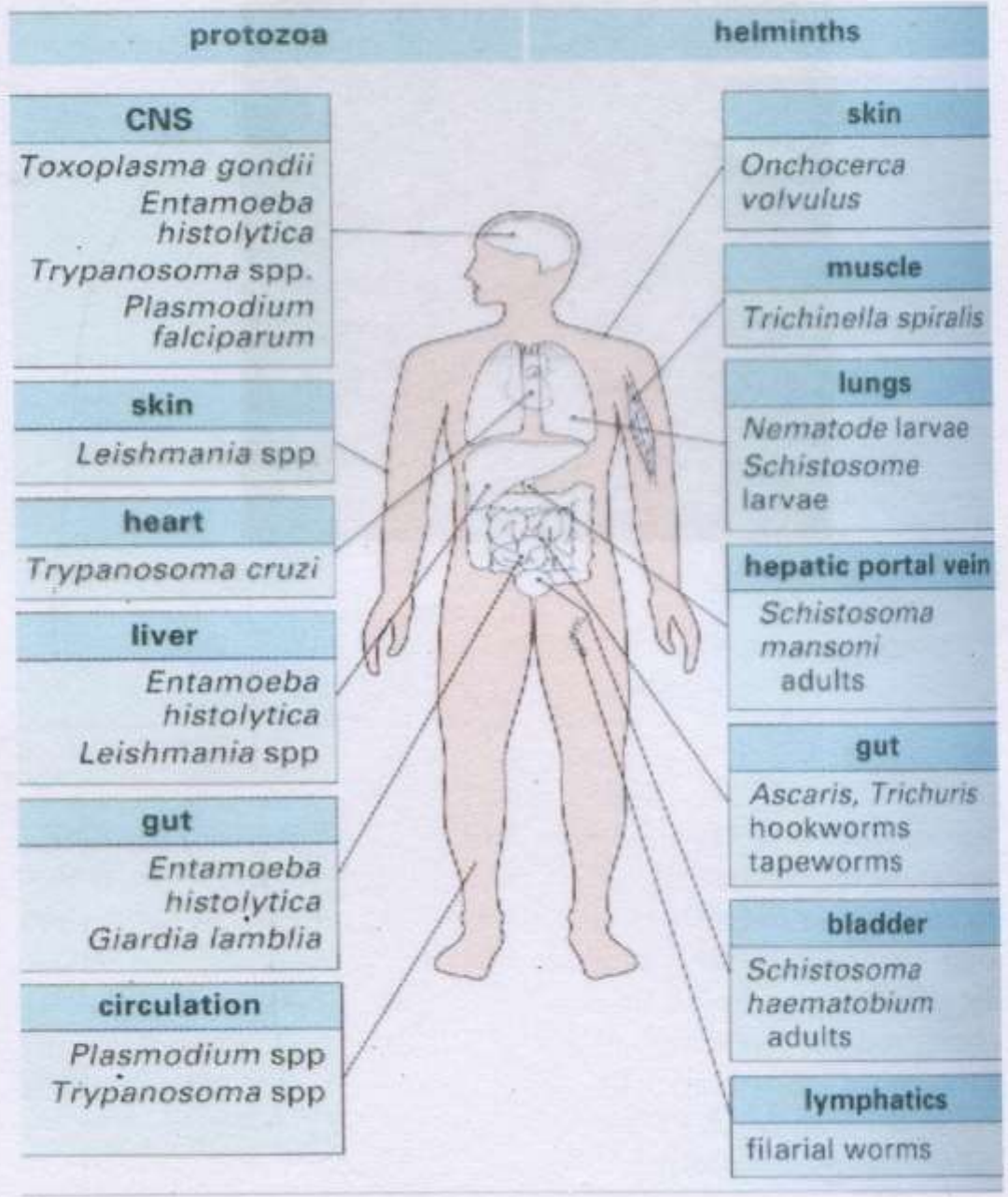
Immunology of parasitic infection

Dr.Eman Albataineh,
Associate Prof. Immunology
College of Medicine, Mutah university
Immunology,

Immunity to Parasites

- Parasites stimulate a number of immunological defense mechanisms
- humoral, cellular responses and innate system
- Immune response depends on the stage and the type of infection
- Most parasites pass through a complicated life cycle helminths are bigger and more complex than protozoa

Examples of parasitic infections



Features of Parasitic infection:

1- Infect large number of people

2- Parasitic infection have common features

Variety and large quantity of Ag

Ability to change their surface Ag

Complicate life cycle

Different mode of entry

3- Most parasites are host specific

4- Host resistance to parasite may be genetic

5- Many parasitic infections are chronic

Effector mechanisms by Immune cells

MACROPHAGES

- Secrete factors that kill parasites without ingestion
- Secrete cytokines that activate other immune cells
- Synthesize nitric oxide that act as parasite toxin
- Activation of macrophages is a general feature of early stage of infection
- Some resistance by protozoa
- IFN gamma –activated macrophages most effective against protozoa

NEUTROPHILS

- Can kill large and small parasites
- Secrete factors that kill parasites without ingestion
- Have granules that contain cytotoxic proteins

PLATELETS

- Cytotoxic activities against larval stages
- Activation are enhanced by cytokines

EOSINOPHILS

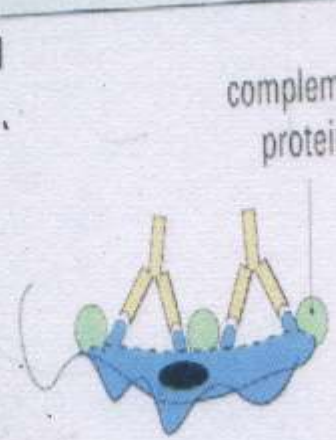
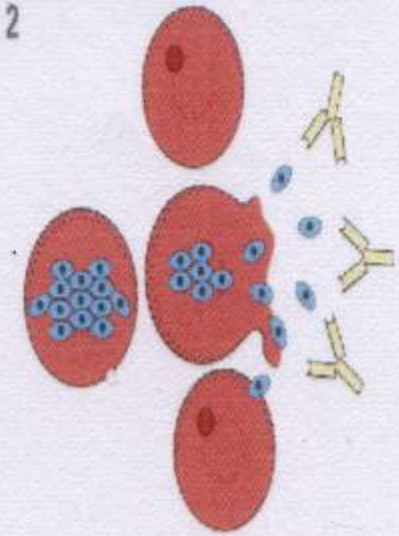
- Characterize helminth infection
- Thought to be specific against tissue parasites
- Limit migration of parasites through the host
- Act in accordance with mast cells
- Have Fc receptors >> ADCC

Role of T cells

- The type of T cells involved is determined by the type and the stage of the infection
- Cytokines enhance protective immunity against intracellular parasites
- ADCC for helminths
- Granuloma in early helminth lesion is good to encapsulate their eggs, if 2^{nd} exposure lead to pathological fibrosis
- TH2 protective against helminths (Ab is IgE) (TH1 is counter protective), complication of over action is allergy and fibrosis and granuloma
- TH1 protective against protozoa and filarial worm from helminth (TH2 is counter protective, IGG and IGM), complication of over action is autoimmunity

Role of Antibodies

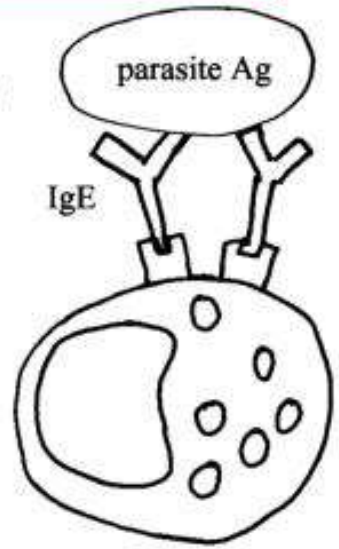
- Parasites induce production of specific and non specific Abs
- Antibodies have several functions on parasites
  - -Act direct damage by complement mediated, plasmodium sporozoite and intestinal worms
  - -ADCC on helminths as schistosomes and intestinal worms
  - -Block attachment to host cells by neutralizing the attachment sites plasmodium sporozoite
  - -Important for Phagocytosis in plasmodium
  - -Infection by protozoan parasites is associated with the production of IgG and IgM. With helminths there is, in addition, the synthesis of substantial amounts of IgE.

parasite	*Plasmodium* sporozoite, intestinal worms, trypanosome	*Plasmodium* sporozoite and merozoite, *Trypanosoma cruzi*, *Toxoplasma gondii*	*Plasmodium*, trypanosome	schistosomes, *Trichinella spiralis*, filarial worm larvae
mechanism	1 	2 	3 	4 
effect	direct damage or complement-mediated lysis	prevents spread by neutralizing attachment site, prevents escape from lysosomal vacuole, prevents inhibition of lysosomal fusion	enhancement of phagocytosis	antibody-dependent cell-mediated cytotoxicity (ADCC)

Pathological effect of the immune response

1- Allergic reactions (type 1 hypersensitivity):

IgE mediated allergy



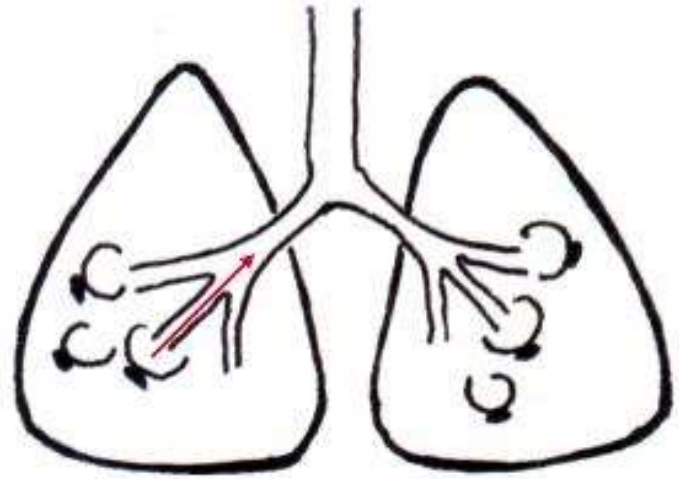
Leaking hydatid fluid ⟶ anaphylactic shock.

Fascioliasis and larva migrans ⟶ bronchial asthma.

Early stages of schistosomiasis, fascioliasis, ascariasis ⟶ Allergic dermatitis.

Pathological Effect of the Immune response

2- Eosinophilic pneumonia:
Migrating larvae of *Ascaris* and hookworms through the lungs.



Loffler's syndrome

3- Autoimmune reactions:
Some parasites have antigens similar to host antigens. These will induce the production of antibodies (autoantibodies) that cross-react with host antigens e.g. in malaria and Chagas' disease.

4- Deposition of immune complex (type 3 hypersensitivity reaction):

Deposition in host tissues and activate the complement system resulting in host tissue damage e.g.

Nephrotic syndrome complicating *Plasmodium malariae* infection.

katayama fever occurring in acute schistosomiasis.

5- Granuloma formation (delayed type hypersensitivity):

Cell-mediated reactions form granulomatous lesions around parasites e.g.

Granuloma formation around *Schistosoma* eggs producing subsequent complications of the disease.

6- Immunosuppression:

Secondary bacterial infection occurs ⟶ death of infants and small children infected with visceral leishmaniasis.

Parasite Immune Evasion strategies.

Immune Evasion | **1- Sequestration of Parasite**

Means: The location of the parasite that makes it inaccessible to the immune response.

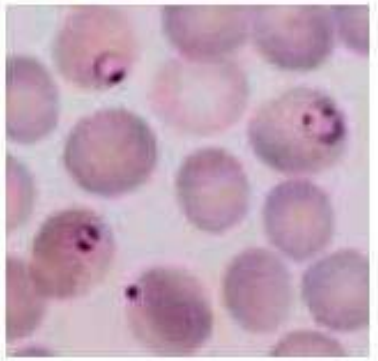
This can be achieved through:

- Intracellular habitat

  e.g. *Plasmodium, Toxoplasma, Leishmania*

Tissue cyst of *Toxoplasma*

Amastigotes of *Leishmania*

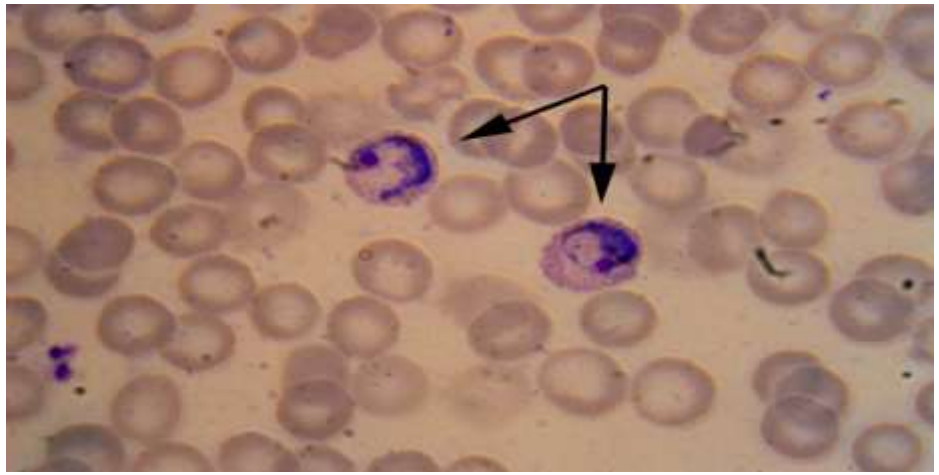


Plasmodium parasite

- Presence of surrounding cyst wall

  e.g. *Trichinella* larva.

Encysted larva of *T.spiralis*



Protozoan immune evasion strategies.

Anatomical seclusion in the vertebrate host.

Parasites may live intracellularly. By replicating inside host cell parasites avoid immune response.

Plasmodium lives inside Red Blood Cells (RBC'S) which have no nucleus, when infected not recognised by immune cells. Other stages of *Plasmodium* live inside liver cells.

Leishmania parasites toxoplasma and *Trypanosoma cruzi* live inside **macrophages**.

2- Luminal Habitat

Intestinal parasites: e.g. *Ascaris, Enterobius* are less exposed to immune factors present in the mucosa

3- Parasite movement

Adult *Ancylostoma*: move away from inflamed tissue to fresh areas.

In larva migrans: Migrating larva escapes the immune response elicited locally.

4- Antigenic modification

- Antigen variation:

  African trypanosomes, malaria parasites.

- Antigen disguise:

  Parasites cover themselves with host proteins to be considered as self and will not be attacked by the immune factors e.g. adult *Schistosoma.*

- Antigen mimicry:

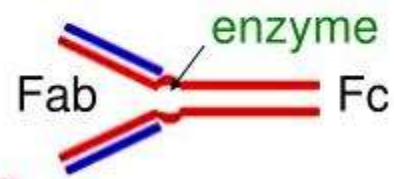
  Parasites produce antigens similar to host antigens so they are not recognized by the host's immune system e.g. *Schistosoma.*

- Antigen shedding:

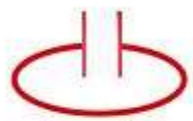
  Parasites shed their antigens in abundance can neutralize antibody response at a distance away from the parasite e.g. *Schistosoma mansoni and Plasmodium falciparum.*

5- Inhibition of Immune Factors

- Cleavage of antibodies: parasite produces a protease enzyme that can cleave immunoglobulin molecule into Fab and Fc portions e.g. *Trypanosoma cruzi.*



- Inactivation of complement: through:
  - Protease activity e.g. *Schistosoma* larva.
  - Acceleration of decay of complement e.g. *Trypanosoma cruzi.*
  - Ejection of membrane attack complex from their surface e.g. *Leishmania.*



- Inhibition of macrophages by several inhibitory mechanisms so they can survive in macrophages e.g. *Leishmania, Toxoplasma, Trypanosoma cruzi.*

X

6- Production of blocking antibodies

Antibodies of little protective effect.

Some helminths produce blocking Abs that combine with helminths Ags making them unavailable for antibodies of high protective effect (antibodies involved in ADCC) : e.g. *Schistosoma*

7- Immunosuppression

Mediated through Ts cells e.g. Visceral leishmaniasis

Immunodiagnosis

- Immunodiagnosis includes:
  - Skin tests.
  - Serological tests.
- Performed when:
  - Failure of detection of parasite by direct methods.
  - Light or chronic infection, to identify Ag or Ab against Ag.

➢ Skin test = intradermal (ID) test

- How?
  - ID injection of 0.1-0.2 ml of prepared Ag in forearm & saline in the other as control.
- Result:
  - Immediate → IgE → wheal & erythema.
  - Delayed → CMI → induration & edema.

➢ Skin test = intradermal (ID) test

- Use:
  - Low cost & rapid.
  - BUT!!!!! Lacks specificity & rarely severe reaction:
  - Montengero ID test for cutaneous leishmaniasis (immediate +ve), is also +ve in Kala Azar after cure.
  - Frenkel ID test for toxoplasmosis (delayed).
  - ID test for amaebiasis (delayed).
  - Casoni test for hydatid disease (immediate & delayed).
  - Bachman ID test for trichinosis (immediate & delayed).
  - ID test for ascaris (immediate).
  - ID test for filariasis (immediate & delayed).

Sterilizing Immunity: Wipe out the parasites completely, meanwhile get a long-term specific resistance to re-infection. Rare!

Non-sterilizing Immunity: Wipe out most of the parasites, but not completely. Common! No parasite, no immunity!

Vaccination

No efficient vaccine preparation has yet been developed for human use against parasites.

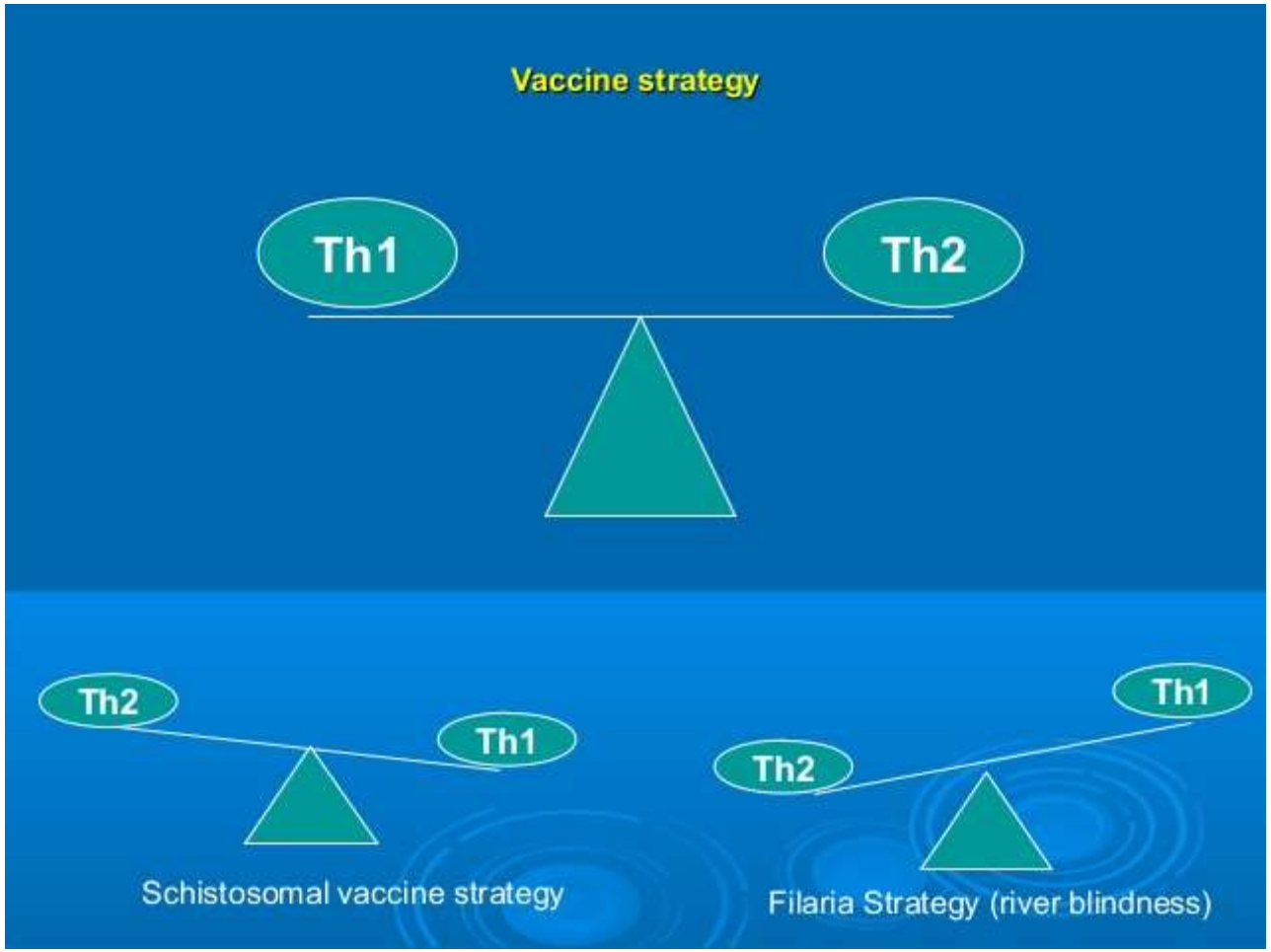
Why?????

- Complexity of the life cycle of the parasite makes the stage to be chosen for vaccine preparation difficult.
- Difficulty of identification and isolation of protective antigen to be used as vaccine.
- Possibility of inducing immunopathological lesions in response to the vaccine.
- Parasites may evade the immunity produced by the vaccine.
- Vaccine preparation may not be equally effective.

Vaccine to schistosoma

- Pathology from schistosomiasis , however, is also associated with a Th2 response. IL-12, a cytokine that shifts T cells away from the Th2 subset, has been shown to reduce granuloma formation and subsequent fibrosis.
- There is hope that administration of egg antigens plus IL-12 could be used as an "anti-pathology" vaccine for preventing granulomatous disease.
- And since the disease caused by schistosomiasis is largely caused by the host response to eggs, rather than the infecting worms themselves, an anti-pathology vaccine might prove to be more effective.

- However, some believe that if down-regulation of the granuloma response is carried too far, leaking egg antigens may elicit toxic effects that could damage the surrounding hepatocytes in the absence of any sequestering reaction.
- Furthermore, since IL-12 stimulates a Th1 response, it subsequently down-regulates IgE production.
- Therefore, a vaccine towards schistosomiasis may have to achieve a balance where a Th2 response is elicited towards the parasite with elevated IgE production while the Th2 response towards the eggs is inhibited.


Vaccine strategy
Th1
Th2
Th2
Th1
Schistosomal vaccine strategy
Th1
Th2
Filaria Strategy (river blindness)