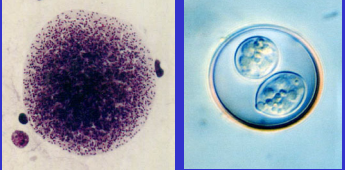


BioMedical Parasitology

Protozoa

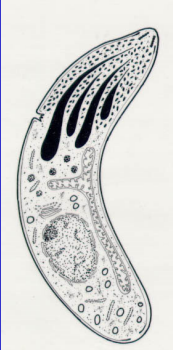
Tissue cyst-forming coccidia



Prof Peter O'Donoghue

1

Apicomplexa







- cluster of anterior organelles designed to facilitate entry into host cell
- Apicomplexa are obligate intracellular parasites

4

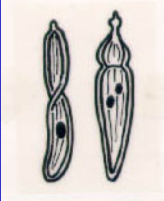

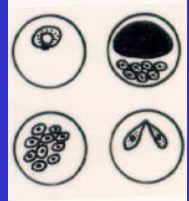
PROTOZOA

65,000 species
(31,250 extant + 33,750 extinct)

flagellates	amoebae	sporozoa	ciliates
			
6,900 species	11,550 species	5,600 species	7,200 species
5,100 free-living 1,800 parasitic	11,300 free-living 250 parasitic	all parasitic	4,700 free-living 2,500 parasitic

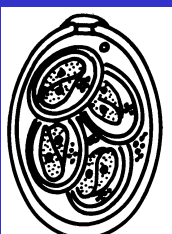


2

APICOMPLEXA

Gregarinidea (modified conoid) (large extracell. gamonts)	Coccidia (conoid complete) (small intracell. gamonts)	Haematozoa (conoid absent) (motile kinete)
		
gregarines	coccidia	haemosporidia/piroplasm


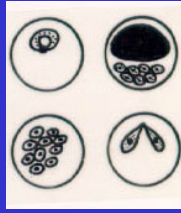
5

SPOROZOA

Apicomplexa (apical complex) (oocysts)	Microspora (unicellular) (spores)	Myxozoa (multicellular) (spores)
		
All parasitic		

3


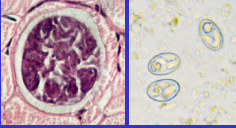
APICOMPLEXA

Coccidia (conoid complete) (small intracellular gamonts)	Haematozoa (conoid absent) (motile kinete)
	
coccidia	haemosporidia/piroplasm

6

Parasite assemblage

COCCIDIA

<ul style="list-style-type: none"> • enteric • monoxenous • fast cycle • acute  <ul style="list-style-type: none"> • <i>Isospora</i> • <i>Eimeria</i> 	<ul style="list-style-type: none"> • tissue cyst-forming • heteroxenous • slow cycle • chronic  <ul style="list-style-type: none"> • <i>Toxoplasma</i> • <i>Sarcocystis</i>
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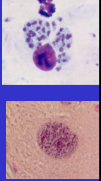
7

Parasite morphology

Toxoplasma gondii cysts

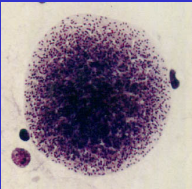
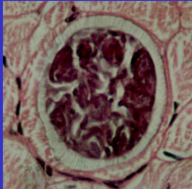
Intermediate hosts
(parasites undergo asexual development)

- infections found in most mammals, including humans
- tachyzoites (schizonts) in macrophages
- bradyzoites (tissue cysts) in muscle/brain
- high prevalence (25-75% seroprevalence)



10

Tissue cyst-forming coccidia

<p><i>Toxoplasma</i> heteroxenous cycle felid-vertebrate 1:2:4 thin cyst wall</p> 	<p><i>Sarcocystis</i> heteroxenous cycle carnivore-herbivore 1:2:4 thick cyst wall</p> 
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8

Parasite morphology

Toxoplasma gondii oocysts

Definitive hosts
(parasites undergo sexual development)

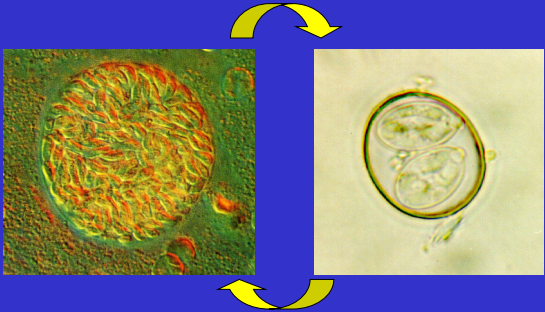
- life cycle discovered in 1970's
- only occurs in felids
- gamogony (gametes) in mucosa
- sporogony (sporozoites) in faeces
- oocysts with isosporid configuration (1:2:4)



11

Parasite morphology

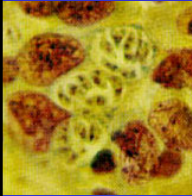
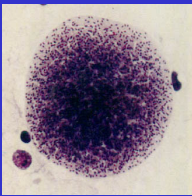
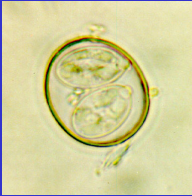
Toxoplasma gondii



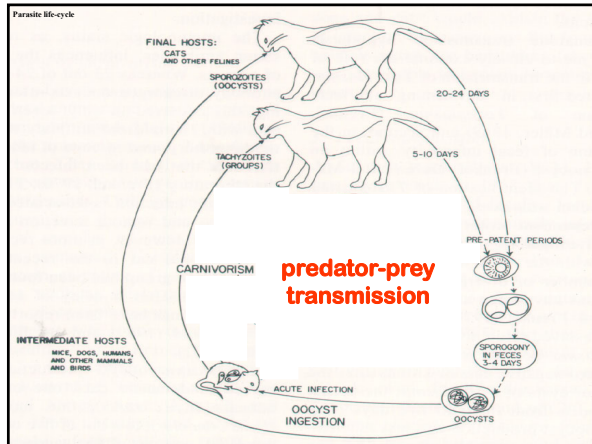
tissue cysts prey-predator oocysts

9

Toxoplasma gondii

intermediate host most vertebrates	definitive host cat	
		
schizonts tachyzoites	tissue cysts bradyzoites	oocysts sporozoites

12

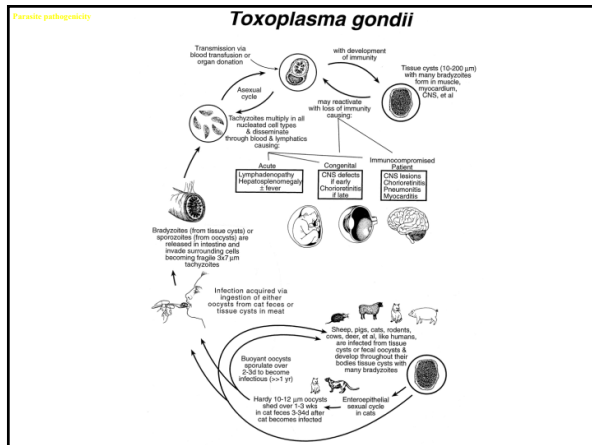


13

ACUTE disease

- most infections asymptomatic
- in some adults, lymphadenopathy, flu-like fever, headache, myalgia
- in postnatal infections, lymphadenitis, myocarditis, CNS involvement, retinochoroiditis
- in immunocompromised, cell lysis, expanding focal lesions, rapid dissemination, encephalopathy, meningoencephalitis

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CHRONIC disease

- tissue cyst formation, esp. in brain, muscles
- quiescent (dormant)
- cysts occupy space (minute lesions with little loss of function)
- contradictory evidence for learning disabilities
- reactivation in immunocompromised patients, space-occupying lesions

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Toxoplasmosis

SYSTEMIC INFECTIONS	ENTERIC INFECTION
<ul style="list-style-type: none"> • in numerous mammals • ACUTE tachyzoite proliferation • CHRONIC tissue cyst formation 	<ul style="list-style-type: none"> • only in cats • ACUTE oocyst production • subclinical protective immunity

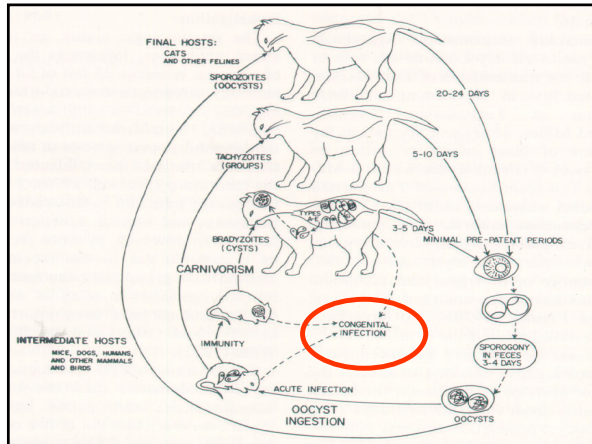
15

Congenital infections

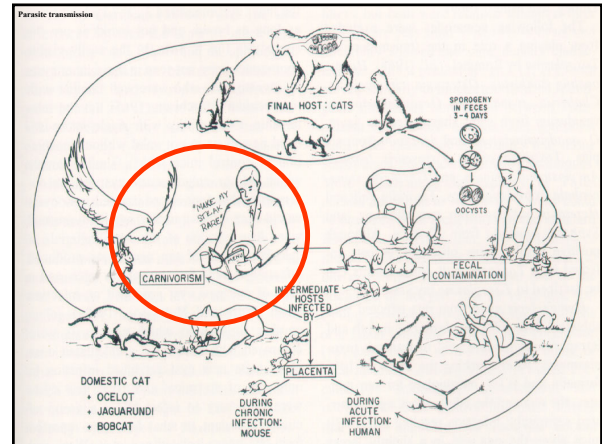
TORCH

- *Toxoplasma/Treponema*
- Other (varicella-zoster/*Listeria/Mycobacterium*)
- Rubella (German measles)
- Cytomegalovirus/*Chlamydia*
- Herpes-simplex/Hepatitis-B/HIV

18



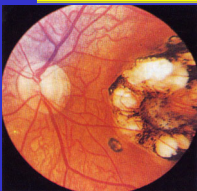
19



22

Parasite pathogenicity


Congenital infections



1st trimester - abortion

2nd trimester - stillbirth

3rd trimester - congenital abnormalities (cerebral calcification, retinochoroiditis, hydrocephalus, microcephaly)



NB: mother must become infected during pregnancy


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Carnivorism

- ingestion of cysts in raw/rare meat (tartare, smallgoods)
- bradyzoites resistant to pepsin
- revert to tachyzoites
- multiply and spread
- cyst formation

Cooking

- heat denaturation
- meat red due to blood
- haemoglobin browns around 65°C
- organisms dead



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Parasite biodiversity


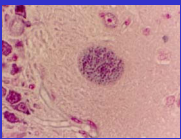
Toxoplasma

Infections acquired

- oocyst ingestion
- transplacental
- transmammmary

Still does not explain high incidence

- epidemiology suggests ascension through food chain

21

Diagnosis

Direct detection (definitive)

- tissue culture
- animal inoculation
- histology/labelling
- radio-imaging
- PCR/DNA

Indirect demonstration (presumptive)

- serology
 - antibodies (IgM/IgG)
 - antigens

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Treatment

Treatment


Treat infections or disease?

- clinically active disease
- diagnosed congenital infections
- symptomatic compromised patients
- pyrimethamine + sulfadiazine + clindamycin

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Enigma

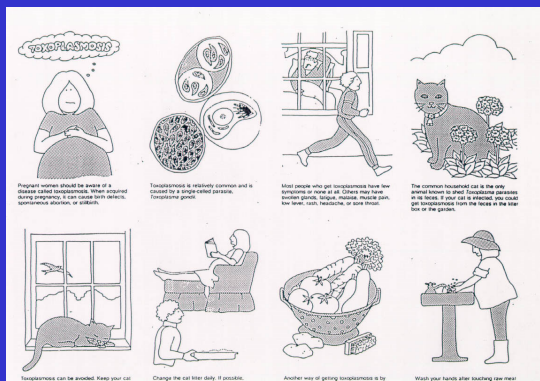
- *Toxoplasma* infections prevalent in many mammals
- infections cause serious reproductive losses in many domesticated species, except cattle
- cattle are refractory to disease (natural & experimental)
- cattle found to have novel genus causing disease, named *Neospora*



28

Prevention

Prevention



Prevent women should be aware of a disease called toxoplasmosis. When untreated during pregnancy, it can cause brain defects, spontaneous abortion, or stillbirth.

Toxoplasmosis is relatively common and is caused by a single-celled parasite, *Toxoplasma gondii*.

Most people who get toxoplasmosis have few symptoms or none at all. Others may have swollen glands, fatigue, muscle aches, pain, low fever, rash, headache, or sore throat.

The common household cat is the only animal known to shed *Toxoplasma gondii* oocysts in its feces. If your cat is pregnant, you could get toxoplasmosis from the feces in the litter box or the garden.

Toxoplasmosis can be avoided. Keep your cat house or indoors or outdoors high, close all doors and windows thoroughly. Wipe or soak kitty-poop magazines that may have come in contact with cat feces in the garden.

Preventives can be avoided. Keep your cat house or indoors or outdoors high, close all doors and windows thoroughly. Wipe or soak kitty-poop magazines that may have come in contact with cat feces in the garden.

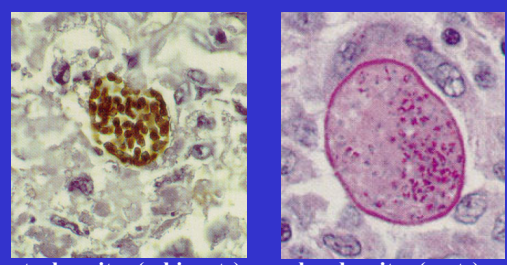
Change the cat litter daily. If possible, something other than your important partner should do this.

Another way of getting toxoplasmosis is by eating raw or undercooked meat. Cook all meat and poultry thoroughly. Wipe or soak kitty-poop magazines that may have come in contact with cat feces in the garden.

Wash your hands after touching law near changing the cat litter or working in garden that cats have access to.

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Neospora



tachyzoites (schizonts) bradyzoites (cysts)

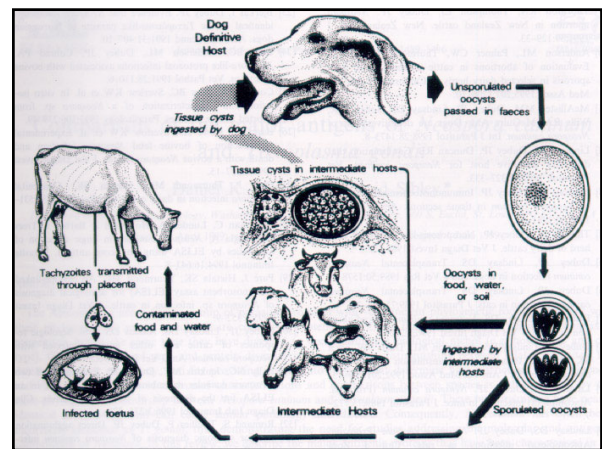
- first associated with ascending paralysis in dogs
- then abortions in various domestic animals

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Behaviour?



27



30

Co-evolution

Despite the number of pathogens, many do not cause overt clinical disease in their hosts because they have evolved together to live in a stable relationship where the existence of neither is threatened.

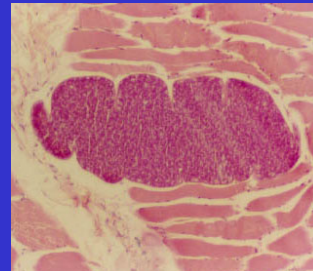
This balance is called ENZOOTIC stability

- the pathogen does not kill the host
- the host does not kill the pathogen

31

Sarcocystis

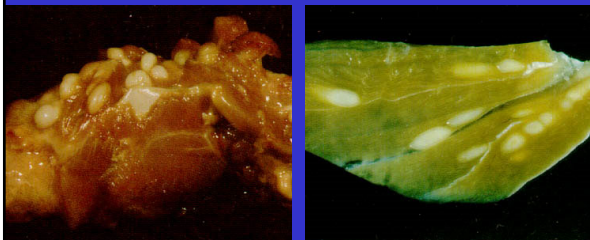
- sarcocysts contain millions of cystozoites
- life cycle discovered in 1970's (predator-prey)



34

Exemplar - Sarcocystis

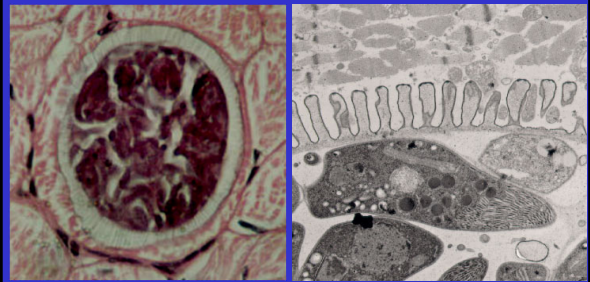
- Tissue cyst-forming coccidian (esp. muscles)
- Macrocysts lead to rejection of carcass from export or condemnation from human consumption
- Prevalence around 5% but low intensity



32

Chronic sarcocystosis

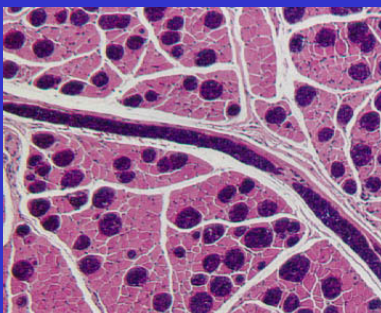
- tissue cyst formation in musculature
- cystozoites in thick-walled cysts



35

Sarcocystis

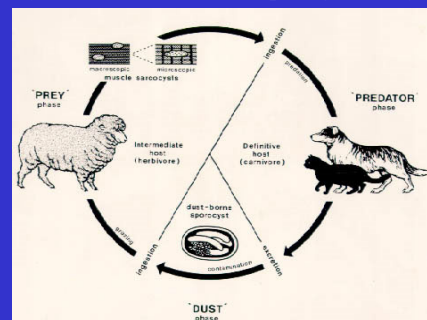
- Microcysts not considered at meat inspection
- Prevalence around 95% and intensity high



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Sarcocystis

- Cysts awaiting uptake by definitive host (predator)
- Two cycles discovered for sheep (dog & cat cycles)



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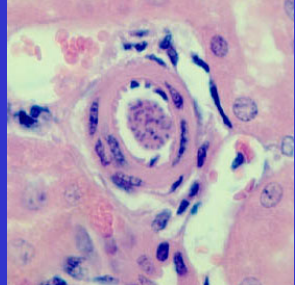
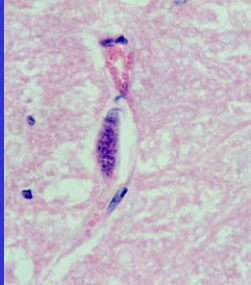
Sarcocystosis

SYSTEMIC INFECTIONS	ENTERIC INFECTION
<ul style="list-style-type: none"> • in numerous mammals, including humans • ACUTE merozoite proliferation • CHRONIC tissue cyst formation 	<ul style="list-style-type: none"> • in numerous carnivores, including humans • ACUTE oocyst production

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Acute sarcocystosis

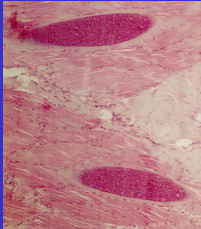
- asexual proliferation in vascular endothelial cells
- schizonts in arterioles then capillaries

40

Humans as intermediate hosts

- tissue cyst formation in muscles causing myositis
- no evidence for pre-cyst vasculitis
- very low prevalence, moderate seroprevalence
- infections acquired through ingesting sporocysts
- contaminated foods, esp. fruit in monkey jungles
- suspected python-monkey cycle



38

Acute sarcocystosis

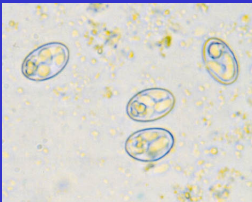
- schizogony linked with acute disease
- characterized by petechial haemorrhages
- possible cause of weaner illthrift/mortality




41

Humans as definitive hosts

- oocyst/sporocyst production in intestinal mucosa
- most asymptomatic, some enteritis ('sarcocystin'?)
- very low prevalence
- infections acquired through ingesting tissue cysts
- *S. suis* in pork
- *S. bovis* in beef



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Acute sarcocystosis

Disease associated with:

- mortality
- morbidity
- reduced weight gain
- reduced wool growth
- reproductive failure (abortion/stillbirth)

- BUT ONLY IN EXPERIMENTAL LABORATORY ANIMALS GIVEN HIGH DOSES
- CONDITION NOT SEEN IN FIELD ANIMALS

WHY?

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Tissue cyst-forming coccidia

Dormant stages awaiting ingestion by predator
 Earlier proliferative stages dangerous in:

- foetal tissues
- neonates
- immunocompromised

Infections do not accumulate with age
 due to premunitive immunity

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Disease is merely the tip of the iceberg
 while the remainder provides stability

The diagram shows an iceberg floating in water. The tip above the water is labeled 'classical disease picture' and 'less severe disease'. The much larger part below the water is labeled 'asymptomatic infection (individual infects others, seroconverts, resists reinfection)' and 'ENZOOTIC STABILITY'.

46

Protection

acquisition of strong protective immunity

The graph plots IgM-ELISA results on a logarithmic scale (2, 8, 32, 128, 512) against time. It shows a 'Low-dose primary infection' followed by 'Homologous lethal challenge' for four groups. Group 1 shows a high peak, while Groups 2, 3, and 4 show progressively lower peaks, indicating the acquisition of protective immunity.

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REVIEW

TISSUE CYST-FORMING COCCIDIA

SYSTEMIC	ENTERIC
<i>Toxoplasma</i>	<i>Toxoplasma</i>
• common	• never
• abortifacient	
<i>Sarcocystis</i>	<i>Sarcocystis</i>
• rare	• rare
• myositis	• enteritis

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Enzootic stability

Absence of clinical disease due to:

- low-dose primary infections (trickle/sporadic) being asymptomatic/subclinical
- solid protective immunity (concomitant not sterile) able to resist super-infection and disease

The graph shows the number of parasites over time after infection. It is divided into an 'acute' phase with a high peak and a 'chronic' phase with a lower, sustained level. The chronic phase is associated with 'premunitive immunity' (not sterile) and 'sterile immunity'.

45