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Aims

At the end of session must.

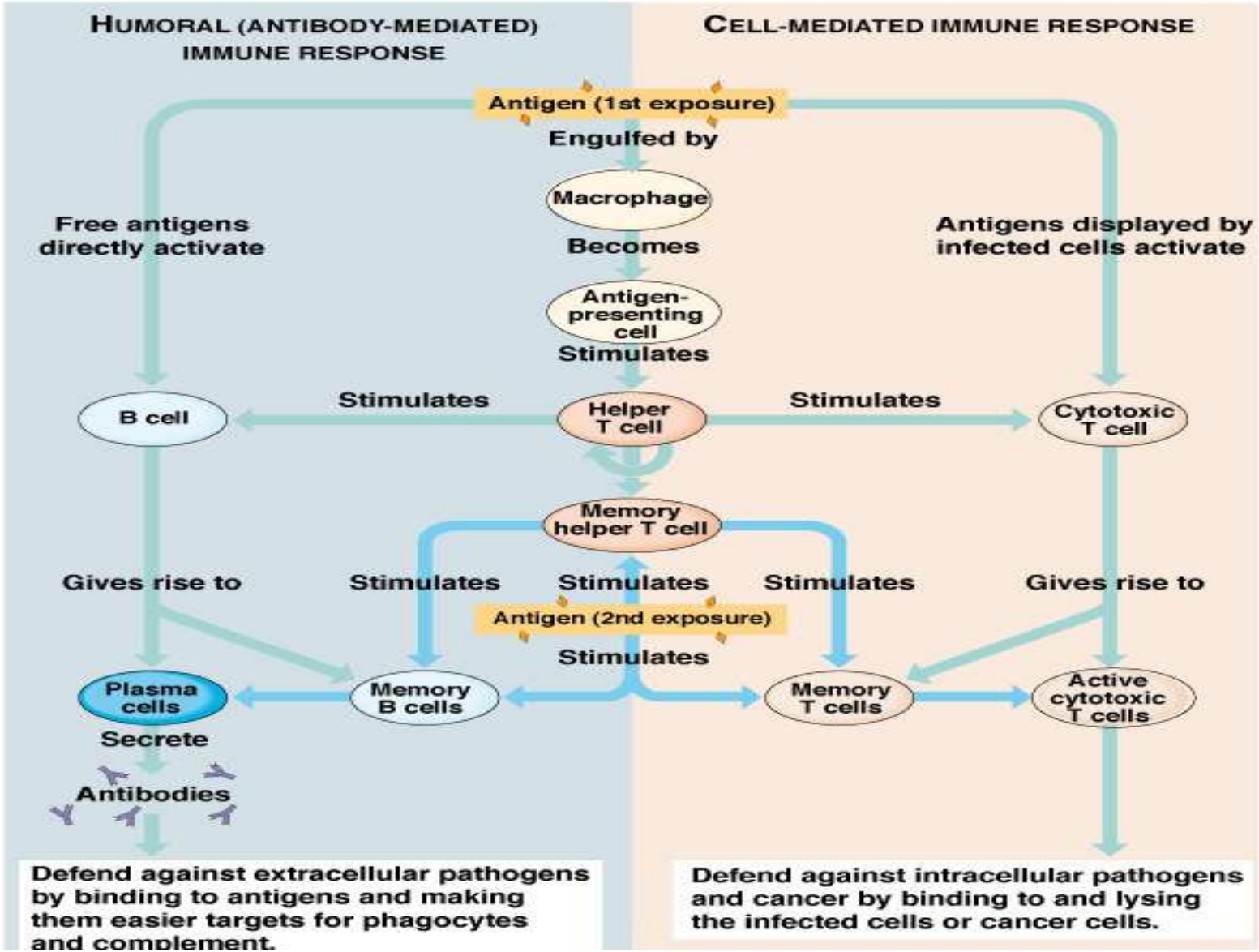
1- know the two lines of the immune response.

2- Estimate the immune responses to different groups of parasites.

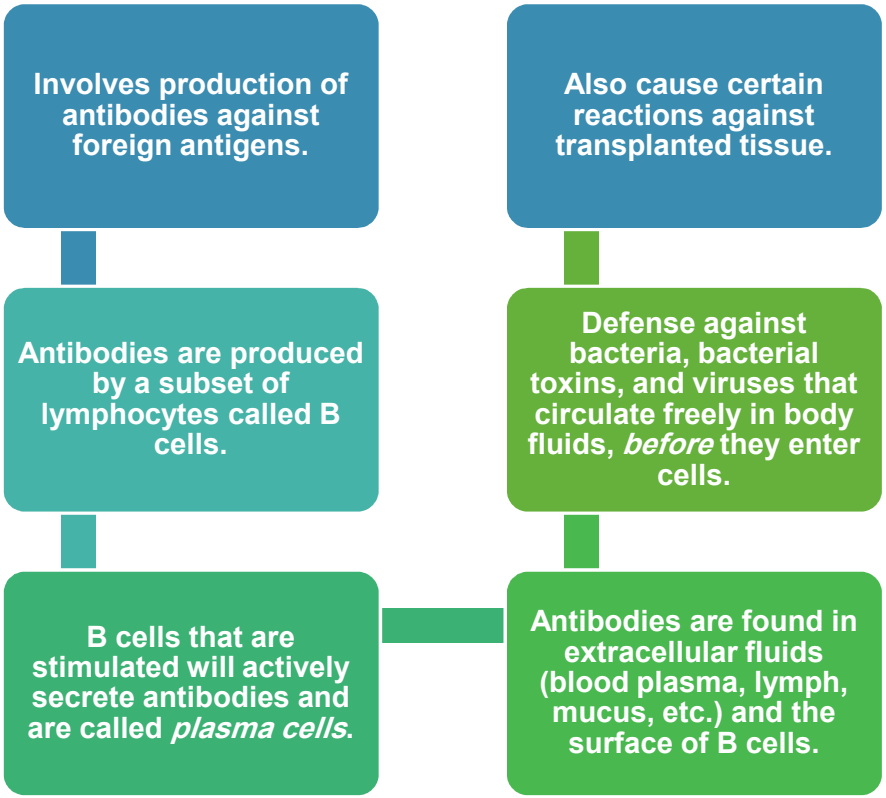
3- Estimate strategies used by parasites to evade their hosts' immune mechanism

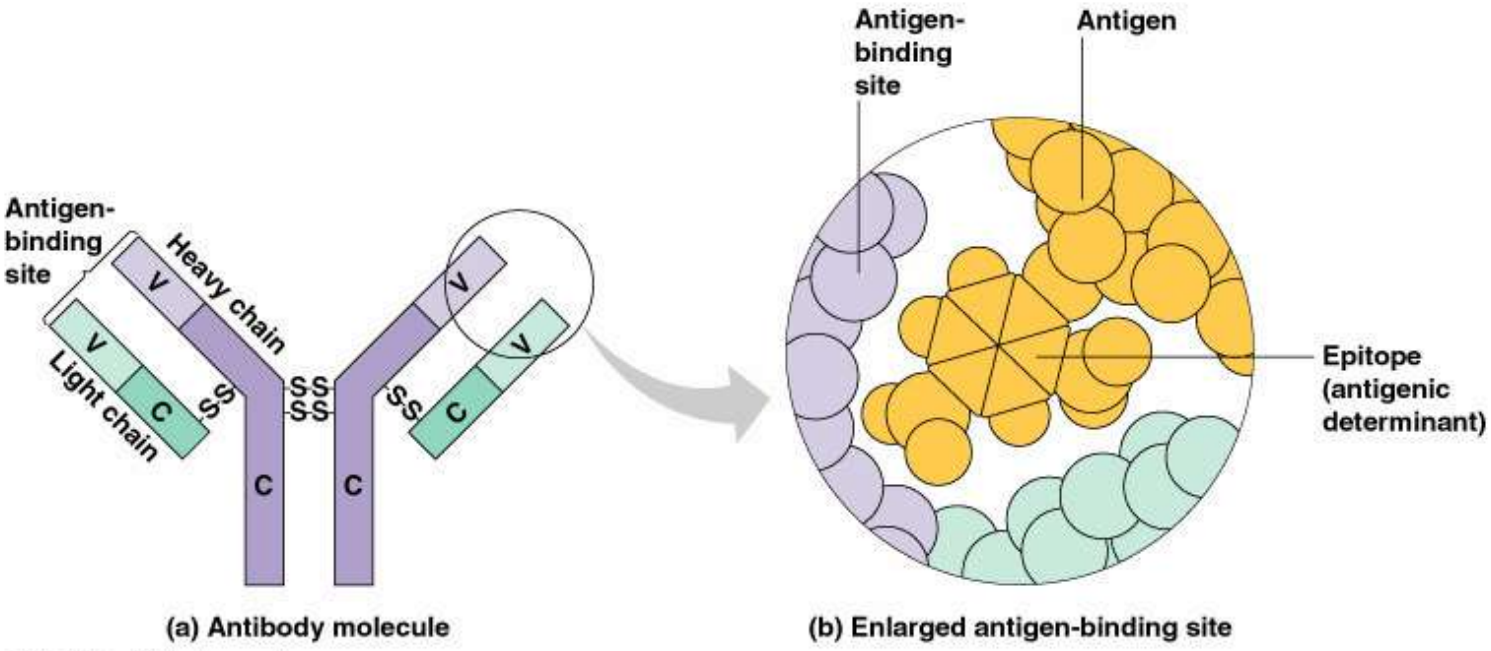
Evidence of Immune response against parasites

Overview of the Immune Response

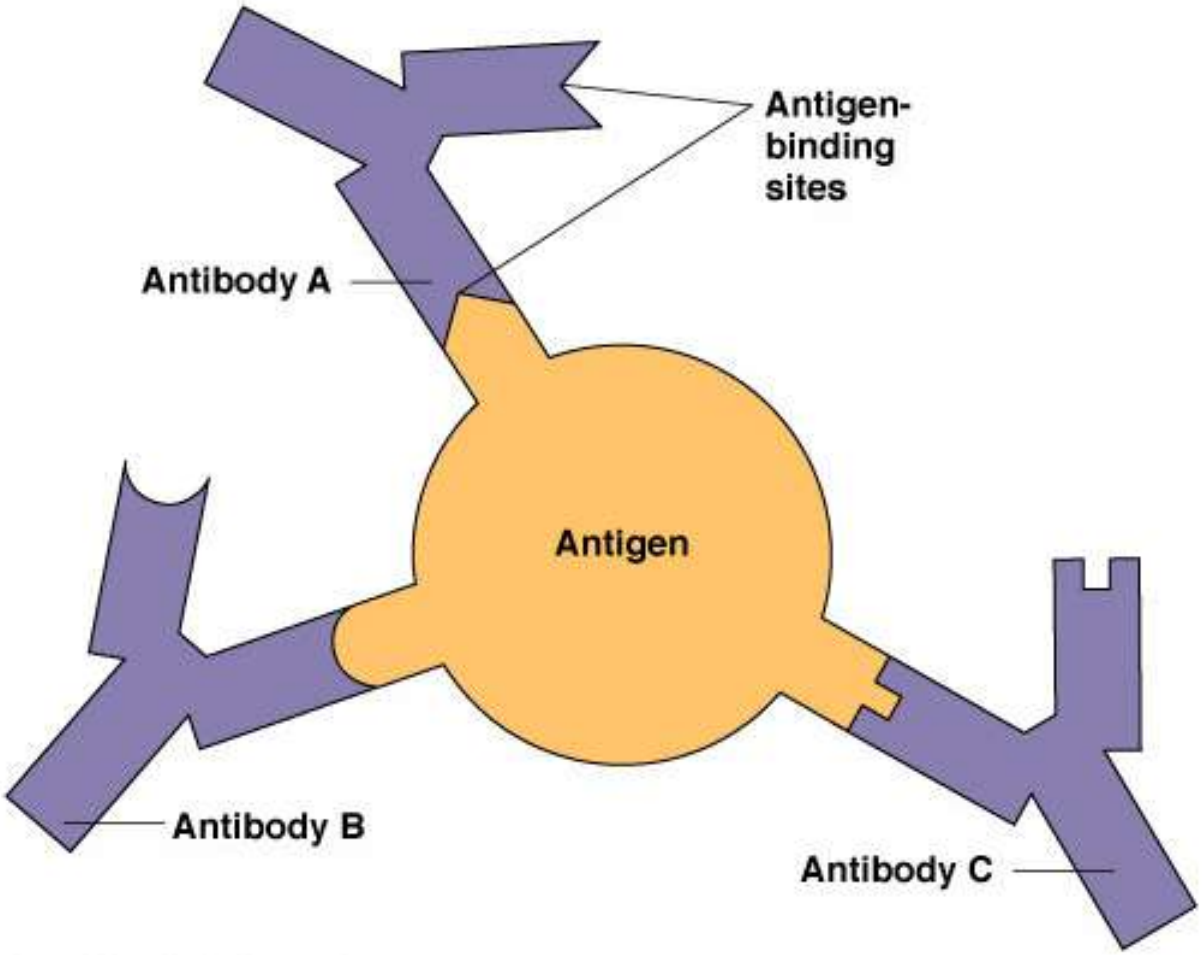

HUMORAL (ANTIBODY-MEDIATED) IMMUNE RESPONSE
CELL-MEDIATED IMMUNE RESPONSE
Antigen (1st exposure)
Engulfed by
Macrophage
Free antigens directly activate
Becomes
Antigens displayed by infected cells activate
Antigen-presenting cell
Stimulates
B cell
Stimulates
Helper T cell
Stimulates
Cytotoxic T cell
Memory helper T cell
Gives rise to
Stimulates
Stimulates
Stimulates
Gives rise to
Antigen (2nd exposure)
Stimulates
Plasma cells
Memory B cells
Memory T cells
Active cytotoxic T cells
Secrete
Antibodies
Defend against extracellular pathogens by binding to antigens and making them easier targets for phagocytes and complement.
Defend against intracellular pathogens and cancer by binding to and lysing the infected cells or cancer cells.

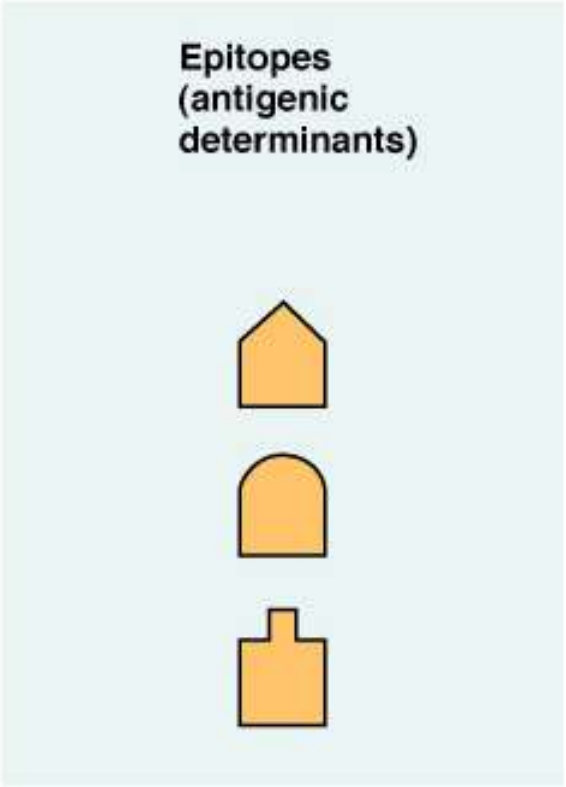
Humoral (Antibody-Mediated) Immunity


Involves production of antibodies against foreign antigens.
Antibodies are produced by a subset of lymphocytes called B cells.
B cells that are stimulated will actively secrete antibodies and are called *plasma cells*.
Also cause certain reactions against transplanted tissue.
Defense against bacteria, bacterial toxins, and viruses that circulate freely in body fluids, *before* they enter cells.
Antibodies are found in extracellular fluids (blood plasma, lymph, mucus, etc.) and the surface of B cells.



Antibodies are Proteins that Recognize Specific Antigens





Epitopes: Antigen Regions that Interact with Antibodies

Immunoglobulin Classes

II. IgM

IgA

- Structure: Dimer
- Percentage serum antibodies: 10-15%
- Location: Secretions (tears, saliva, intestine, milk), blood and lymph.
- Half-life in serum: 6 days
- Complement Fixation: No
- Placental Transfer: No
- Known Functions: Localized protection of *mucosal* surfaces. Provides immunity to infant digestive tract.

I. IgG

Structure: Monomer

Percentage serum antibodies: 80%

Location: Blood, lymph, intestine

Half-life in serum: 23 days

Complement Fixation: Yes

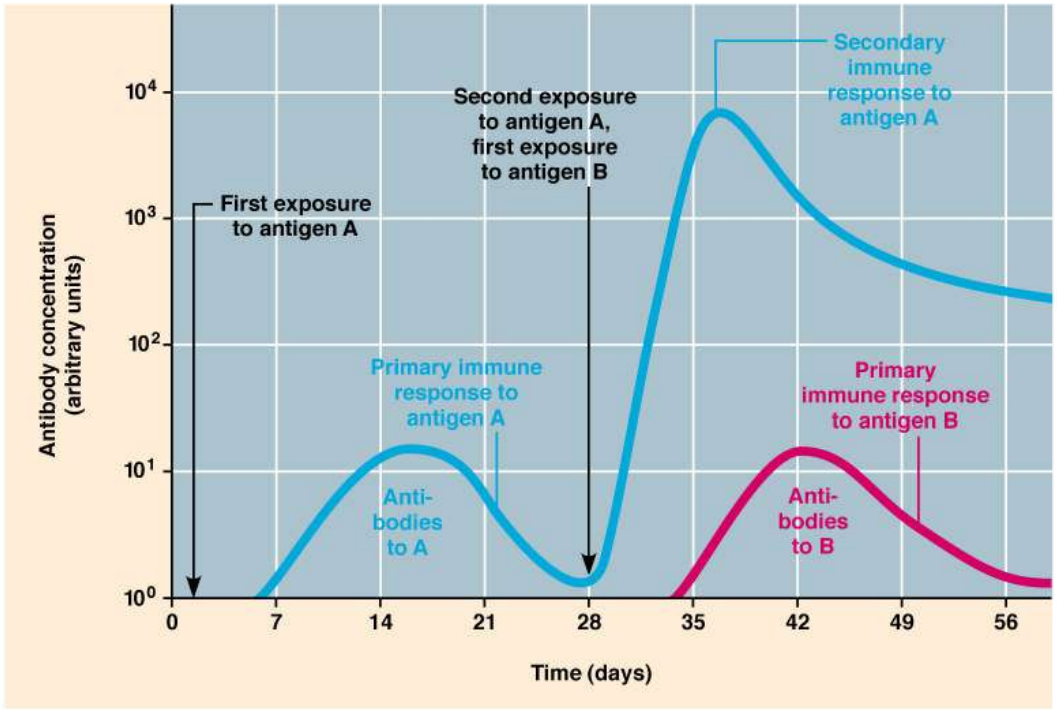
Placental Transfer: Yes

Known Functions: Enhances phagocytosis, neutralizes toxins and viruses, protects fetus and newborn.

IgE

- **Structure: Monomer**
- **Percentage serum antibodies: 0.002%**
- **Location: Bound to mast cells and basophils throughout body. Blood.**
- **Half-life in serum: 2 days**
- **Complement Fixation: No**
- **Placental Transfer: No**
- **Known Functions: Allergic reactions. Possibly lysis of worms.**

- IgD



Antibody Response After Exposure to Antigen

II-T Cells and Cell Mediated Immunity

- Antigens that stimulate this response are mainly *intracellular*.
- Requires constant presence of antigen to remain effective.
- Unlike humoral immunity, cell mediated immunity is not transferred to the fetus.
- Cytokines: Chemical messengers of immune cells.
  - Over 100 have been identified.
  - Stimulate and/or regulate immune responses.
    - Interleukins: Communication between WBCs.
    - Interferons: Protect against viral infections.
    - Chemokines: Attract WBCs to infected areas.

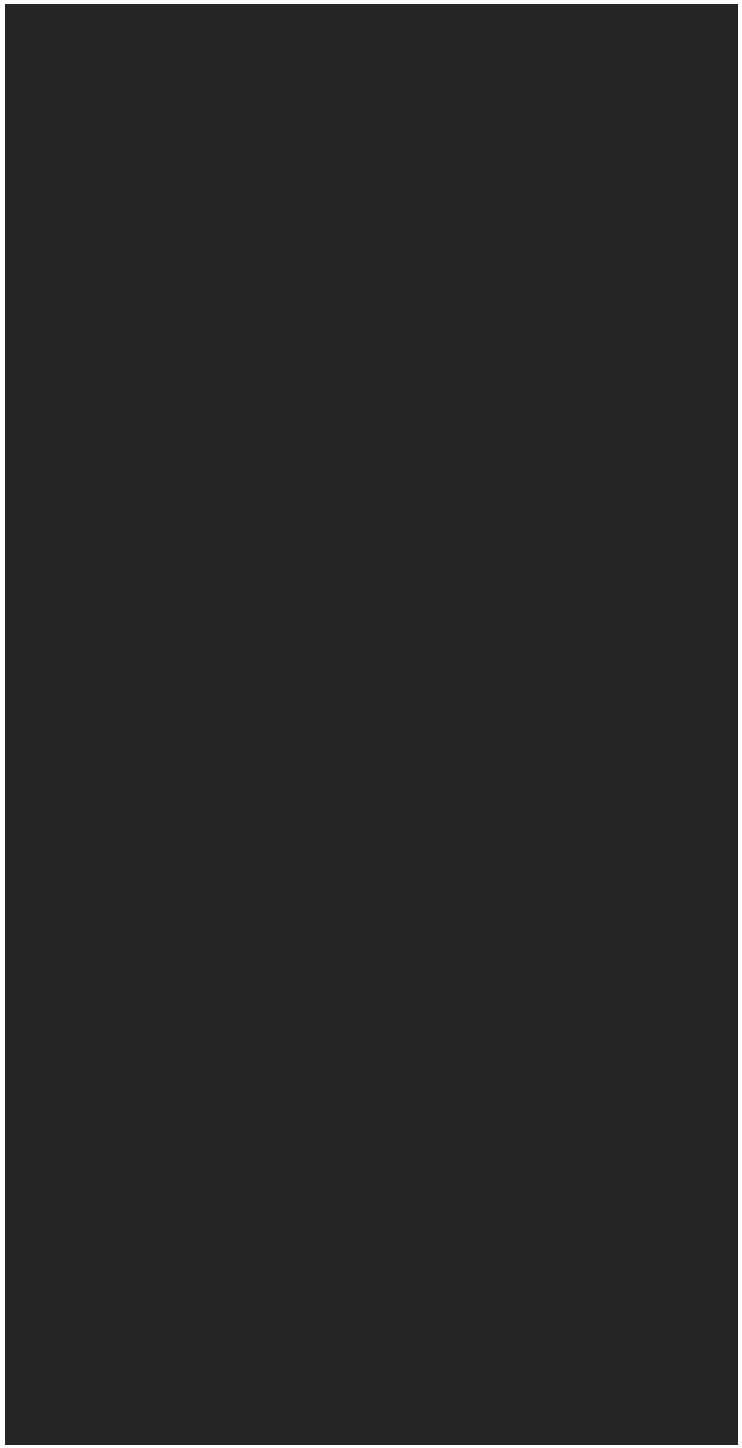
Cells of primary immune response

Activated Macrophages:
Stimulated phagocytes.

- **Stimulated by ingestion of antigen**
- **Larger and more effective phagocytes.**
- **Enhanced ability to eliminate intracellular bacteria, virus-infected and cancerous cells.**

2. Natural Killer (NK) Cells:

- **Lymphocytes that destroy virus infected and tumor cells.**
- **Not specific. Don't require antigen stimulation.**
- **Not phagocytic, but must contact cell in order to lyse it.**

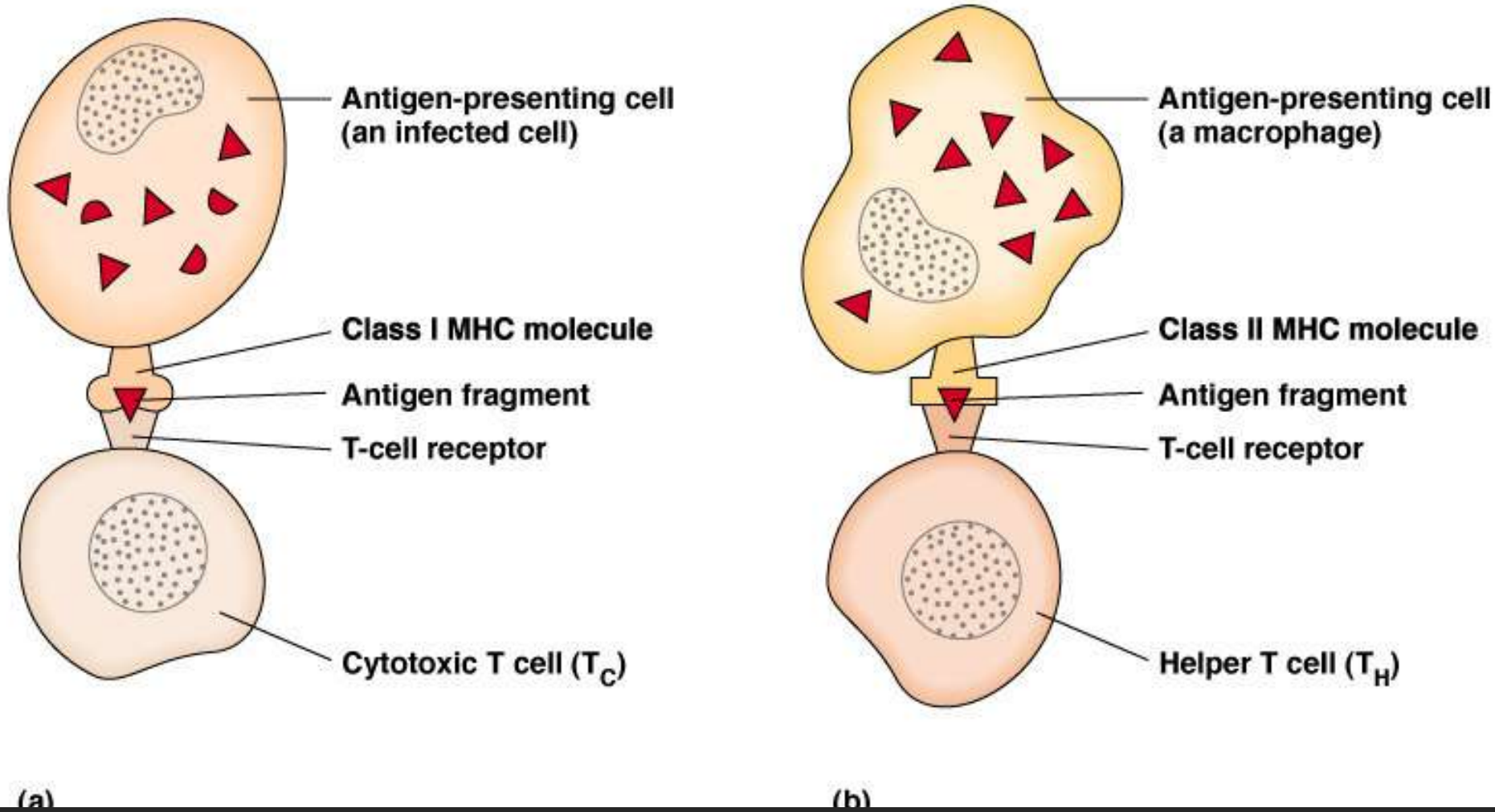


- Involves specialized set of lymphocytes called T cells that recognize foreign antigens on the surface of cells, organisms, or tissues:
  - Helper T cells
  - Cytotoxic T cells
- T cells regulate proliferation and activity of other cells of the immune system: B cells, macrophages, neutrophils, etc.
- Defense against:
  - Bacteria and viruses that are inside host cells and are inaccessible to antibodies.
  - Fungi, protozoa, and helminths
  - Cancer cells
  - Transplanted tissue

T Cells and Cell Mediated Immunity

Cellular Components of Immunity:

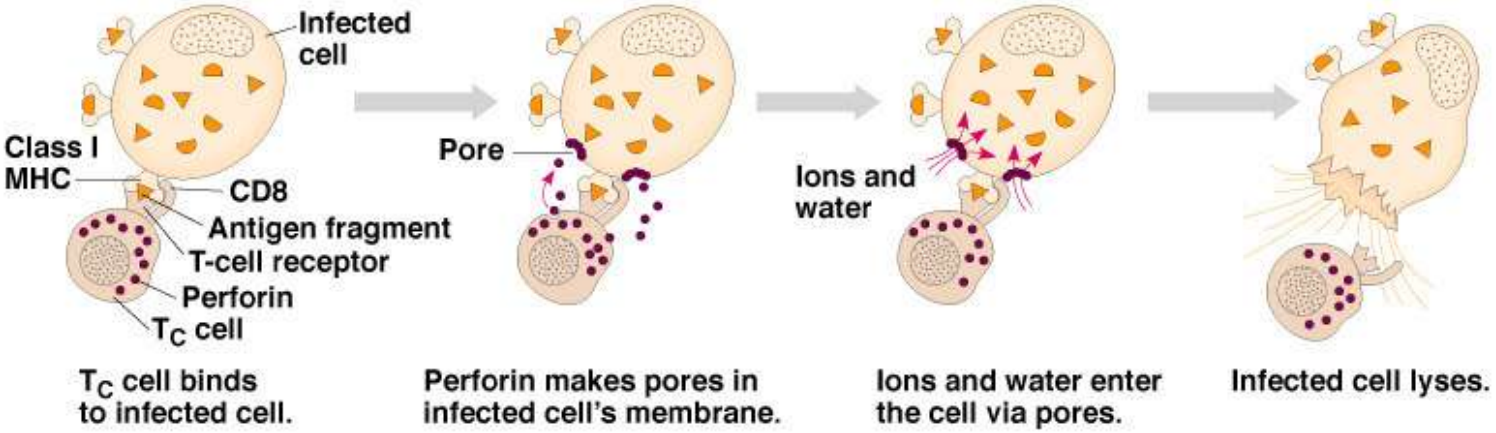
- T cells are key cellular component of immunity.
- T cells have an antigen receptor that recognizes and reacts to a specific antigen (T cell receptor).
- T cell receptor only recognize antigens combined with major histocompatability (MHC) proteins on the surface of cells.
  - MHC Class I: Found on all cells.
  - MHC Class II: Found on phagocytes.
- Clonal selection increases number of T cells.



T Cells Only Recognize Antigen Associated with MHC Molecules on Cell Surfaces

2. Cytotoxic T (Tc) Cells: Destroy target cells.

- Most are CD8 while, CD4 negative ($CD4^-$).
- Recognize antigens on the surface of all cells:
  - Kill host cells that are infected with viruses or bacteria.
  - Recognize and kill cancer cells.
  - Recognize and destroy transplanted tissue.
- Release protein called *perforin* which forms a pore in target cell, causing lysis of infected cells.
- Undergo apoptosis when stimulating antigen is gone.



(a)

Cytotoxic T Cells Lyse Infected Cells

3. Delayed Hypersensitivity T (T_D) Cells:

Mostly T helper and a few cytotoxic T cells that are involved in some allergic reactions (poison ivy) and rejection of transplanted tissue.

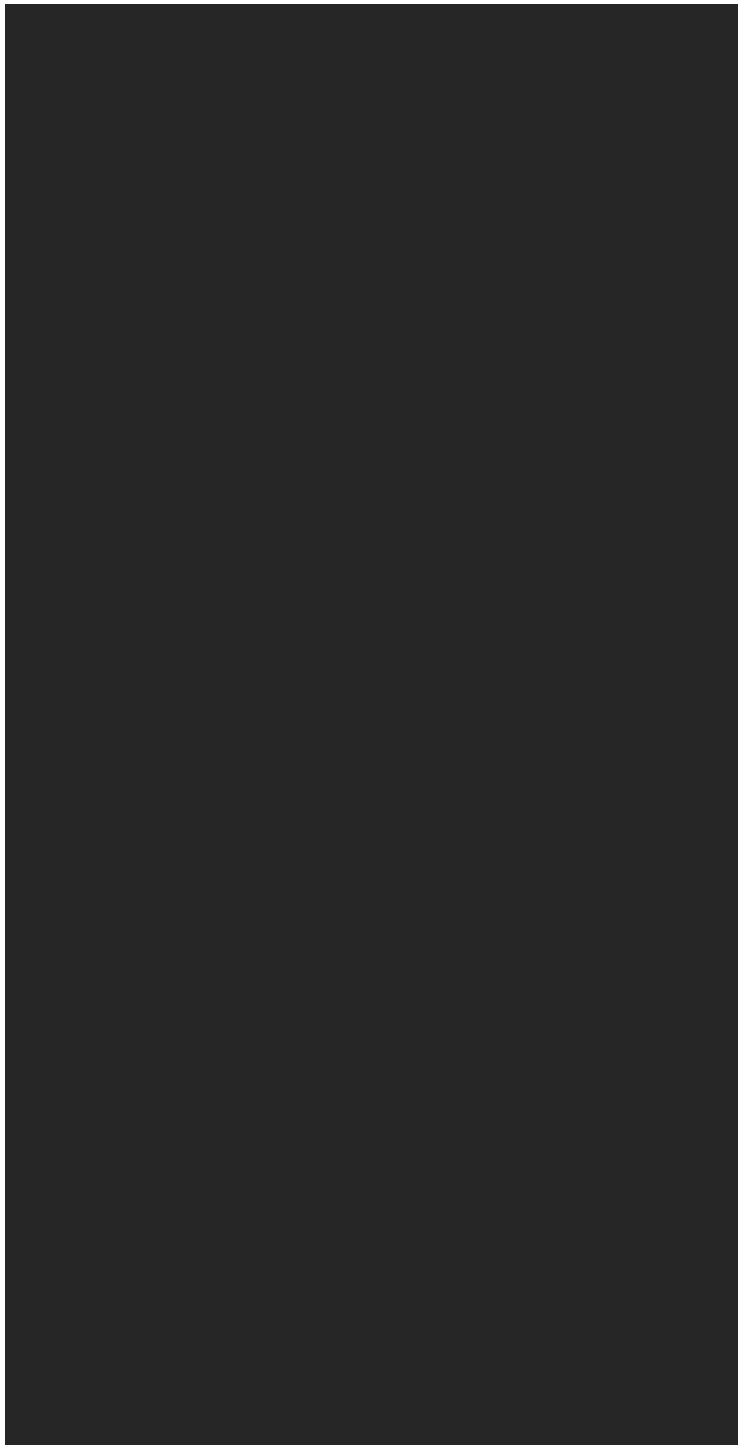
4. T Suppressor (Ts) Cells: May shut down immune response.

T Cells and Cell Mediated Immunity Types of T cells

Central role in immune response.

1. **T Helper (T_H) Cells:**
   - **Most are $CD4^+$**
   - **Recognize antigen on the surface of antigen presenting cells (e.g.: macrophage).**
   - **Activate macrophages**
   - **Induce formation of cytotoxic T cells**
   - **Stimulate B cells to produce antibodies**

Vertebrate Immune responses to Protozoan parasites.



Innate immune responses.

In vertebrates, extracellular protozoa are eliminated by phagocytosis and complement activation.

T cell responses.

- Extracellular protozoa - Th2 cytokines released for antibody production.
- Intracellular protozoa - Cytotoxic lymphocytes (CTL's) kill infected cells. Th1 cytokines produced to activate macrophages, CTL's & DTH response also involved.

Combination of innate and acquired immune responses.

Antibody + Complement, e.g. lysis of blood dwelling trypanosomes.

Antibody / complement plus neutrophils or macrophages against malaria merozoites. Activated macrophages can be effective against many intracellular protozoa, e.g. *Leishmania*, *Toxoplasma*, *Trypanosoma cruzi*.

CD8+ cytotoxic T cells respond parasite infected host cells, e.g. *Plasmodium* infected liver cell.

Vertebrate Immune responses to helminth infections.

Most helminths extracellular & too large for phagocytosis.

For the larger worms, e.g. some gastrointestinal nematodes host develops inflammation and hypersensitivity. Eosinophils & IgE activated to initiate inflammatory response in the intestine or lungs to expel the worms. These histamine elicited reactions are similar to allergic

The **acute response** after previous exposure can involve an IgE and eosinophil mediated systemic inflammation which results in expulsion of the worms.

Chronic exposure

to worm antigens can cause **chronic inflammation**:

- Delayed type hypersensitivity (DTH), Th1 / activated macrophages which can result in granulomas.
- Th2 / B cell responses increase IgE, mast cells & eosinophils activate inflammation.

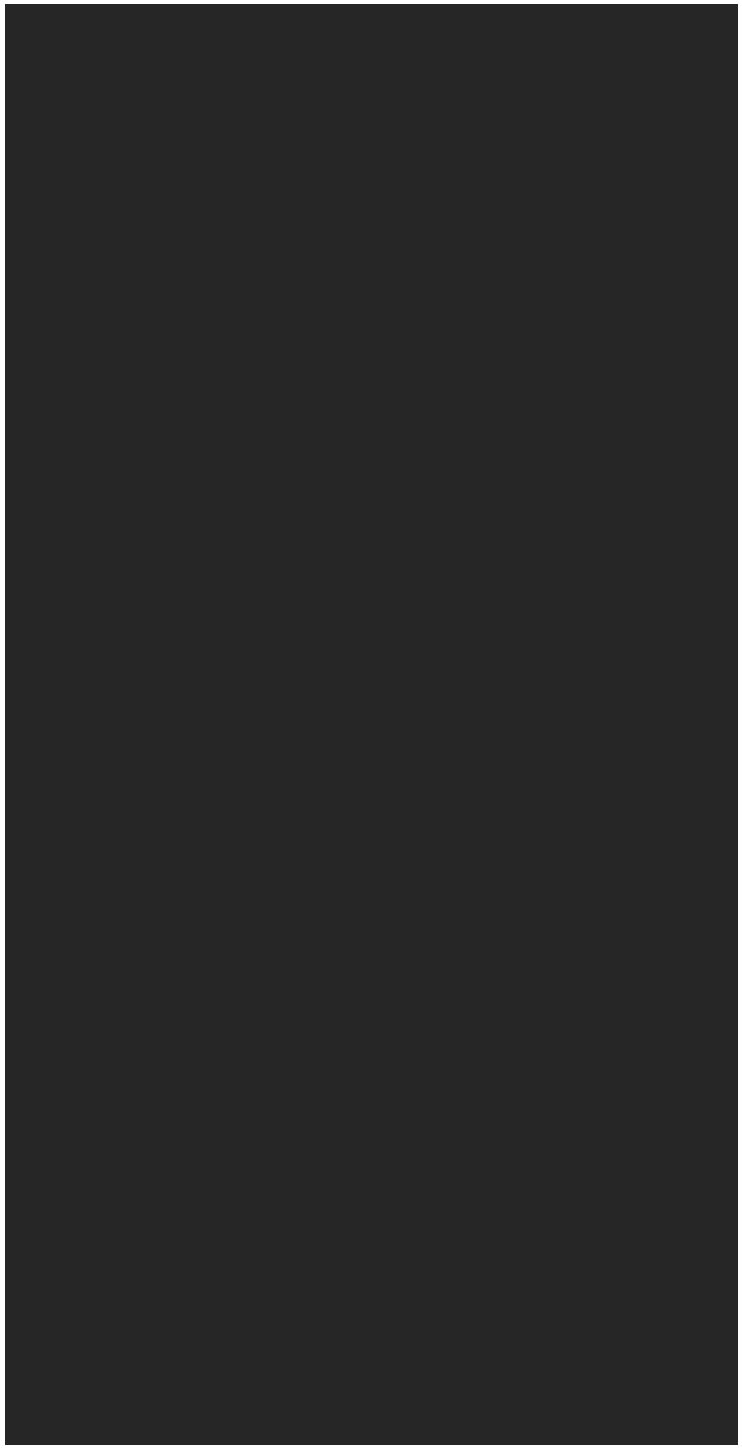
Parasite Immune Evasion – Evasion strategies.

Why the parasite should evade from the immune response?

Parasites need time in host to complete complex development, to sexually reproduce & to ensure vector transmission.

Chronic infections (from a few months to many years) are normal, therefore parasite needs to avoid immune elimination.

Parasites have evolved immune evasion strategies.



Protozoan immune evasion strategies.

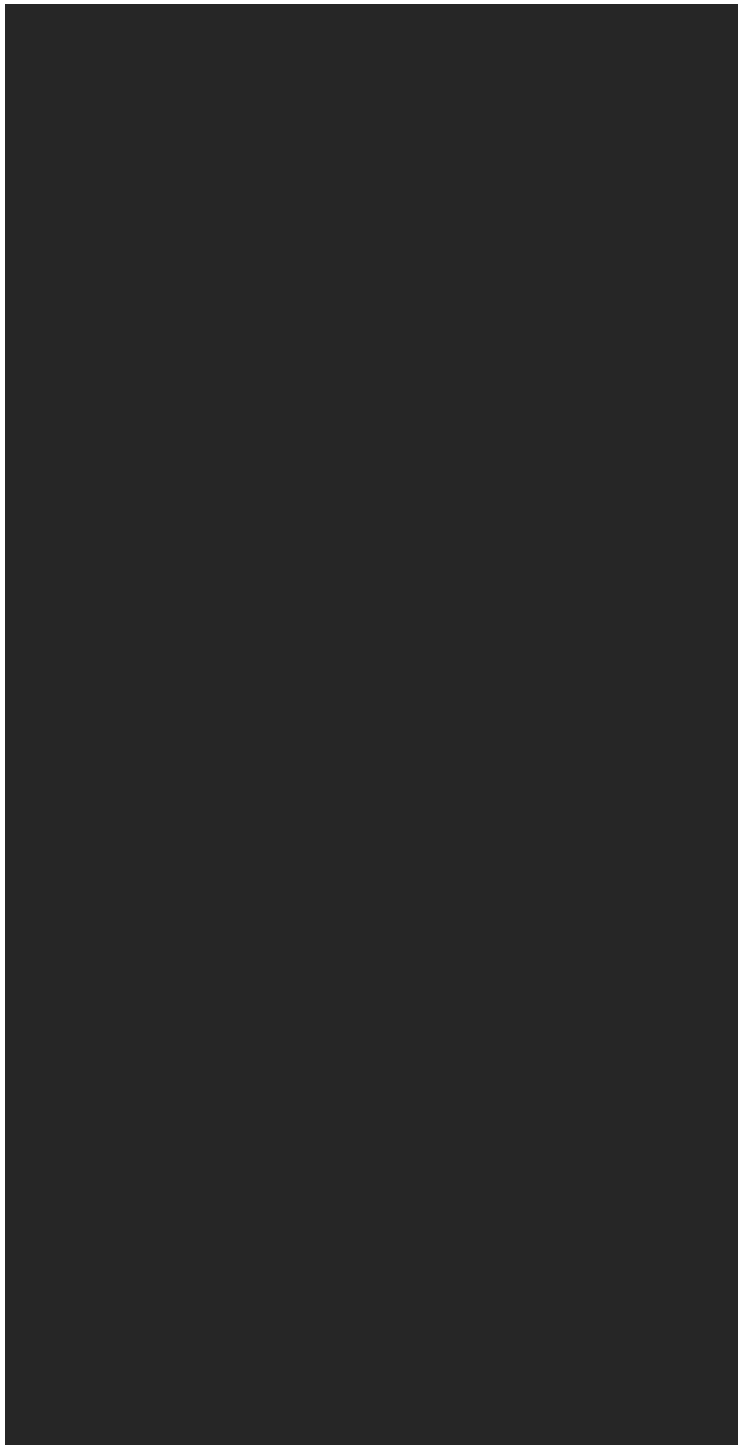
1- Trypanosomes

have one surface glycoprotein that covers the parasite.

This protein is immunodominant for antibody responses.

Trypanosomes have "gene cassettes" of variant surface glycoproteins (VSG's) which allow them to switch to different VSG.

VSG is switched regularly. The effect of this is that host mounts immune response to current VSG but parasite is already switching VSG to another type which is not recognised by the host.

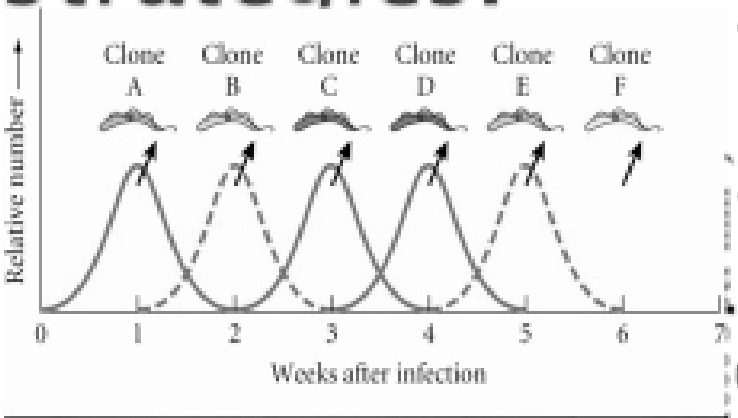


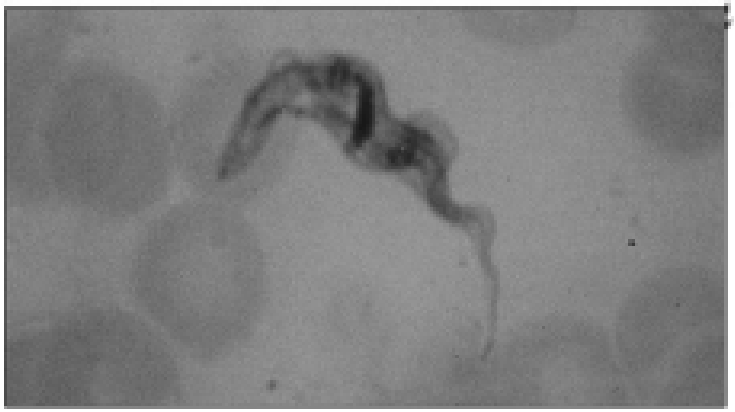
. A parasite expressing the new VSG will escape antibody detection and replicate to continue the infection.

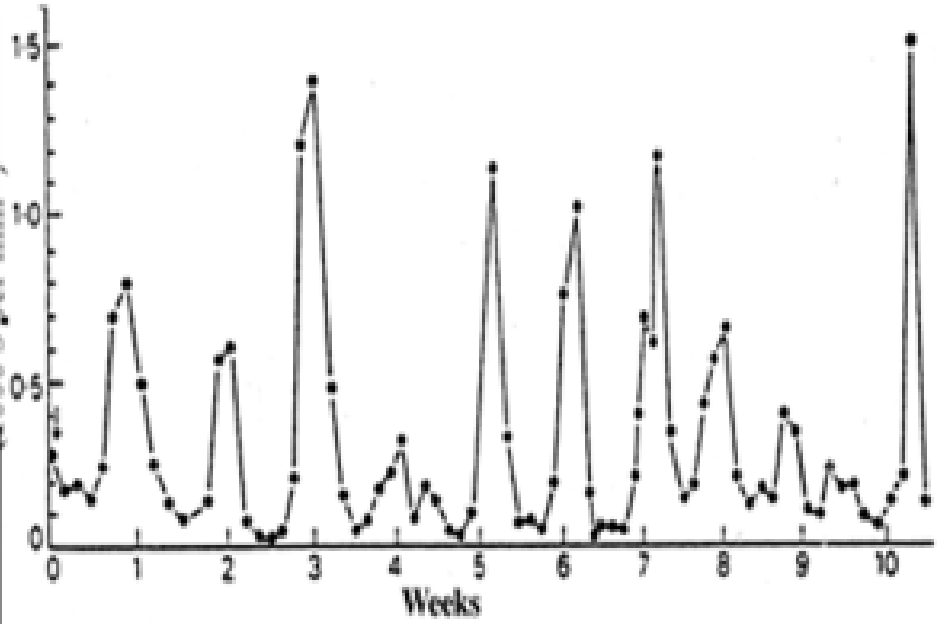
This allows the parasite to survive for months or years.

Up to 2000 genes involved in this process.

Protozoan immune evasion strategies.







After Ross, P. (1910), Proc. Royal Soc. London, B82, 411

After each peak, the trypanosome population is antigenically different from that of earlier or later peaks.