

Pneumocystis jirovecii and *Toxoplasma gondii*:
A Tale of Two Parasites or
Opportunistic Infections In Immuno-deficient Hosts
Charles Knirsch, MD, MPH

Protozoan Parasites

1. *Toxoplasma gondii*

2. The Malarias

Plasmodium falciparum

Plasmodium vivax

Plasmodium ovale

Plasmodium malariae

3. Diarrheal disease-causing protozoa:

Giardia lamblia

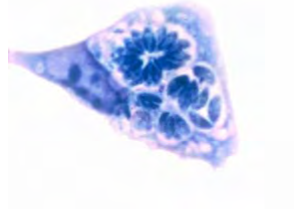
Entameba histolytica

Cryptosporidium parvum

Cyclospora cayetanensis

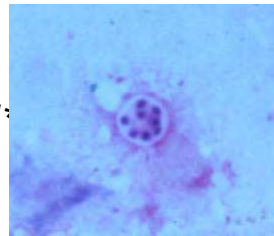
Protozoa:

Toxoplasma gondii



and

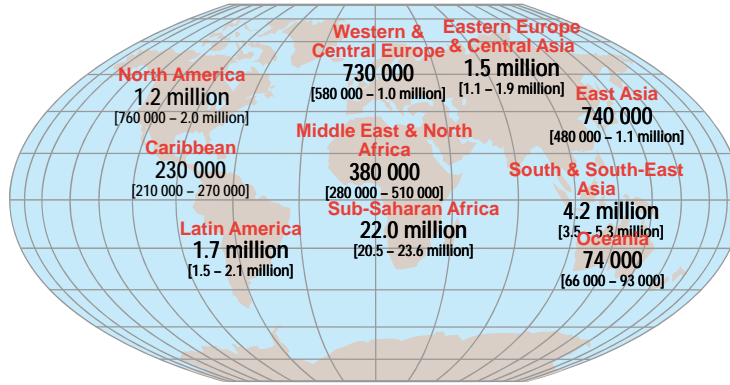
Pneumocystis jirovecii
formerly *P. carinii*



*actually an unusual fungus



Adults and children estimated to be living with HIV, 2007

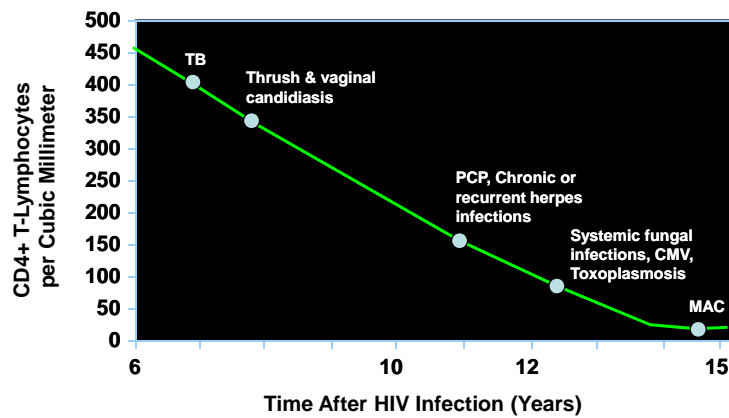


Total: 33 million (30 – 36 million)

And the Band Played On

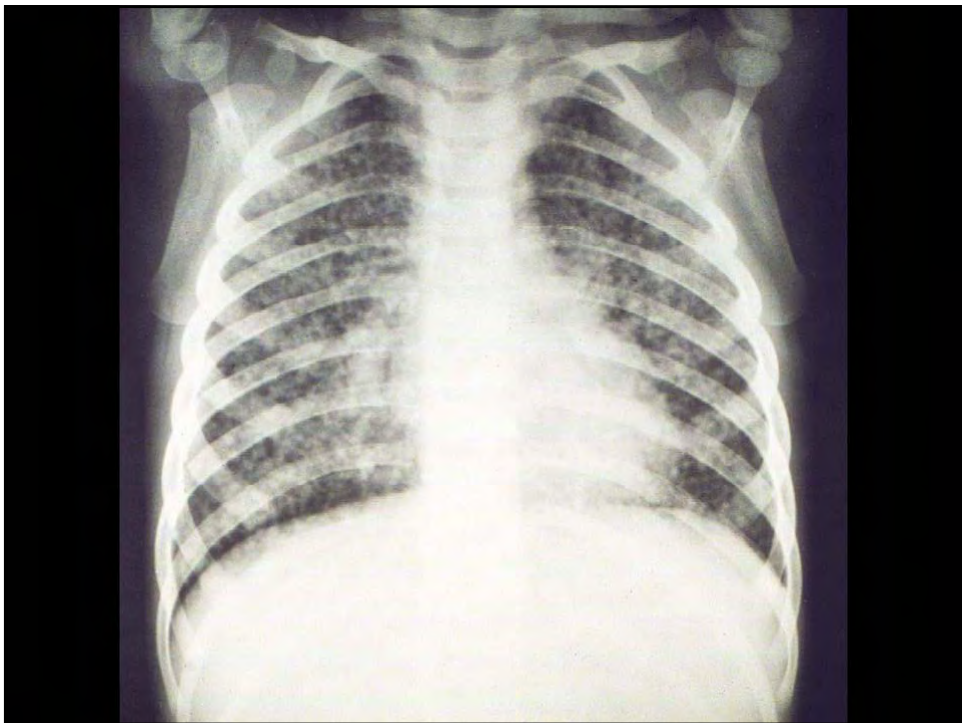
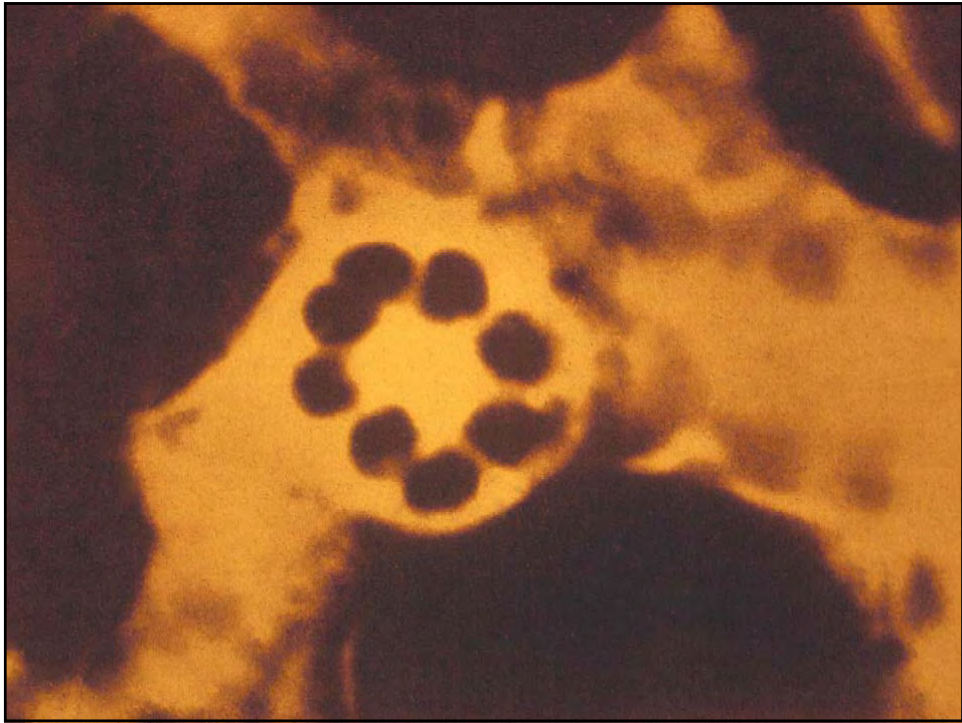
- Politics, people and the AIDS epidemic
- CDC April 1981: “This guy should go back to medical school if he can’t find some simple neoplasm”
- June 1981 MMWR: Pneumocystis pneumonia in young men
- GRID

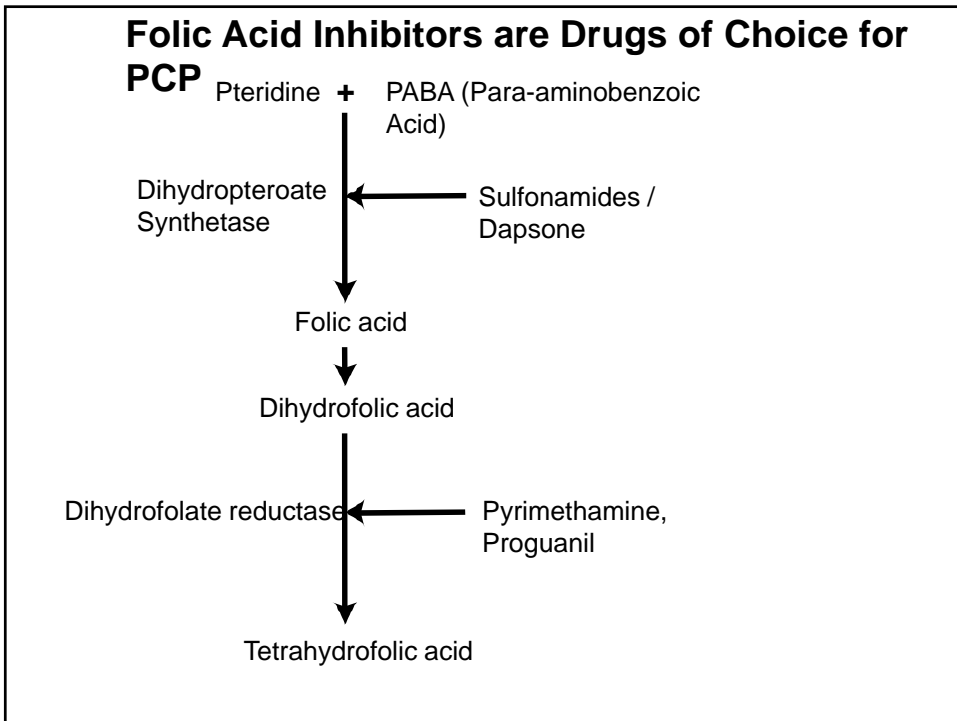
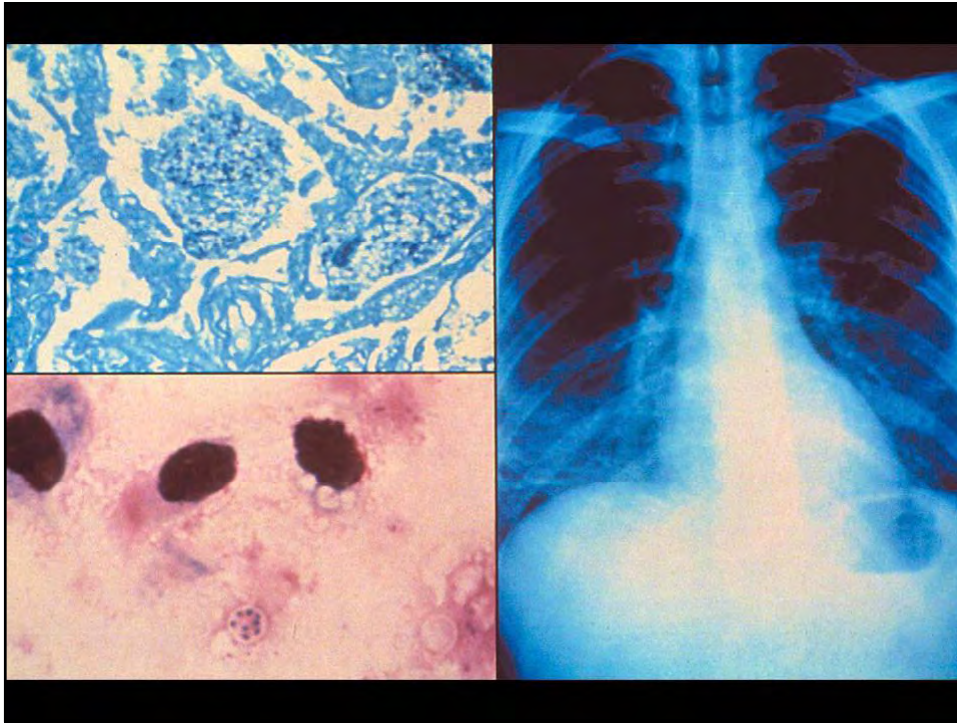
Opportunistic Infections Associated with Progressive Immunodeficiency



Pneumocystis jirovecii (PCP)

- Commensal organism and opportunistic pathogen
- Morphologically resembles protozoan
- Difficult to grow in vitro
- Life cycle???
 - Cyst stage : 5 μ m in diameter with 4-8 sporozoites
 - Trophozoite : 2-5 μ m in diameter – attach to cell surfaces





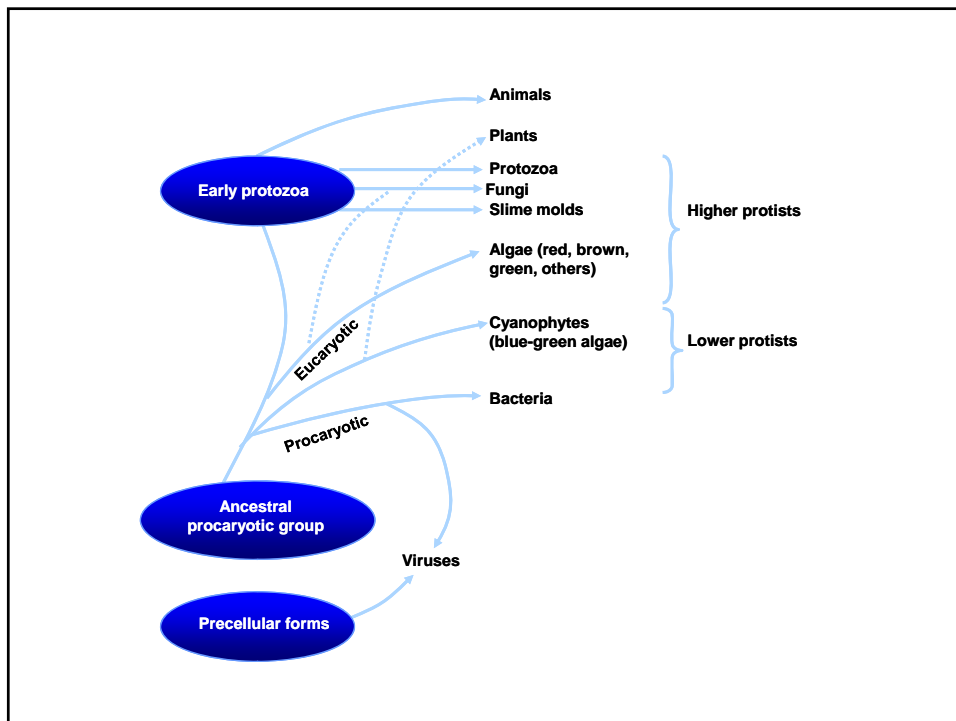
Is *P. carinii* a Fungus or Protozoon?

Protozoon

- Morphology
- Inability to culture in vitro
- Response to anti-protozoal drugs

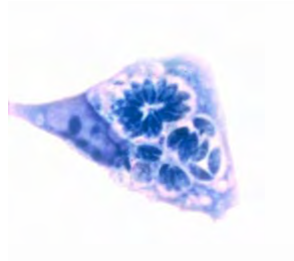
Fungus

- Ribosomal rRNA sequence homology
- ELF3

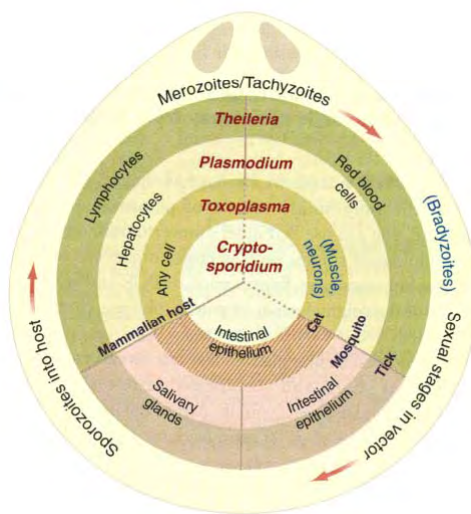


Protozoa:

Toxoplasma gondii

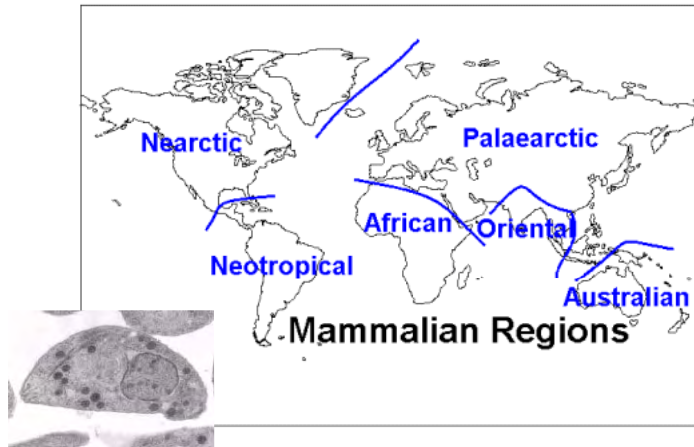


The Apicomplexa



Toxoplasma gondii
The Plasmodia (malaria)
Cryptosporidium hominis

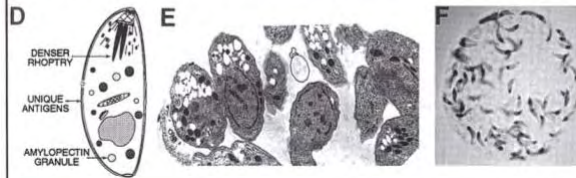
Toxoplasma gondii infects all mammals and all tissues in each of them.



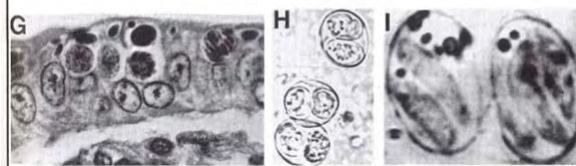
TACHYZOITE (acute, active infection)

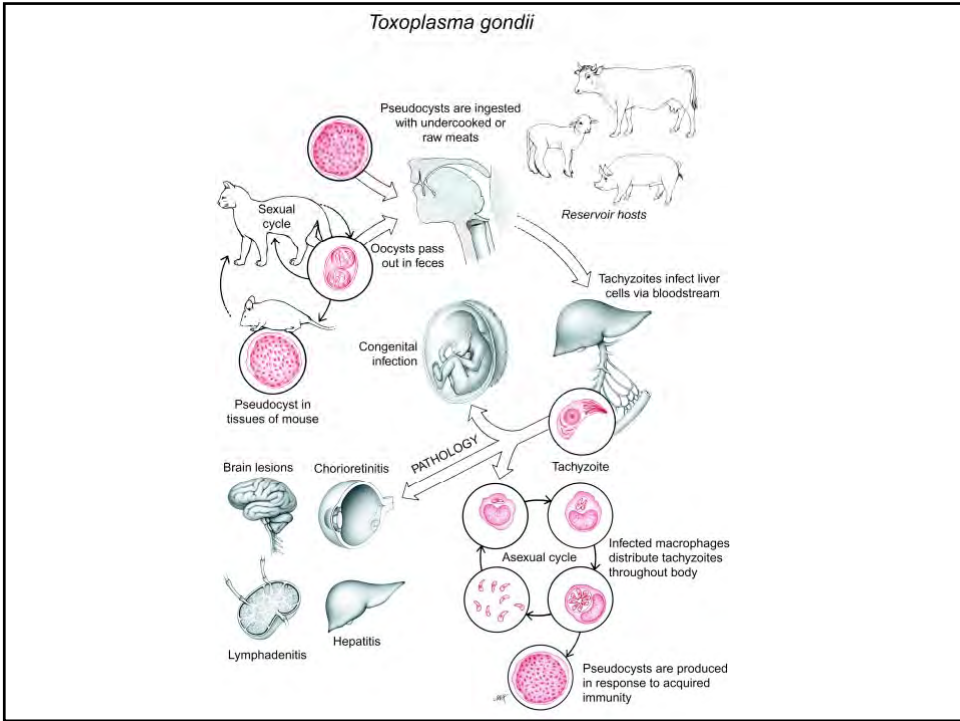


BRADYZOITE IN CYST (latent infection)



SPOROZOITE IN OOCYST (feline intestine and soil)





Felines are the definitive hosts for *Toxoplasma gondii*

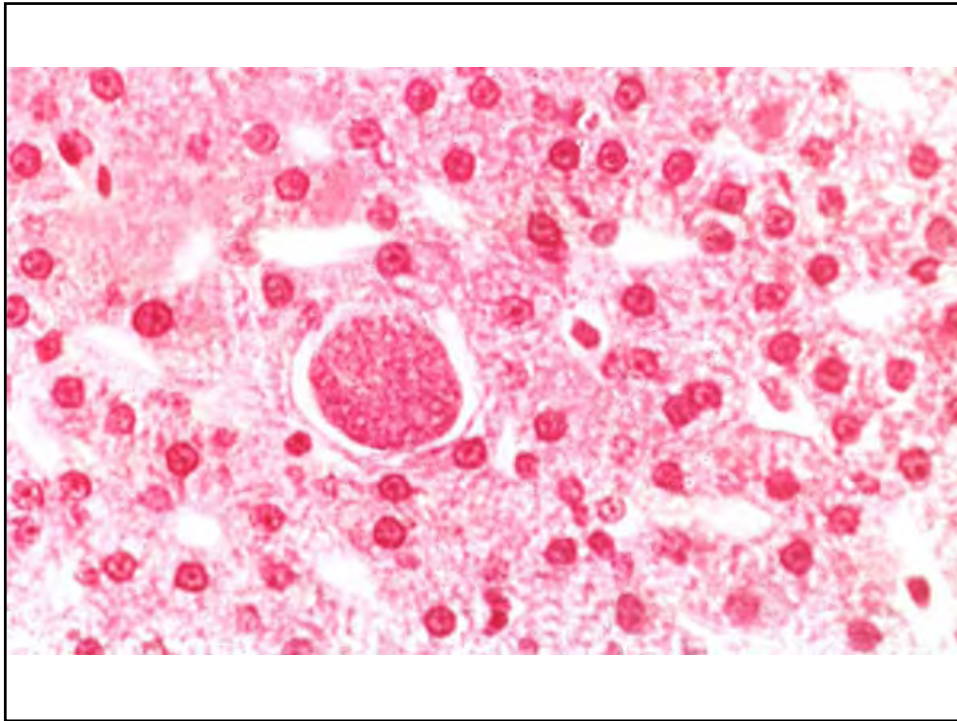


Oocysts of *Toxoplasma gondii*

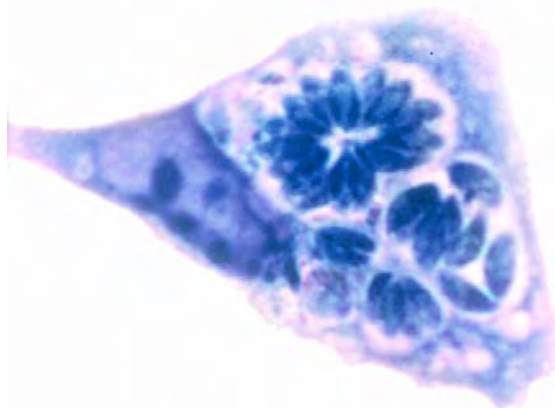


Rack of lamb is usually served rare



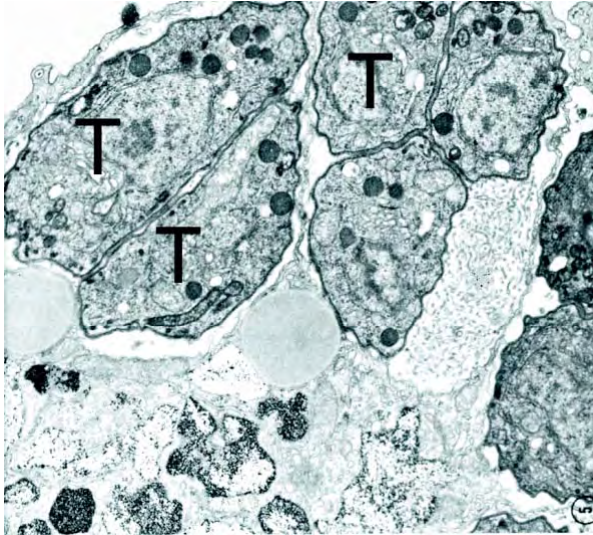


Macrophage Infected With *Toxoplasma gondii**



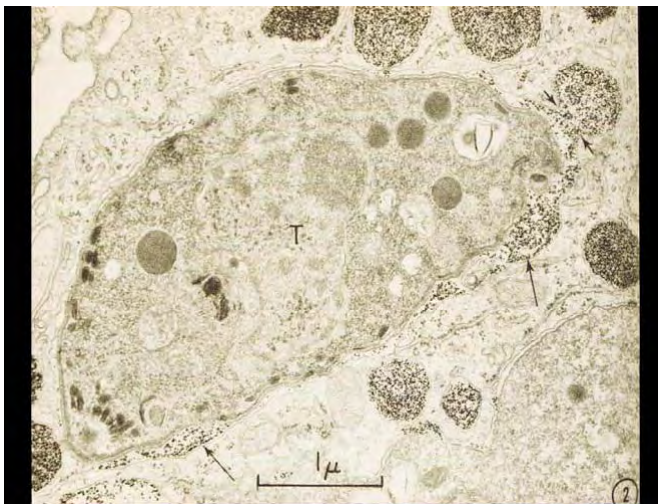
* The hunter becomes the hunted

Toxoplasma gondii in culture



Trophozoites (T) prevent fusion of lysosomal membranes to the parasitophorous vacuole, thereby escaping digestion

Toxoplasma gondii in culture



Heat-killed organisms cannot prevent fusion of lysosomal membranes with the parasitophorous vacuole

Clinical Disease:

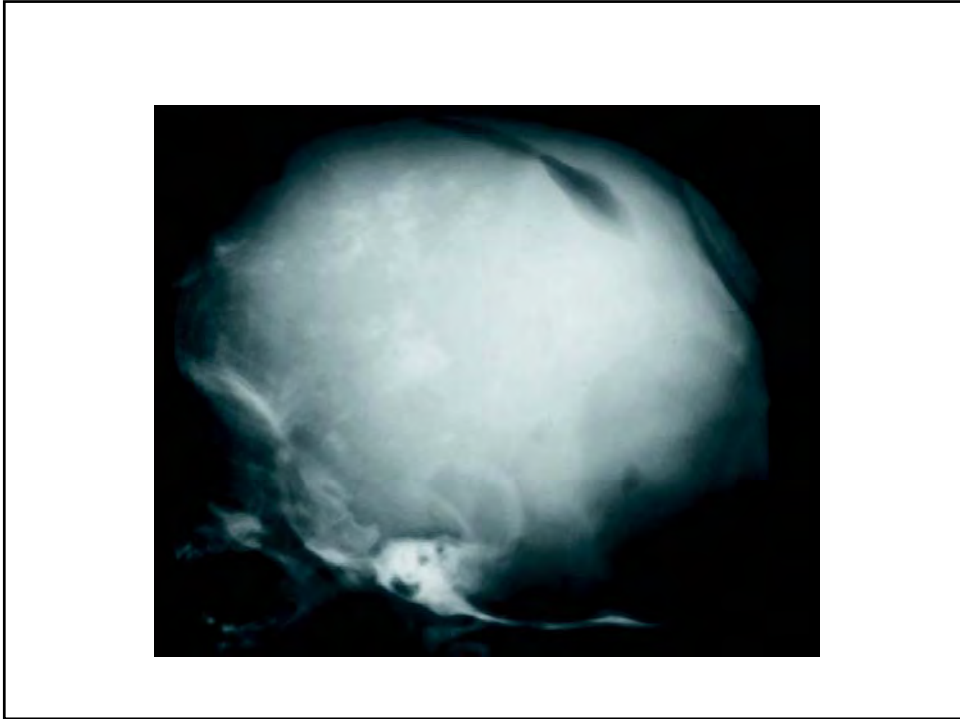
Congenital

Adult-acquired

AIDS-related

Congenital Toxoplasmosis





Congenital Toxoplasmosis

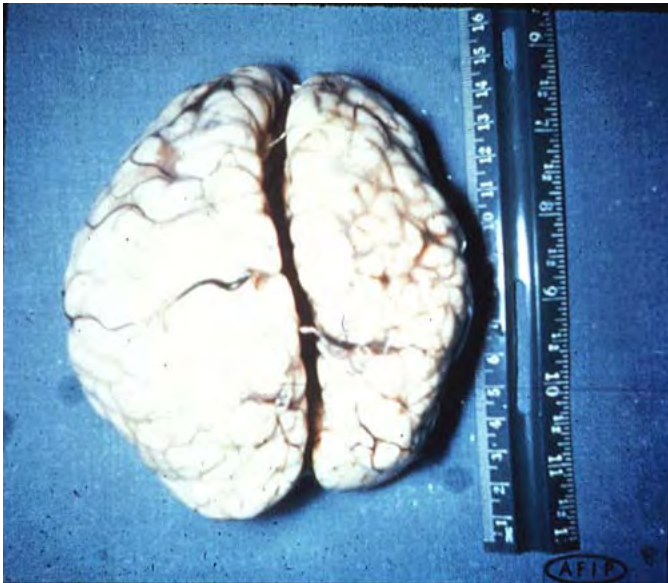


Photo courtesy: Gary Baumbach, M.D., Department of Pathology, University of Iowa College of Medicine

Congenital Toxoplasmosis:

Still Birth

Chorioretinitis

Mental Retardation

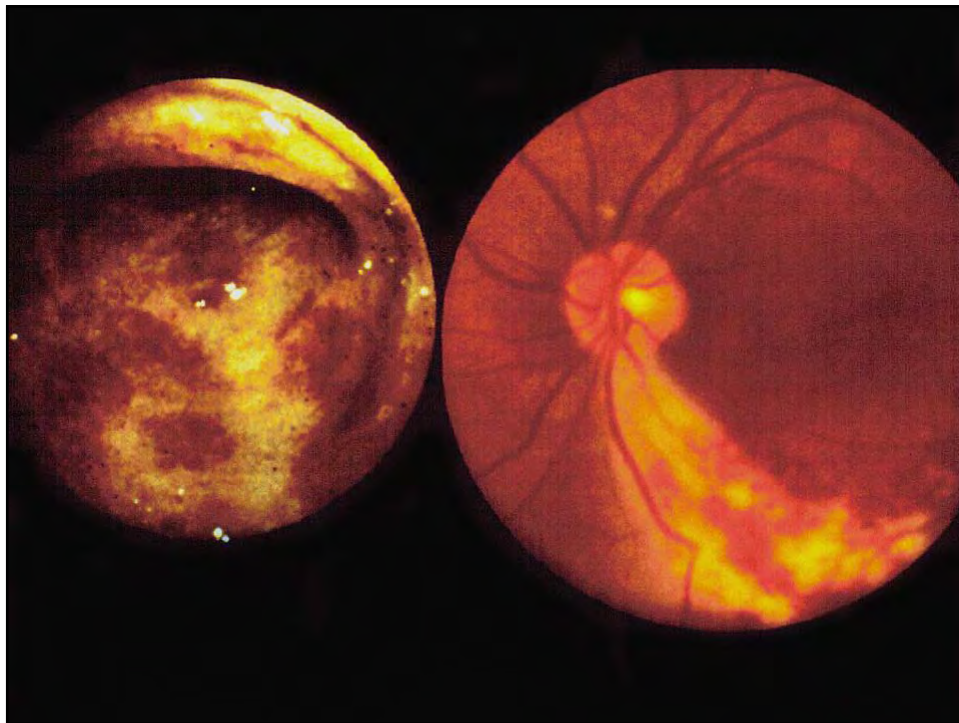
Congenital Toxoplasmosis Following Maternal Infection During First and Second Trimester*

Not Infected	73%
Subclinical Infection	13%
Mild Infection	7%
Severe Infection	6%

* From Desmonts and Couvier, NEJM 290: 1110, 1974

Toxoplasma Ocular Disease

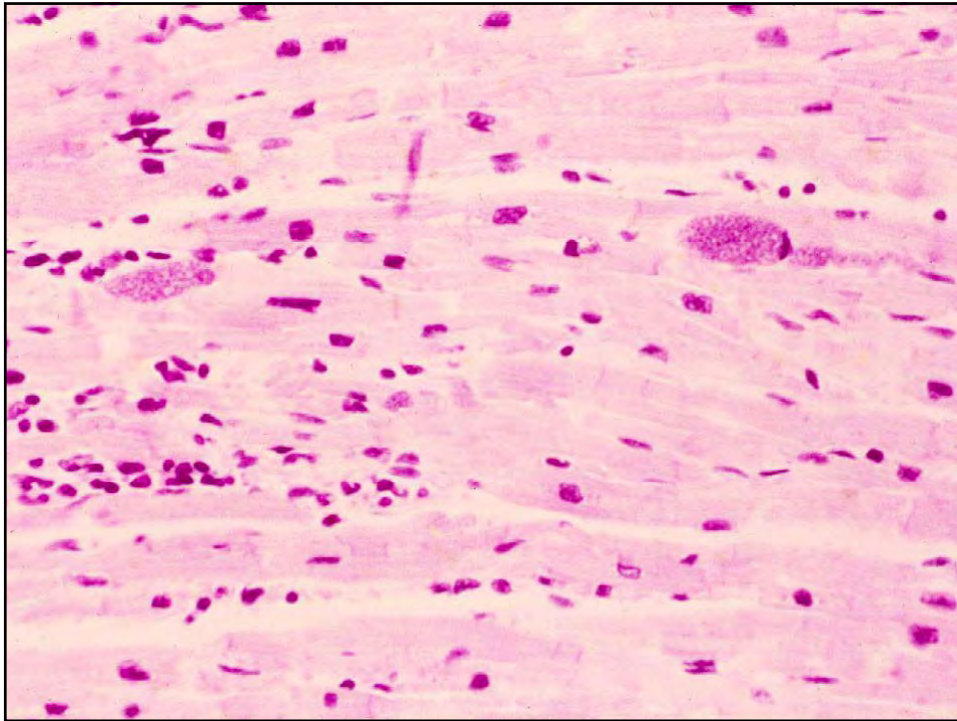
- Usually from congenital infection manifesting in adults
 - Episodic flares may destroy retinal tissue
 - Specific treatment necessary



Adult-Acquired Toxoplasmosis

Infection by Blood or Organ Transplant

- Parasitemia (WBC's) for up to 1 year post infection
- Heart, bone marrow, liver, kidney donors
 - Dangerous when recipient toxo (-)
- Myocarditis, diffuse lymphadenopathy



Adult-Acquired Toxoplasmosis

Signs and symptoms:

Lymphadenopathy

Fever

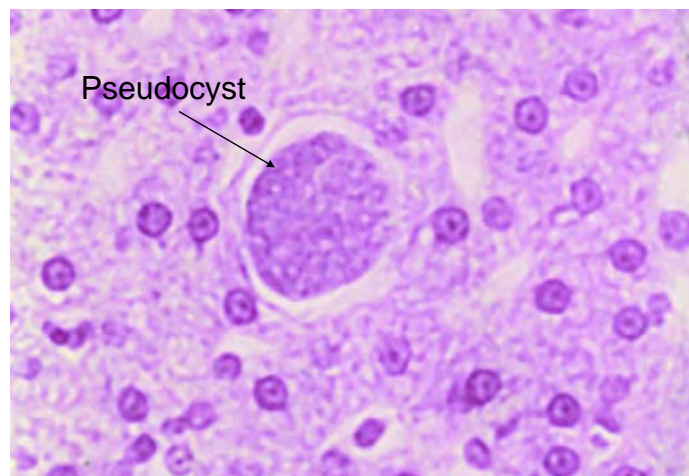
Headache

Chronic Malaise

Differential Diagnosis of Lymphadenopathy

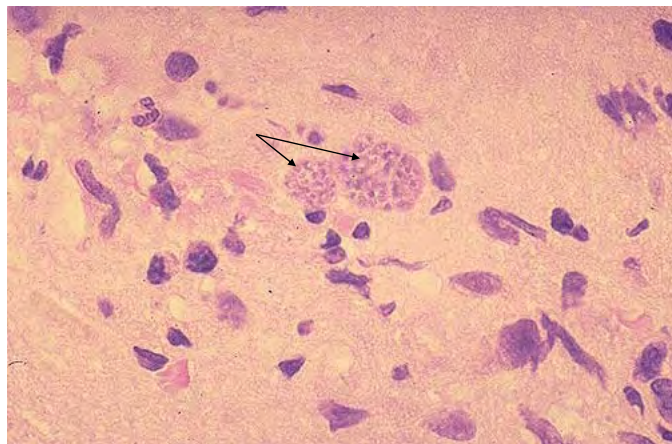
	<i>Toxoplasmosis</i>	<i>Inf. Mono</i>	<i>Lymphoma</i>
Lymphadenopathy Without Other Symptoms	+++	+	+++
Pharyngitis	+	+++	+
Monocytosis, Eosinophilia	+++	+	+++
Atypical Lymphocytes	+	++++	+
Anemia	0	+	+++
Positive Heterophil	0	++++	0
Altered Liver Function	0	++++	++
Hilar Lymphadenopathy	+	+	+++
Lymph Node Pathology	Reticulum Cells	Germinal Cells	Bizarre Cells

Pseudocyst of *Toxoplasma gondii* in Liver



AIDS-related Disease

Pseudocysts of *Toxoplasma gondii* in a microglial nodule with a variety of inflammatory cell types in an HIV/AIDS patient



AIDS-related Disease:

1. CD4 < 200 and reactivation of latent infection
2. Encephalitis
 1. Diffuse inflammation and swelling
 2. Localized ring enhancing lesions on CT scan
 3. Herniation
 4. Death if untreated



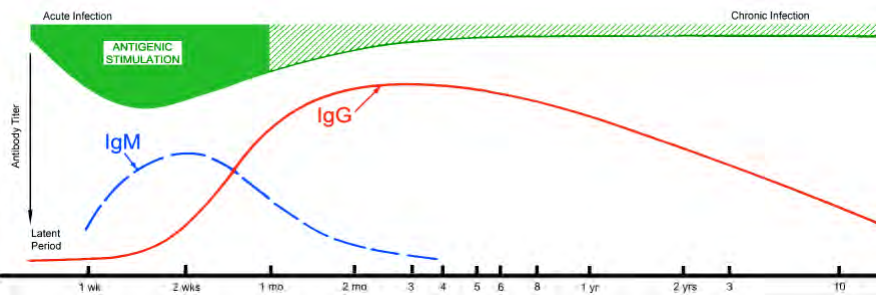
Toxoplasma abscess in the brain would appear as a ring-enhancing lesion with CT scan.

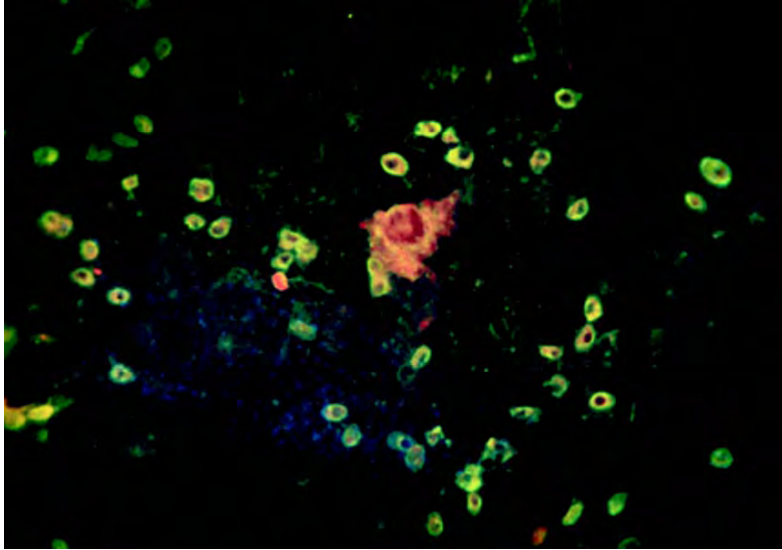


CT Scan

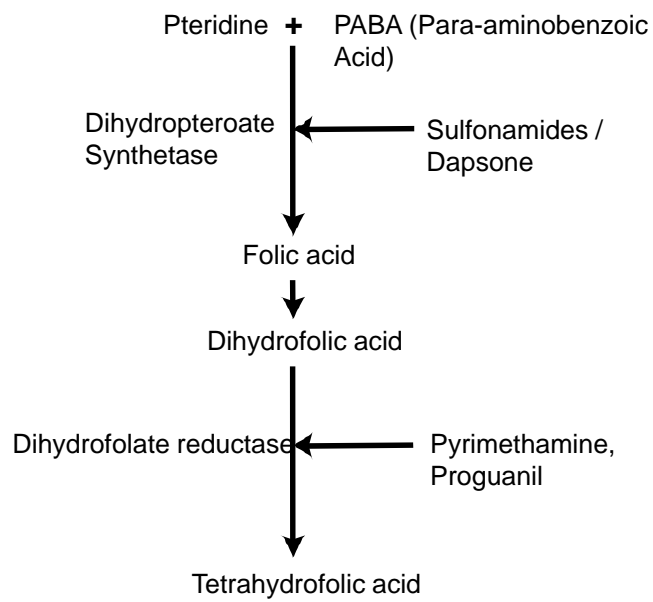
Diagnosis

Serological correlates in acute and chronic infection



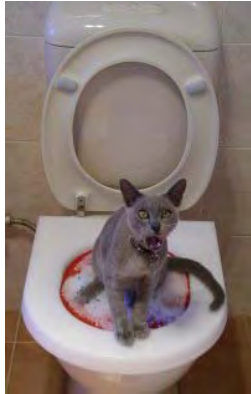


Folic Acid Inhibitors are Drugs of Choice



Prevention:

1. Prevent pregnant women from handling cat litter
2. Avoid eating raw or under-cooked meats



Trained cat



Automated litter collection box

Host status

- *Pneumocystis carinii*
 - No Life cycle!
 - Lung disease in AIDS
 - Malnourished children
 - Organ Transplants
- *Toxoplasma gondii*
 - Cat definitive host
 - Disease: Host status
 - CNS Disease in AIDS
 - Congenital Infections
 - Organ Transplants

Some Good News Regarding Extinction:

Smallpox - eliminated
(probably)



Polio - nearly gone



Yaws - almost eliminated



Onchocerciasis - on its way out



The Most Common Neglected Infections of Poor People

Disease	Number of Cases	Population at-risk
Ascariasis	807 million	4.2 billion
Trichuriasis	604 million	3.2 billion
Hookworm	576 million	3.2 billion
Amebiasis	500 million	ND
Schistosomiasis	200 million	0.6 billion
Lymphatic Filariasis	120 million	1.0 billion
Trachoma	84 million	0.5 billion
Onchocerciasis	18 million	0.1 billion
Chagas Disease	16 million	0.1 billion
Leishmaniasis	12 million	0.4 billion
Leprosy	0.4 million	ND
Dracunculiasis	0.01 million	ND

Global Network for Neglected Tropical Diseases

<http://www.GNNTDC.org>

- Schistosomiasis Control Initiative
- International Trachoma Initiative
- Helen Keller International
- Liverpool School - GAELF
- Human Hookworm Vaccine Initiative
- Earth Institute at Columbia Univ.
- Task Force for Child Survival
 - Mectizan Donation Program
 - Albendazole Donation Program
 - Mebendazole Donation Program



GNNTDC
GLOBAL NETWORK
FOR NEGLECTED TROPICAL
DISEASE CONTROL



More Bad News:

Most vector-borne diseases are on the rise

