

Fighting the Enemy Within!

phagocytic leukocyte

## Immune / Lymphatic System

lymphocytes attacking cancer cell

lymph system

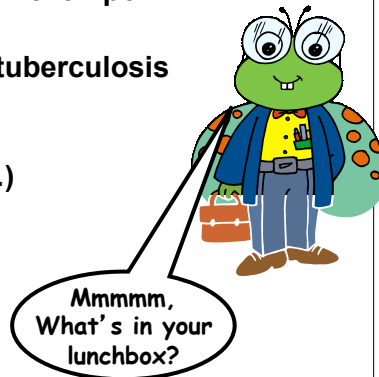
### Avenues of attack

- **Points of entry**
  - ◆ digestive system
  - ◆ respiratory system
  - ◆ urogenital tract
  - ◆ break in skin
- **Routes of attack**
  - ◆ circulatory system
  - ◆ lymph system

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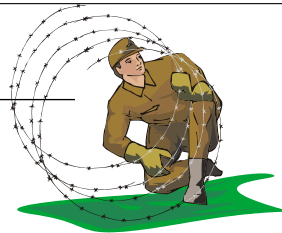
## Why an immune system?

- **Attack from outside**
  - ♦ **animals must defend themselves against invaders (pathogens)**
    - viruses
      - ♦ HIV, flu, cold, measles, chicken pox
    - bacteria
      - ♦ pneumonia, meningitis, tuberculosis  
Lyme disease
    - fungi
      - ♦ yeast ("Athlete's foot"...)
    - protists
      - ♦ amoeba, malaria
- **Attack from inside**
  - ♦ **cancers = abnormal body cells**



## Lines of defense

- **1st line: Non-specific barriers**
  - ♦ **broad, external defense**
    - "walls & moats"
  - ♦ skin & mucous membranes
- **2nd line: Non-specific patrols**
  - ♦ **broad, internal defense**
    - "patrolling soldiers"
  - ♦ **leukocytes = phagocytic WBC**  
(macrophages)
- **3rd line: True immune system**
  - ♦ **specific, acquired immunity**
    - "elite trained units"
  - ♦ **lymphocytes & antibodies**
    - **B cells & T cells**


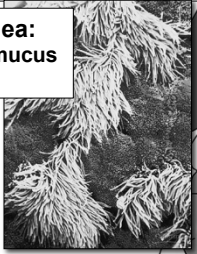

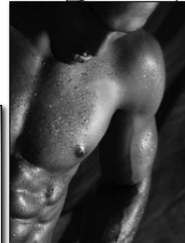


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**1st line: Non-specific External defense**

- **Barrier**
  - skin
- **Traps**
  - mucous membranes, cilia, hair, earwax
- **Elimination**
  - coughing, sneezing, urination, diarrhea
- **Unfavorable pH**
  - stomach acid, sweat, saliva, urine
- **Lysozyme enzyme**
  - digests bacterial cell walls
  - tears, sweat

Lining of trachea: ciliated cells & mucus secreting cells

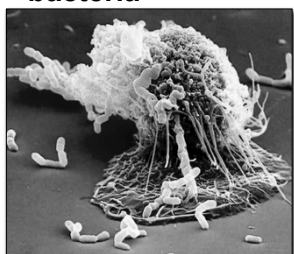





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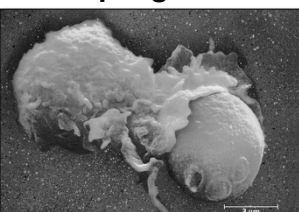
**2nd line: Non-specific patrolling cells**

- **Patrolling Cells & Proteins**
  - ♦ Attack pathogens, but don't "remember" for next time
  - leukocytes
    - ♦ phagocytic white blood cells
    - ♦ macrophages, neutrophils, natural killer cells (not killer T)
  - complement system
    - ♦ proteins that destroy cells
  - inflammatory response
    - ♦ increase in body temp.
    - ♦ increase capillary permeability
    - ♦ attract macrophages

bacteria



macrophage

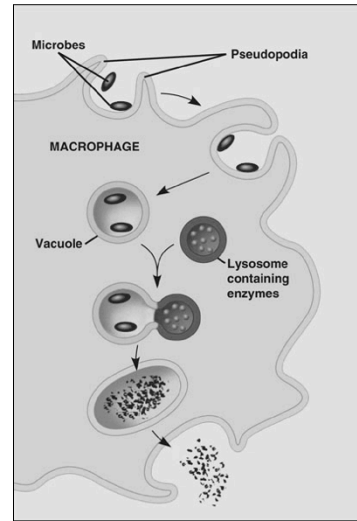


yeast

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## Leukocytes: Phagocytic WBCs

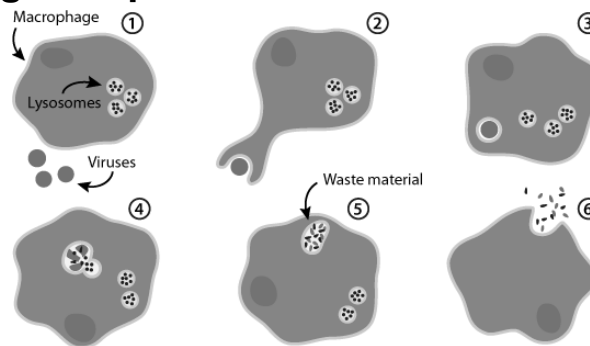
- **Role of phagocytic cells**
  - ◆ ingest pathogens
  - ◆ digest in lysosomes
- **Neutrophils**
  - ◆ most abundant WBC (~70%)
  - ◆ ~ 3 day lifespan
- **Macrophages**
  - ◆ “big eater”, long-lived
  - ◆ Use lysosomes to digest
- **Natural Killer Cells**
  - ◆ destroy virus-infected cells & cancer cells



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## Macrophages

- **Means “BIG EATER” and is a white blood cell that engulfs microscopic invaders, such as bacteria, viruses, fungi and parasites.**

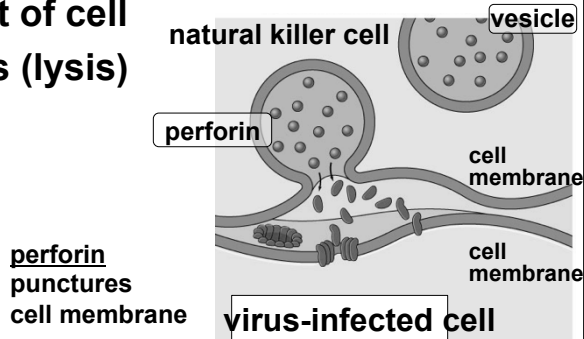
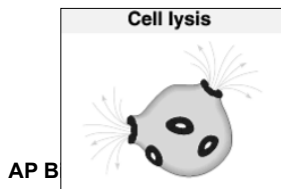


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**Destroying cells gone bad!**

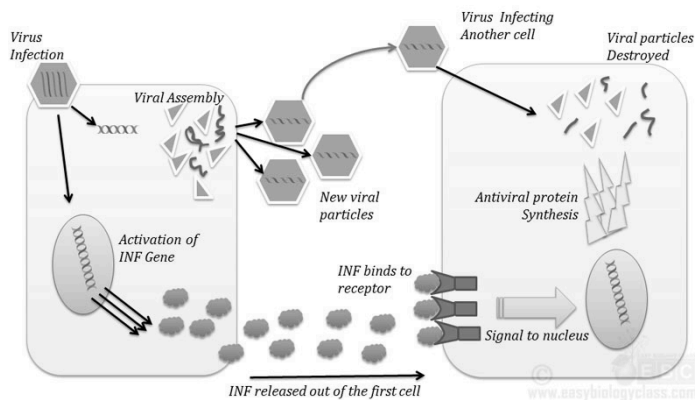
- **Natural Killer Cells** perforate cells
  - ◆ **release perforin** protein
  - ◆ **insert into membrane of target cell**
  - ◆ **forms pore allowing fluid to flow in & out of cell**
  - ◆ **cell ruptures (lysis)**
    - **apoptosis**



**Interferons**

- **The first cell gets activated and releases INF that bind to an unaffected cell and initiates the synthesis of antiviral proteins.**

**ANTIVIRAL ACTION OF INTERFERON (INF)**

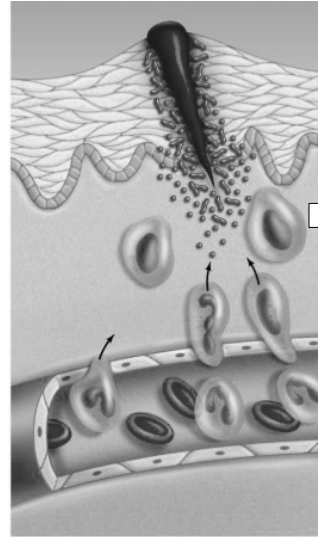


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## Inflammatory Response

- **Damage to tissue triggers local non-specific inflammatory response**
  - ◆ **release chemical signals**
    - **histamines & prostaglandins**
  - ◆ **capillaries dilate (vasodilation) and become more permeable**
    - **delivers macrophages, RBCs, platelets, clotting factors**
      - ◆ **fight pathogens**
      - ◆ **clot formation**



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## Fever

- **When a local response is not enough**
  - ◆ **system-wide response to infection**
  - ◆ **activated macrophages release interleukin-1**
    - **triggers hypothalamus in brain to readjust body thermostat to raise body temperature**
  - ◆ **higher temperature helps defense**
    - **inhibits bacterial growth**
    - **stimulates phagocytosis**
    - **speeds up repair of tissues**
    - **causes liver & spleen to store iron, reducing blood iron levels**
      - ◆ **bacteria need large amounts of iron to grow**



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**3rd line: Acquired (active) Immunity**

▪ **Specific defense with memory**

B cell

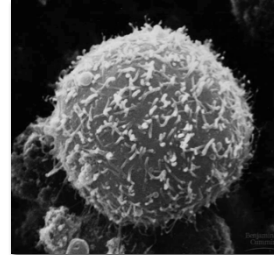
◆ lymphocytes

▪ B cells

▪ T cells

◆ antibodies

▪ immunoglobulins



▪ **Responds to...**

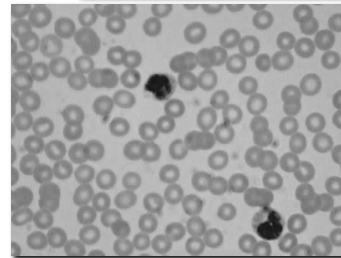
◆ antigens

▪ cellular name tags

◆ specific pathogens

◆ specific toxins

◆ abnormal body cells (cancer)



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**How are invaders recognized?**

▪ Antigens

◆ cellular name tag proteins

▪ “self” antigens

◆ no response from WBCs

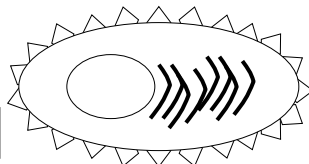
▪ “foreign” antigens

◆ response from WBCs

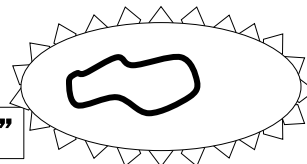
◆ pathogens: viruses, bacteria, protozoa, parasitic worms, fungi, toxins

◆ non-pathogens: cancer cells, transplanted tissue, pollen

“self”



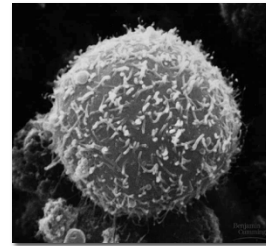
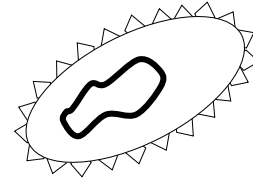
“foreign”



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### B cells

- Attack, learn & remember pathogens circulating in blood & lymph
- Produce specific antibodies against specific antigen
- Types of B cells
  - ◆ plasma cells
    - immediate production of antibodies
    - rapid response, short term release
  - ◆ memory cells
    - continued circulation in body
    - long term immunity



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### Acquired Immunity

- **The third line of the immune response is internal, specific and acquired. Foreign pathogens are recognized by the presence of unrecognized antigens. Foreign antigens are also found on the surface of cancer cells, transplanted tissue and allergens such as pollen. The third line of defense involves the response of B lymphocytes that produce antibodies and the humoral cell response.**

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## **B Lymphocytes**

- **B-lymphocytes mature in the bone marrow and they are part of our humoral response. The pathogen will be detected in the blood or lymph fluid. B cells can be found as either plasma cells or memory cells.**
- **Humoral=Bloodstream**
- **Uses antibodies in response to antigens**

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## **Steps in B-Cell Response**

- **Foreign invader (pathogen) with foreign antigens (proteins-glycoproteins) enters the blood stream.**
- **Patrolling B-cells with surface antibodies contact the foreign invader.**
- **B-cells with complementary antigen-antibody complex will bind.**
- **Bound B-cells become activated.**

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## Antibodies

- **Proteins that bind to a specific antigen**
  - ◆ multi-chain proteins
  - ◆ binding region matches molecular shape of antigens
  - ◆ each antibody is unique & specific
    - millions of antibodies respond to millions of foreign antigens
  - ◆ tagging “handcuffs”
    - “this is foreign...gotcha!”

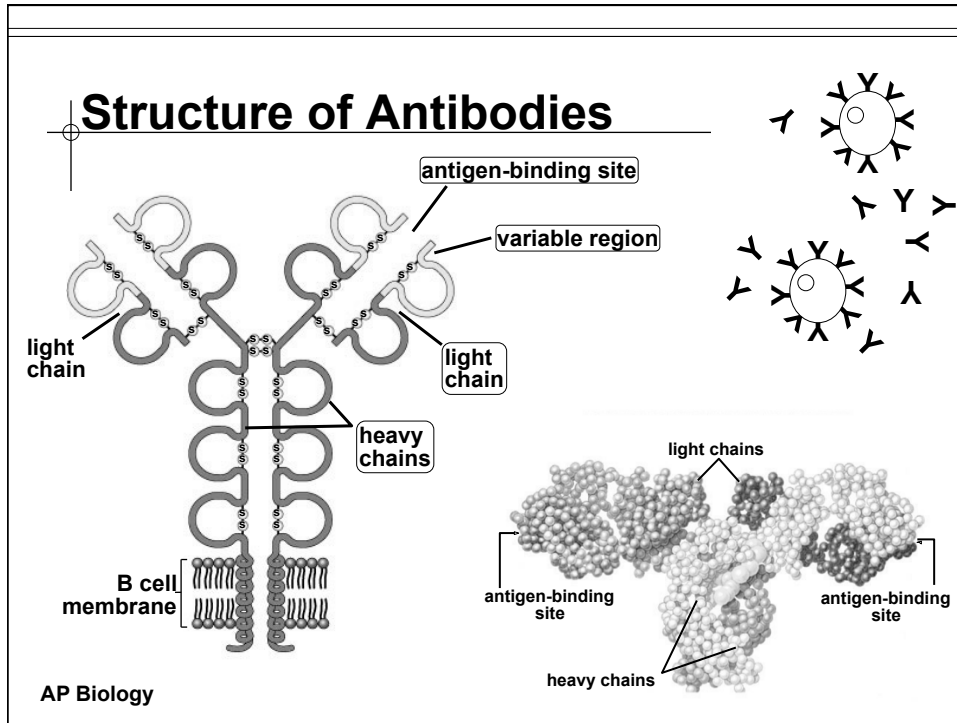
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## B-Cell Response (continued)

- Activated B-cells will clone themselves “clonal selection”
- B-cells may differentiate into plasma cells.
- Plasma cells release protein antibodies into blood and attach to the pathogen/ antigen and cause it to clump. (Target)

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### B-Cell (continued)

- Macrophages will engulf and partially digest the pathogen. Fragments will be incorporated into the cell membrane. These are not called “antigen presenting cells”
- Memory B cells are stored for future exposure.

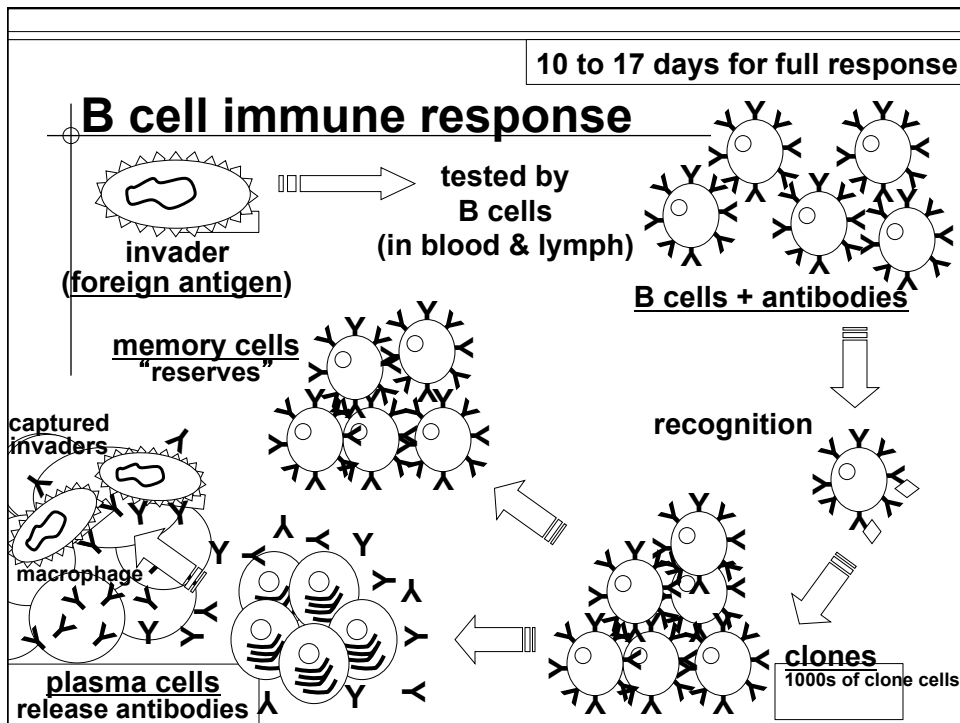
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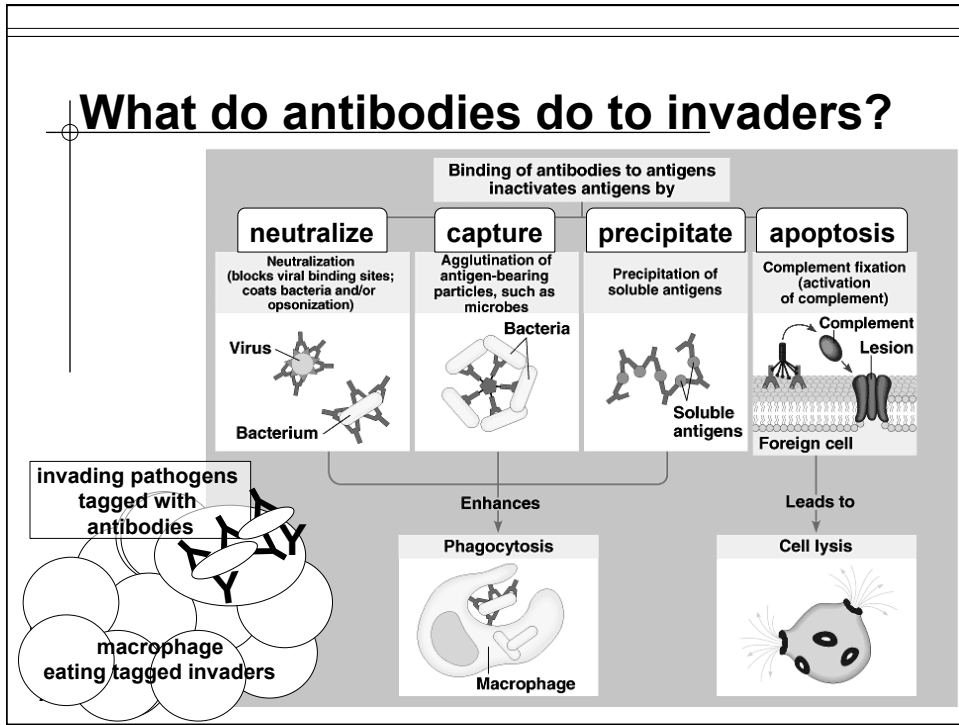
### Memory B-Cells

- Memory B-cells will remain in the bloodstream allowing for rapid immune response upon the second exposure. Once the clumped pathogens are engulfed by the macrophage, the macrophage will present protein fragments of the foreign pathogen on the surface and is referred to as an antigen presenting cell. Since the pathogen is now detected, the T-cell response is not activated.**

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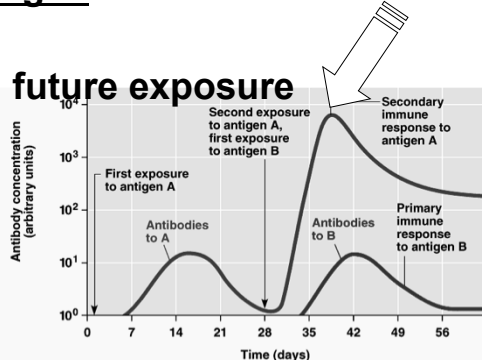
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## Vaccinations (Active)

- Immune system exposed to harmless version of pathogen
  - ◆ stimulates B cell system to produce antibodies to pathogen
    - “active immunity”
  - ◆ rapid response on future exposure
  - ◆ creates immunity without getting disease!
- Most successful against viruses





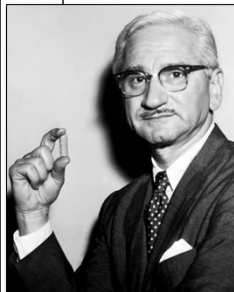
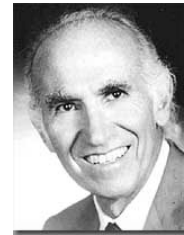
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1914 – 1995

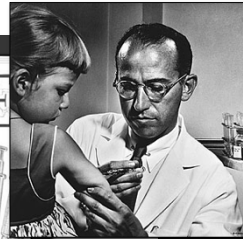
## Jonas Salk

April 12, 1955

- Developed first vaccine
- ◆ against polio
- attacks motor neurons



Albert Sabin  
1962  
oral vaccine



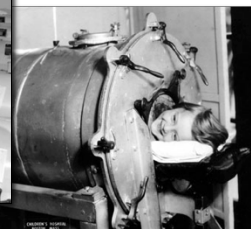
## Polio Epidemics



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1994:  
Americas polio free



## Passive Immunity (\*last page)

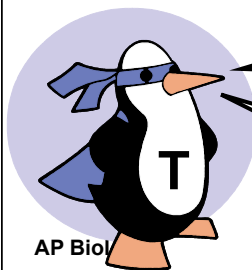
- **Obtaining antibodies from another individual**
  - ◆ **maternal immunity**
    - antibodies pass from mother to baby across placenta or in mother's milk
    - **critical role of breastfeeding in infant health**
      - ◆ mother is creating antibodies against pathogens baby is being exposed to
  - **Injection**
    - ◆ injection of antibodies
    - ◆ short-term immunity



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**What if the attacker gets past the B cells in the blood & actually infects (hides in) some of your cells?**

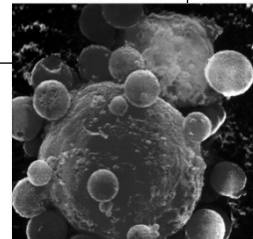
**You need trained assassins to recognize & kill off these infected cells!**



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**Attack of the Killer T cells!**

**But how do T cells know someone is hiding in there?**



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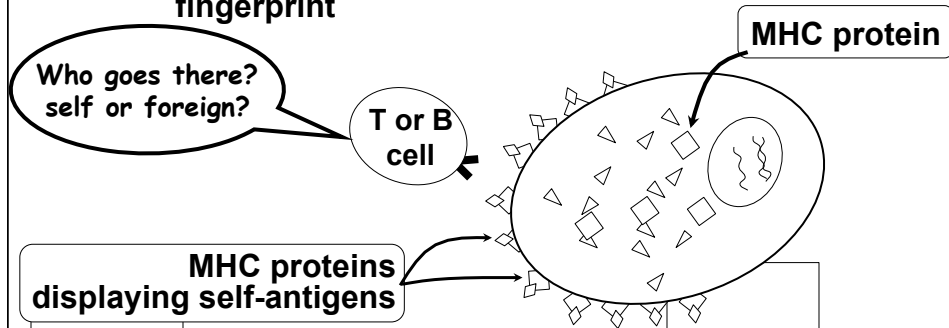
### T-Cell Response

- The T-cell response is often referred to as a cell mediated response because the pathogen is now located within a cell. Remember the end of the B-cell response, the pathogen was engulfed by the macrophage. Within the macrophage protein complexes known as major histocompatibility complexes or MHC's will carry pathogen fragments on the surface of the cell and act as antigen presenting cells (APC's).

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### How is any cell tagged with antigens?

- Major Histocompatibility (MHC) Proteins
  - ◆ proteins which constantly carry bits of cellular material from the cytosol to the cell surface
  - ◆ “snapshot” of what is going on inside cell (self or foreign)
  - ◆ give the surface of cells a unique label or “fingerprint”

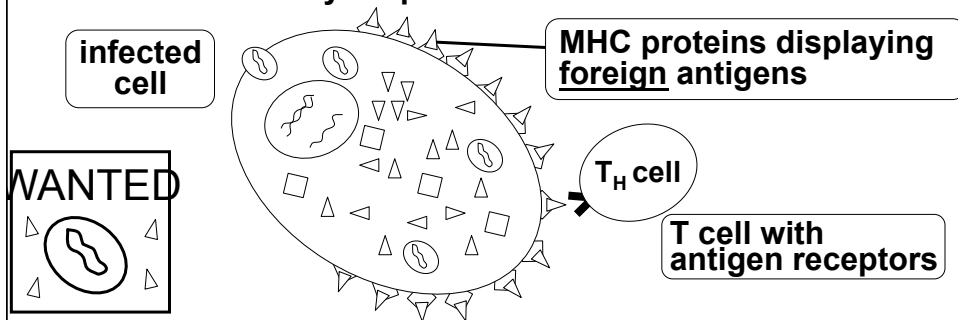




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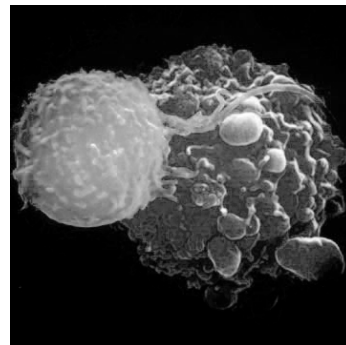
**How do T cells know a cell is infected?**

- **Infected cells digest some pathogens**
  - ◆ **MHC proteins carry pieces to cell surface**
    - foreign antigens now on cell membrane
    - called **Antigen Presenting Cell (APC)**
      - ◆ macrophages can also serve as APC
  - tested by **Helper T cells**



**T cells**

- **Attack, learn & remember pathogens hiding in infected cells**
  - ◆ recognize antigen fragments
  - ◆ also defend against “non-self” body cells
    - cancer & transplant cells
- **Types of T cells**
  - ◆ helper T cells
    - alerts rest of immune system
  - ◆ killer (cytotoxic) T cells
    - attack infected body cells



T cell attacking cancer cell

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**T-Cell Response**

- **APC infected -OR- APC activated macrophage is inside the organism.**
- **MHC's carry foreign antigen fragments to the surface.**
- **Helper T-cells with complimentary receptors bind to the APC, and if activated, release interleukins and T-cells begin to clone themselves.**

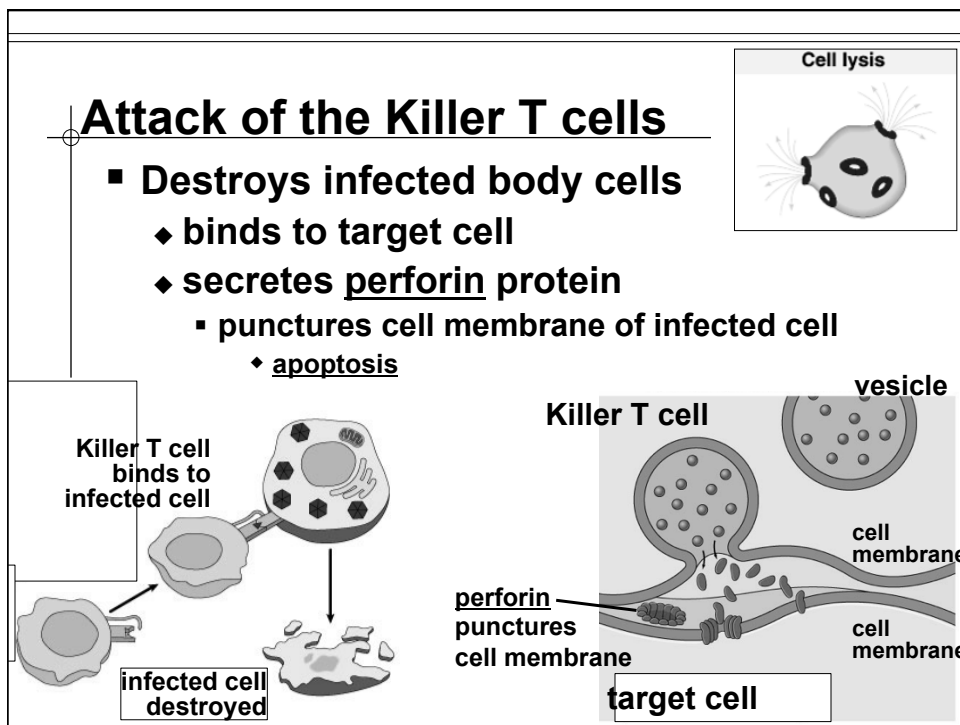
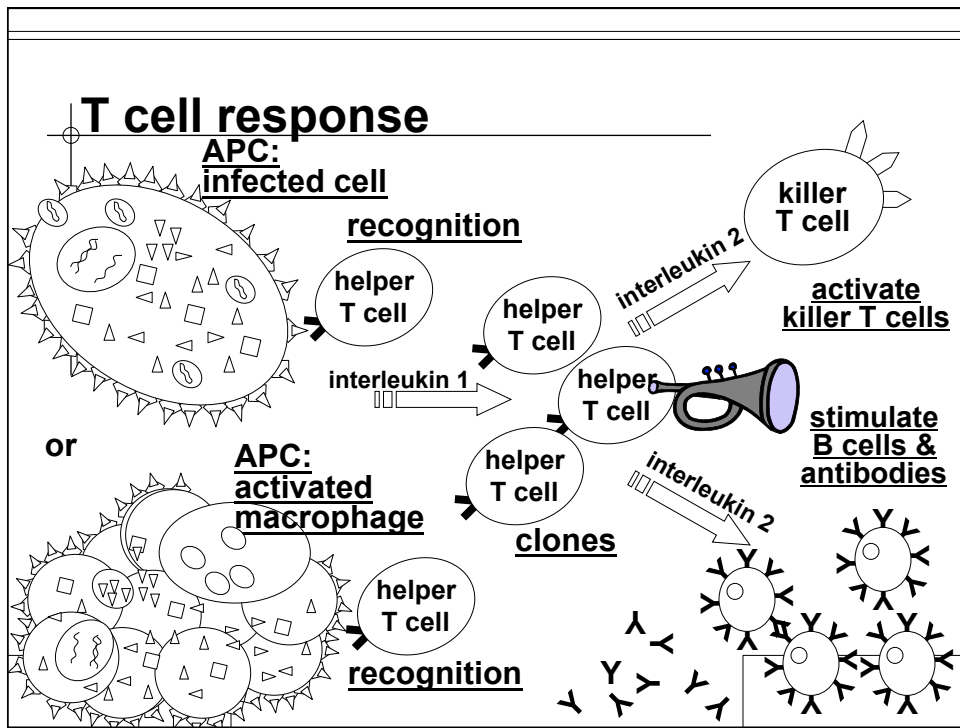
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**T-Cell (continued)**

- **Interleukin 2 activates killer T-cells which bind to the infected macrophage and release perforins, which puncture the cell so it lyses and gets destroyed.**
- **Interleukin 2 also stimulates B-cells and antibodies.**

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## Lymphocytes Review

- **B cells**
  - ◆ mature in bone marrow
  - ◆ humoral response system
    - “humors” = body fluids
    - attack pathogens still circulating in blood & lymph
  - ◆ produce antibodies
- **T cells**
  - ◆ mature in thymus
  - ◆ cellular response system
    - attack invaded cells
- **“Maturation”**
  - ◆ learn to distinguish “self” from “non-self” antigens
    - if react to “self” antigens, cells are destroyed during maturation

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## Immune Response

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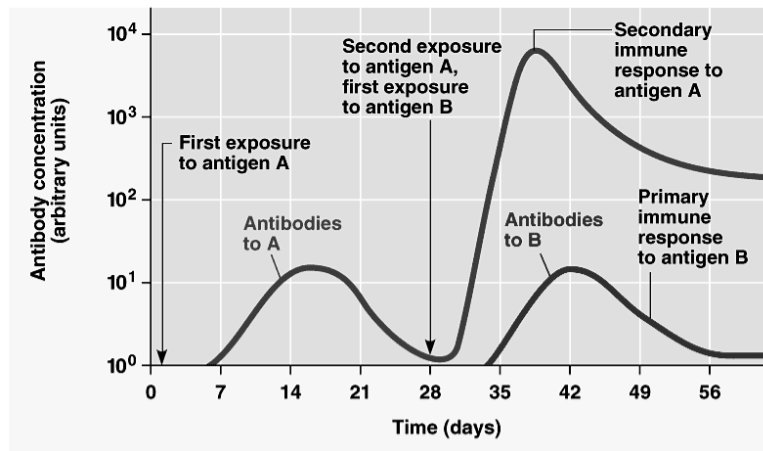
graph TD
    A[skin] --> B[pathogen invasion antigen exposure]
    B --> C[free antigens in blood]
    B --> D[antigens on infected cells]
    C --> E[humoral response]
    D --> F[cellular response]
    E --> G[B cells]
    F --> H[T cells]
    G --> I[plasma B cells]
    G --> J[memory B cells]
    H --> K[memory T cells]
    H --> L[cytotoxic T cells]
    B --> M[macrophages APC]
    M -- alert --> G
    M -- alert --> H
    I --> N[antibodies]
    J --> O[antibodies]
    
```

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### Active Immunity

- After the body's exposure to an antigen, the body will fight it and produce antibodies against a future infections.
- This will speed up the response time because there are so many more antibodies to join the fight.

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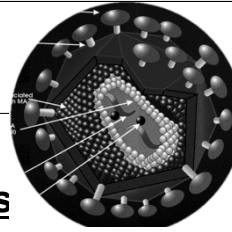
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**HIV & AIDS**

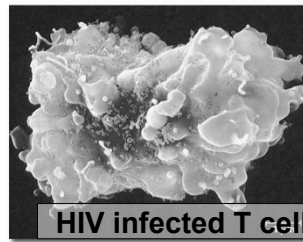
▪ **Human Immunodeficiency Virus**

- ◆ virus infects (WBC's) **helper T cells**
  - helper T cells don't activate rest of immune system: killer T cells & B cells
  - also destroys helper T cells

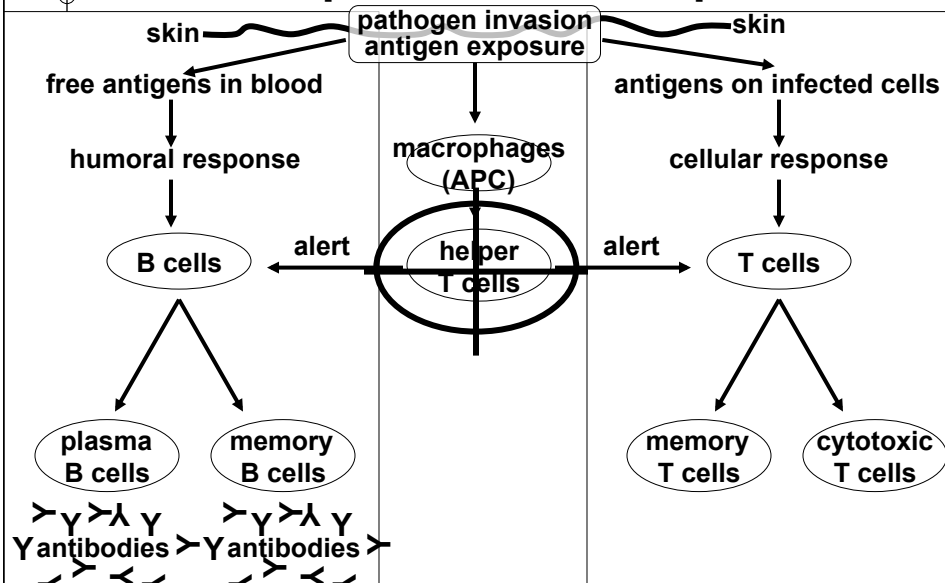


▪ **AIDS: Acquired ImmunoDeficiency Syndrome**

- ◆ infections by opportunistic diseases
- ◆ death usually from
- ◆ "opportunistic" infections
  - pneumonia, cancers



**HIV Interrupts Immune Response**



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**Immune System Malfunctions**

- **Auto-immune diseases**
  - ◆ immune system attacks own molecules & cells
    - lupus
      - ◆ antibodies against many molecules released by normal breakdown of cells
    - rheumatoid arthritis
      - ◆ antibodies causing damage to cartilage & bone
    - diabetes
      - ◆ beta-islet cells of pancreas attacked & destroyed
    - multiple sclerosis
      - ◆ T cells attack myelin sheath of brain & spinal cord nerves
- **Allergies**
  - ◆ over-reaction to environmental antigens
    - allergens = proteins on pollen, dust mites, in animal saliva
    - stimulates release of histamine

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