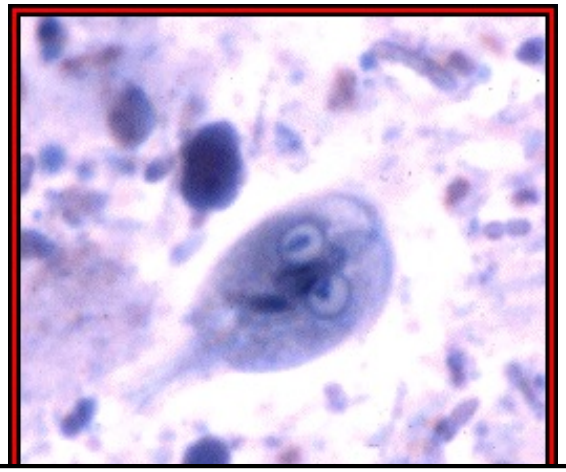
True parasites are eukaryotic organisms living in/on other eukaryotes

Protozoa are single-cellular parasites that can be intracellular or extracellular



Giardia parasite in feces stain.
Image shows protozoa from bottom

Helminths aka parasitic worms are multicellular and can be up to meters long and still live inside host.

Ancylostoma (hookworm)

Extracellular Protozoa

- Live in mucosal tissue.

Giardia lamblia live in host intestines. These protozoa inhibit phagocytosis, and the main adaptive immune response is **IgA**.

Giardia infection is a zoonosis from beavers and high asymptomatic rate.

- Replicates in bloodstream.

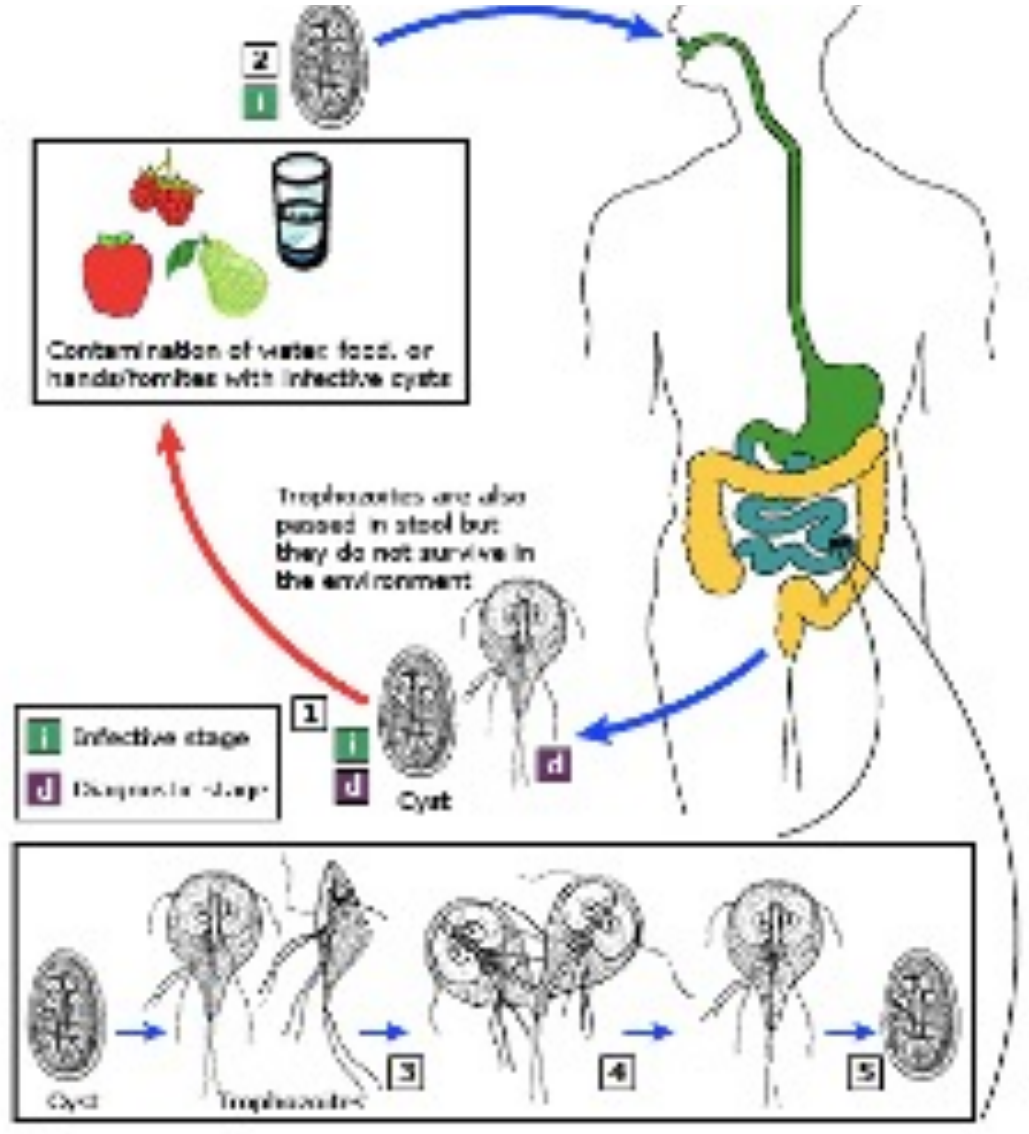
Trypanosoma brucei. These blood dwelling trypanosomes are transmitted between hosts via a tsetse fly vector. The incidence of infection is confined to vector area.

Main immune responses is **IgG** to VSGs.

Human trypanosomiasis is a zoonosis from cows.

- 200 million symptomatic infections (Giardiasis = diarrhea) each year worldwide.
- Up to 90% of infections are asymptomatic. Thus, Giardia infection is strongly underdiagnosed and underreported.
- Almost no mortality. Considered a zoonosis

Giardia lamblia Life cycle



Giardia lamblia

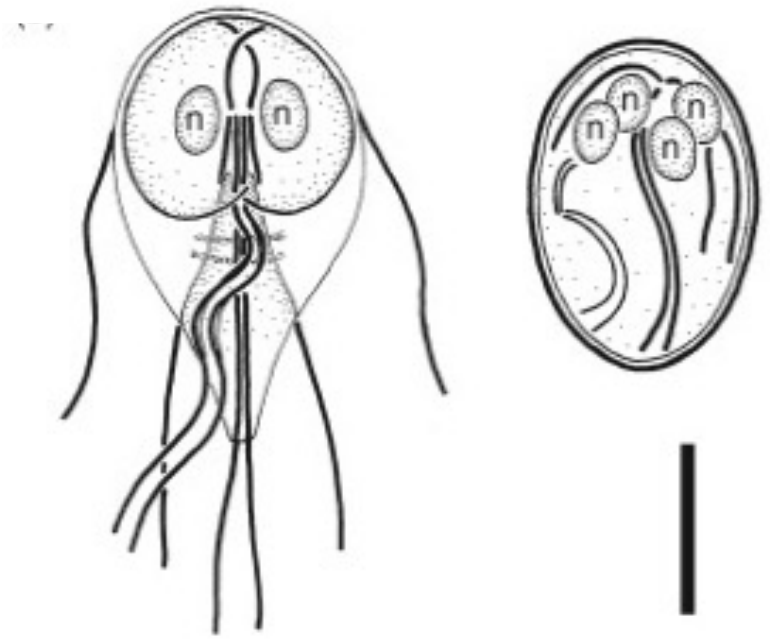
- Parasites attach to mucosal epithelium and can survive for weeks in the host.
- Trophozoite form is replicating form in intestine.

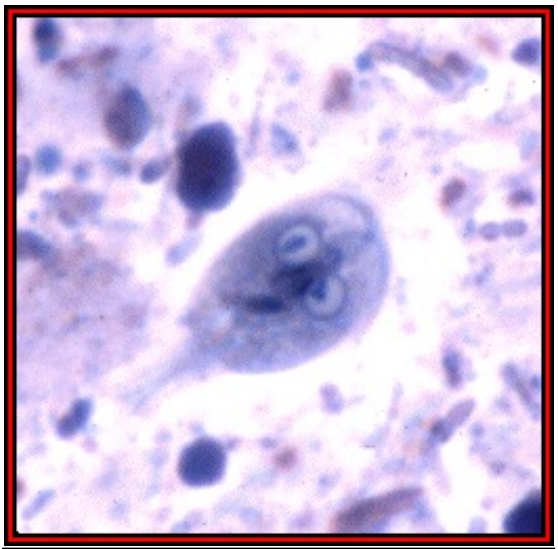
Trophozoite form of Giardia.

Ventral side flattened for attachment to mucosal cell wall.

Giardia lamblia

- Cyst form passed in feces.
- Beaver = main animal reservoir in North America.
- But dogs and cats may be reservoir.
- Many mammals can be infected.

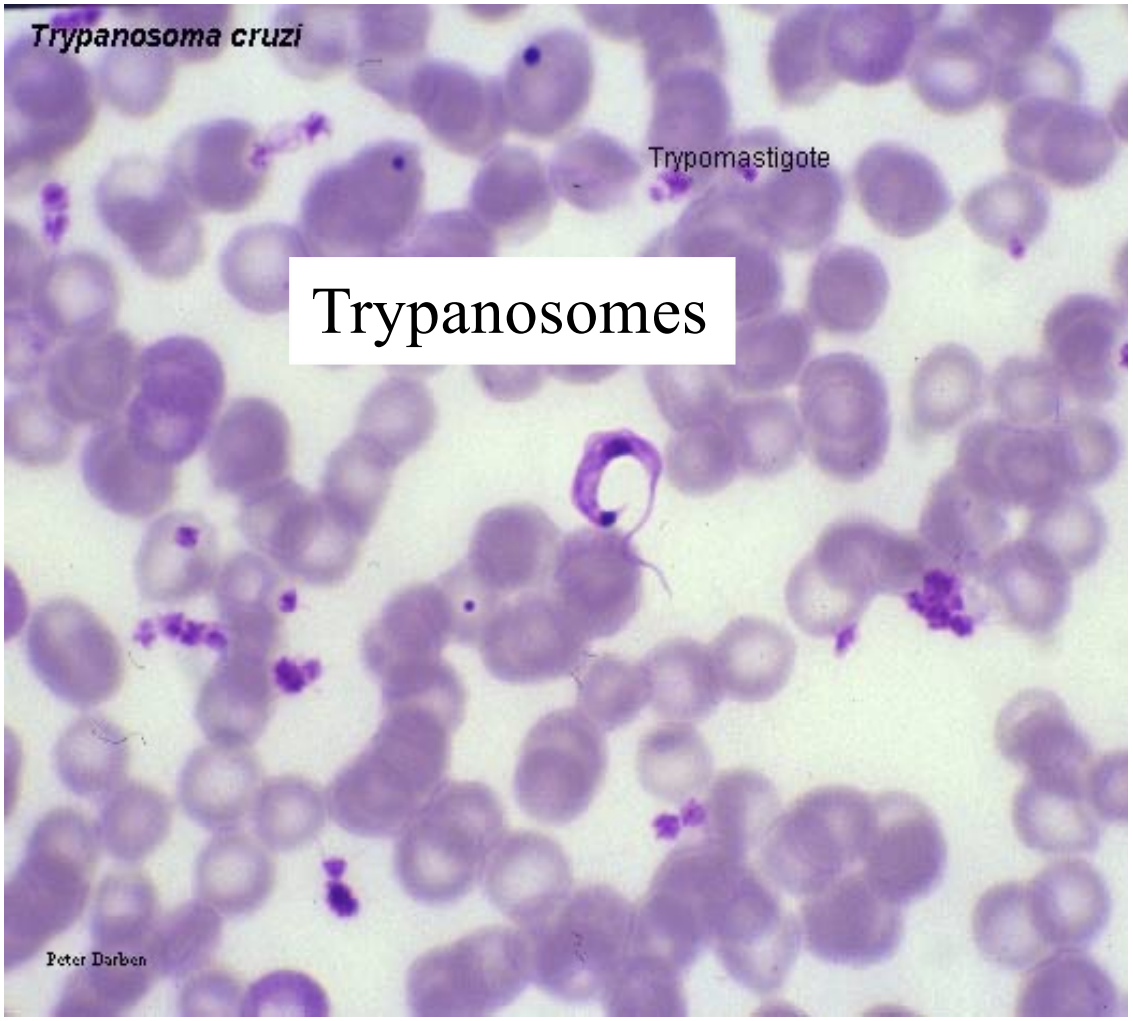




A single trophozoite has two identical nuclei.

Left. Viewing bottom or ventral side of trophozoite with flagella. Replicating form in intestine.
Right. Cyst form passed in feces for transmission. Giardia cysts can survive for 1–3 months in 10'C/50'F water or 1-7 weeks in soil.

African trypanosomiasis is caused by *Trypanosoma brucei*

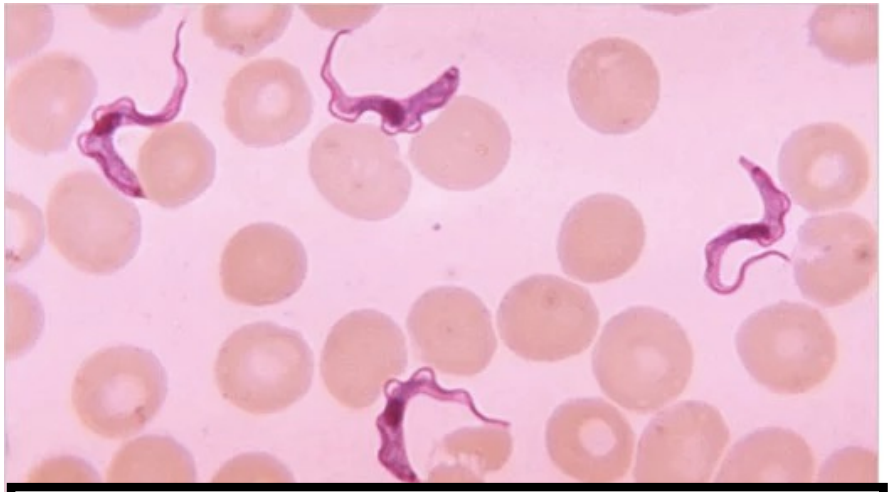


In 1903, David Bruce identified motile, vibrating parasites in the blood of livestock "nagana" with tsetse fly transmission to humans possibly causing sleeping sickness.

Trypansomiasis is a zoonosis from cows/horses.

Trypanosoma brucei

Trypanosomes live extracellularly in blood

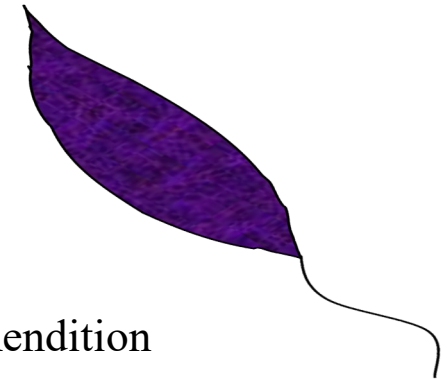


Trypansomes in blood smear

T. brucei protozoa are spread by bite of tsetse flies. The parasites live extracellularly in the bloodstream and the infection is normally controlled by IgG that eliminate the parasites. However, *T. brucei* can evade IgG in blood through antigenic variation.

If parasite escapes antibodies, they can spread to brain and cause neurological disease (sleeping sickness).

Immune Response to Trypanosomes



Beatty Rendition
of Trypanosome

Innate immunity

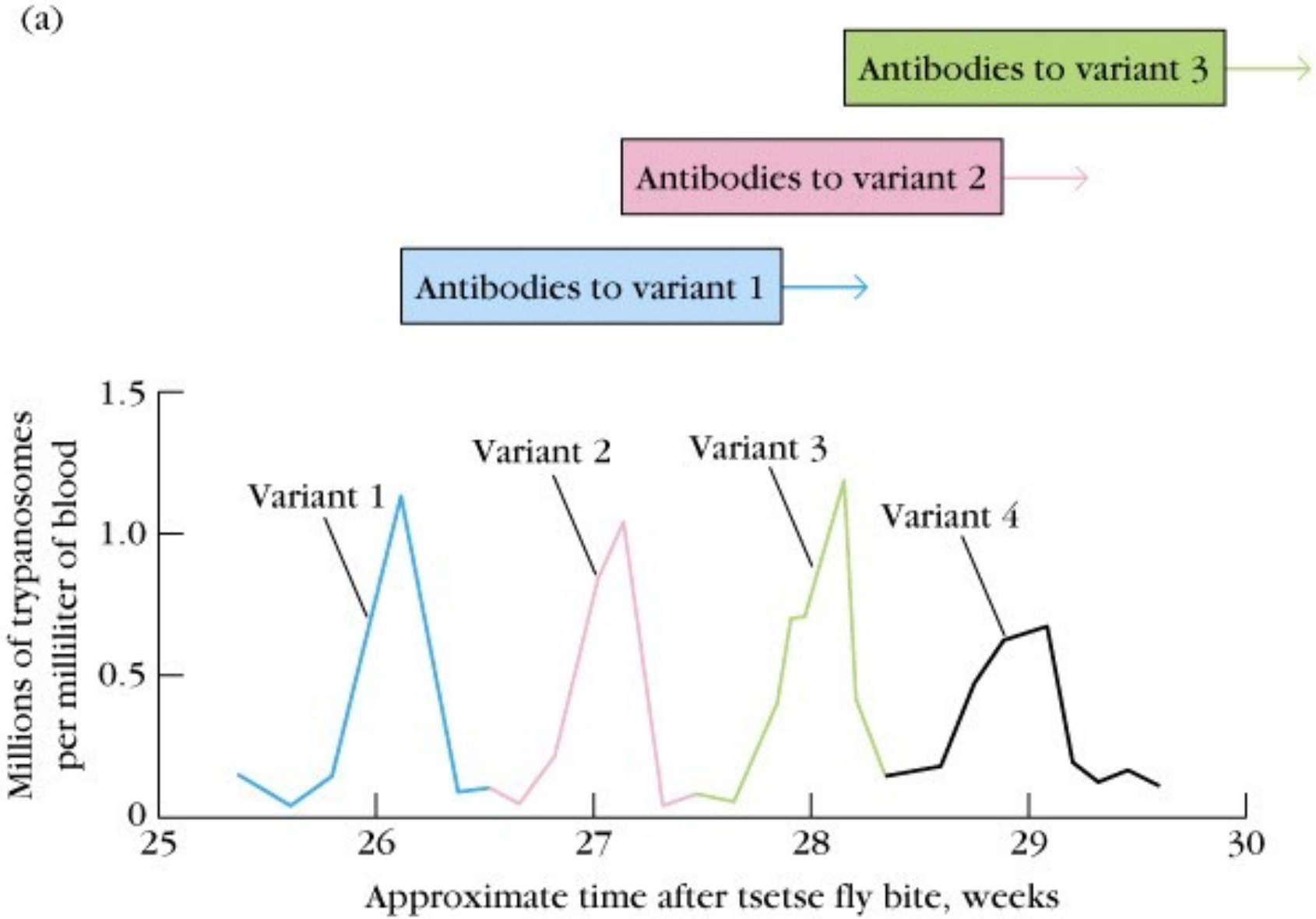
Because of size, these parasites
are hard to eliminate by phagocytosis.
Can activate inflammation but often inhibited.

Adaptive immunity

IgG elimination of parasites by neutralization and ADCC.
However, antigenic variation with the ability of the parasite to to change the primary antigen: variable surface glycoproteins (VSGs) helps evade IgG.

Antigenic variation- VSGs

Change in surface antigens displayed by the pathogen allows escape from antibody mediated responses.



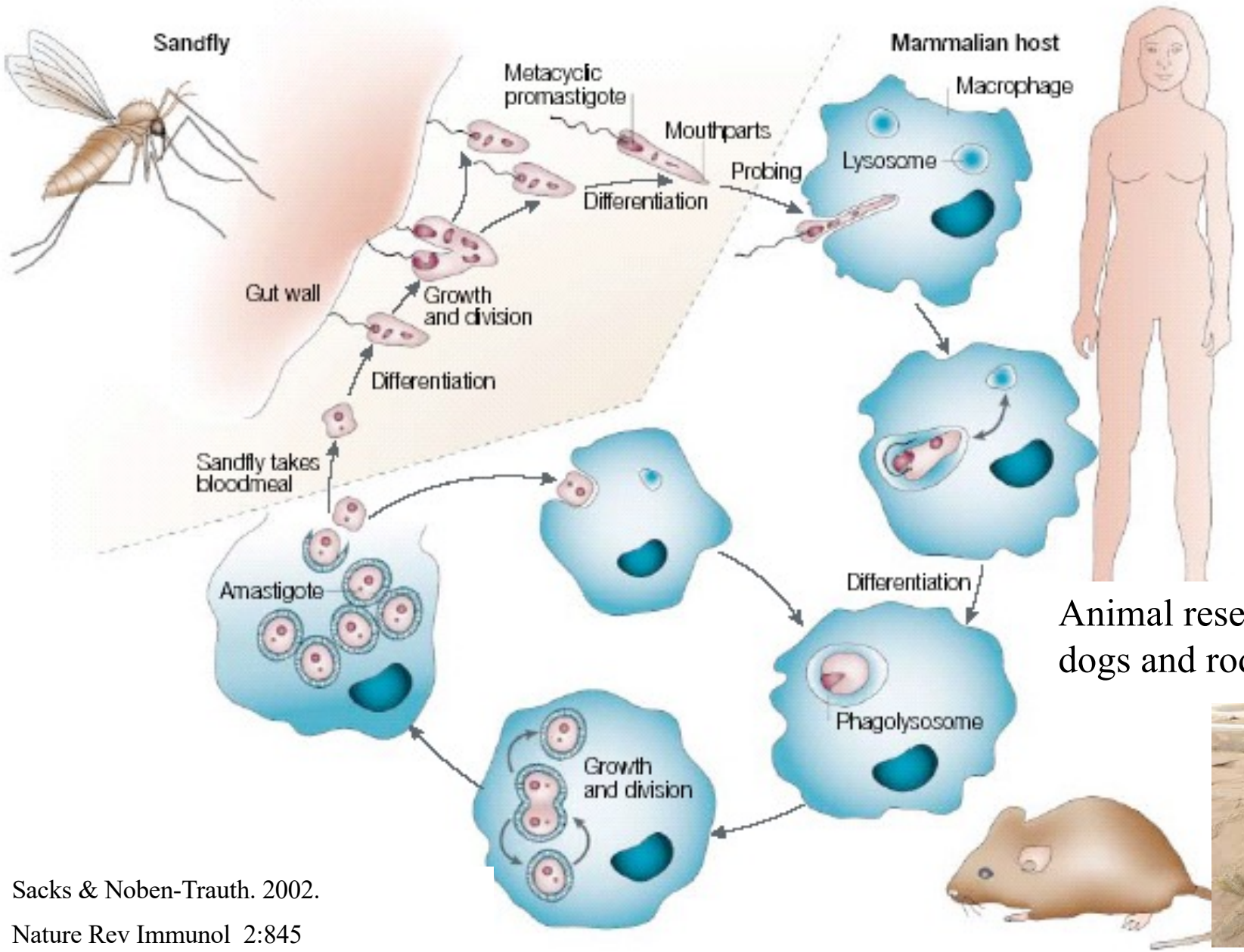
Intracellular Protozoa

- **Malaria (*Plasmodium*)** infects liver cells and RBCs. Immune responses-CTLs to liver form, IgG to RBC form.

- Protozoa that replicate in vacuole.
  - ***Leishmania chagasi*** infects macrophages. Transmitted by sandflies. Main immune response is Thelper cytokines activating macrophages.
  - ***Toxoplasma gondii*** lives in muscle and neurons as cysts.

Location of replication affects disease caused and type of immune response needed to eliminate.

Example 1- Leishmania lifecycle



Animal reservoir primarily dogs and rodents

Sacks & Noben-Trauth. 2002.

Nature Rev Immunol 2:845

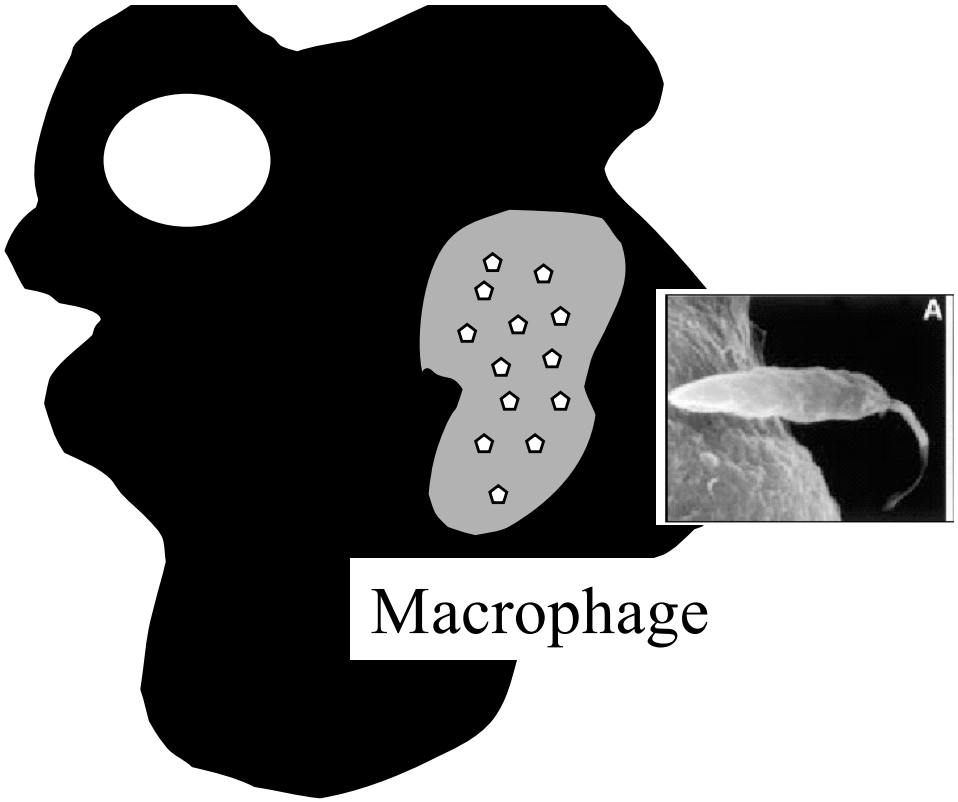
WARNING

Leishmania disease slides coming--- please do not watch if you feel uncomfortable with images of disease.

WARNING

Leishmania infect macrophages

Leishmania lesions are sites of **chronic inflammation**.
Infected macrophages need to be activated by cytokines from Thelper cells to kill parasites in vesicles. But these infected macrophages also cause non-specific damage and immunopathology causing tissue damage.



Macrophage

Mucocutaneous leishmaniasis

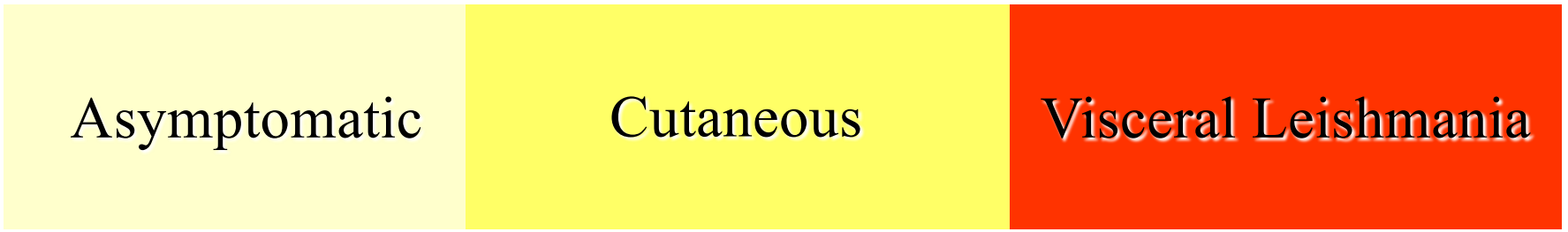
Leishmania triggered disease

Cutaneous

Visceral

Mucocutaneous

Leishmania infections present a spectrum of clinical disease

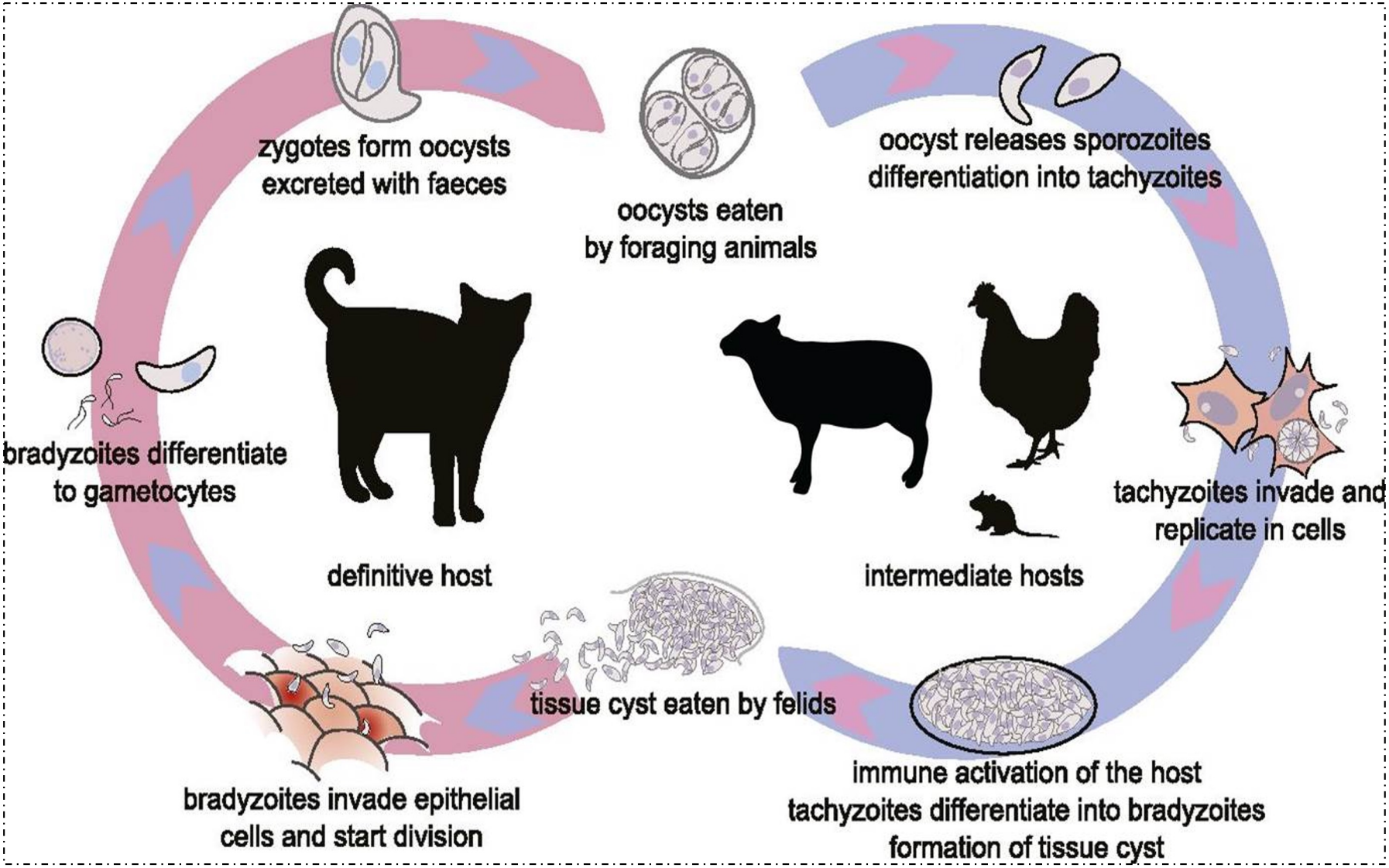


What factors impact the disease manifestation?

- The parasite? Different species- cause different diseases
- The host immune response? YES– too little is bad and too much is worse.
- The transmitting insect? has little influence……. maybe in intial infection.

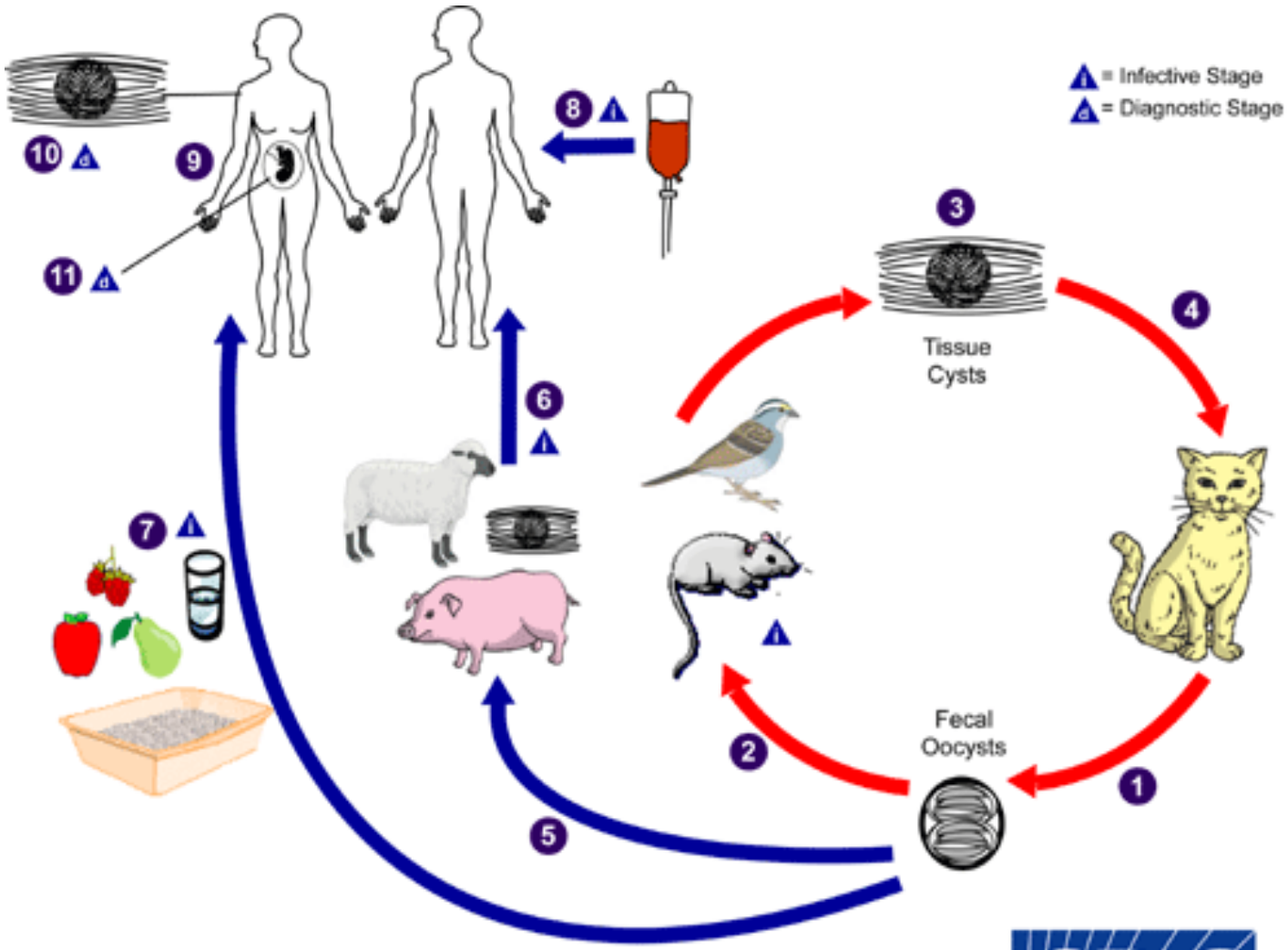
Scrapping lesion for parasites

Toxoplasma gondii animal lifecycle



Felines are ONLY definitive host. Mice are common intermediate host, but many species can be intermediate hosts. Humans are considered dead-end host so a true zoonosis.

Life cycle of *Toxoplasma gondii*

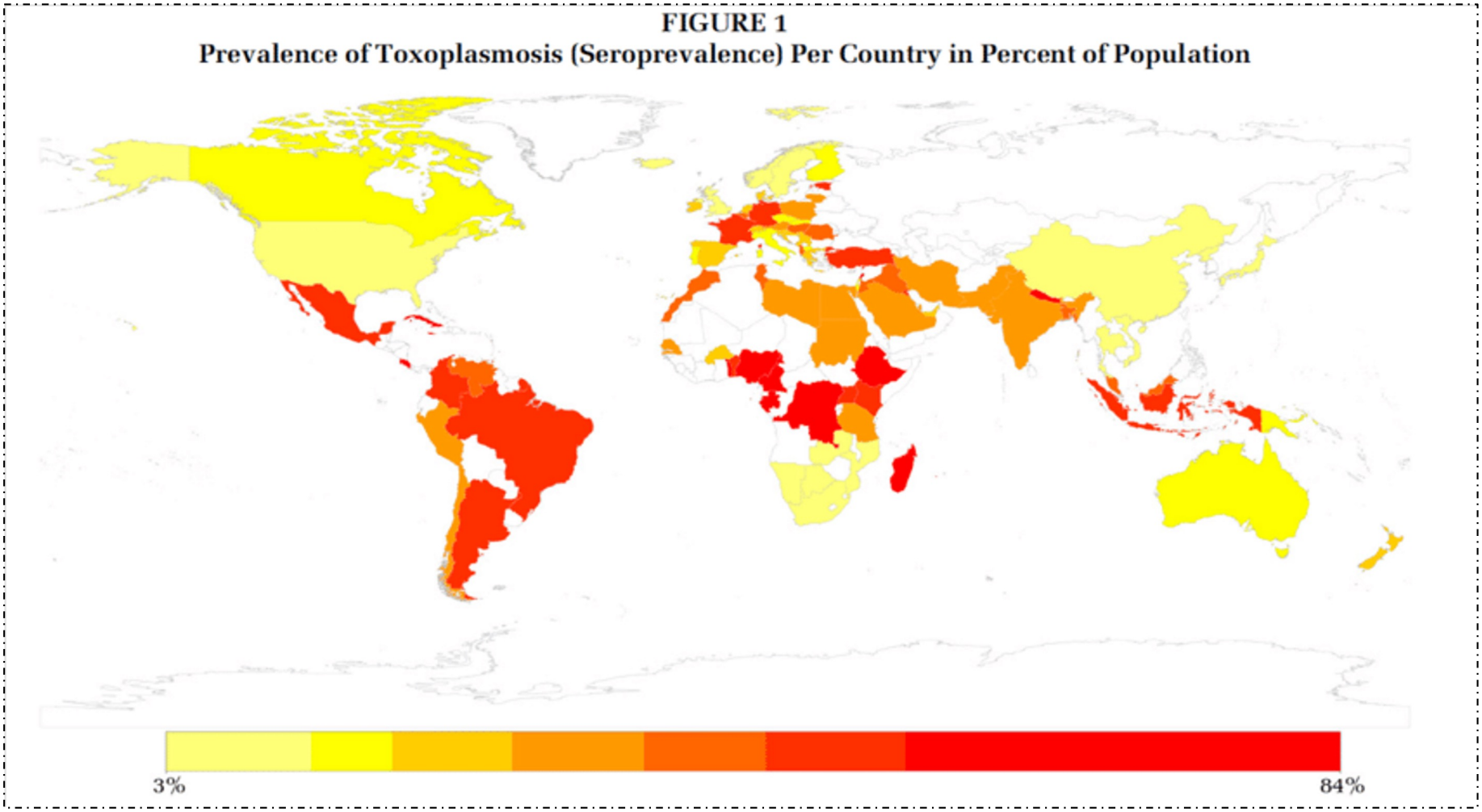


Toxoplasmosis in humans is zoonosis caused by *T. gondii*.

Normal life cycle is cats and rodents.

Oocysts are ingested by mice (or humans) and form tissue cysts primarily in muscle or nerve cells. Humans can also be infected by ingesting undercooked meat from animals that have cysts in tissue.

Seroprevalence of *Toxoplasma gondii*



Prevalence of antibodies to toxoplasma antigens in humans in US -9-11%, Canada 17%, France 47%, Brazil 50%.
Assumption is IgG antibodies mean past or current infection.