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.

Immune system = The cells and organs involved in defense against pathogens and cancer.

1) Lymph Organs:
   A. Primary lymph organs
   > Bone marrow - make B lymphocytes (B-cells) & T-lymphocytes (T-cells)
   > Thymus – where T-cells mature.
1. **Review Immune Organs & Cells. Pg 164 Wiki text**

**Immune system** = The cells and organs involved in defense against pathogens and cancer.

1) **Lymph Organs:**
   A. **Primary lymph organs**
      > Bone marrow - make B lymphocytes (B-cells) & T-lymphocytes (T-cells)
      > Thymus – where T-cells mature

   B. **Secondary lymph organs**
      > Lymph nodes - activate lymphocytes, where B cells mature
      > Lymphatic & blood vessels - transport immune cells
      > Tonsils – first line of defense from inhaled substances
      > Brain – microglia
      > Spleen - activate lymphocytes
      > Intestines - Peyer’s patches
      > Appendix - on cecum
      > Liver - Kupffer cells

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3) **3 Lines of Defense from Pathogens! Pg 162 Wiki text**

A) **External Innate Immunity (non-specific)**
   - External barriers to entry for orifices of the body. KEEP PATHOGENS OUT!

B) **Internal Innate Immunity (non-specific)**
   – If a pathogen makes it past external barriers and gets inside, a non-specific internal defense happens.

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**Adaptive or Acquired Immunity (specific)**
Involves: > **Lymphocytes** (T-cells & B-cells)
   > **Antibodies** (a.k.a. immunoglobulins)
1) Innate Immunity (non-specific)

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

- Epithelial membranes
  - skin blocks entrance of pathogens into body
  - sweat is acidic and has lysozymes that are antimicrobial.
- Stomach acid - kills ingested microorganisms
- Respiratory tract - mucus & alveolar macrophages
- Urinary / genital defense = pH barriers
  - acidic vagina & urethra
- Eyes - Lysozyme in tears is antimicrobial

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.
- Complement proteins – proteins that cause inflammation and poke holes in bacteria to lyse them.
**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 cells makes blood vessels “leaky” so WBC can escape

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 Helper T-cells (see later in notes)**

   - Phagocytes then send chemical “Cries for help” = **cytokines, chemokines**
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.
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.

Activation of Internal Innate Immunity

1. Neutrophil and monocytes attack pathogen in blood, secrete pyrogens (fever)

2. Extravasation of macrophages in tissue

2. macrophages eat pathogen, become APC (will activate T-cells, & cry for help (cytokines & chemokines)

3. Mast cells release histamine (start redness & swelling)

4. Cytokines & chemokines cells of adaptive immunity
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

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

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.
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 phagocytize pathogens.
     > Memory T cells (T\(_M\))
       - retain memory of a specific antigen
     > 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.

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 of both Plasma B-cells & Memory B cells that have antibodies specific to the antigen.

Activated T-cells stimulate B-cells (plasma cells) to make antibodies to an antigen.
Plasma B-cell (the white blobs) with antibodies (the yellow Y’s), attacks the pathogen by binding to it.

I’m hit! I’m hit!
Go on without me!!!

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.
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 immunity).
- Exposure of B-cell to its specific antigen causes release of antibodies to bind to antigens.
- Causes clonal production of more B-cells with antibodies:
  A) plasma B cells for immediate defense, and
  B) memory B cells for future encounters.

Effects of antibodies:
- Activate complement proteins
- Agglutination reaction (antibodies sticks antigen-bearing cells together)
  “tags” pathogenic cells so they’re recognized & destroyed by phagocytes.

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).
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 adaptive immunity, which keeps a memory of pathogen.
   C. _________ = Cell that is part of antibody-mediated adaptive immunity
7. Cell from #6 above can make _________ (otherwise known as immunoglobulin)
8. Cell from #6 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 ___________)

1) _________
   • _________
   • _________
   • _________
   • _________

2) _________
   • _________
   • _________
   • _________
   • _________

Click HERE for blank flow diagram of immune categories

Click HERE for KEY
Review

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

Types of T and B Cells
  T-cell formation and activity
  \(T_h, T_c, \text{ and } T_{\text{reg}}\)
  B-cell formation and activity

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.
vaccination $\rightarrow$ $1^\circ$ immune response $\rightarrow$ memory cells

**Primary response:** takes ~2 weeks for good production of plasma B-cells with antibodies (high antibody titer,) and memory B-cells after 1$^{st}$ 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.
Vaccinations and Halt of Communicable Disease: THE SCIENCE

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY</th>
<th>MOST RECENT REPORTS OR ESTIMATES OF U.S. CASES</th>
<th>PERCENT DECREASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>21,053</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td><em>H. influenzae</em> (invasive, &lt;5 years of age)</td>
<td>20,000</td>
<td>31</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>117,333</td>
<td>2,8903</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Hepatitis B (acute)</td>
<td>66,232</td>
<td>18,800^3</td>
<td>72%</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>18,711</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>5841</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>28,639^3</td>
<td>86%</td>
</tr>
<tr>
<td>Pneumococcal disease (invasive, &lt;5 years of age)</td>
<td>16,069</td>
<td>1,900^4</td>
<td>88%</td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>16,316</td>
<td>11</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Rotavirus (hospitalizations, &lt;3 years of age)</td>
<td>62,500^3</td>
<td>12,500^3</td>
<td>80%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>9</td>
<td>&gt;99%</td>
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<tr>
<td>Congenital Rubella Syndrome</td>
<td>152</td>
<td>11</td>
<td>99%</td>
</tr>
<tr>
<td>Smallpox</td>
<td>29,005</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>26</td>
<td>96%</td>
</tr>
<tr>
<td>Varicella</td>
<td>4,085,120</td>
<td>167,490^5</td>
<td>96%</td>
</tr>
</tbody>
</table>


Vaccinations and Halt of Communicable Disease: THE CONTROVERSY

Do vaccinations cause Autism????

NO!
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.

---

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.
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.

Herd Immunity: How It Works

- Percent Vaccinated: 0%
- Percent Vaccinated: 25%
- Percent Vaccinated: 50%
- Percent Vaccinated: 75%
- Percent Vaccinated: 90%
- Percent Vaccinated: 95%

- Infected
- Unvaccinated
- Vaccinated
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).

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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:

> *rheumatoid arthritis* – attack on connective tissue of synovial joints.
> *rheumatic heart disease* – antibodies produced from strep throat attack heart valves.
> *lupus* – nuclear proteins.
> *multiple sclerosis* – attacks myelin sheaths on neurons.
> *Grave’s disease* – attack on thyroid gland TSH receptor.
> *Crohn’s disease* – attack on cecum of large intestine.
> *diabetes* (certain forms) – destruction of beta cells in the pancreas.
> *Myasthenia gravis* – destruction of nicotinic cholinergic receptors on skeletal muscles.
Review

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

Classification of Immunity

Autoimmune Disorders