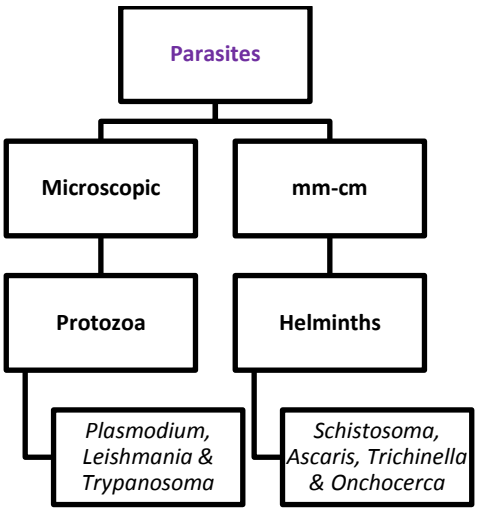
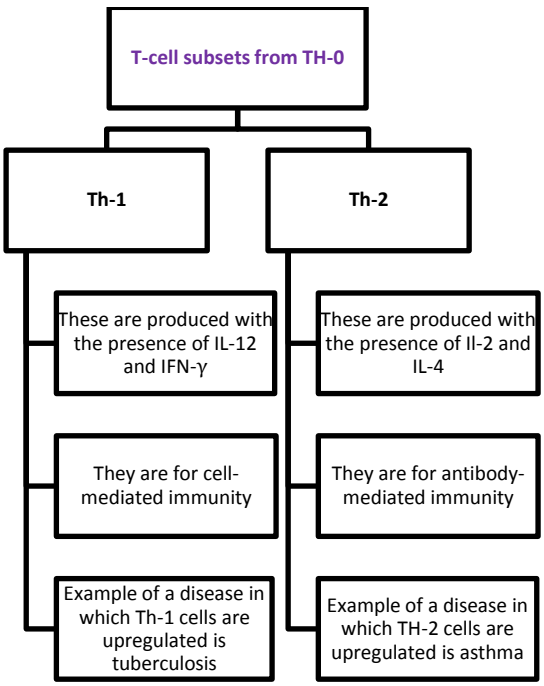
Unit VII – Problem 9 – Immunology: Immunity to Parasitic Infections



- **Sites of infection:**
  - **Protozoa**: CNS, skin, heart, liver, gut and circulation.
  - **Helminths**: skin, muscle, lungs, hepatic portal vein, gut, bladder and lymphatics.
- **Effector mechanisms of immunity:**
  - **Innate immunity:**
    - ✓ Phagocytes (macrophages and neutrophils).
    - ✓ Eosinophils (which play an important role in parasitic infections) and platelets.
    - ✓ Complement.
  - **Acquired immunity:**
    - ✓ Antibodies.
    - ✓ T-lymphocytes: which are of 2 types:
      - ❖ *CD4+ helper T-cells.*
      - ❖ *CD8+ cytotoxic T-cells.*
- **General principles of killing parasites:**
  - **Small parasites** → they are killed by phagocytosis.
  - **Large parasites** → extracellular killing.
  - **Extracellular parasites** → they are killed by antibodies and complement.
  - **Intracellular parasites (ex. Leishmania)** → they are killed by cell-mediated immunity
- **Mechanisms by which specific antibody controls some parasitic infections:**
  - Binding of antibody to the parasite → activating complement → leading to complement-mediated lysis of the parasite.
  - Antibodies neutralize parasites and inhibit their attachment to new healthy cells by binding to attachment sites present on the cell surface of parasites.
  - Antibodies enhance phagocytosis when their Fc portion binds to receptors found on the surface of macrophages (opsonization).
  - Antibody-Dependent Cell-mediated Cytotoxicity (ADCC): in which antibodies will bind to phagocytes and enhance the release of cytotoxic mediators from them.
- **The major immune response required to kill leishmania → cell-mediated immunity.**
- **Mechanisms of evasion of host defenses:**
  - **Evading killing by macrophages:**
    - ✓ Parasites can prevent the fusion of lysosomes with phagosomes.
    - ✓ Parasites can exit the phagosome and move to the cytoplasm where lysosomes can't affect them.
    - ✓ Parasites can be resistant to lysosomal enzymes (a good example is leishmania).
  - **Antigenic variation**: parasites present for long time in the host can mutate and change their antigens. Therefore, the old immune response will not be effective anymore against the new antigens.

- **Shedding of soluble antigens**: parasites can release soluble/free antigens which will bind to antibodies and inhibit them from binding to the parasites themselves. Soluble antigens:
  - ✓ They can bind to free antibodies.
  - ✓ They can bind to antibodies which are present on the surface of killer cells.
  - ✓ The presence of large quantities of antigens might lead to B-cells & T-cells tolerance → which will stop the immune response.
  - ✓ These antigens can activate all B-cells (even those which are not specific for the antigen itself) → and therefore leading to the dilution of the immune response.
  - ✓ They can inhibit the inflammatory response.
- **Surface disguise التنكُّر with human-like antigens**: the immune will think that these antigens are not foreign and they are normally present in the body.
- **Suppression of host defense/immune response.**

- **Leishmania:**
  - Protozoan parasite طفيلي ينتمي إلى الأوليات
  - In the mammalian host → amastigotes avoid lysosomal killing and survive inside macrophages (multiplying intracellularly).
  - **Cell-mediated immunity is the mechanism by which leishmania is going to be killed:**
    - ✓ CD4+ helper T-cells → they will produce interferone-γ (IFN-γ) → which will activate macrophages → leading to upregulation of nitric oxide (NO) intermediates → eventually killing leishmania.
- **T-cell subsets:**



  - **Antigen-presenting cells can also induce Th-0 cells to differentiate to:**
    - ✓ Th-17: which is important in inflammatory responses and autoimmunity.
    - ✓ Treg: which is important in immune tolerance, lymphocyte homeostasis and regulation of immune responses.
- **Th-1 is upregulated in leishmania by converting Th-0 to Th-1. Th-1 cells produce TNF & IFN-γ which will enhance the action of macrophages. On the other hand, macrophages produce IL-12 which promotes/enhances the production of Th-1 cells (A CYCLE!). Note that IFN-γ which is produced by Th-1 cells is suppressive to Th-2 cells especially when Th-1 cells are produced in high quantities.**