




Immuno-Evasion



protozoa



helminths




arthropods

Professor Peter O'Donoghue

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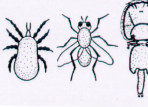
PARASITOLOGY

Protozoa



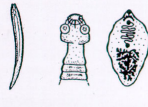
flagellates amoebae sporozoa ciliates
(coccidia) (haematozoa)

Arthropods



arachnids insects crustacea
(ticks) (flies) (mites) (fleas) (lice)

Helminths




nematodes cestodes trematodes
(roundworms) (tapeworms) (flukes)

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Interactions


PARASITE

- needs food supply
- place to develop
- place to propagate



HOST

- resist infection
- moderate disease
- develop protection



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Evolutionary arms race

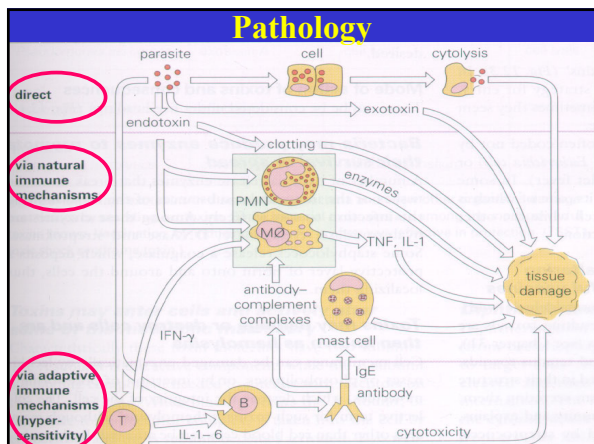
Host immune system works to:

- repel/destroy invaders
- undertake damage control
- protect against re-infection

Parasites develop survival strategies to avoid:

- innate immune responses
- acquired immune responses

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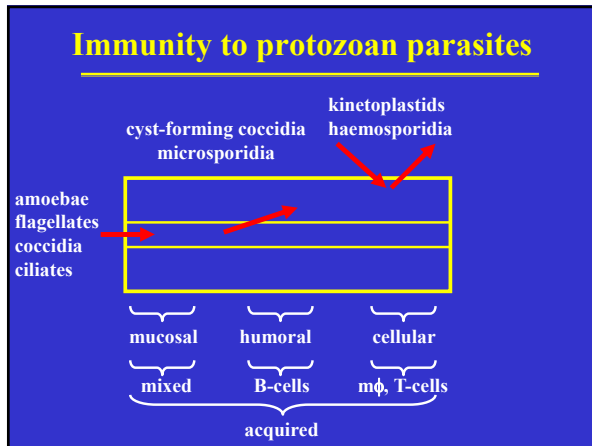
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Pathology due to parasites

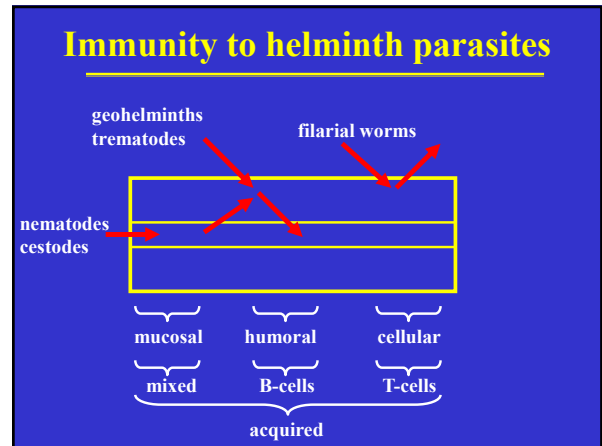
Abnormalities arise due to:

- direct effects of parasites
 - structural (cell lysis, tissue trauma, lesions)
 - functional (loss, regulation, obstruction)
- host responses to infection
 - innate immune responses
 - phagocytosis, antimicrobial proteins
 - inflammation
 - acquired immune responses
 - humoral (antibodies)
 - cell-mediated (cytotoxicity)
 - hypersensitivity

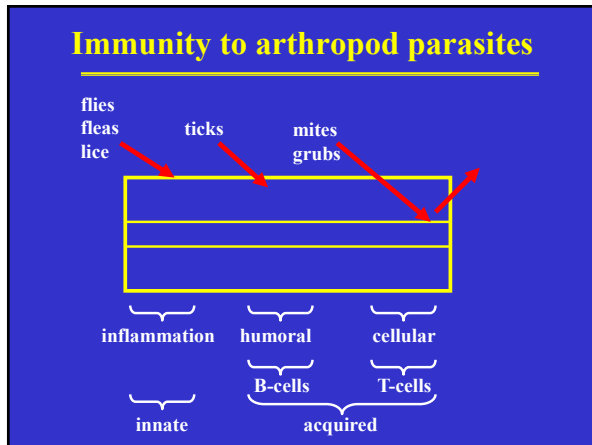
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- ### How do parasites survive it all?
- Become less aggressive
(parasite - commensal - symbiote)
 - Learn to avoid host immune system
(evasion mechanisms)
 - Host-parasite evolutionary arms race
(middle ground = enzootic stability)

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Immuno-evasion

HIDE - CHANGE - SUBVERT

These strategies improve parasite survival
(colonization, development, reproduction)

but still allows host immune system to limit
disease and provide some protection

Remember: overt virulence resulting in
host mortality is not in best interest of
most parasites - better to be sneaky!

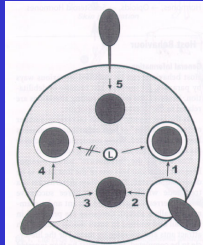
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Innate immunity	Acquired immunity
nonspecific mechanisms	specific mechanisms
phagocytosis inflammation	cell-mediated & humoral responses

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Strategies to avoid INNATE responses

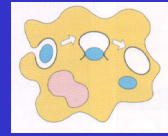
- kill phagocytes using toxins (common for bacteria, suspected for some parasites)
- best to avoid phagocytic lysis altogether (common for protozoa)
 - develop in cytoplasm
 - parasitophorous vacuole
 - produce inhibitory proteins
 - produce anti-oxidants



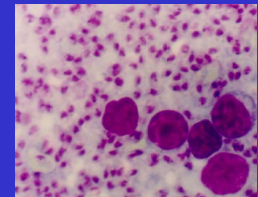
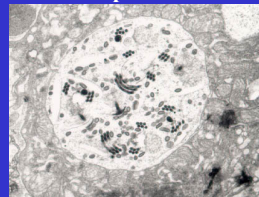
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Intracytoplasmic development

- penetrate membrane directly into cytoplasm
- microspora



escape from phagolysosome
– amastigotes of *Leishmania*, *T. cruzi*

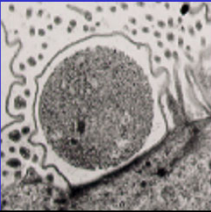


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Parasitophorous vacuole

- intracellular yet extracytoplasmic location
- live in vacuole lined by host membranes
- or host + parasite materials

Cryptosporidium



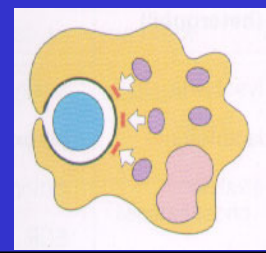
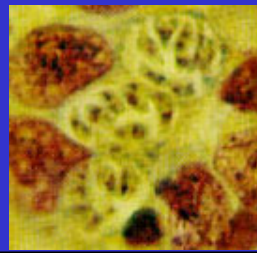
Sarcocystis



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Inhibitory proteins

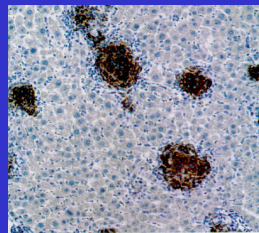
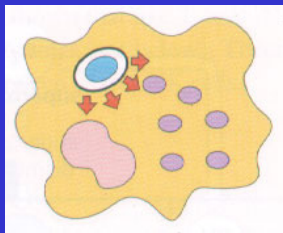
- fusion of phagosome and lysosome inhibited e.g. *Toxoplasma gondii* tachyzoites



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Anti-oxidants

- parasites resist killing by ROI and/or RNI (reactive oxygen/nitrogen intermediates) using anti-oxidants e.g. *Leishmania*, *Plasmodium*



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Strategies to avoid ACQUIRED responses



HIDE



CHANGE



SUBVERT

- conceal antigens

- antigen variation

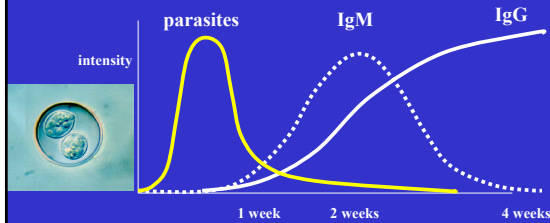
- immunosuppress

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HIDE 1: hit-and-run

Rapid transient infections, e.g. coccidia

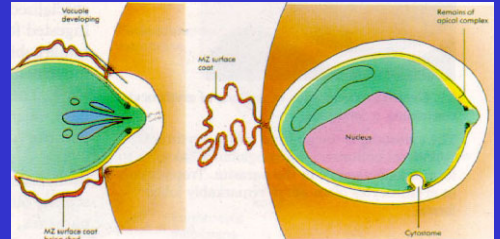
- short prepatency and patency
- outrace immune responses



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HIDE 2: antigen presentation

- do not express antigens (hide in cytoplasm)
- shed antigenic coat e.g. *Plasmodium*
- inhibit MHC recognition (implied)

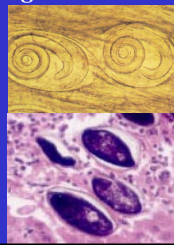


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HIDE 3: inert sites

Infect host tissues where lymphocyte populations are absent or reduced

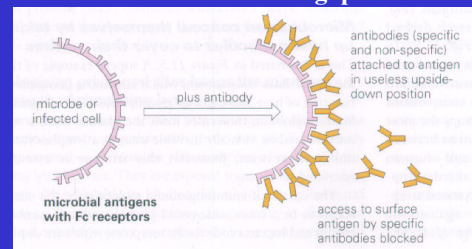
- gastro-intestinal lumen e.g. *Giardia*
- central nervous system e.g. *Naegleria*
- joints e.g. *Onchocerca*
- embryo e.g. *Toxoplasma*
- intragenomic e.g. *Karyolysus*
- intracystic e.g. hydatid cysts
- encapsulation e.g. *Trichinella*
- granuloma e.g. *Schistosoma*



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HIDE 4: antigenic mimicry

- mimic host antigens e.g. *Plasmodium*
- coat with host antigens e.g. *Schistosoma*
- coat with host antibodies e.g. protein A

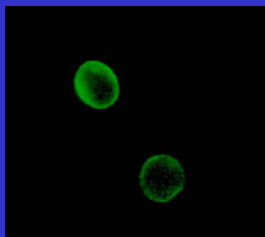


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CHANGE 1: mutation

antigenic drift

Giardia axenic culture
drift over >10 generations



Trichomonas culture
drift over 20 generations



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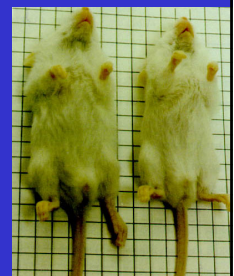
CHANGE 2: recombination

genetic shift

(well known for human/avian influenza virus)

implicated for exceptionally virulent strains

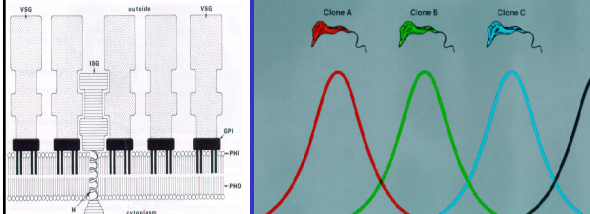
- *Toxoplasma* RH (lacking cysts)
- *Giardia* 'Polly' (zoonotic, petechia)



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CHANGE 3: gene switching

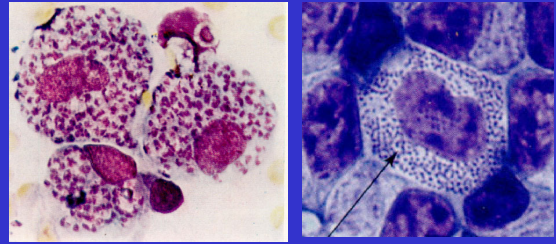
- best known example: *Trypanosoma* VSG's (variant-specific glycoproteins) (up to 1,000 genes but only one governing expression)
- occurs for many other parasites (esp. protozoa)



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SUBVERT 1: target immune cells

- macrophages
Toxoplasma, Leishmania
- lymphocytes
Theileria

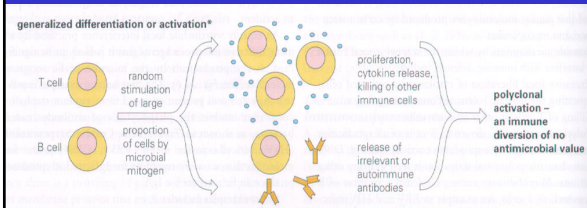


impaired function, impaired division, cell death

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SUBVERT 2: produce exotoxins

- induce polyclonal activation (T cell mitogens)
- immunodiversion (saturate host with irrelevant antigens) (e.g. many worms)
- produce proteolytic enzymes (cleave Ig)



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SUBVERT 3: immunosuppress host

- induction of suppressor cells
- proteinase destruction of host effector molecules
- inhibit host proteinases/cytokines
- malaria immunosuppression linked to down-regulation of cytotoxic T cells

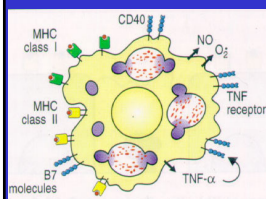


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Immuno-evasion - summary

INNATE IMMUNITY (avoid phagocytes)

- develop in cytoplasm
- parasitophorous vacuole
- inhibitory proteins
- anti-oxidants



ACQUIRED IMMUNITY (avoid lymphocytes)

- HIDE (conceal antigens)**
 - hit-and-run
 - antigen presentation
 - inert sites
 - antigenic mimicry
- CHANGE (antigen variation)**
 - mutation
 - recombination
 - gene switching
- SUBVERT (modulate)**
 - target immune cells
 - produce exotoxins
 - immunosuppress host

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