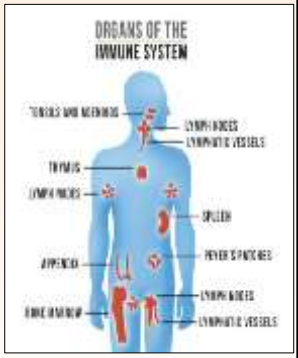
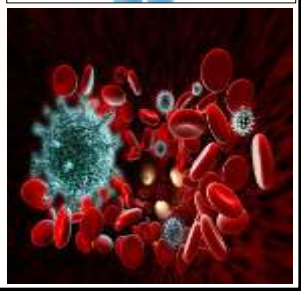
## Ch. 11: Immune Physiology (modified 6/21)

**Objectives:**

1. Review immune organs & cells.
2. Two categories of immunity: innate vs adaptive
3. Understand functions of adaptive immunity cells (T-cells and B-cells)
4. Natural vs artificial immunity
4. Understand autoimmunity disorders.



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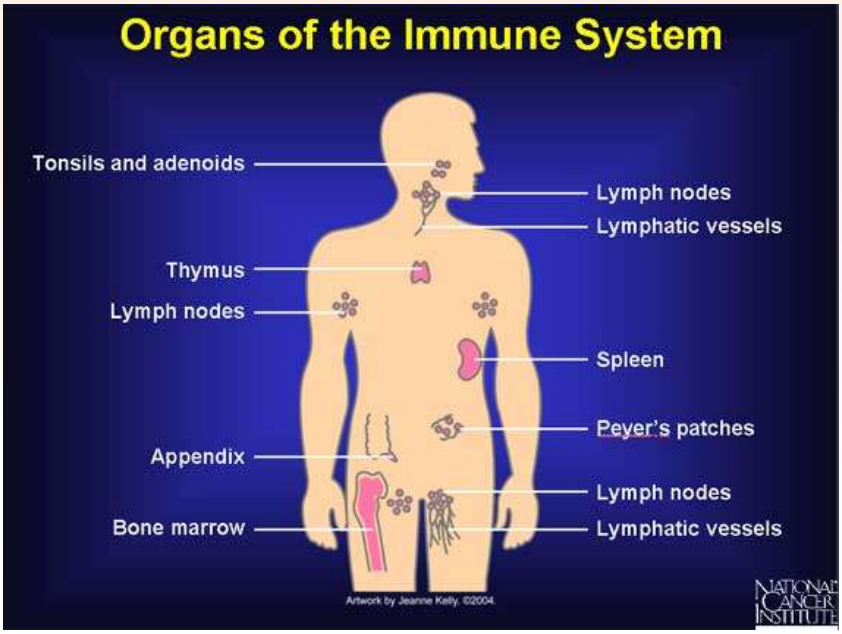
## 1. *Review* Immune Organs & Cells.

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## 1. *Review* Immune Organs & Cells. Pg 164 Wiki text

**Immune system** = The cells & organs that defend against pathogens & cancer.

**1) Lymph Organs:**

**A.** *Primary lymph organs*

> **Bone marrow** – where lymphoctyes (and all WBCs, RBCs, platelets) produced.
> **Thymus** – where T-cells mature

**B.** *Secondary lymph organs*

> **Lymph nodes** – where lymphocytes "activated", where B cells mature.

> **Lymphatic & blood vessels** – transport immune cells

> **Tonsils** – first line of defense from inhaled pathogens
> **Alveolar macrophages** – defend against pathogens in lungs.

> **Brain** – has microglia for defense

> **Spleen** – activate lymphocytes

> **Intestines** – have Peyer's patches for defense

> **Appendix** – on cecum.

> **Liver** – have Kupffer cells for defense

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## 3 Lines of Defense from Pathogens! Pg 162 Wiki text

**Innate**

**A) External Innate Immunity (non-specific)**

**External barriers to pathogen entry**

**B) Internal Innate Immunity (non-specific)**

**Once pathogen enters body, internal non-specific defenses**



**Adaptive**

**Adaptive or Acquired Immunity (specific)**

**Defense involving antibodies, for long-term and specific protection from antigens. (involves T and B lymphocytes)**

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# 1) Innate Immunity (non-specific)

## A. External Innate Defense (barriers to keep things OUT of your body)

- **Epithelial membranes**
  **>** skin **–** physically blocks pathogen entry.

  > Sweat – is acidic and antimicrobial.
- **Stomach acid –** kills bacteria
- **Respiratory tract** –mucus, cilia for removal of pathogens.
  Alveolar macrophages destroy pathogens.
- **Urinary / genital defense =** both are acidic (antimicrobial)
- **Eyes –** lysozymes in tears is antimicrobial.

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# 1) Innate Immunity (non-specific)

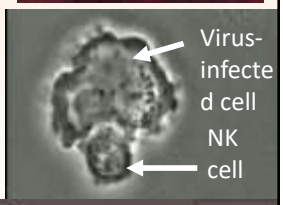
## B. Internal innate defense (if things get in, try & kill them without antibodies)

**Step 1. Phagocytic WBC Cell response**.

> Neutrophils & Monocytes in blood can phagocytize bacteria.

> WBCs secrete **endogenous pyrogens** = cause fever (kills bactreia)

> WBCs secrete **cytokines & chemokines** –chemical cries for help.




**Step 2. Natural killer (NK) cells**

> secrete **interferons** kills viruses.

> **toxic granules -** destroys tumor and cancer cells

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# 1) Innate Immunity (non-specific)

## B. Internal innate defense (if things get in, try & kill them without antibodies)

**Step 1. Phagocytic WBC Cell response**.

> Neutrophils & Monocytes in blood attack, engulf, & kill pathogens

> WBCs secrete **endogenous pyrogens** to cause **fever response.**

> WBCs secrete chemical cries for help (**cytokines & chemokines**)

**Step 2. Natural killer (NK) cells**

> secrete **interferons** to kill viruses.

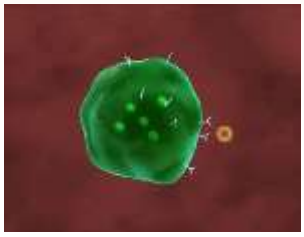
> **toxic granules** to kill tumor/cancer cells.

**Step 3. Inflammatory response**

> **Mast cells** – secrete histamine for inflammation response

> **Complement proteins** – kill bacteria by poking holes in them.

*Mast cell secreting histamine*



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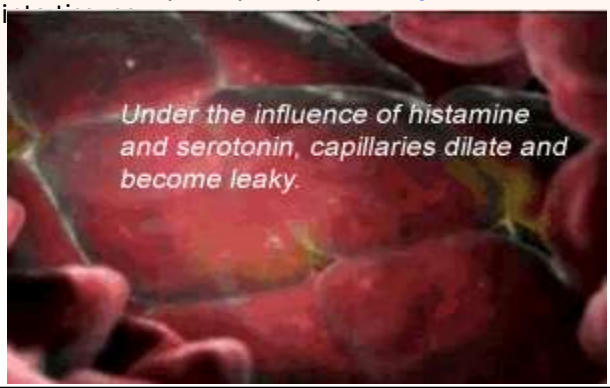
**Step 1: Phagocytic WBC response:**

**1.** In bloodstream - **Neutrophils & Monocytes are phagocytes** that destroy pathogens & secrete endogenous pyrogens (cause fever).


**2.** Histamine secreted by mast (basophil) cells makes blood vessels "leaky" so WBC can escape, especially **monocytes** which "**extravasate**" out of capillary

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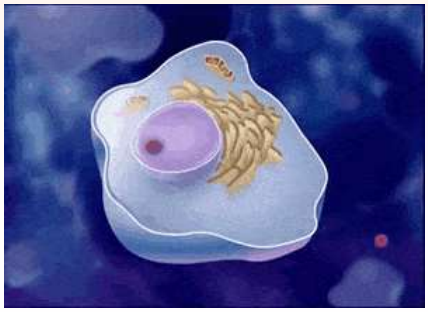
**Step 1: Phagocytic WBC response:**

**3.** Monocytes migrate from blood into tissues by ***extravasation*** to become **Macrophages** that destroy pathogens in tissue.

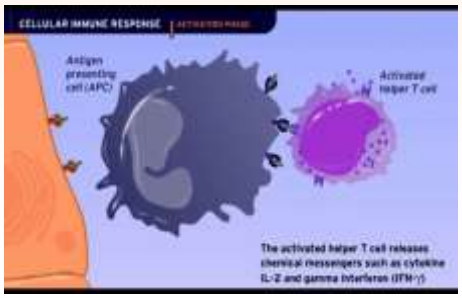
**4.** Macrophages places pathogen's antigen it cell surface – now macrophage is called an **Antigen-Presenting Cell APC).**

***APCs will activate T Cells see later in notes)***

- Phagocytes then send chemical "Cries for help" = **cytokines, chemokines**



*A macrophage becoming an APC*




*An APC activating a helper T-cell*

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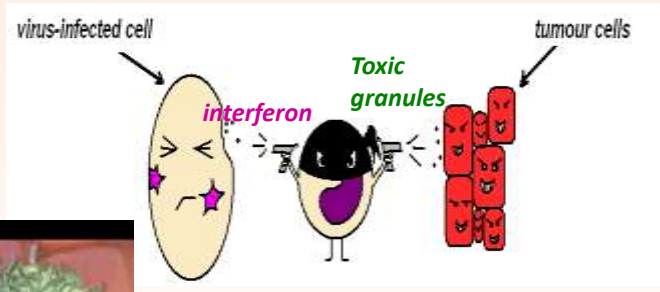
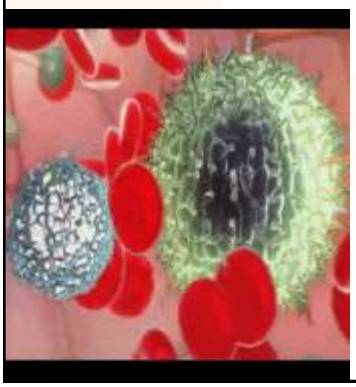
**Step 2. Natural Killer (NK) Cell response**

- are activated by cries for help (cytokines, chemokines)
- release interferon to kill virus-infected cells.
- release toxic granules to kill tumor cells.



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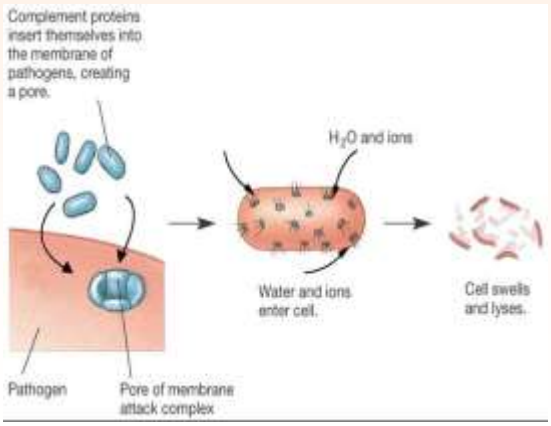
**Step 3. Inflammatory Response**

- **Mast cells** – secrete **histamine** for inflammation. Causes vasodilation of blood vessels. (Allows more WBCs to enter into tissue as macrophages!)

- **Complement proteins** - kill bacteria by making holes in them (bacteria burst!) & cause inflammation.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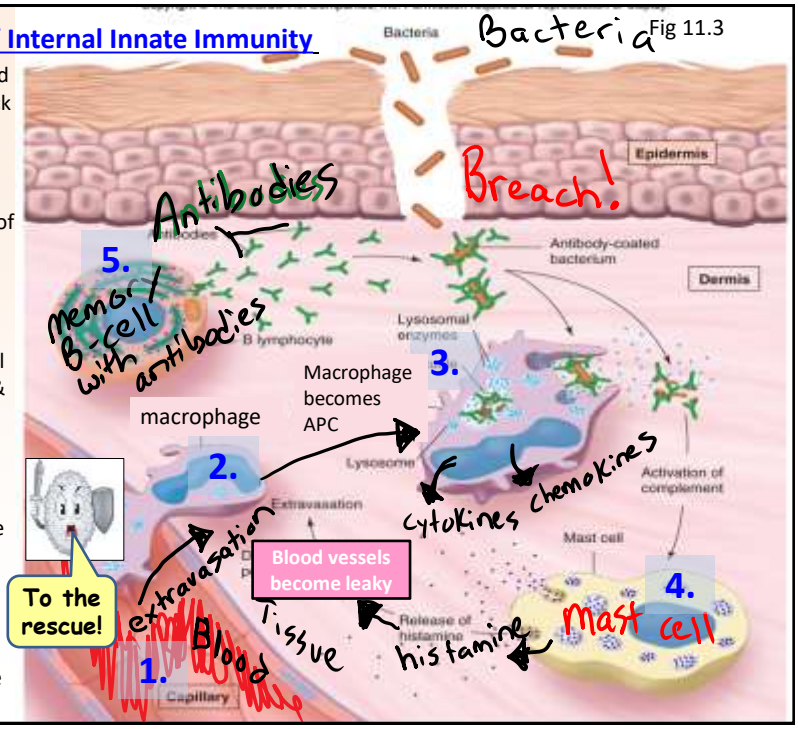
**Activation of Internal Innate Immunity** Fig 11.3

1. Neutrophil and monocytes attack pathogen in blood, secrete pyrogens (fever)
2. Extravasation of monocyte in tissue
3. macrophages eat pathogen, become **APC** (will activate T-cells, & cry for help (cytokines & chemokines)
4. Mast cells release histamine (start redness & swelling)
5. Cytokines & chemokines call cells of adaptive immunity

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# Review

**> Review of Immune Organs and Cells**

**> Innate Immunity (2 types)**

**External innate immunity** (keep pathogens OUT)

**Internal innate immunity** (activate when pathogens get in)

↓

**> Activation of Internal Innate immunity**

- **Neutrophils & monocytes** (phagocytic cells in blood that attack pathogens)
  - > secrete endogenous pyrogens (fever)
  - > secrete chemical cries for help (cytokines & chemokines)
- **Phagocytic cells in tissue** (macrophages, which become APC)
- **Natural killer (NK) cells**
  - > interferon to kill viruses & toxic granules to kill tumor cells
- **Mast cells**
  - > secrete histamine for inflammation response (edema, redness, pain, vasodilation)
- **Complement proteins**
  - > poke holes in bacteria to lyse them

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**Activation of Adaptive Immunity – or long term specific defenses**

## Adaptive immunity:

**Provided by lymphocytes**

> Are produced in bone marrow

> T-lymphocytes (**T-cells**) & B-lymphocytes (**B-cells**)

> T-cells mature in **thymus**.

- Are involved in **Cell-Mediated Immunity**
- T-cells must activate first in order to activate B-cells

> B-cells mature in lymph nodes & spleen, and produce **antibodies**.

- Are involved in **Antibody-Mediated Immunity**

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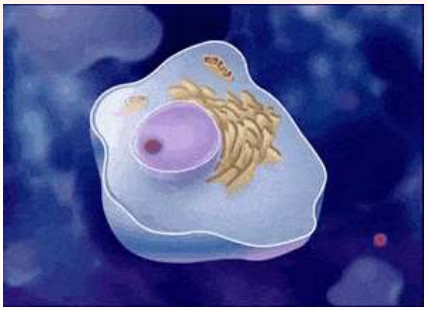
# *How do T-cells get "activated"?*

**By Antigen-Presenting Cells (APCs) of the internal innate immunity**

- APC presents antigen to Helper T-cells
- Helper T-cell then is ACTIVATED!



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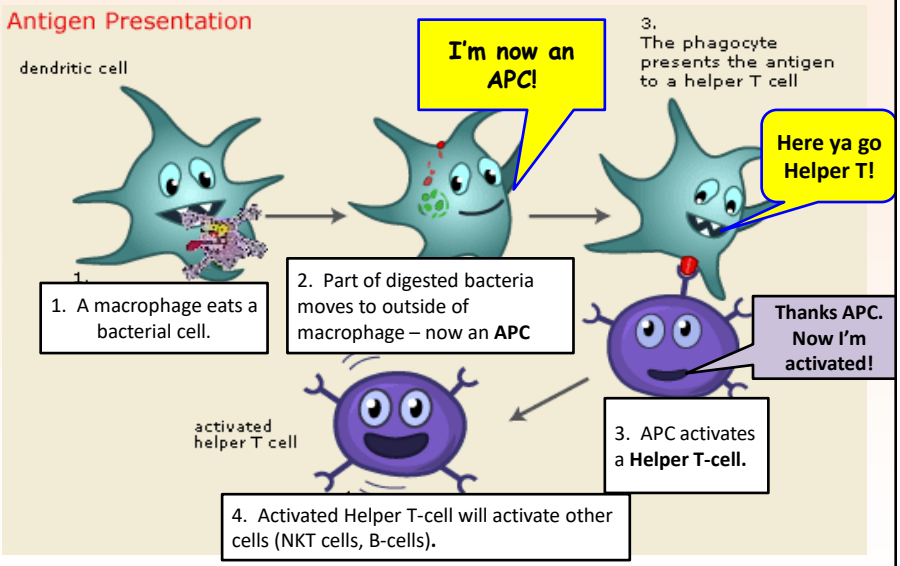


Tissue **macrophages** engulf pathogen. *Part of pathogen moves to outside of macrophage – now an **antigen-presenting cell (APC)**, and APC then activates **Helper T-cells**.*

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# Two types of Adaptive Immunity:

**1. Cell-Mediated Immunity (T-cells!)**

•**Helper T-cells** (activated by APCs)
Now activates other T-cells:

> **Cytotoxic T cells ($T_C$)**
- can kill pathogens directly

> **Memory T cells ($T_M$)**
-retain memory of pathogen, to kill later.

> **Regulatory T-cells ($T_{reg}$)**
– inhibit $T_C$ and B cells.
– may guard against allergies & autoimmune disease.

• **Helper T-cells** activate **B-cells** to make antibodies.

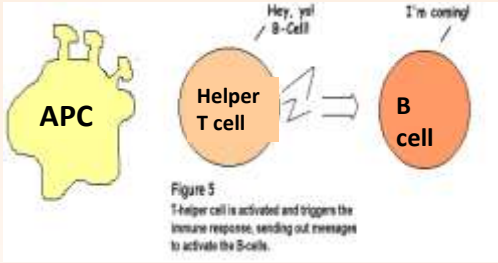

Figure 5
T-helper cell is activated and triggers the immune response, sending out messages to activate the B-cells.

**2. Antibody-Mediated Immunity (B-cells)**

•**B-cells** are activated by Helper T-cells) & make **antibodies** (or immunoglobulins) specific to the pathogen.

•Results in formation 2 types of B-cells
> Plasma B cells

> Memory B cells

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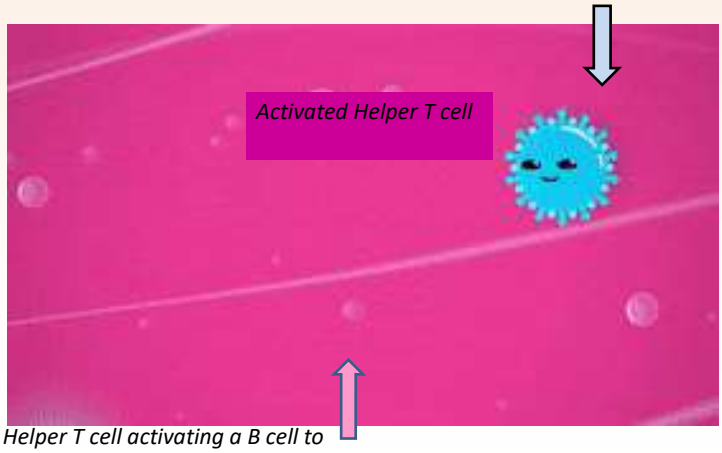
**Activated T-cells** stimulate **B-cells (plasma cells)** to make **antibodies** to an antigen**.**




*Helper T cell activating a B cell to make antibodies specific to pathogen*

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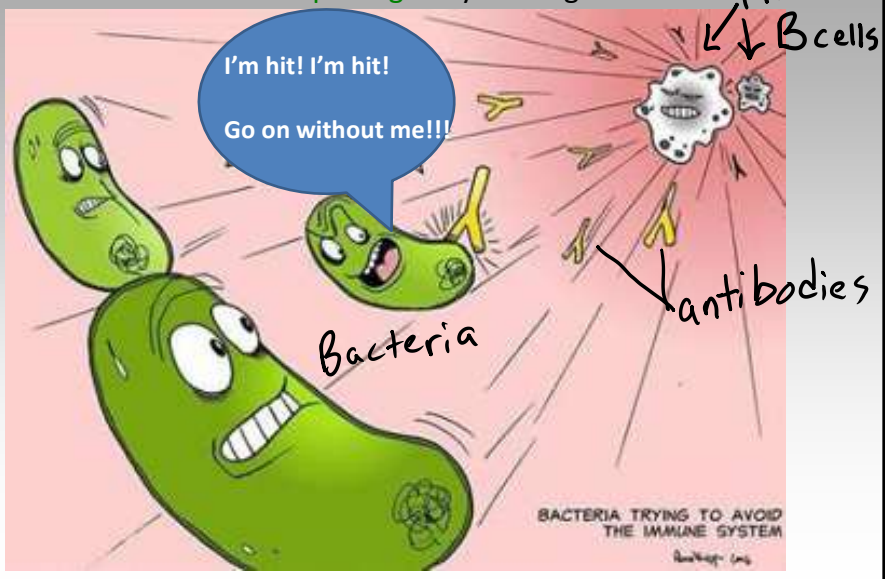
**Plasma B-cell** (the white blobs) with antibodies (the yellow **Y**'s), attacks the pathogen by binding to it.

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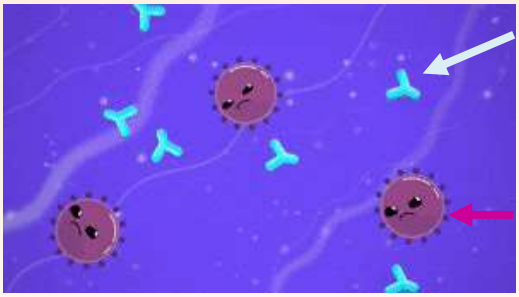
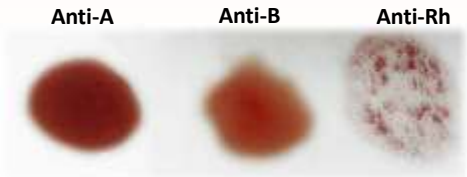



**Antibodies** of B-cells stick to antigen on **pathogen cells** and "stick them together" – process called **agglutination.**

The agglutinated blob will attract macrophages, which will engulf the blob & destroy it.




**Agglutination used in blood typing test**

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# More about B-Cells

> Activated by stimulation by activated Helper T-cells.

> produce **antibodies (immunoglobulins)** to specific antigens

> Provides ***humoral (or antibody-mediated, or specific immu***


> Exposure of B-cell to its specific antigen causes release of antibodies to bind to antigens.

> causes clonal production of 2 types B-cells with antibodies:

A) **plasma B cells** – ready to fight NOW.

B) **memory B cells** – wait to fight for later.

*Clonal replication of B cells*

**Effects of antibodies:**

- Activate complement proteins
- Agglutination reaction (antibodies sticks antigen-bearing cells together)
  "tags" pathogenic cells so they're recognized & destroyed by phagocytes.

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## Action of B Lymphocytes

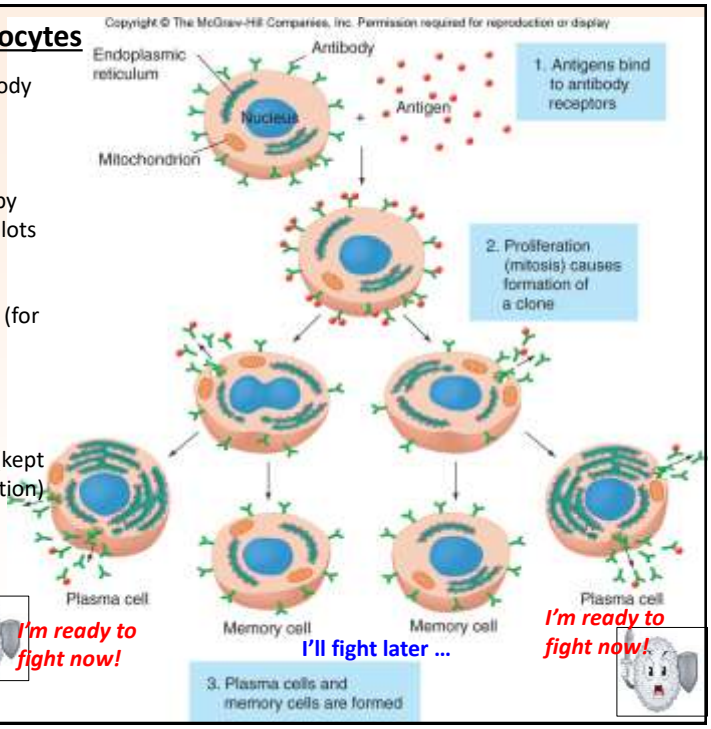
**1.** Antigen binds to antibody receptors on B-cells.

**2.** On contact with the antigen B-cells replicate by **cloning** to make lots and lots more B-cells.

**3. Plasma B-cells** formed (for immediate action),

and

**Memory B-cells** formed (kept in storage for later activation)

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**Sequence of events, from entry of pathogen into the body to the formation of antibodies:**

1. Bacteria enters tissue from a break in skin.
2. _____ = Phagocytic non-specific WBC in the blood stream.
3. _____ = Cell that extravasates from blood vessel into tissue. (is now called an _____)
4. _____ = Phagocytic cell in tissue, which finds pathogen, kills it, and puts antigen on its surface.
5. _____ = Cell of cell-mediated adaptive immunity, which becomes activated by interaction with the cell in #4 above.
6. Activated cell from #5 above can now activate these cells:
   - A. _____ = Cell of cell-mediated adaptive immunity, which directly kills pathogen.
   - B. _____ = Cell of cell-mediated adapted immunity, which keeps a memory of pathogen.
   - C. _____ = Cell that is part of antibody-mediated adaptive immunity)
7. Cell from 6C above can make _____ (otherwise known as immunoglobulins)
8. Cell from 6C above encounters its pathogen and the following happens:
   - A. _____
   - B. _____

Click **HERE** for blank flow diagram.

Click **HERE** for KEY

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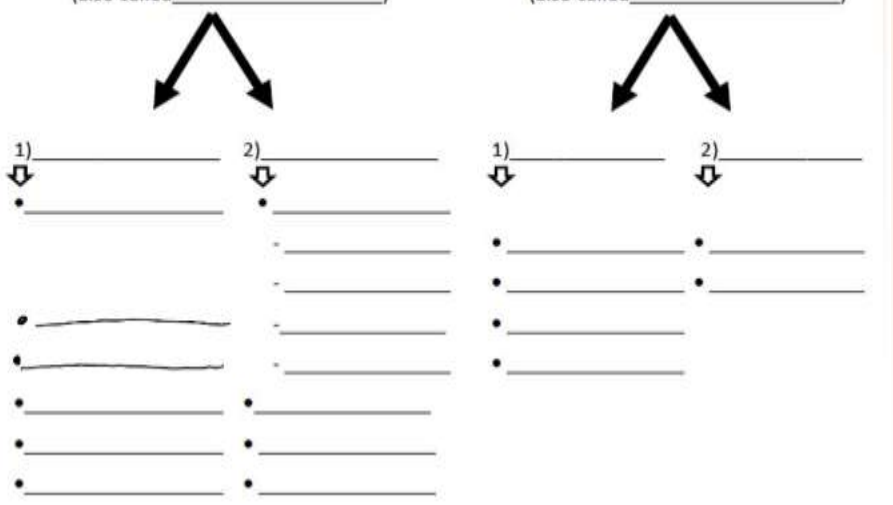
**CATEGORIES OF IMMUNITY:**

Innate Immunity (also called_____) Vs Adaptive Immunity (also called_____)




Click **HERE** for blank flow diagram of immune categories

Click **HERE** for KEY

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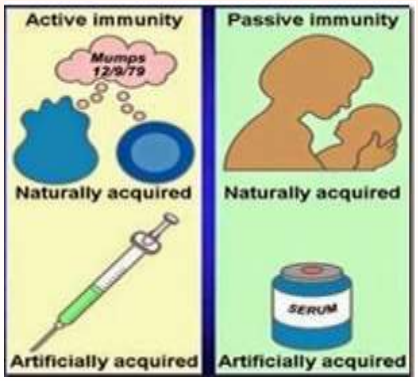
## Classification of Immunity

**1) Active immunity** = get immunity (antibodies) that you produce from actual exposure (natural) to disease organism or from vaccination (artificial exposure).

**2) Passive Immunity** = get immunity (antibodies) from source outside your body: Natural (breast milk) or artificial (injection of antibodies).




**Active Immunity**

**Active natural immunity** -
Make antibodies after exposed to sick person

**Active artificial immunity** -
Make antibodies after get vaccination

**Passive Immunity**

**Passive natural immunity** -
Receive antibodies From breast milk

**Passive artificial immunity** -
Receive antibodies From injection

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## 4. Autoimmunity Disorders

### Problems with the Immune Response

**autoimmunity** – when immune cells attack self; can be B or T cells.

*** Abnormal T-cells from Thymus associated with most autoimmune disorders!

**Ex. Of autoimmune disorders we've covered:**

> *rheumatoid arthritis* – attack on connective tissue of synovial joints.

> *rheumatic heart disease* – antibodies produced from strep throat attack heart valves.

> *multiple sclerosis* – attacks myelin sheaths on neurons.

> *Grave's disease* – attack on thyroid gland TSH receptor.

> *Myasthenia gravis* – destruction of nicotinic cholinergic receptors on skeletal muscles.

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# Review

Adaptive Immunity
- Cell-mediated adaptive immunity
- Antibody-mediated adaptive immunity

Types of T and B Cells
- T-cell formation and activity
- $T_H$, $T_C$, and $T_{reg}$
- B-cell formation and activity

Classification of Immunity

Autoimmune Disorders

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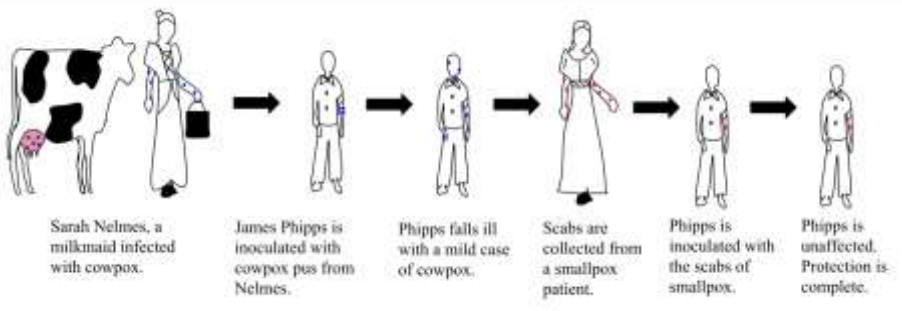
## Vaccinations

- Late 1700s → Edward Jenner noticed milkmaids rarely had smallpox.
- Jenner reasoned that milkmaids were immune to smallpox because they had been exposed to cowpox.
- To test his hypothesis, he inoculated a boy with cowpox pathogens and then with smallpox pathogens. As predicted, the boy did not contract smallpox.

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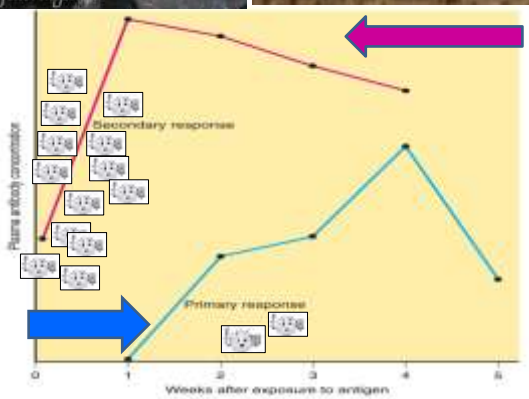
**vaccination** → 1° immune response → memory cells


**Primary response**: takes ~ 2 weeks for good production of plasma B-cells with antibodies (**high antibody titer,**) and memory B-cells after 1st exposure.




**Secondary response:** have lots of memory B-cells that were stored & waiting for future exposure = **stronger, faster immune response!**

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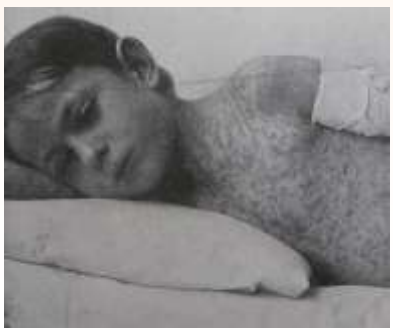
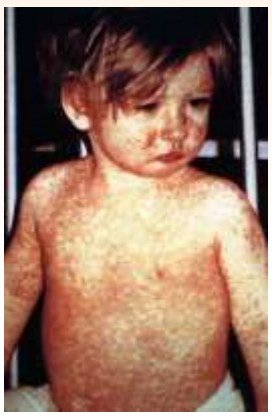
**Vaccinations and Halt of Communicable Disease: THE SCIENCE**

**Example of Vaccine Effectiveness:**

In the United States, before measles vaccine became available in the mid-1960s was estimated over 530,000 cases with 500 deaths per year. After vaccine – has been **99.9% decrease** in incidence of the disease.





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## Vaccinations and Halt of Communicable Disease: THE SCIENCE

| DISEASE | PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY* | MOST RECENT REPORTS OR ESTIMATES† OF U.S. CASES | PERCENT DECREASE |
|---|---|---|---|
| Diphtheria | 21,053 | 0† | 100% |
| *H. influenzae* (invasive, <5 years of age) | 20,000 | 31‡ | >99% |
| Hepatitis A | 117,333 | 2,890§ | 98% |
| Hepatitis B (acute) | 66,232 | 18,800§ | 72% |
| Measles | 530,217 | 187† | >99% |
| Mumps | 162,344 | 584† | >99% |
| Pertussis | 200,752 | 28,639† | 86% |
| Pneumococcal disease (invasive, <5 years of age) | 16,069 | 1,900‡‡ | 88% |
| Polio (paralytic) | 16,316 | 1† | >99% |
| Rotavirus (hospitalizations, <3 years of age) | 62,500** | 12,500†† | 80% |
| Rubella | 47,745 | 9† | >99% |
| Congenital Rubella Syndrome | 152 | 1† | 99% |
| Smallpox | 29,005 | 0† | 100% |
| Tetanus | 580 | 26† | 96% |
| Varicella | 4,085,120 | 167,490§§ | 96% |

http://www.immunize.org/catg.d/p4037.pdf

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## Vaccinations and Halt of Communicable Disease: THE CONTROVERSY

Do vaccinations cause Autism????

NO!

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## Vaccinations and Halt of Communicable Disease: THE CONTROVERSY

**Where did the controversy start?**

A study originally published in journal ***Lancet*** by **Andrew Wakefield in 1995** claimed that his study of **12 children** showed that the 3 MMR (measles, mumps, rubella) vaccines taken together (1st at 1 year, then at 5 -6 yrs) could alter immune systems, causing intestinal woes that then reach, and damage, the brain (autism?)

**Scientific community responded:**

> Dozens of epidemiological studies found no merit to his work
> His claims were based on a tiny sample size.
> The British Medical Journal called his research "fraudulent."
> The British journal ***Lancet*** retracted his publication.
> The British medical authorities stripped him of his license.

**Problem:**

People still believe Wakefield. Groups of people began to NOT vaccinate their children.

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## Vaccinations and Halt of Communicable Disease:

> Nationwide, vaccination rate against diseases has stayed at 90 % or higher, but % in some of the country now well below that, making those communities more vulnerable to disease outbreak.

There has been an increase in cases of Measles, Mumps is the US – especially in counties where vaccination rate below 90%.

> Medical doctors & epidemiology experts say that vaccination rate of ~95 % needed to protect a community by "herd immunity".

> **Herd immunity** = indirect protection from infectious disease when a large % of population has become immune (natural or vaccination-acquired) it reduces potential exposure of non-immune people (aren't or can't be vaccinated) to that disease.

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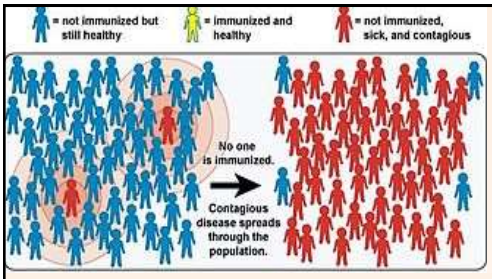


## Herd Immunity

The **top box** shows an outbreak in a community in which a **few people are infected (shown in red)** and **the rest are healthy but unimmunized (shown in blue);** the illness spreads freely through the population.

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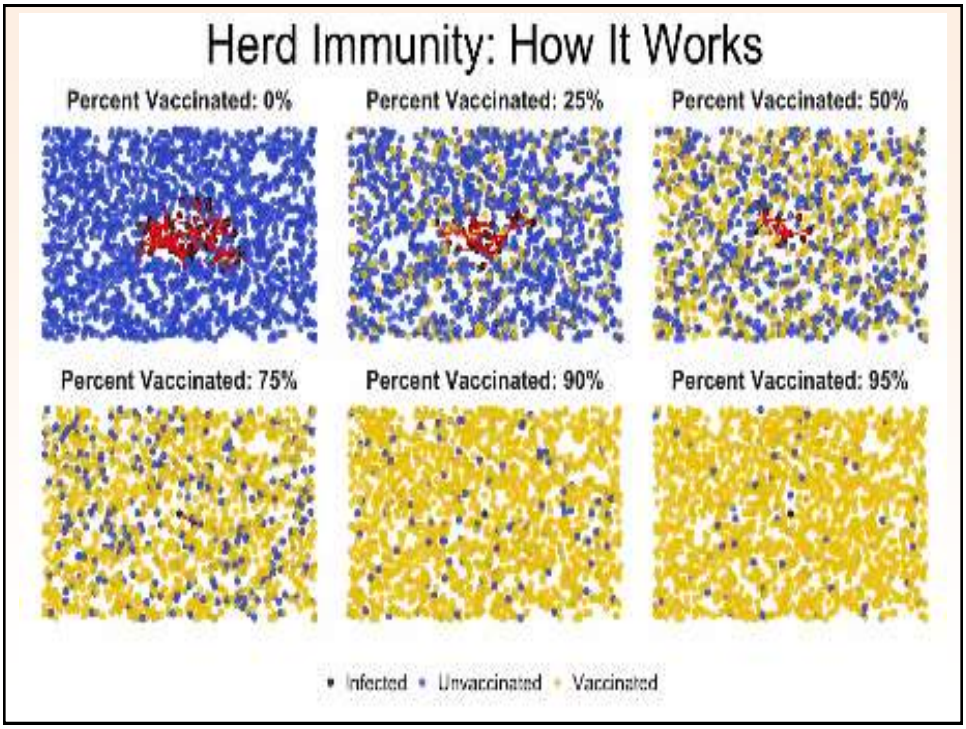


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# Review

Vaccination

- History of vaccination
- Action of vaccinations on immunity
- Controversy on vaccinations
- *[There shouldn't be!!!]*

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