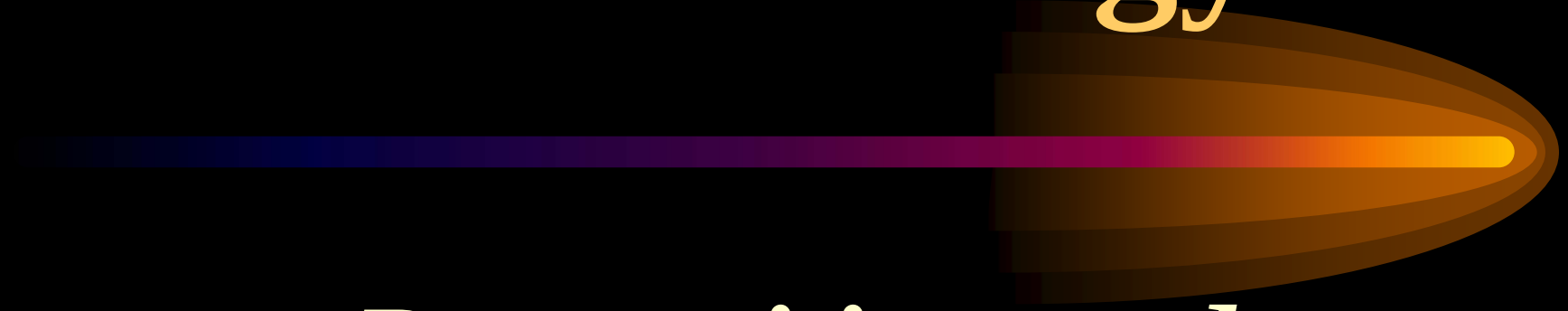
Immunology



Recognition and Response

Immunology, before the germ theory of disease

- Disease was believed to have a spiritual cause, thus cures and treatments were also spiritual

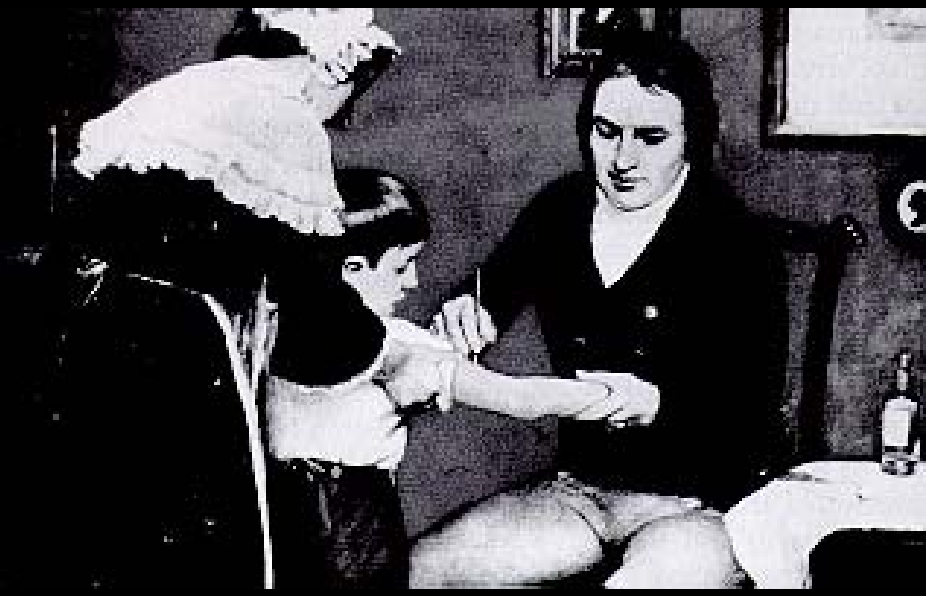
  - During the Plague of Athens, 430 BC becoming immune after exposure was recognized

  - The idea that diseases were caused by living things led to new ideas about treatment and prevention

Bishop healing a disease

Historical Perspective

- *Immunis* Latin for exempt
- Ancients recognized
- Process of variolation
- Edward Jenner and small pox-1798



Jenner vaccinating

Vaccination

- Vaccine from "*vacca*" from Latin for cow
- L. Pasteur's work on rabies
  - Joseph Meister
- Vaccination was not accepted at first
- Mechanisms discussed below

Discovery of mechanisms of immunity

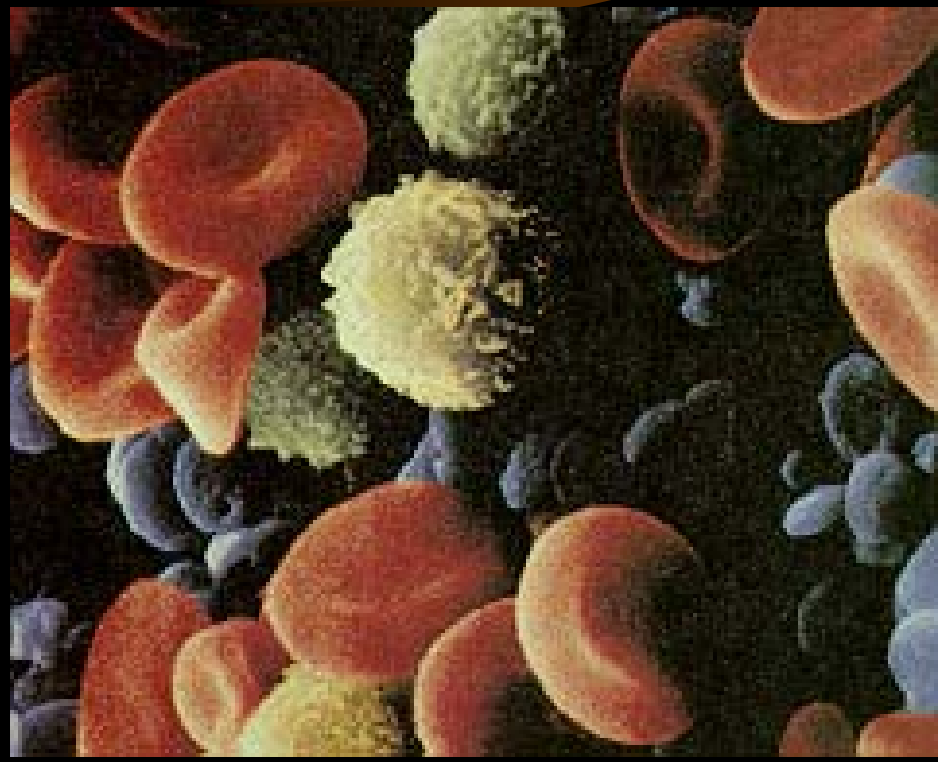
- Emile Von Behring
  1890- humoral
  1901-Nobel Prize
- Elie Metchnikoff
  1883, cellular
  1908-Nobel Prize
- Humoral or Cellular?

  Until 1950s unsettled

Elie Metchnikoff

Innate (nonspecific) immunity

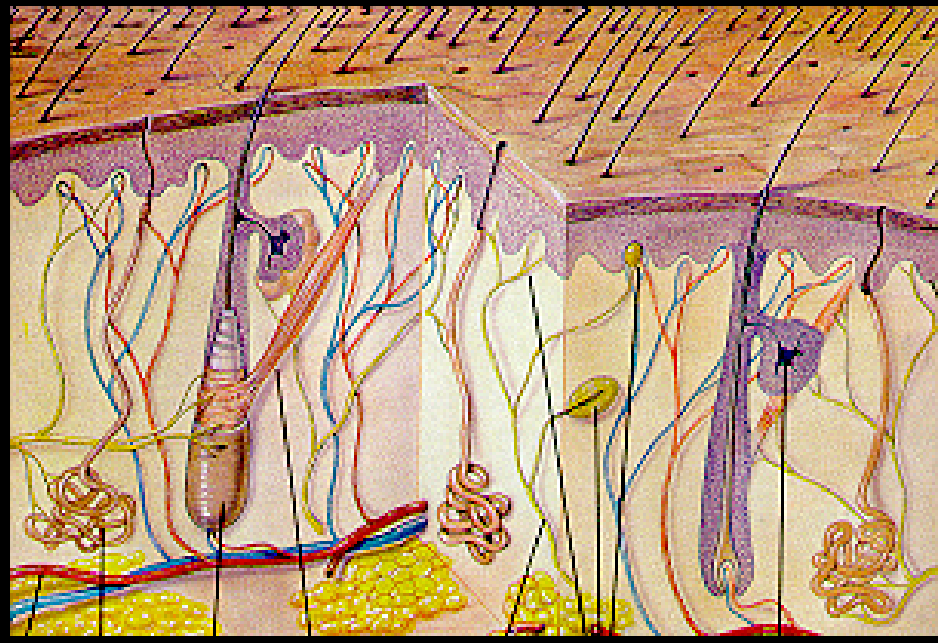
- 4 Barriers to infection:
  -Anatomic
  -Physiologic
  -Endocytic
  -Inflammatory
- Innate immunity cannot be “boosted”



RBCs, Leukocytes, platelets

Anatomic barriers to infection, Skin

- Skin has 2 layers:
  - Epidermis
    - dead at maturation
    - no blood vessels
    - frequent desquamation
    - dry, salty, acidic, sebum
    - Normal flora
  - Dermis
    - rich in blood vessels
    - macrophages, etc.
    - sebaceous glands

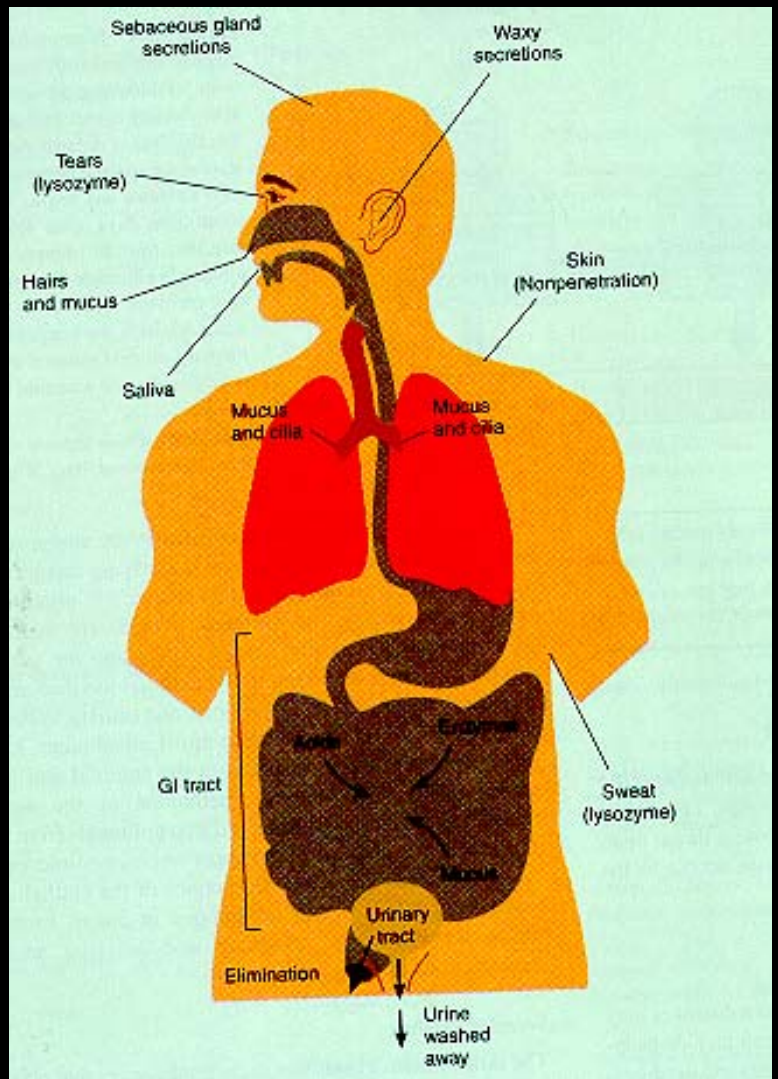


Skin with 2 layers

Other anatomic barriers to infection

The body is a donut

- GI tract
  - Body as a donut
  - Mouth
  - Stomach
  - Normal flora
  - Small intestine
  - Large intestine



Respiratory Tract

- Aerosolization
  - Air is generally clean
  - Molds, spores, etc, rare
  - Droplet dissemination
    - Sneezing, coughing
- Role of mucus (rhinitis)
- Role of cilia
  - (ciliary escalator)
- Alveolar macrophages

Coughing accelerates aerosolization

Bronchial cilia

Uro-genital Tract

- Initial 1/3 generally not sterile
  - Role of urine, flushing action, pH
- The male: Infections less common
  - BPH (Benign prostrate hyperplasia)
- The female: Infections more common
  - Architectural issues
  - Normal flora, pH, cervical plug
  - PID (Pelvic Inflammatory Disease)
- Other Body Openings
  - Eyes and ears

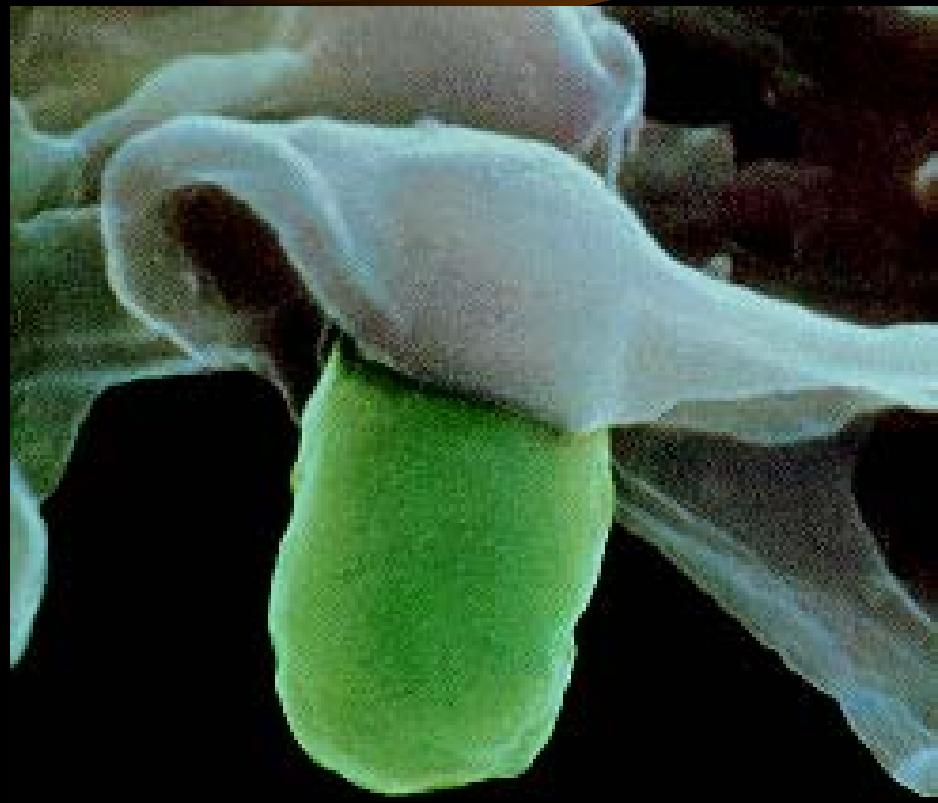
Physiologic barriers to infection

- Phagocytic, endocytic
  - ingestion of microbes
  - monocytes
  - macrophages
  - neutrophils
  - eosinophils-less active
- Soluble factors:
  - lysozyme, interferon, complement
- Others: temp, pH,
  - O_2 tension

Macrophage ingesting *E. coli*

Inflammation

- “setting on fire”
- recognized by 1600BC
- Celus, Roman MD
- “rubor et tumor cum calore et dolore”
  - KNOW HOW TO TRANSLATE THIS -



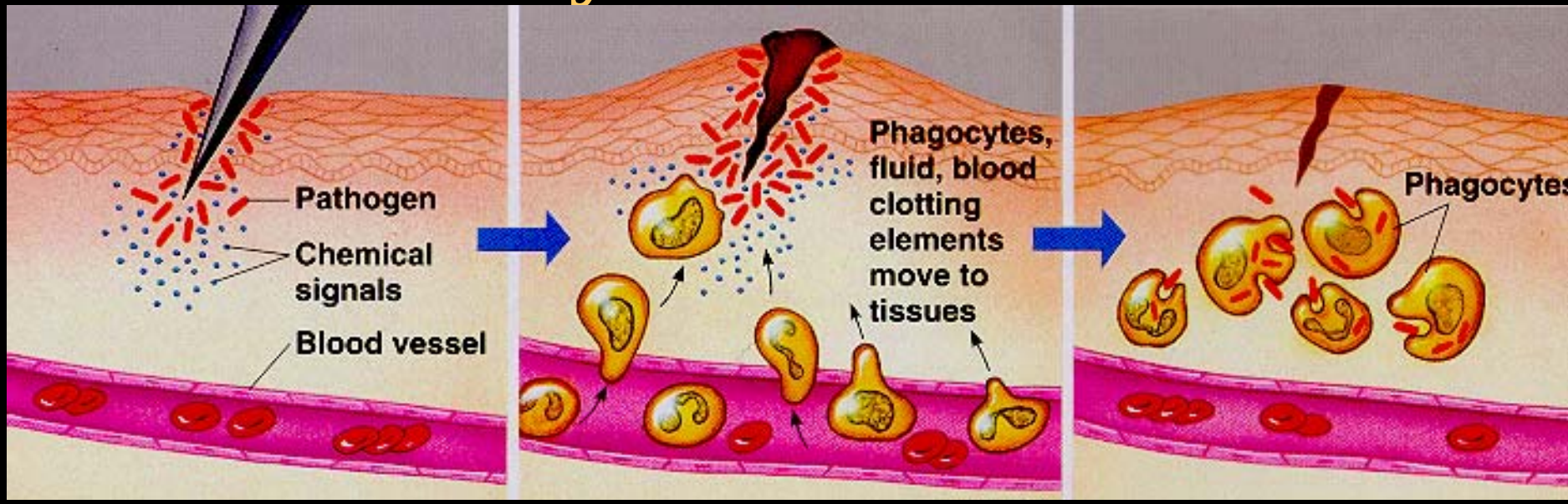
Phagocyte ingesting bacterium

Events in Inflammation

- **Mediators of inflammation**
  - **Cellular injury induces various cells (macrophages, PMNs, endothelial cells, etc) to release mediators of inflammation**
    - **Prostaglandins, histamines, cytokines, etc.**
- **Early inflammatory events:**
  - **Vasodilatation: increased blood flow (rubor, calor)**
  - **Marginalization and diapedesis (tumor)**
  - **Exudate = edema (tumor)**
- **Enhanced pain reception (dolore)**
- **Late inflammatory events:**
  - **Macrophage clearance of dead cells and microorganisms**
  - **Tissue repair by fibroblasts result in scars or granulomas**

- **Prolonged inflammation is generally pathogenic**

Summary of Inflammation



- Injury to tissues releases mediators of inflammation, cytokines ,
- histamine, and prostaglandins (PGE2)
- Vasodilation, increased blood flow (*rubor, calore)*
- Increased capillary permeability with outflow of fluids and cells resulting in edema (fluids) and diapedesis (cells) in tissues (*tumor*)
- Release of bradykinin & PGE2, upregulate pain receptors (*dolore*)
- Chemotaxis is the attraction of inflammatory cells to injury
- Tissue repair, scarring, and granulomas

Impact of systemic inflammation

•Fevers result from systemic inflammation

-Hypothalamus-controls body temperature

-Prostaglandins

-Leukocytes release pyrogenic cytokines: IL-1, IL-6, TNF

-KNOW HOW THEY WORK

-what about aspirin, etc.

-What about cold symptoms?

-Anaphylaxis?

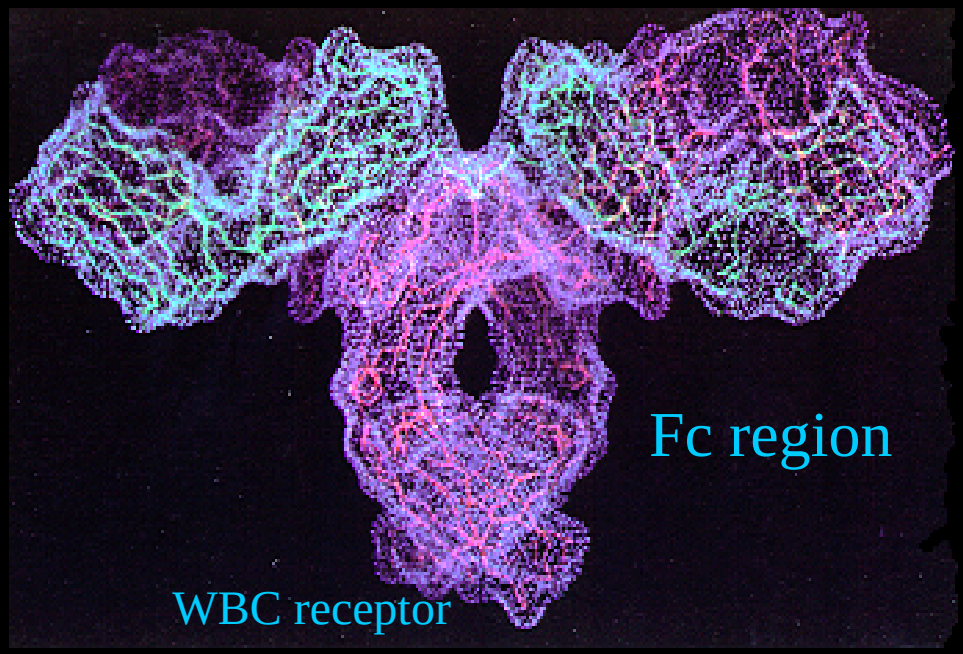
Malaria as Ague and Fever

Specific Immunity

- **The seminal event of specific immunity is immunologic memory**
- **Primary immune response**
  - 7-12 days after exposure
  - Sets up antibody and cytotoxic cellular reactants and memory mechanisms
- **Secondary immune responses**
  - Results from memory mechanisms
  - Rapid response, 3-4 days, generally symptomless

Humoral Immunity

- Antibody is produced by **Plasma cells** (B-cells)
- IgM, first to appear,
  - a pentamer
- IgG, most important,
  - crosses placenta
- IgA, secretory antibdy
  - in gut, in milk, a dimer
- IgE, parasites & allergies
  - receptor for mast cells, basophils, eosinophils



Antibody molecule

CD4+, T-Helper cells

- T-Lymphocytes, the major players in Cell-Mediated-Immunity (the CMI)

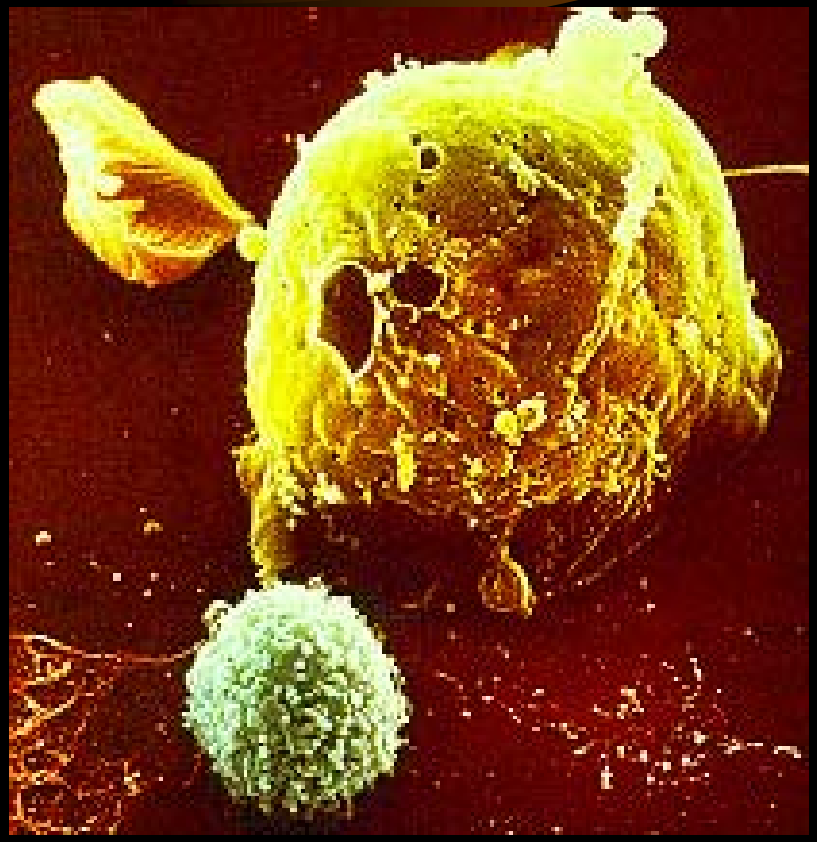
- Primarily are cytokine secretor cells
  - Their secreted cytokines, the interleukins:
    - Control production of antibodies
    - Stimulate macrophage activities
    - Produce some antimicrobial agents

  - up-regulation and down-regulation of immune responses

  - maturation of CD8+ cells to Cytotoxic lymphocytes

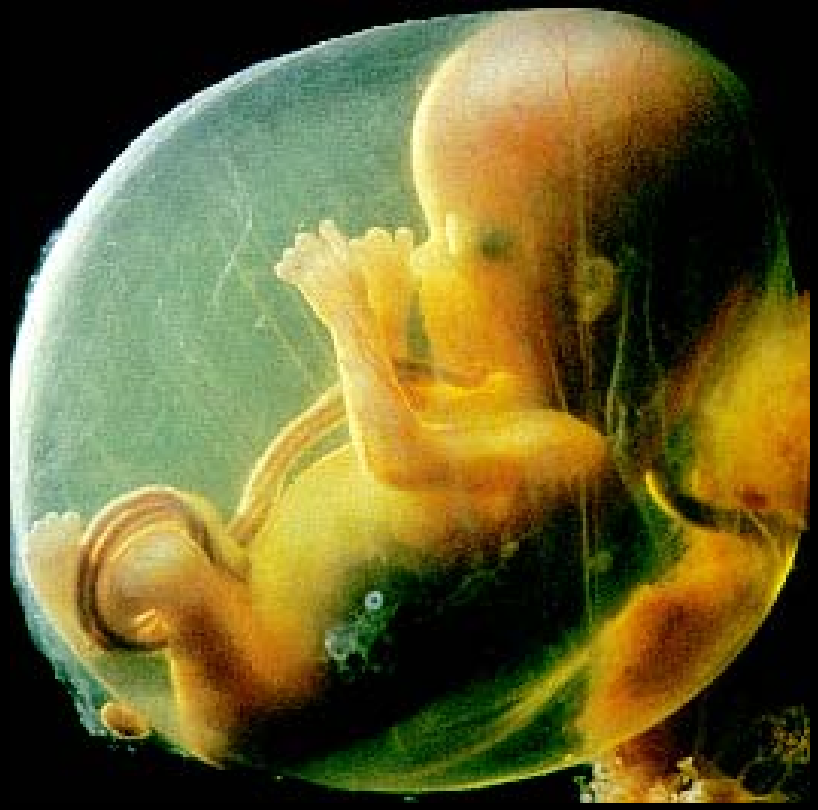
CD8+, cell-mediated immunity

- CD8+
- generally do not produce cytokines
- Cytotoxic Killer cells
  - antigen specific Ctls
  - effective against :
    - intracellular pathogens
      - TB, viruses, etc.
    - cancer cells
    - tissue graft rejection



Ctl lysis of Cancer cell

Active and Passive immunity



Transplacental passive immunity

- Active immunity
  - pathogen exposure
  - vaccination
- Passive immunity
  - Gamma globulin
  - Transplacental
    - IgG
  - Breast feeding
    - IgA