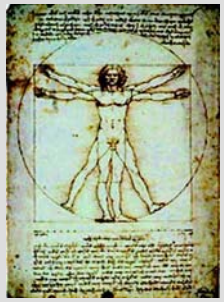
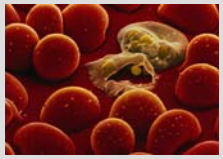
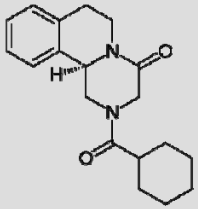
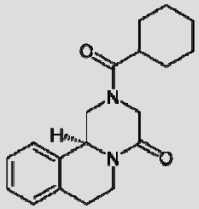








University of São Paulo
Institute of Biomedical Sciences
Department of Parasitology
Unit for Drug Discovery
Carsten Wrenger

Toxoplasma gondii

Taxonomy of *Toxoplasma*

Protozoa

Apicomplexa

Sporozoa (Sub.classe Coccidia)

Eucoccidiida

Sarcocystidae

Toxoplasma

T. gondii

Intermediate host: HUMAN

Definitive host: CAT

Toxoplasma gondii

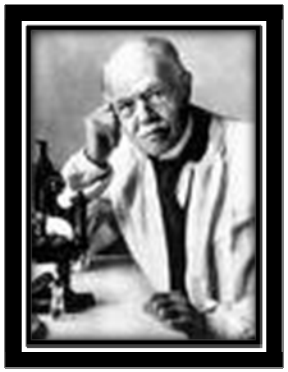
1) History
2) Biology of the parasite
3) Clinical aspects
4) Transmission
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

Toxoplasma gondii

1) History
2) Biology of the parasite
3) Clinical aspects
4) Transmission
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

Toxoplasma gondii

- First isolated in Tunisia in 1908



Charles Nicolle
(1866-1936)

Louis Hubert Manceaux
(1865-1943)

Alfonso Splendore
(1871-1953)

Brasil

Ctenodatylus gondi

North African Rodent called "gundi"

• In 1923 congenital transmission was described, and a diagnostic test established by A. Sabin and H. Feldmann

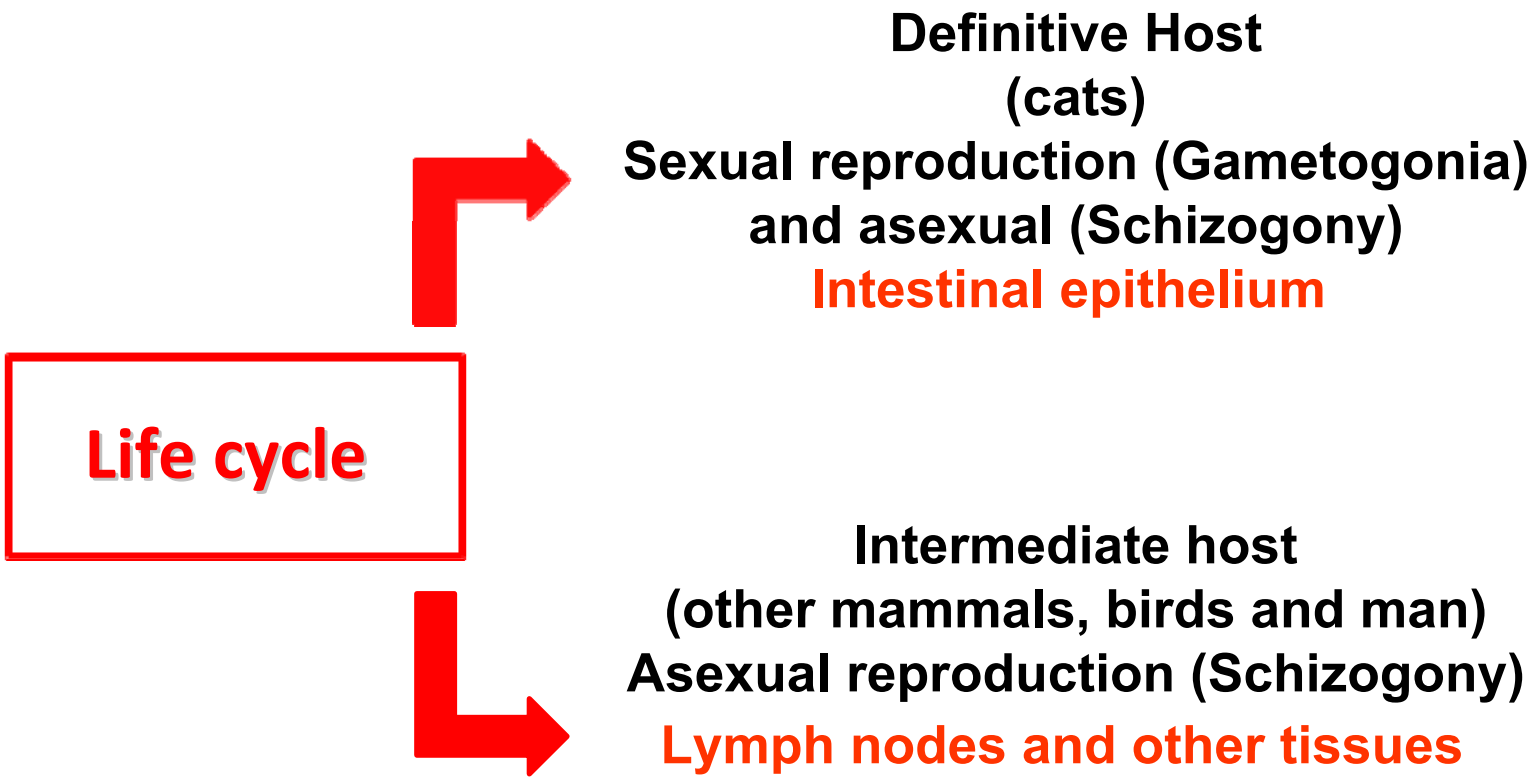
• In 1956 it was postulated that the infection would be by ingestion of raw meat infected with cysts, proven in 1965.

•The complete life cycle was discovered only in 1970.

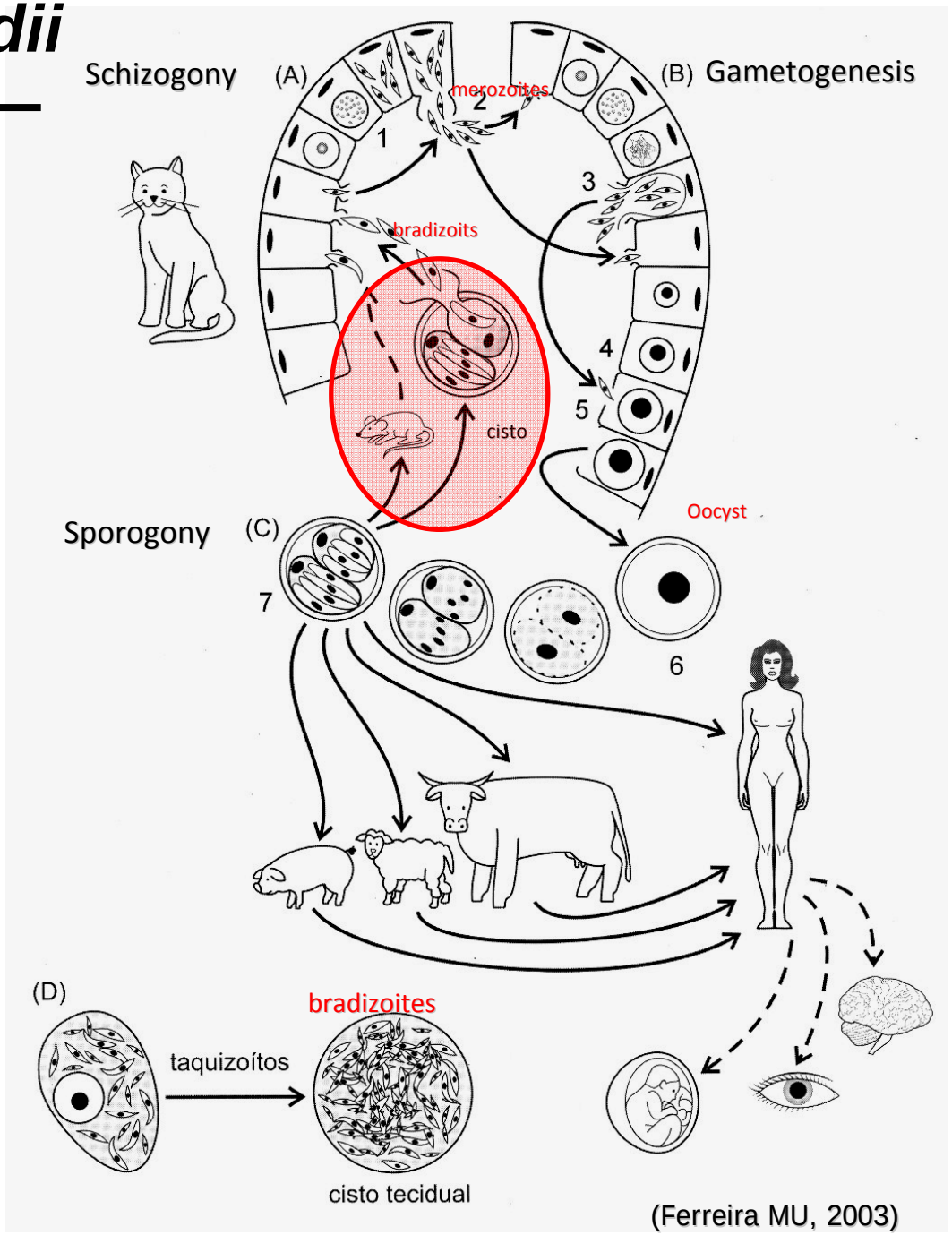
Toxoplasma gondii

1) History
2) Biology of the parasite
3) Clinical aspects
4) Transmission
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

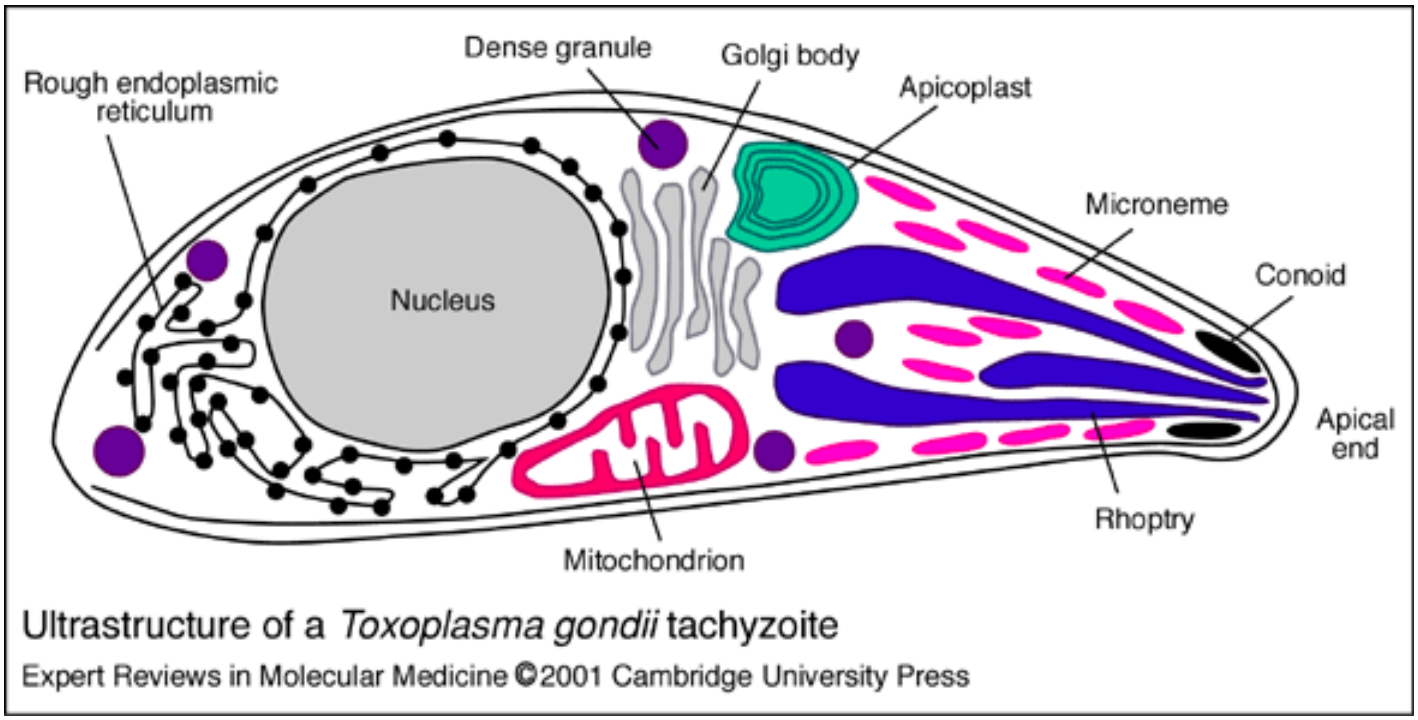
Life Cycle of *T. gondii*



Life Cycle of *T. gondii*



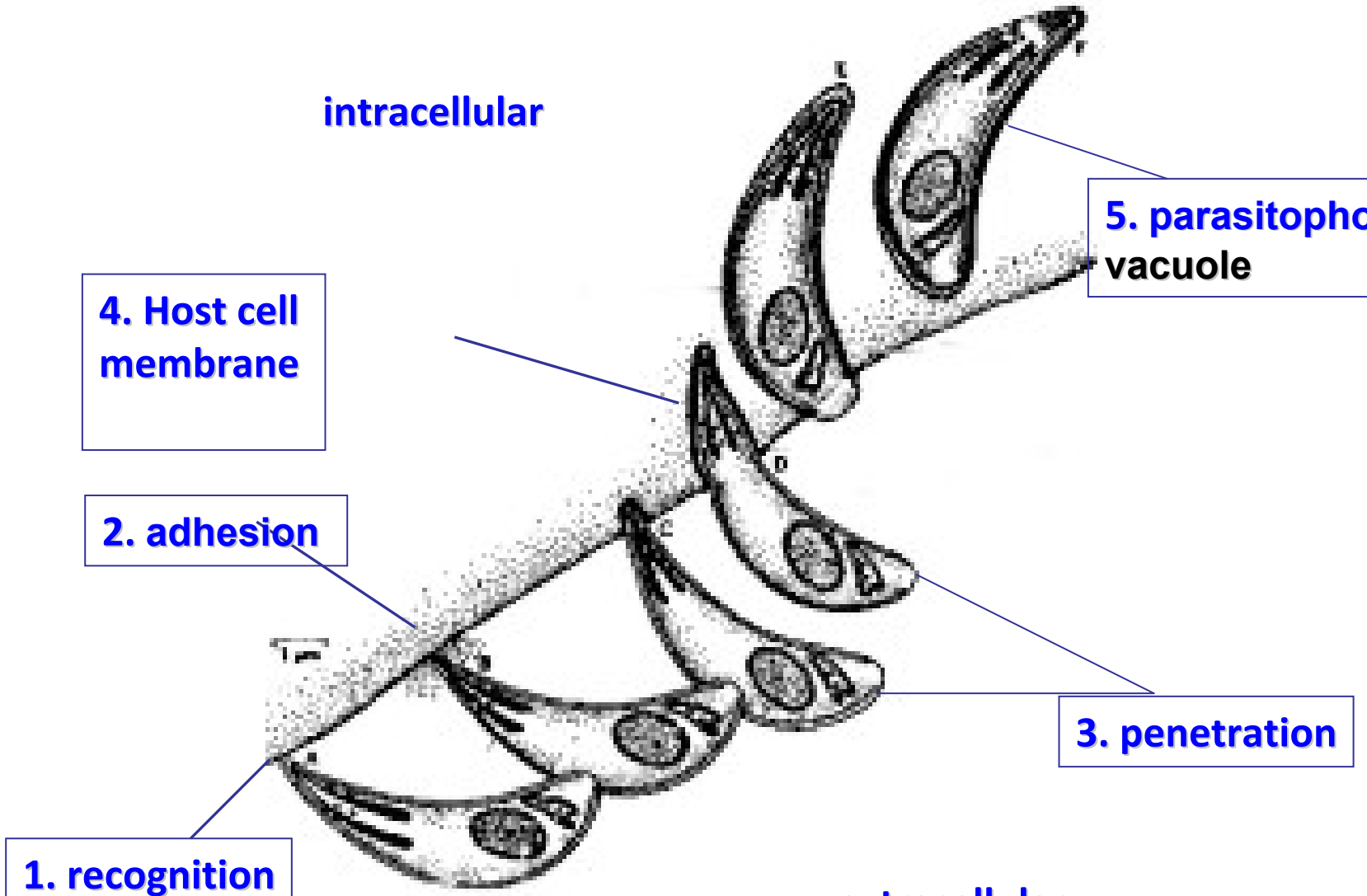
Apicomplexa - Structure of *T. gondii*



Ultrastructure of a *Toxoplasma gondii* tachyzoite

Complexo apical: conóide, anel polar (dois), microtúbulos, roptrias, micronemas e grânulos densos

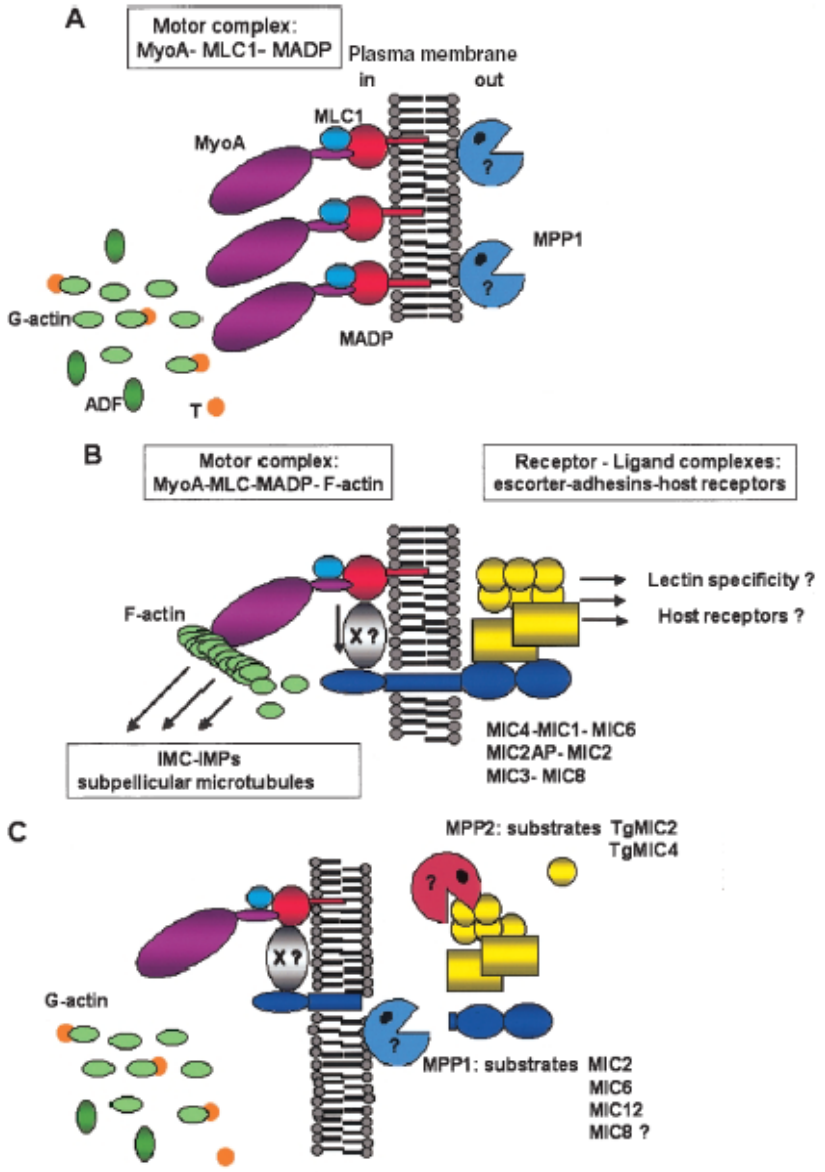
Invasion of *T. gondii*



Invasion of *T. gondii*

Locomotion and invasion is Active and depends on an "engine“ actin-myosin and Proteins similar to thrombospondin on the surface

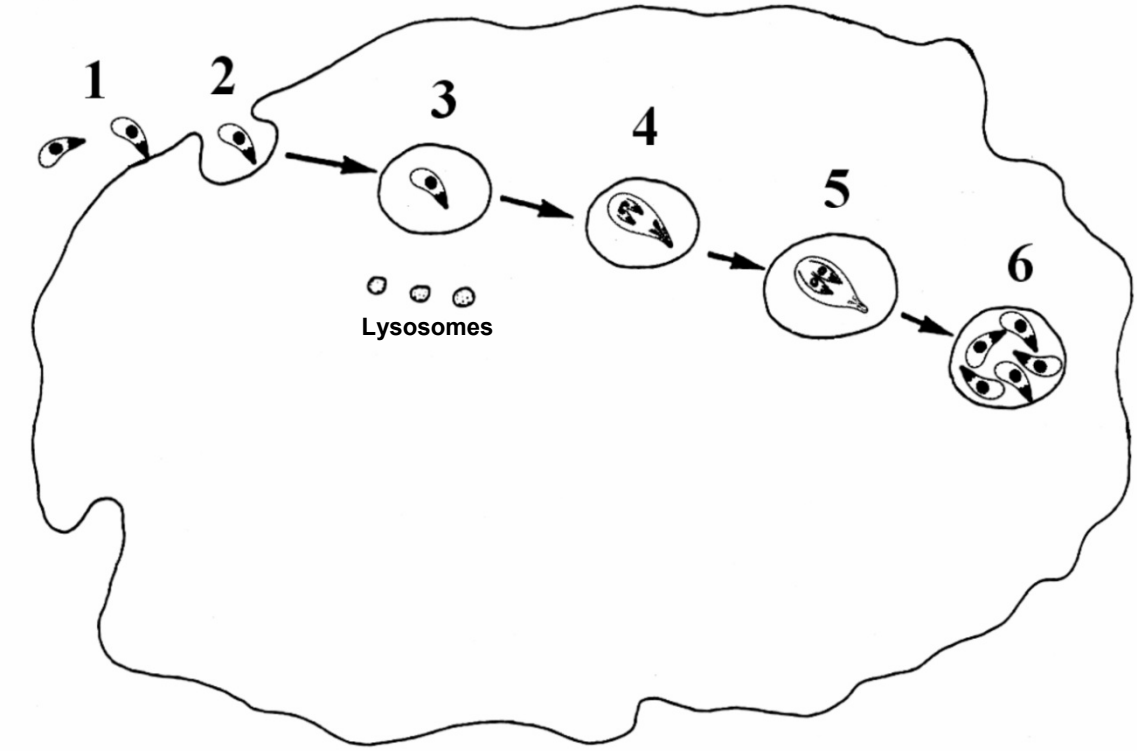
Active movement of T. gondii



(Opitz e Soldati, 2002)

Toxoplasma prevents the fusion of lysosomes

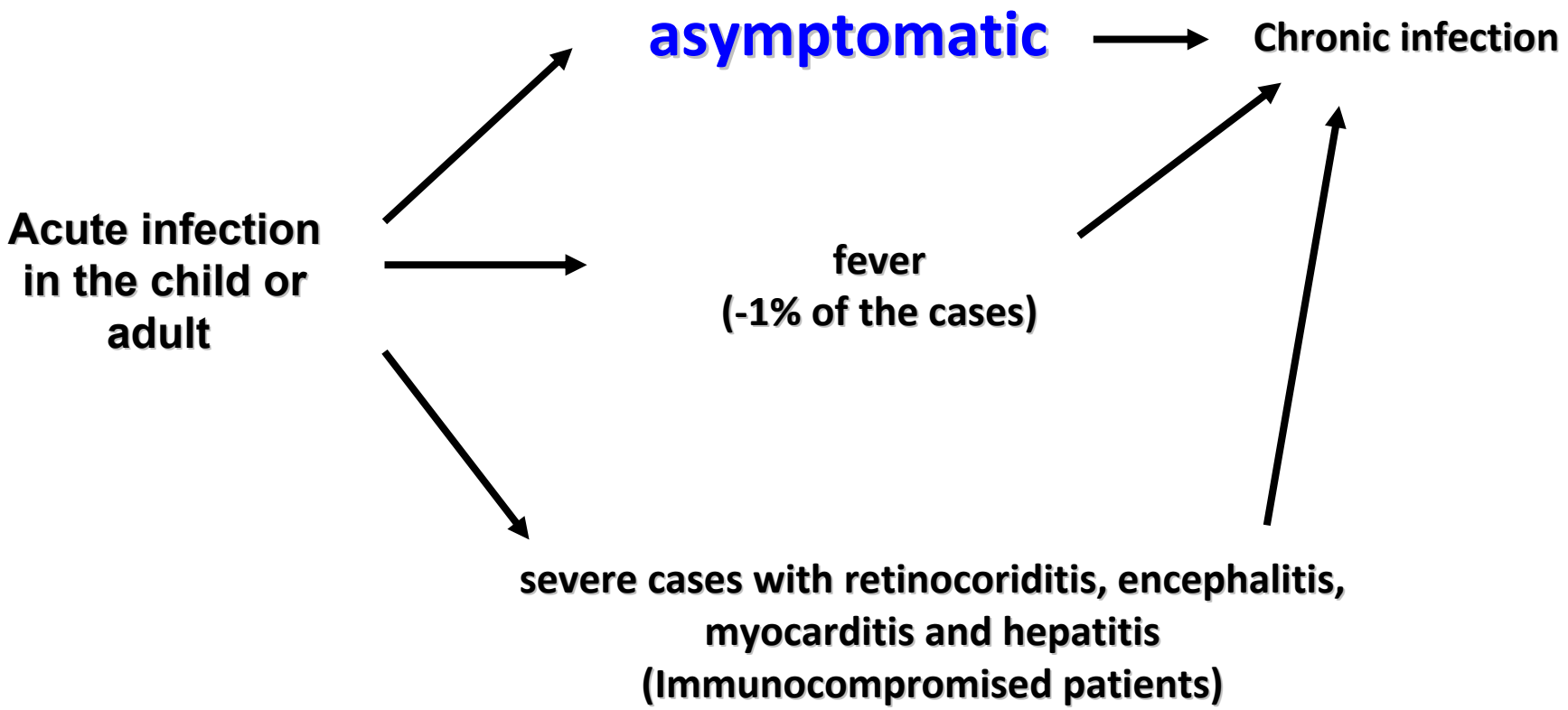
“Probably due to microneme proteins"



Toxoplasma gondii

1) History
2) Biology of the parasite
3) Clinical ascpects
4) Transmission
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

Clinical aspects



Clinical aspects

One of the most severe forms of the disease with varied symptoms:

- **First trimester** - 10x greater chance of miscarriage.

- **Second trimester** - abortion, premature birth with or without sequelae.

- **Third trimester** - The child may be born normal and present later symptoms.

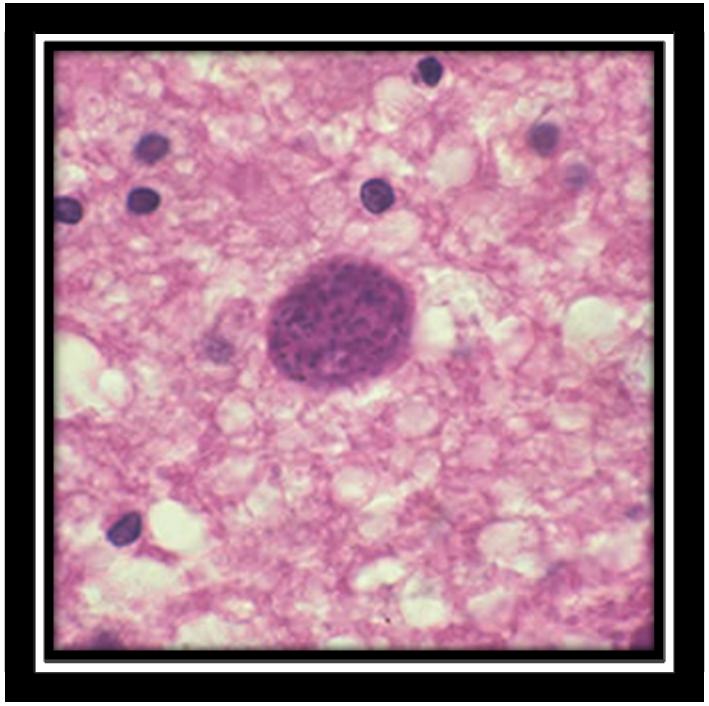
Large number of fatal cases

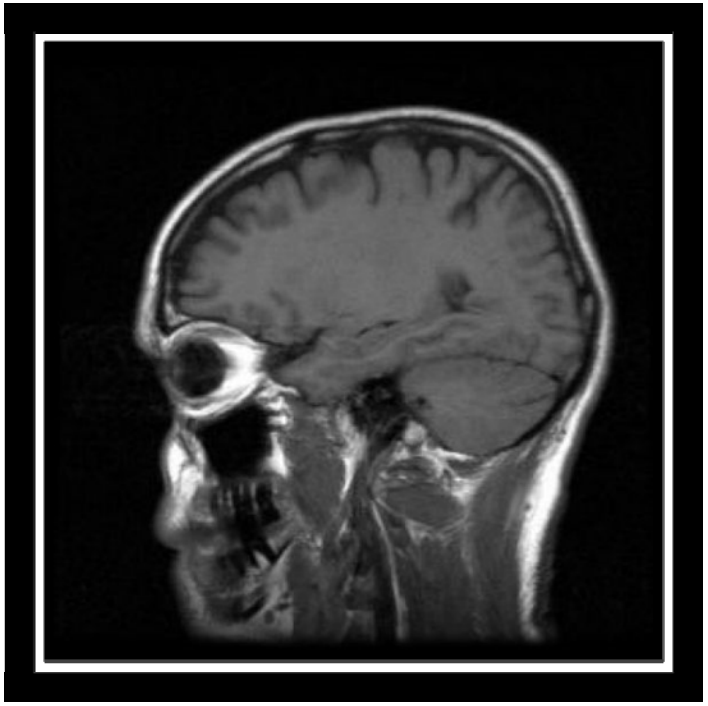
Symptoms of Toxoplasmosis

Toxoplasma gondii

1) History
2) Biology of the parasite
3) Clinical aspects
4) Mechanisms of Pathogenesis
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

Mechanisms of Pathogenesis

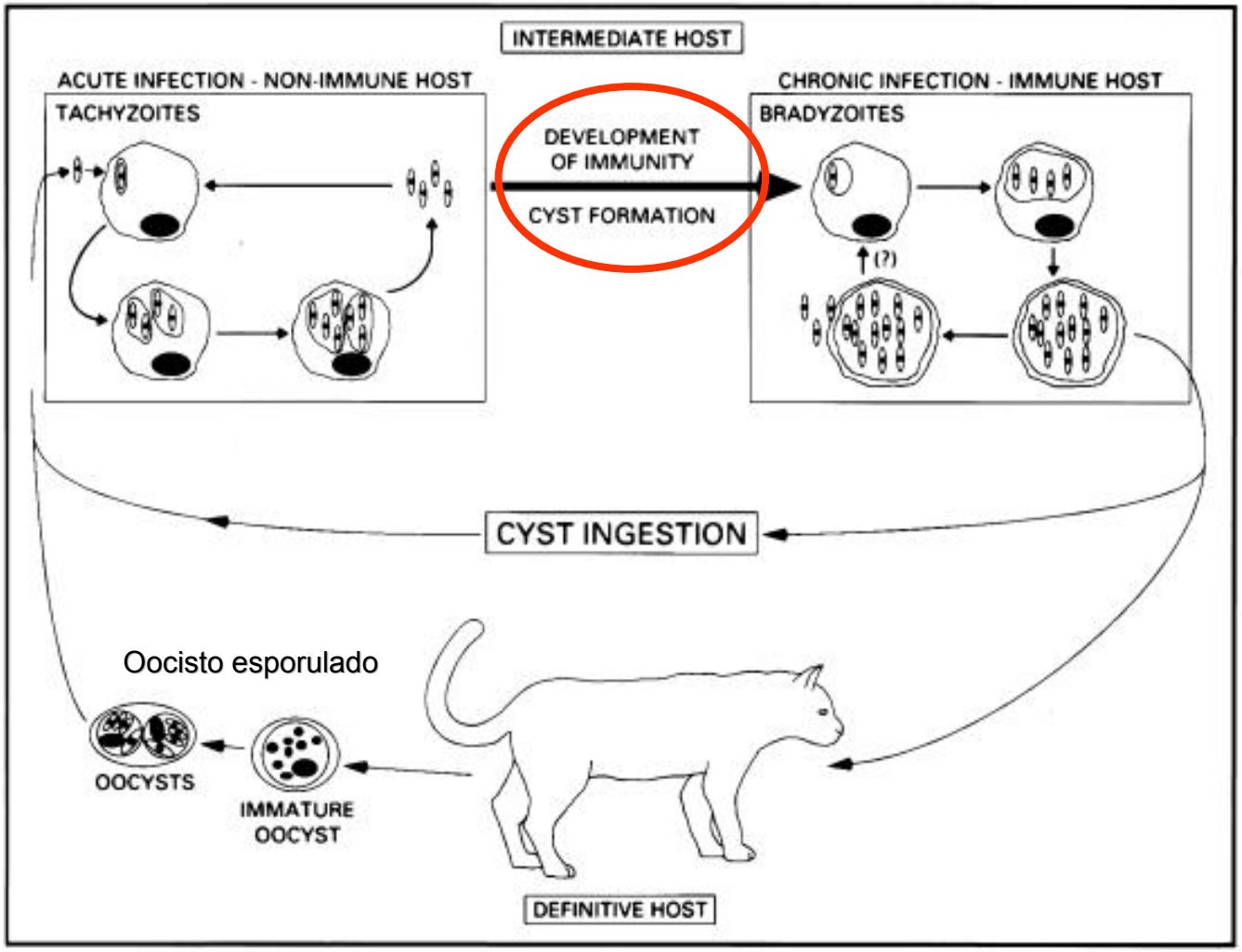




Bradyzoites lodged in a CNS cell cyst

Response to *T. gondii* infection

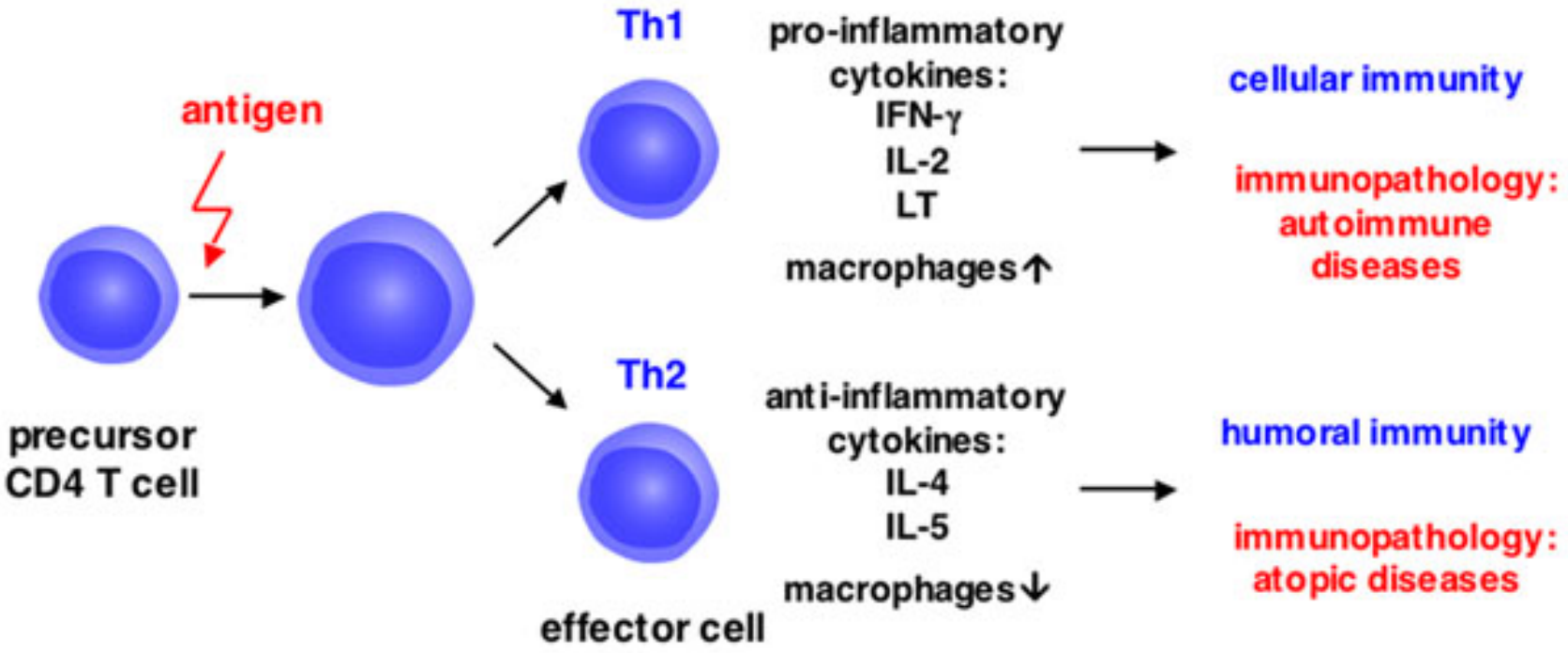
Intermediate host



Definitive host

Denker, 1998

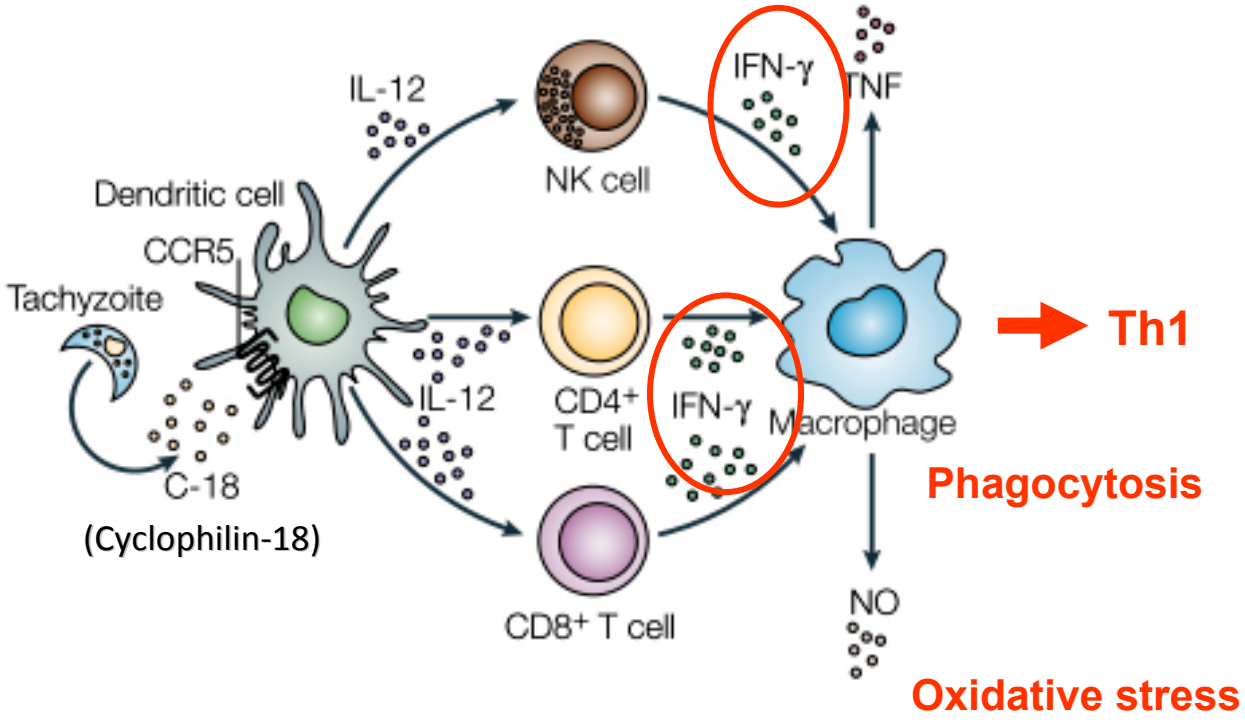
Response to *T. gondii* infection



Chang e Lewin, 2007

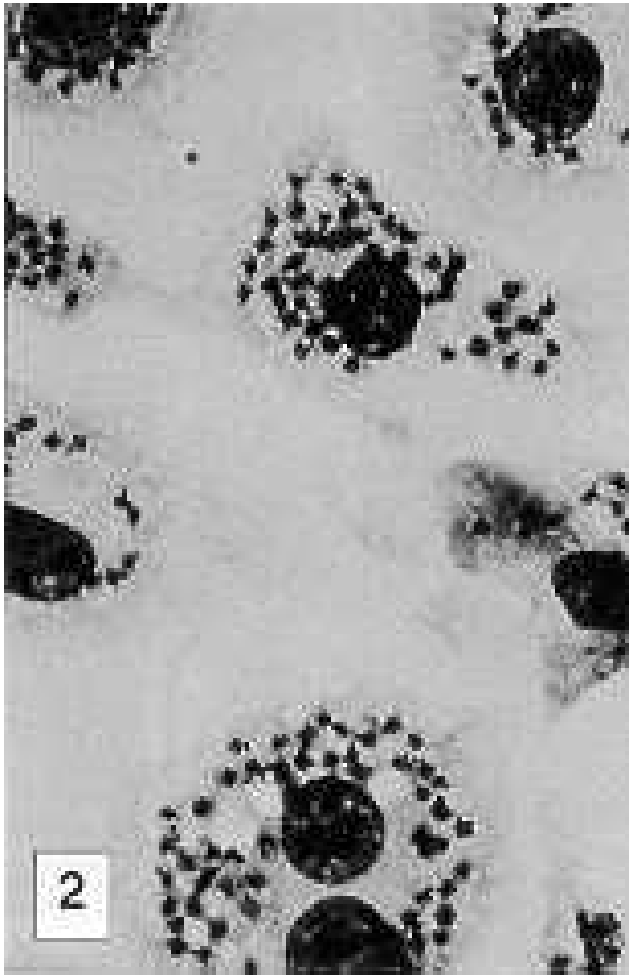
Response to *T. gondii* infection

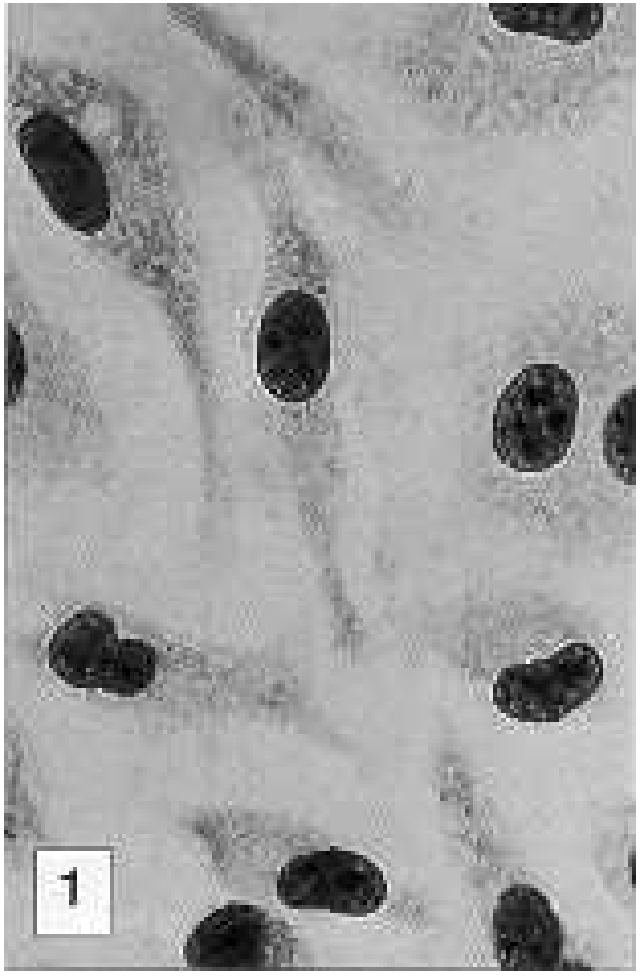
Because of its intrinsic virulence, *T. gondii* induces a potent interleukin 12-dependent cell mediated immune response (IL-12).



Aliberti, 2005

Superoxide and nitric oxide (NO) are destroying parasites within cells

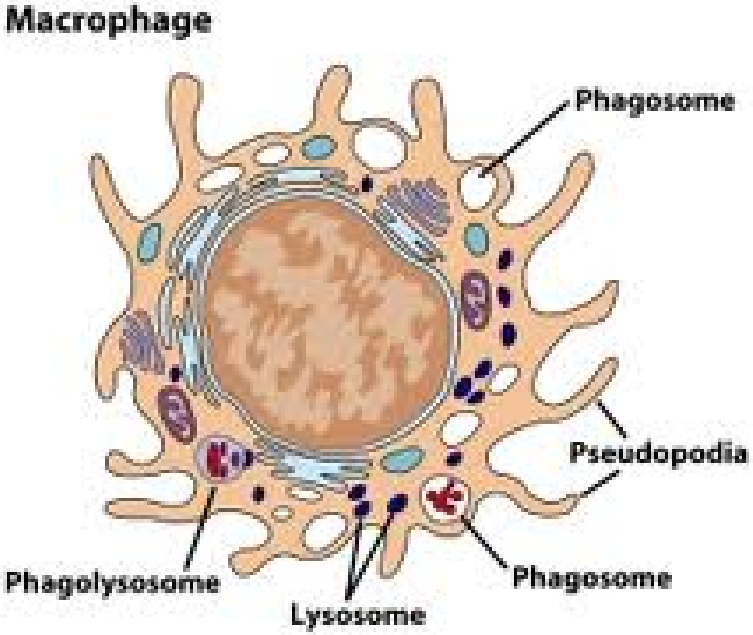




- IFNγ

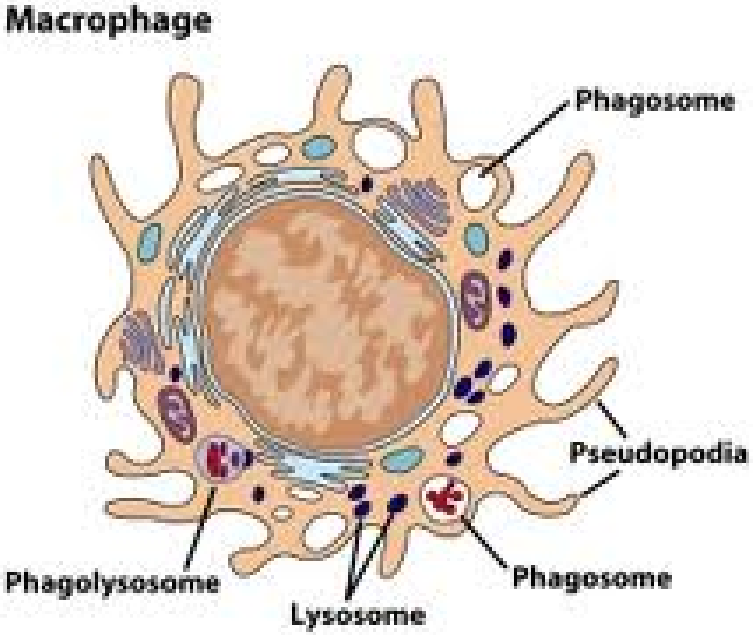
+ IFNγ

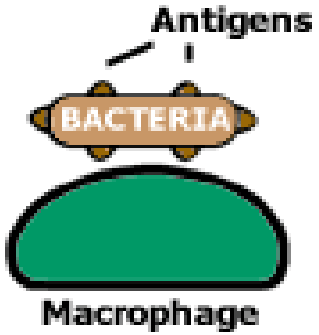
Cellular immune response to *T. gondii* infection



Springer pictures

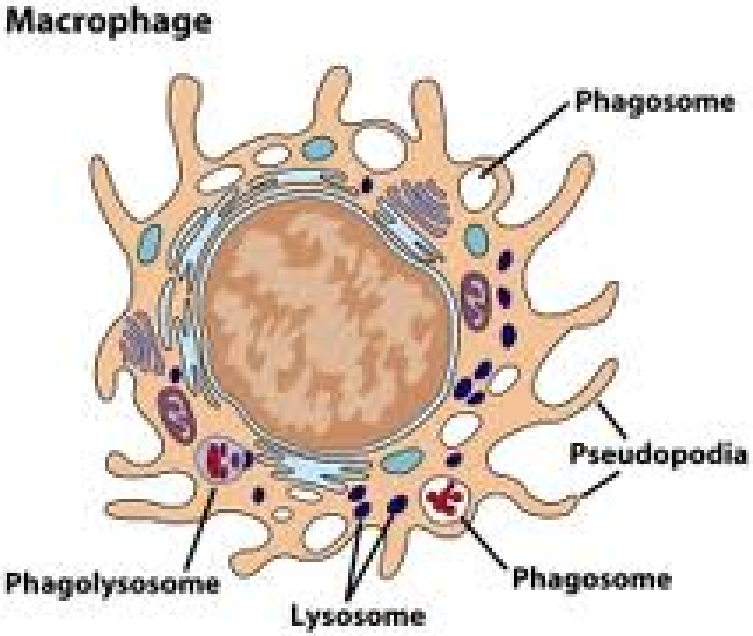
Cellular immune response to *T. gondii* infection

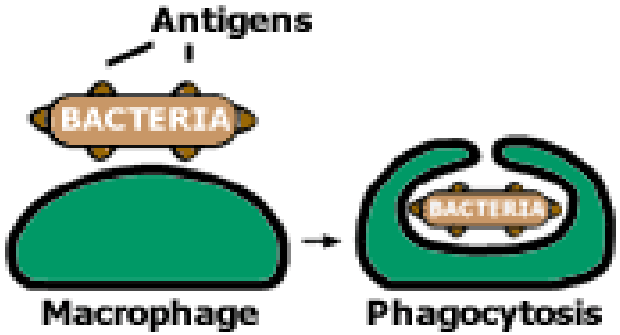




Springer pictures

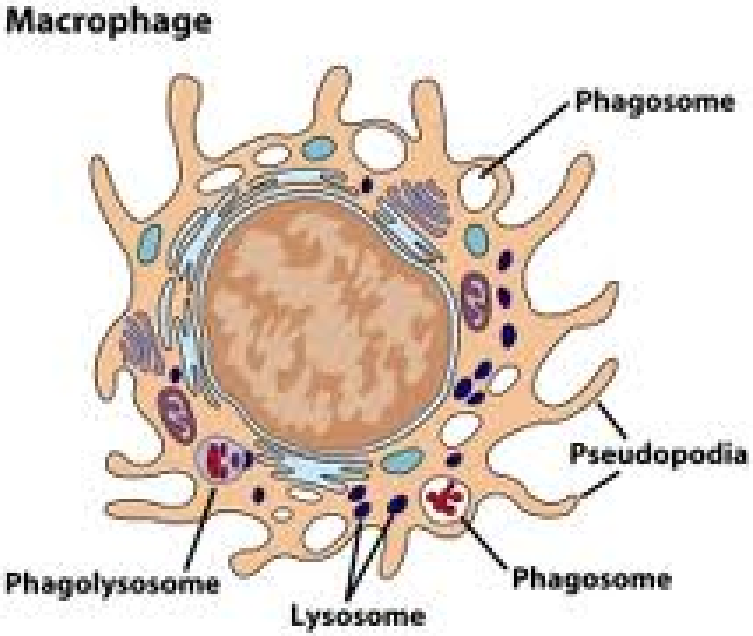
Cellular immune response to *T. gondii* infection

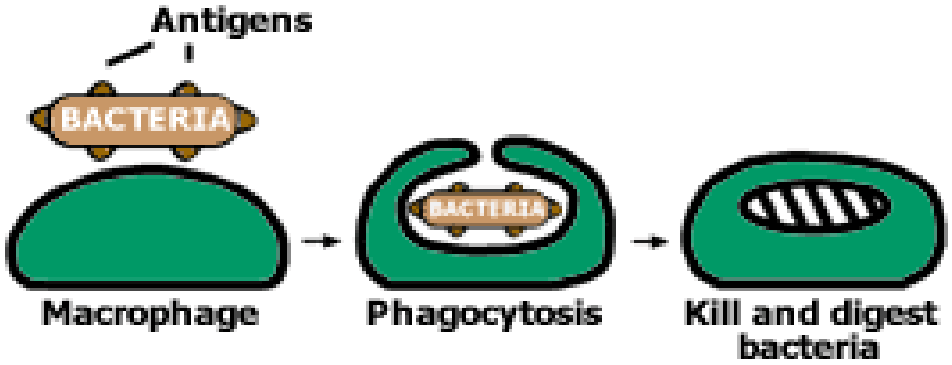




Springer pictures

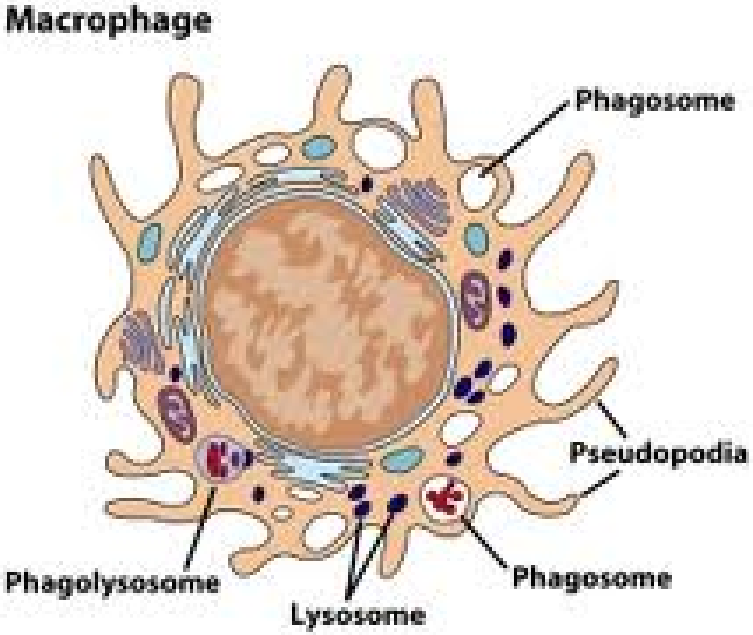
Cellular immune response to *T. gondii* infection

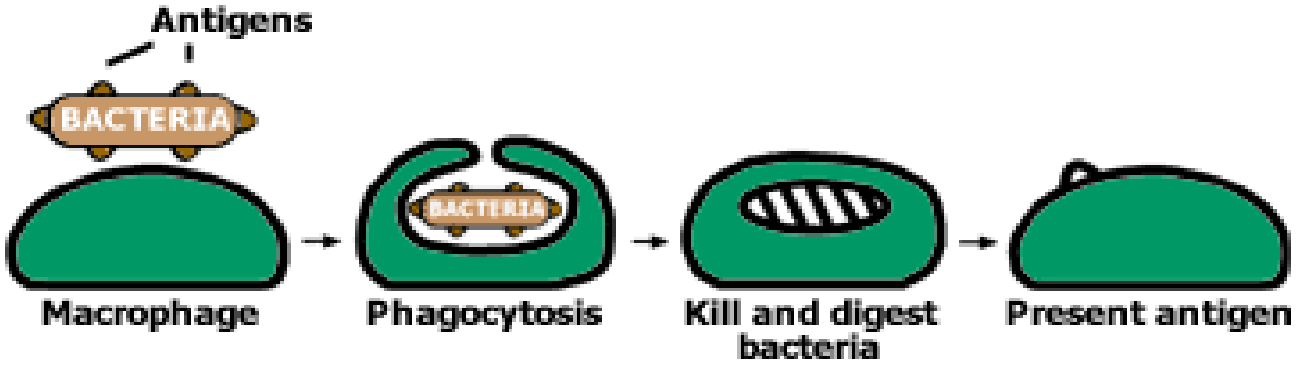




Springer pictures

Cellular immune response to *T. gondii* infection

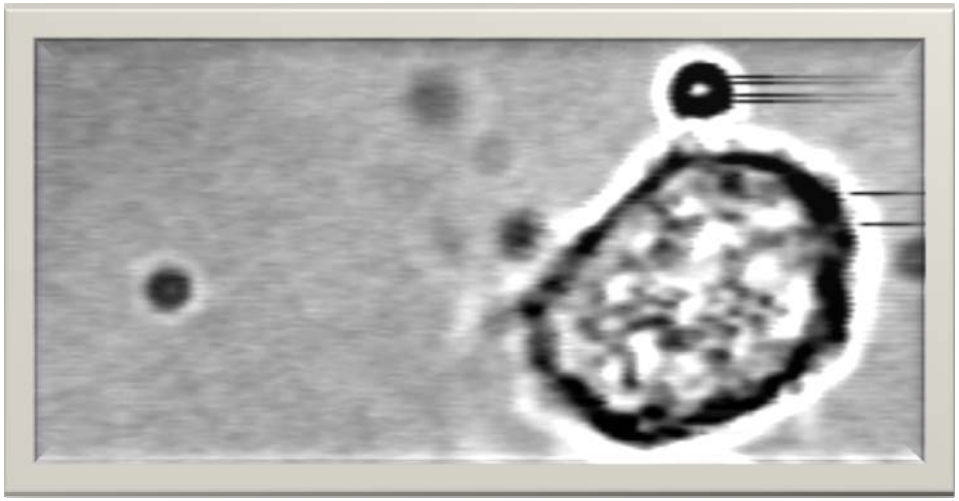




Springer pictures

Response to *T. gondii* infection

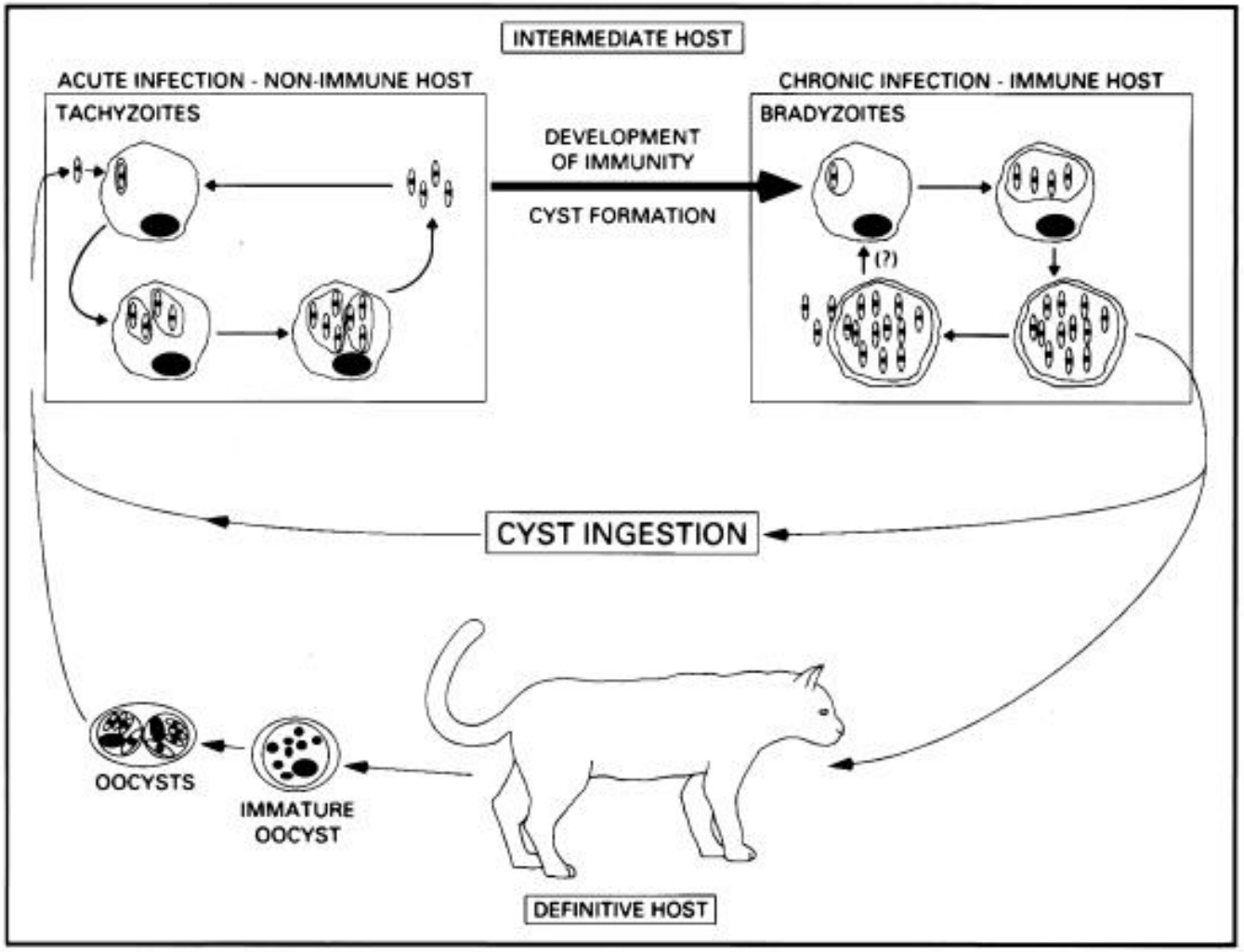
- IFNγ



+ IFNγ

Gazzinelli, 2005

Response to *T. gondii* infection



Denker, 1998

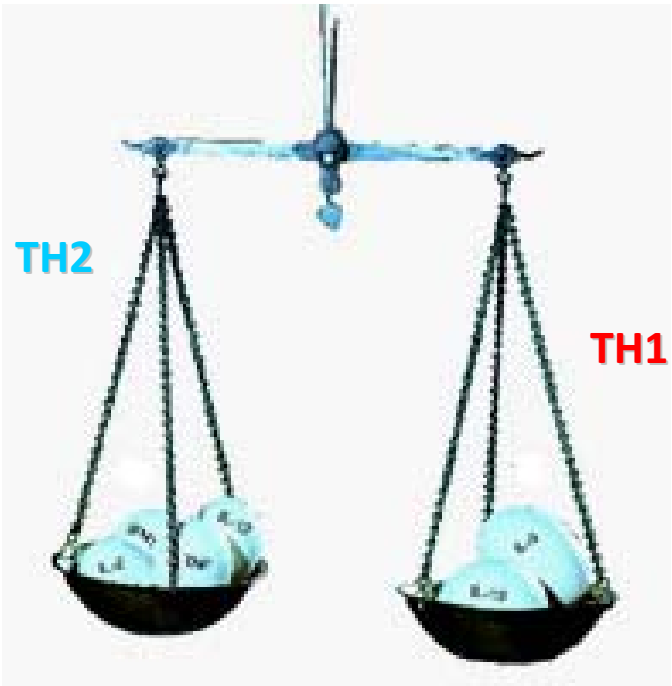
Immune response to *T. gondii* infection

Predominante TH2 response or no response

IL-10
TGF β

"REPLICATION"

Taquizoites
Rupture of the cysts



more pronounced expression of TH1-type cytokines

IFNγ
TNFα

"CONTROL"

Bradizoites (Cysts)
Chronic infection

Epidemiology

- Almost perfect parasite: Approx. 70% of humans had contact with *T. gondii*

Epidemiology

- Almost perfect parasite: Approx. 70% of humans had contact with *T. gondii*

- High incidence in countries with eating habits (raw meat?): France 96%, Germany 70%, Brazil 50-80%

Epidemiology

- Almost perfect parasite: Approx. 70% of humans had contact with *T. gondii*
- High incidence in countries with eating habits (raw meat?): France 96%, Germany 70%, Brazil 50-80%
- Domestic cats are an important source of oocysts: 2-20 million oocysts per infected cat are eliminated daily! The cat's infection can last up to a year.

Epidemiology

- Almost perfect parasite: Approx. 70% of humans had contact with *T. gondii*
- High incidence in countries with eating habits (raw meat?): France 96%, Germany 70%, Brazil 50-80%
- Domestic cats are an important source of oocysts: 2-20 million oocysts per infected cat are eliminated daily! The cat's infection can last up to a year.
- Sporadic contaminations occur with water-borne oocysts that can lead to local epidemics

Município do PR tem surto de toxoplasmose

CURITIBA - Um surto de toxoplasmose assusta a população de Santa Isabel do Ivaí, cidade de 9,3 mil habitantes, a 580 quilômetros de Curitiba. A Secretaria da Saúde confirmou 65 casos da doença e há pelo menos 70 suspeitos aguardando resultados de exames. Entre casos confirmados estão os de três mulheres grávidas. Ainda não há uma conclusão sobre como o protozoário Toxoplasma gondii, causador da infecção, propagou-se entre a população.

anterior
Secretaria vai distribuir remédios por Sedex
próxima
Arqueólogos encontram objetos

7 day later...

Transmissão - A água consumida na cidade vem sendo apontada como uma das principais suspeitas de ter transmitido o parasita à população. Os técnicos acreditam que a água - o município tem sistema próprio de distribuição, independente do sistema estadual - foi contaminada pelas fezes de uma gata, que vivia próximo de um dos reservatórios. A secretaria está oferecendo R$ 100 para quem conseguir capturá-la. "Para as análises que estamos fazendo, ela é importante", disse a secretária.

O parasita que causa toxoplasmose usa os animais como hospedeiro, sobretudo os gatos. Além da água, a doença pode ser transmitida por alimentos crus, como carnes e verduras.

Toxoplasma gondii

1) History
2) Biology of the parasite
3) Clinical aspects
4) Transmission
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

Diagnostics

- **Parasitological diagnosis**

  - demonstration of the organism in biopsy or necropsy

  - intraperitoneal inoculation in lymph node, liver or spleen biopsy mouse

  - culture of the parasites in fibroblasts

  - PCR for the detection of ribosomal DNA of the parasite in samples of tissue and amniotic fluid. iagnóstico parasitológico

Diagnostics

- **Serological diagnosis**

  - detection of antibodies

  IgM - acute phase

  IgG - chronic phase

  - ELISA, immunofluorescence and haemagglutination

Treatment

- Indicated only for severe cases and pregnant women, infection of immunocompetent adults does not require therapy

Treatment

- Indicated only for severe cases and pregnant women, infection of immunocompetent adults does not require therapy

- Pyrimethamine and Sulfonamides in combination - they act in a synergistic manner by blocking the
- pathways of p-aminobenzoic acid
- the cycle of folic acid (vertebrates can use pre-synthesized folic acid, not Toxoplasma)

- Alternatively: Clindamycin and Tetracycline

Toxoplasma gondii

1) History
2) Biology of the parasite
3) Clinical aspects
4) Transmission
5) Epidemiology
6) Diagnostics and treatment
7) Prevention and Control

Prevention and control

- Proper cooking of the meats

Prevention and control

- Proper cooking of the meats
- Wash hands with soap and water after handling raw meats

Prevention and control

- Proper cooking of the meats
- Wash hands with soap and water after handling raw meats
- Avoid contact with cat feces

Prevention and control

- Proper cooking of the meats
- Wash hands with soap and water after handling raw meats
- Avoid contact with cat feces
- Clean daily the domestic environments contaminated with feces of cats with boiling water and wash well the hands after these tasks

Prevention and control

- Proper cooking of the meats
- Wash hands with soap and water after handling raw meats
- Avoid contact with cat feces
- Clean daily the domestic environments contaminated with feces of cats with boiling water and wash well the hands after these tasks
- Sand boxes should be covered

Prevention and control

- Proper cooking of the meats
- Wash hands with soap and water after handling raw meats
- Avoid contact with cat feces
- Clean daily the domestic environments contaminated with feces of cats with boiling water and wash well the hands after these tasks
- Sand boxes should be covered
- Serology in early pregnancy to differentiate pregnant women with chronic infection from those who may contract acute infection.

Prevention and control

- Proper cooking of the meats
- Wash hands with soap and water after handling raw meats
- Avoid contact with cat feces
- Clean daily the domestic environments contaminated with feces of cats with boiling water and wash well the hands after these tasks
- Sand boxes should be covered
- Serology in early pregnancy to differentiate pregnant women with chronic infection from those who may contract acute infection.
- Treatment of pregnant women