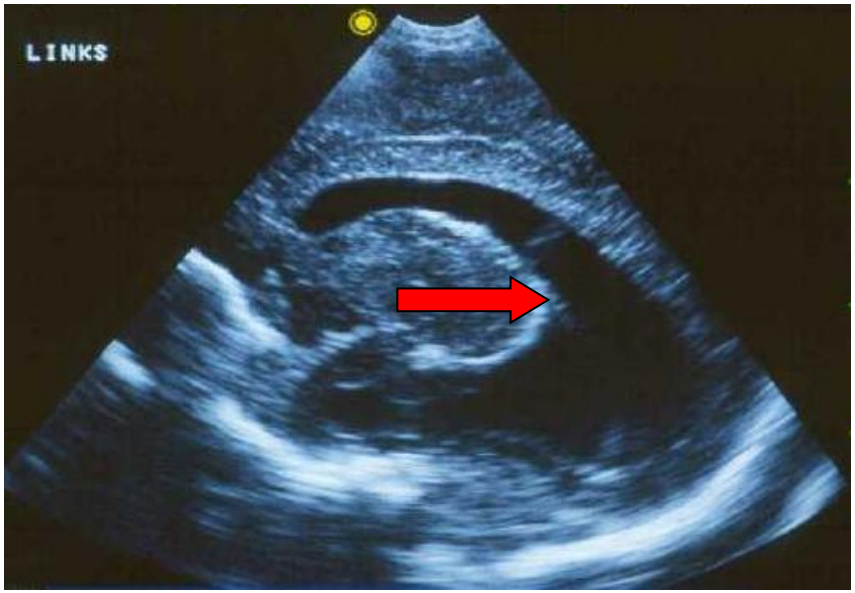




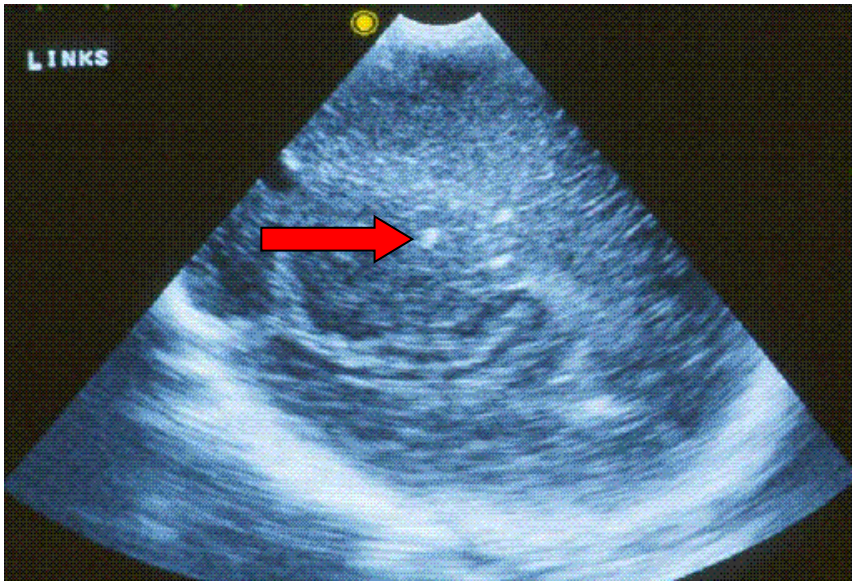
hydrocephalus

Sonography (frontal lamella)

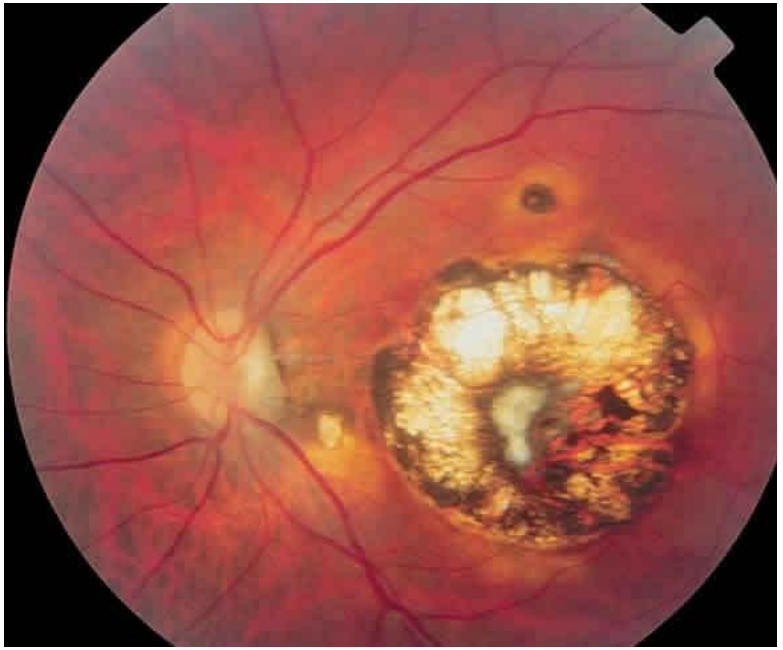
Hydrocephalus

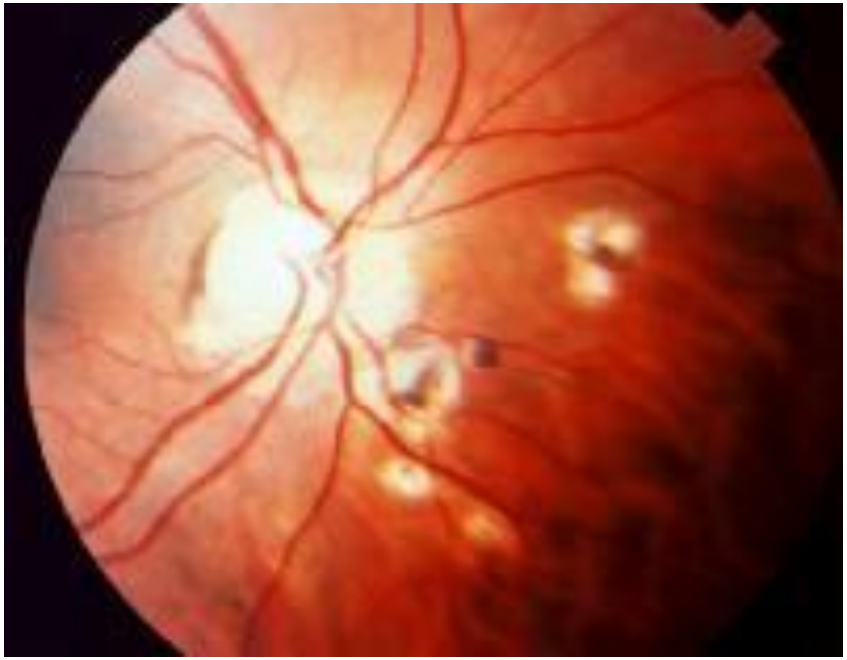


Calcifications



Congenital chorioretinitis





Management of examinations during and after pregnancy

3 examinations during pregnancy (each trimester)

Ab IgM, IgA, IgE and IgG

Positive results

Amniotic fluid: PCR

Newborns: IgM, Western Blot IgG

Interpretation of the results – serology

Infection during or very early before pregnancy

HIGH RISK!!!!!

- **Negative – woman in danger**

should undergo all three examinations during pregnancy!!!!

Acute phase

Elevation of IgM, IgA, IgE

Latent phase

Elevation of IgG

Avidity of Ab

Therapy

Pyrimethamine + Sulfadiazine + Folate

Spiramycine

(prevents transplacentary transmission, not treatment)

Affected children (for 1 year)

Pyrimethamine + Sulfadiazine + Folate

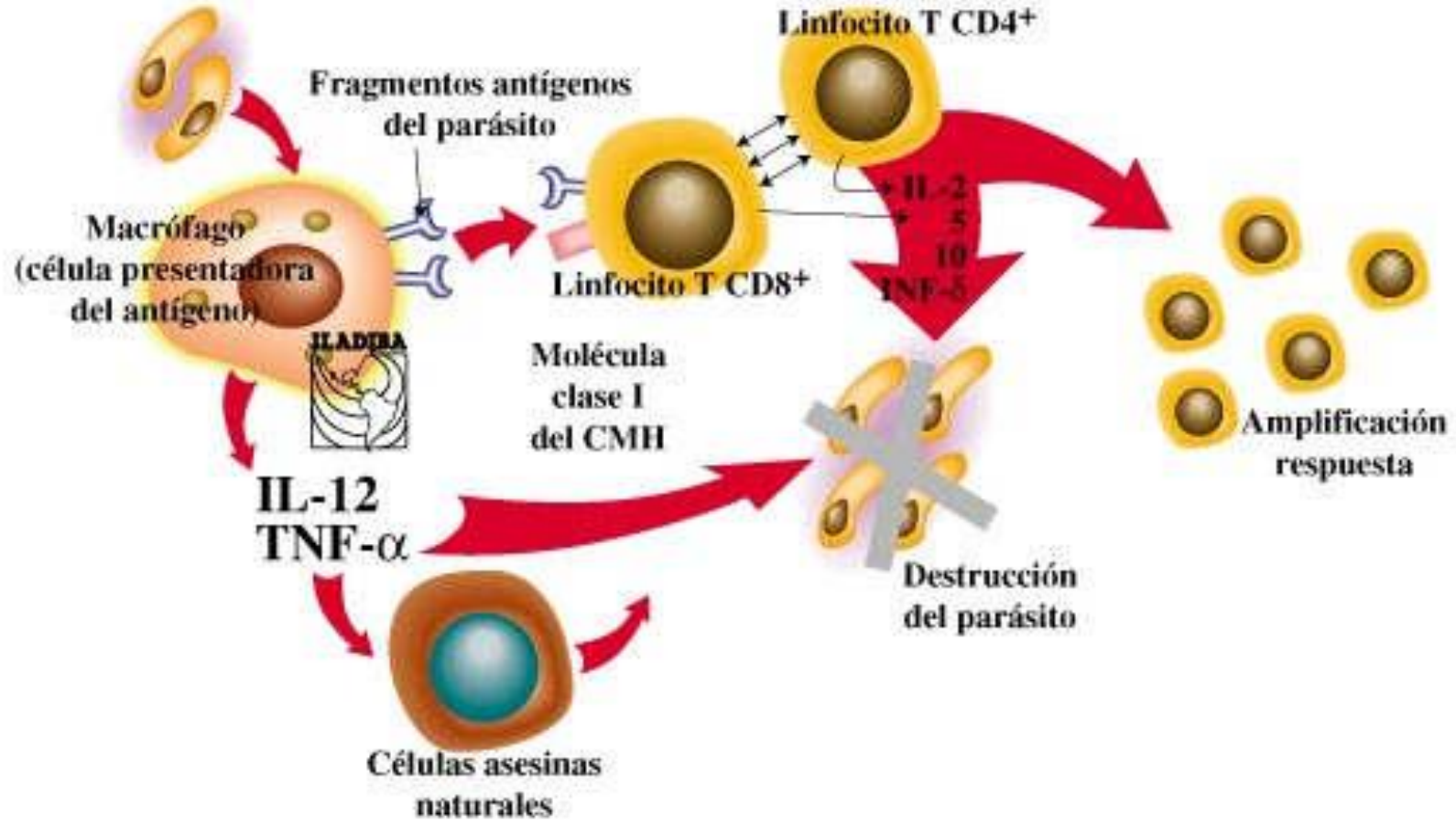
Immunosupresion

Reactivation of latent infection

tissue cysts

Impaired immunity is unable to control infection

Immunosupression



Disease

Subacute onset

CD4 less than 100/ul

Main form of manifestation:

Toxoplasmic encephalitis

Focal neurological deficit (motoric, dysarthry)

Cefalea

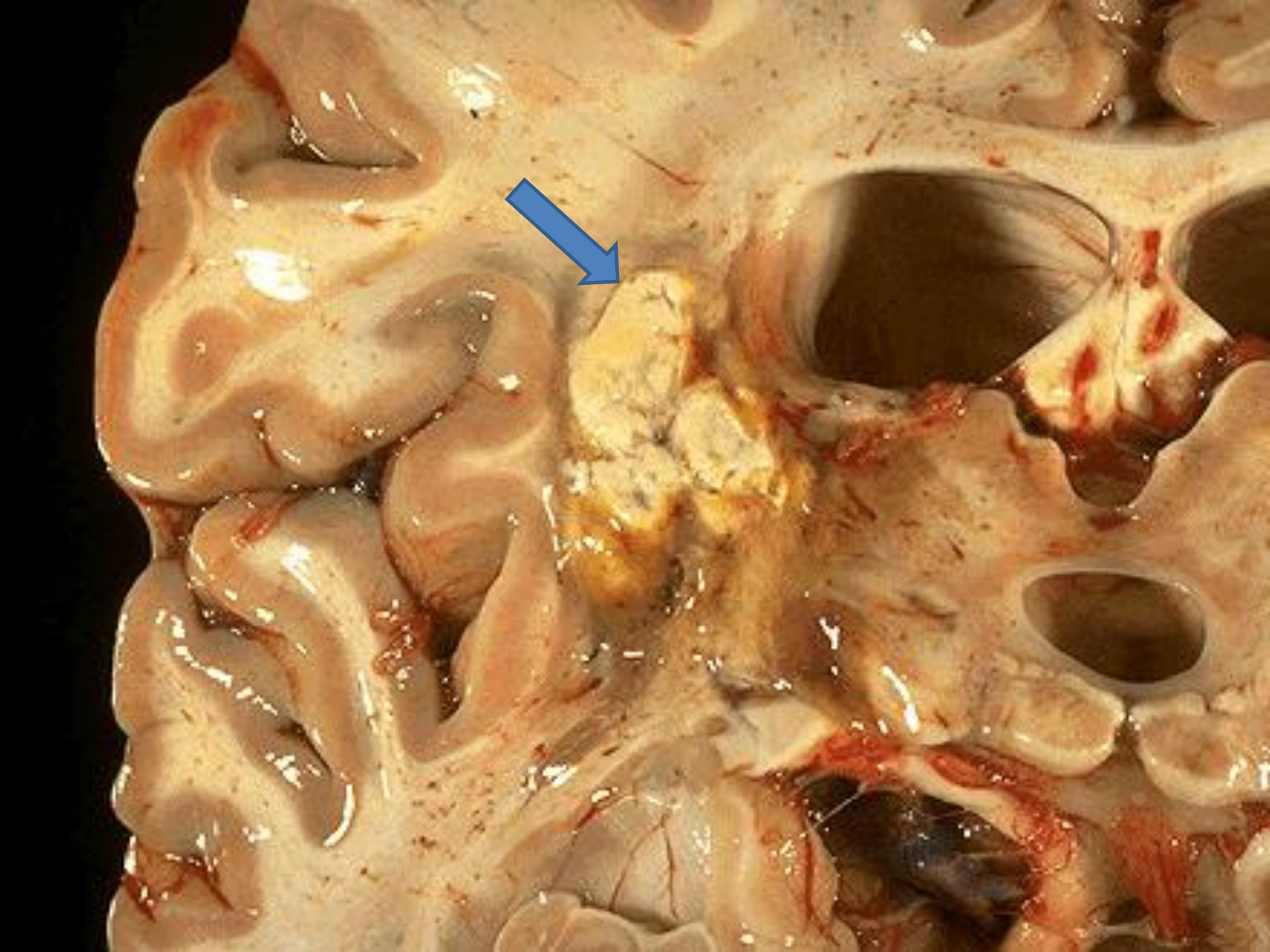
Personality changes

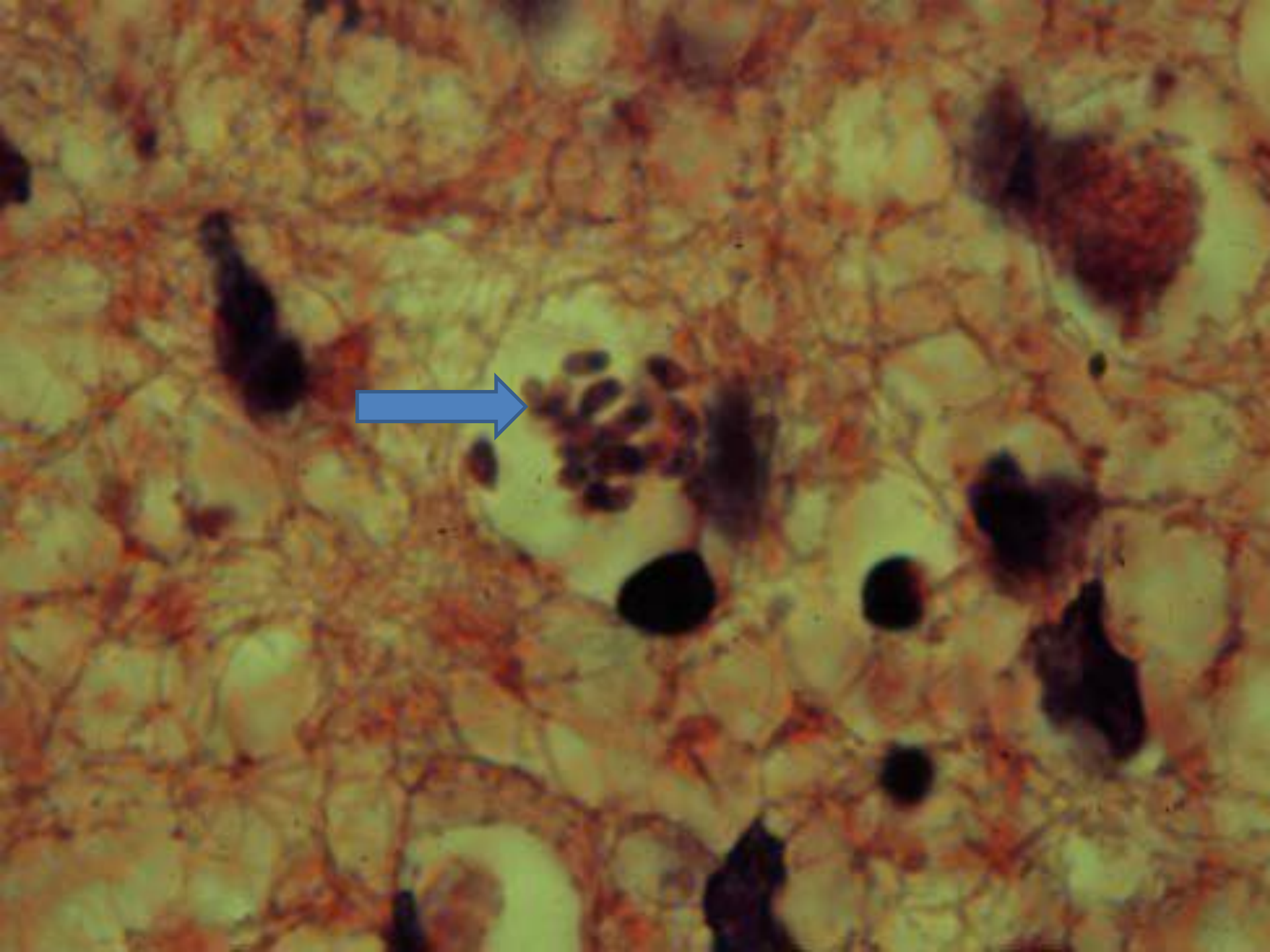
Elevated temperature

Seizures

Cerebellum

Meningism





Extracerebral toxoplasmic infections (except ocular form) are extremely rare

Ocular form

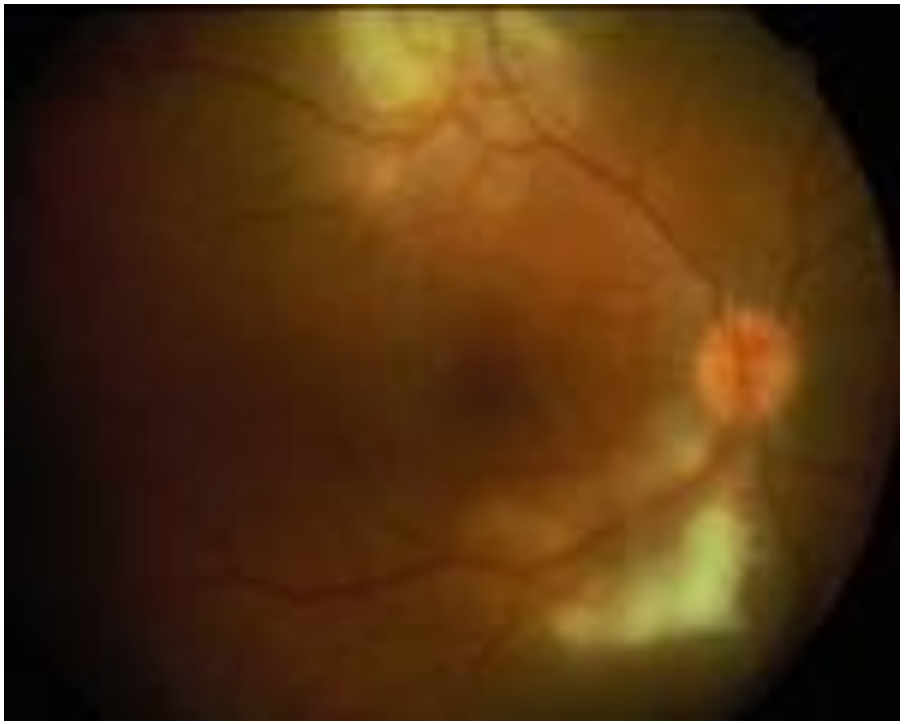
Chorioretinitis: impairement of vision, scotomas, pain, photophoby

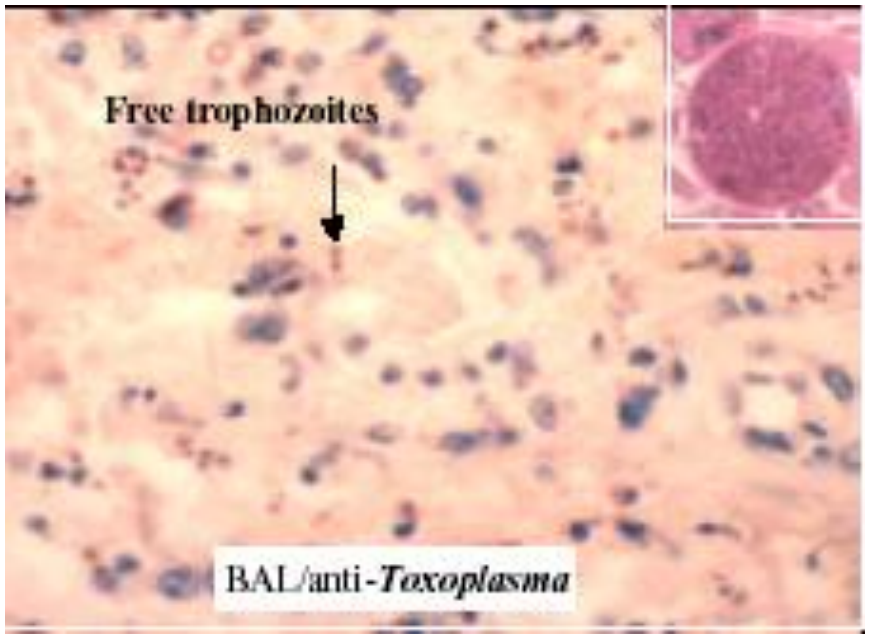
Pulmonary form

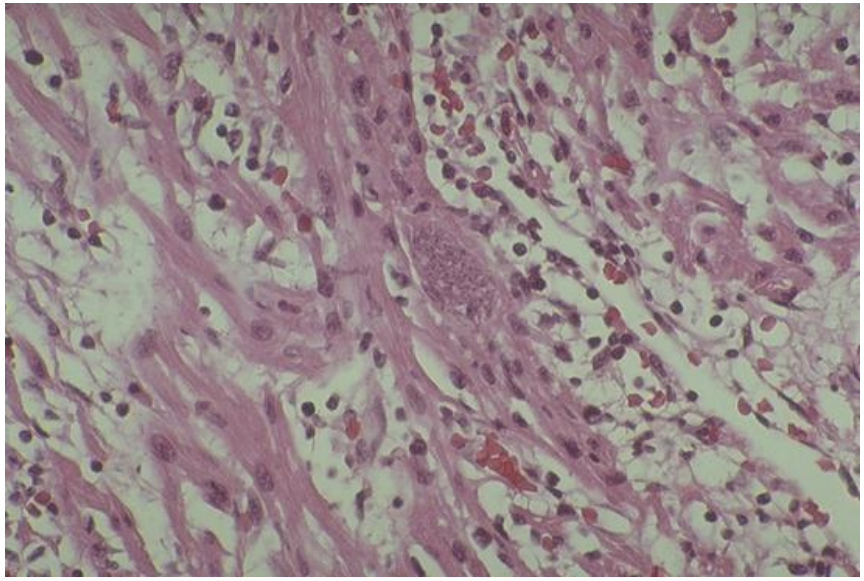
similar to *Pneumocystis* pneumonia

Disseminated form

high temperature, sepsis-like syndrome, DIC…




Free trophozoites
BAL/anti-*Toxoplasma*



Diagnostics

Serology important in HIV+ also

Patients with **elevated IgG** biggest risk

Cerebral toxoplasmosis

CSF:

mild pleocytosis with increased mononuclear cells

elevated protein

Intrathecal production of anti *T. gondii* IgG:

$$\frac{\text{CSF Sabin-Feldman dye test titer (reciprocal)} \times \text{Total serum IgG}}{\text{Total CSF IgG} \times \text{Serum dye test titer (reciprocal)}}$$

Values higher than 1 – toxoplasmic encephalitis

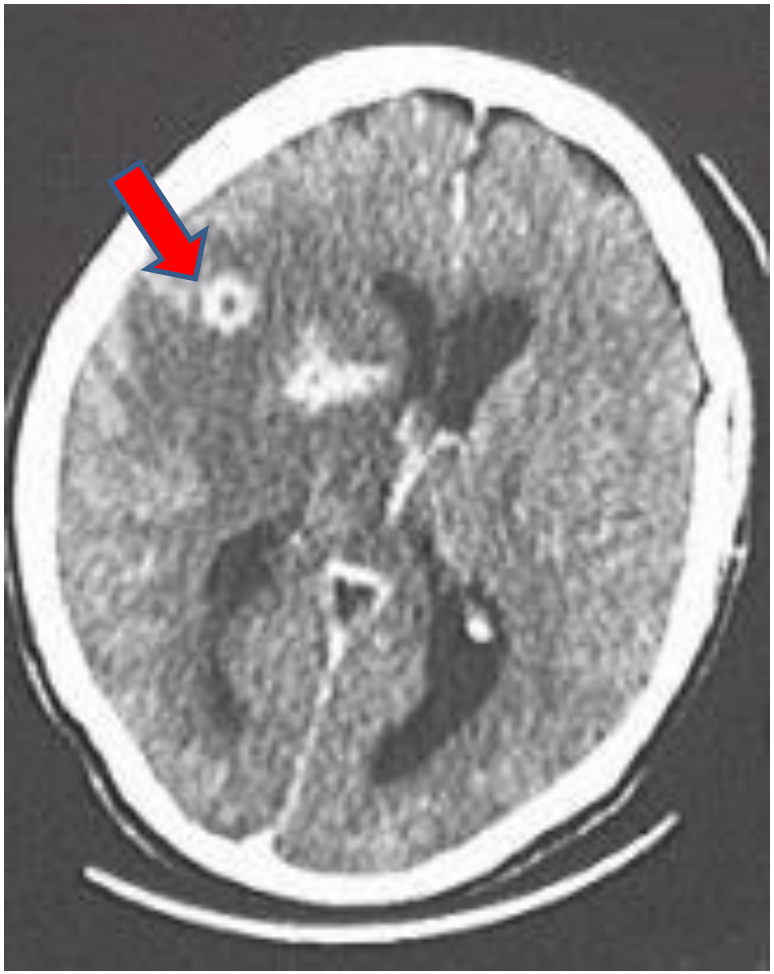
PCR is very important method in establishment of dg

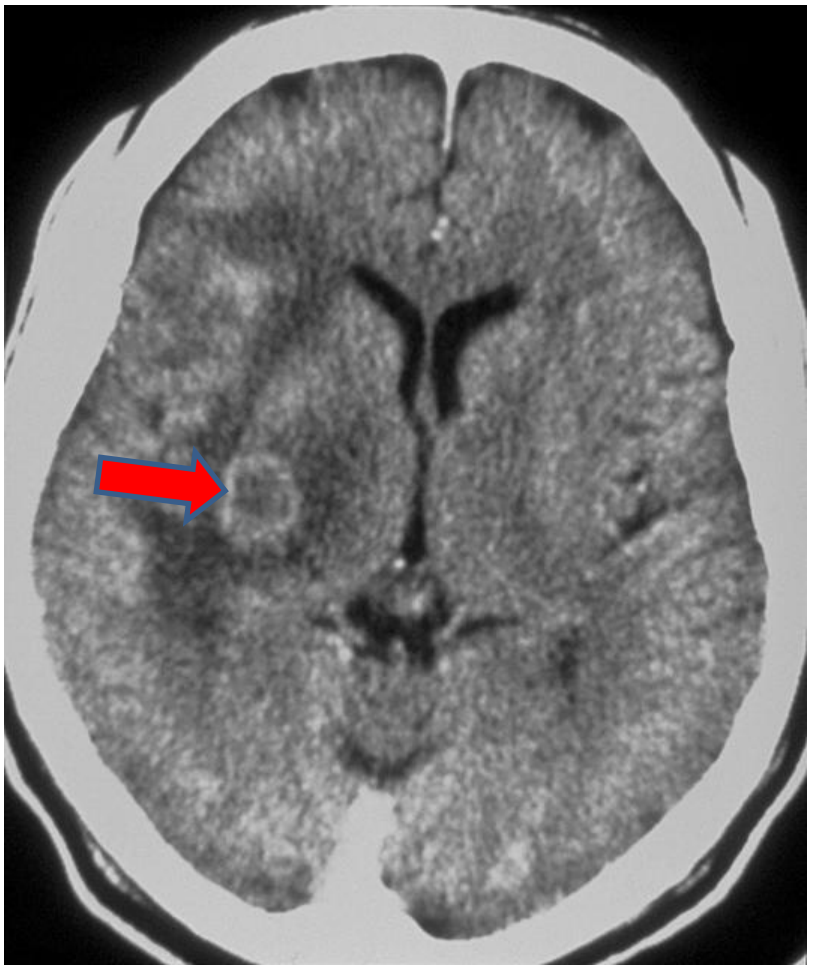
- PCR – CSF (12-70%)
  BAL
  vitreous a aqueous humor
  amnious fluid

- **CAVE!** Positive PCR in CSF doesn´t always mean toxoplasmic encephalitis; tissue cysts can be present for a long period and become disrupted

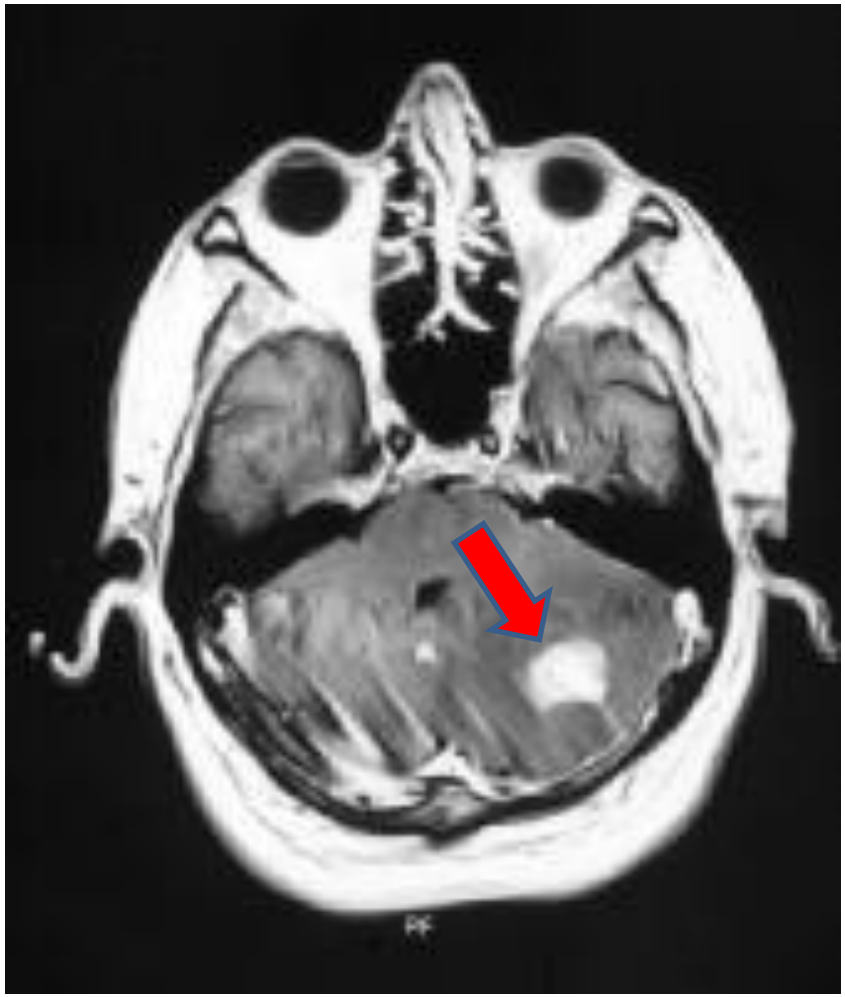
CT:

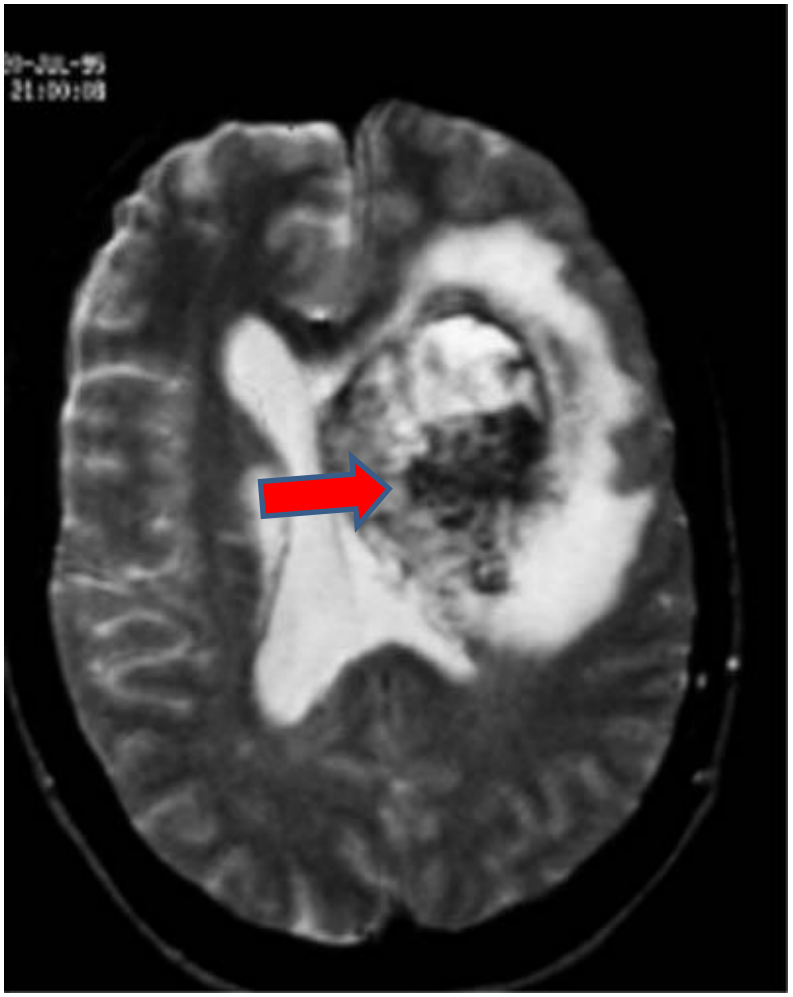
ring enhancing hypodense lesions



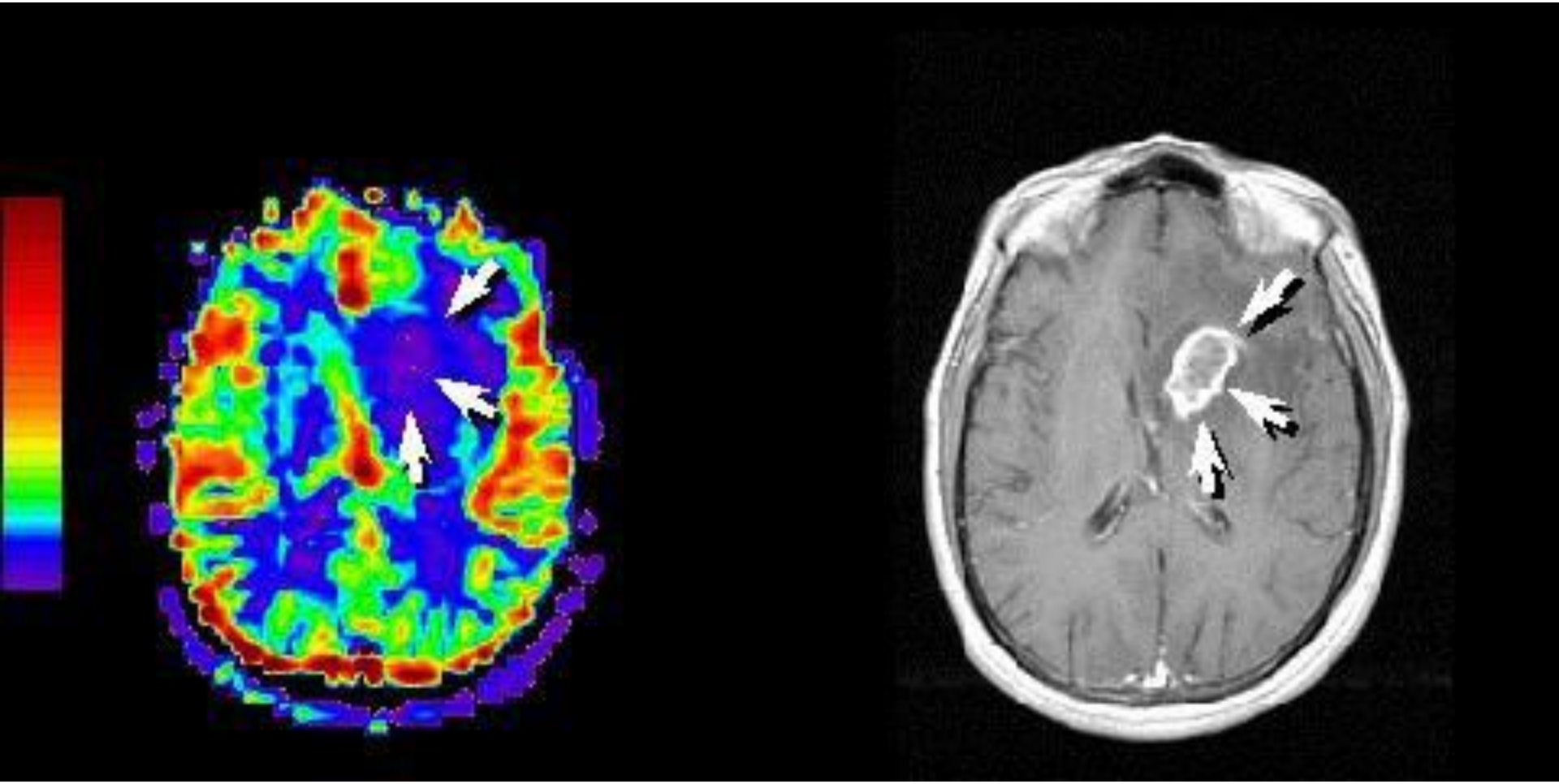


NMR – abnormal signal, very sensitive method

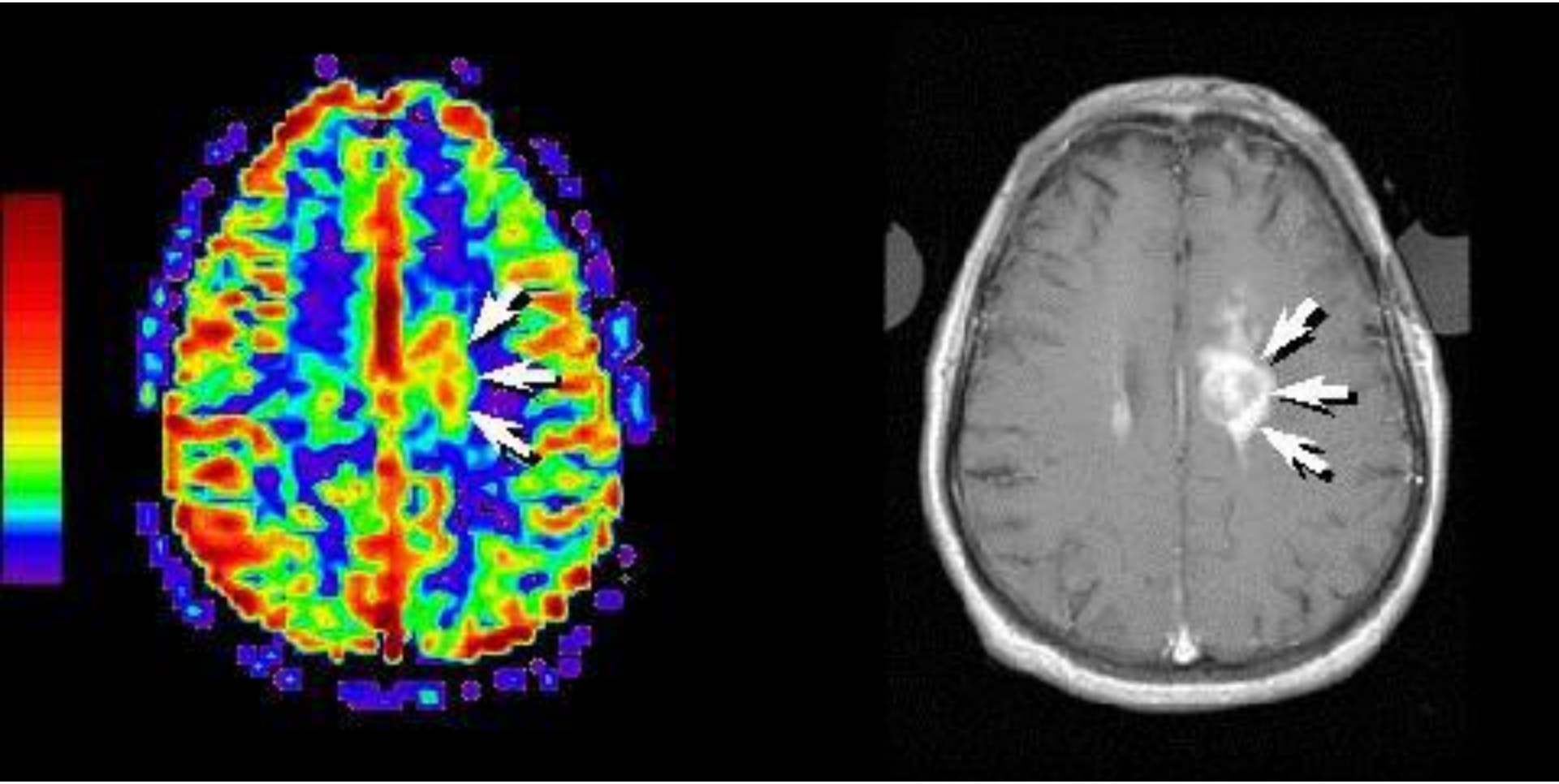




PET: lesions correspond to areas with **decreased interception of glucose**



Dif Dg: Lymphoma – lesions with increased interception of glucose

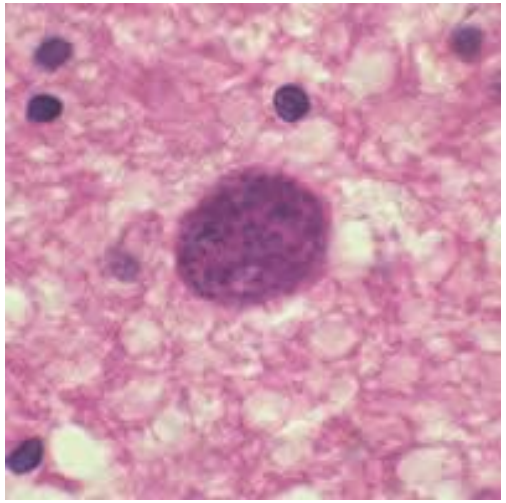


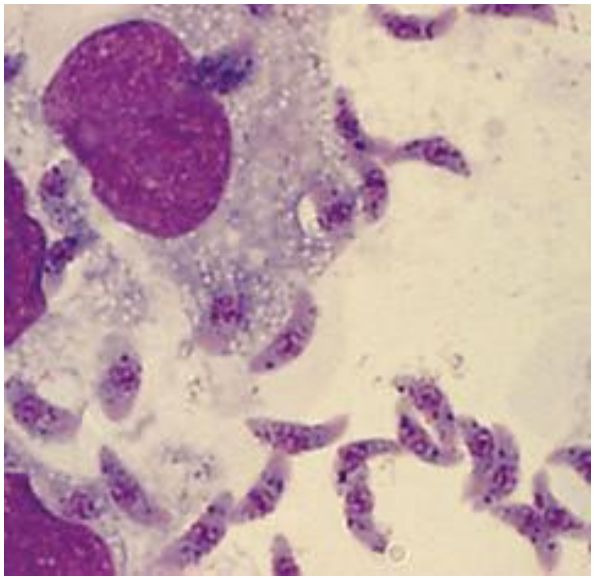
Biopsy of affected organ (Gamma knife in the toxoplasmic encephalitis)

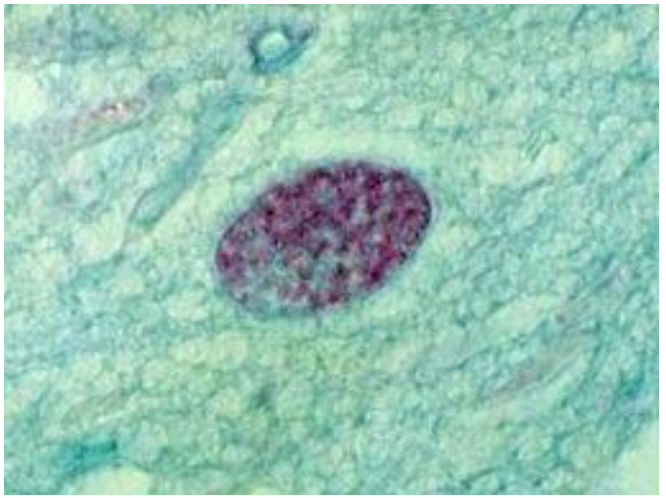
granulomatous reaction with gliosis;

necrosis,

presence of tachyzoites or tissue cysts







Therapy

Pyrimethamin

Initial dose 200 mg po; after 50-75 mg/day po in combination with

Folic acid

10 mg/day po; in combination with

Sulfadiazine

4-6 g/day po

After completion the therapy - lifelong prophylaxis

Therapy leads to improvement of the symptoms within 3 days

Corticosteroids are used in patients with oedema of the brain and symptoms of increased intracranial pressure

Therapy of acute phase of infection: 3-6 weeks

Prophylaxis

Pyrimethamine

50 mg/d PO plus

Sulfadiazine

1-1.5 g/d PO plus

Folic acid

10 mg/d PO

Prophylaxis

Alternative Regimens	
Pyrimethamine* alone	50 mg q24 hours
Pyrimethamine* plus one of the following:	25-50 mg q 24 hours
Atovaquone	1,500 mg q12 hours
Clarithromycin	1,000 mg q12 hours
Azithromycin	1,200-1,500 mg q24 hours
Dapsone	100 mg BIW

Secondary prophylaxis

Trimethoprim-sulfamethoxazole	1 DS tablet qd
	2 DS tablet tiw
Pyrimethamine*/dapsone	50 mg qw/50 mg qd
	50 mg BIW/100 mg BIW
	75 mg qw/200 mg qw
Pyrimethamine*/sulfadoxine	3 tablet every 2 weeks
	1 tab BIW

Follow the basic standards of hygiene

Food must be always properly cooked

CD4 under 100/ul – always prophylaxis

CD4 over 100/ul + opportunistic infection: always prophylaxis

Latent infection with toxoplasma: personality changes?

Male

- Low superego strenght
- Protension
- Suspecting, jealous, dogmatic
- Low IQ
- High Eysenck s lie score
- Low harm avoidance
- Reserved, detached, critical

Female

- Warmhearted, outgoing, easygoing
- Superego
- Trustig, accepting conditions, tolerant
- Worldly, polished,
- Controlled, socially precise