Acquired immunity

- Innate defense immunity cannot always destroy pathogens during infection.
- Acquired immune response center around the ability of the body to distinguish between self and non-self and involves specific response after exposure to a foreign substance:
  - Humoral (antibody-mediated) response – antibody attack free microbes in the body.
  - Cell-mediated response – specialized cells attack infected or abnormal (cancer) cells.
- Lymphocytes and macrophages are important to the development of acquired immunity.
- If overstimulated, can cause harm to host (hypersensitivity).

Antigen and antibody

- **Immunogens** – substances that trigger host immune responses.
- **Antigens** (Ag) – substances that react with products of the immune response (i.e. antibody & specialized cells):
  - Large proteins, large DNA/RNA, other cellular components of microbes are good antigens.
  - Small molecules (hapten) are poor antigens; but when combined with a large molecules (carrier) can still elicit an immune response.
- **Antibody** (Ab) – Immunoglobulins (Ig)
  - Glycoproteins produced by host that bind to antigens an antigenic determinant on the antigen (epitope).
  - “Specific” – recognize and bind to only the antigen that stimulate its initial production (but occasionally, they cross-react).
Overview of the immune response components

- B lymphocytes
- T lymphocytes
- Natural killer (NK) cells
- Major histocompatibility complex molecules (MHC)
- Macrophages (antigen-presenting cells, APC)
- Cytokines

B Cells – humoral response

- Derived from lymphoid stem cells of the bone marrow
- Circulate the body in through lymph and blood (~10-15% of peripheral blood cells)
- Each B lymphocyte (B cell) can make one and only one type of antibody (immunoglobulin).
- Each B cell will take the immunoglobulins it makes and place them into its cell membrane with the specificity-bearing side outward
- Antigens are presented to the B cells. Only those B cells that bind to the antigen can complete their development into antibody-secreting plasma cells and divide repeatedly

T cells – cell-mediated response

- Some of the lymphoid stem cells travel to the thymus and mature into T lymphocytes
- 4 kinds:
  - Cytotoxic T cells (T_C) directly kill invaders.
  - Helper T cells (T_H) aid B and other T-cells to do their jobs, and HIV lives in and kills them.
  - Suppressor T cells (T_S) suppress the activities of B- and other T-cells so they don’t overreact.
  - Delayed hypersensitivity T cells (T_D)
- Do NOT produce antibody; but control antibody production
- Has T-cell receptor (TCR) protein on cell surface - Tissue transplant rejection, cellular immunity to certain microbial infection, cytotoxicity of virus-infected & tumor cells
**Natural Killer (NK) cells**
- Do not response to specific Ag. That is, it has NO Ag-specific recognition ability
- Contain cytotoxic granules kill virus-infected cells, tumor cells and Ab-coated target
- Employed by both specific and non-specific immune response

**Antigen presenting cells (APC)**
- B cells – effective at presenting antigen to which its antibody is directed
- Macrophages – very effective at presenting the phagocytosed/digested microbial components

**MHC molecules**
- Proteins on cell surface that immune system used to identify a cell as either foreign or self
- Class I (MHCI)
  - on every cell in the body
  - Aid T cells in surveying for ‘self’ and what proteins a cell is making
- Class II (MHCII)
  - Only on special APCs
  - Recognized by T cells to initiate an immune response
Cytokines

- Cytokines produced by B or T cells are called lymphokines
- Allow communication between cells and the immune systems

Overview of acquired specific immunity

Two ways to acquire immunity
- Active - YOU produce the Ab
- Passive – OTHERS produce the Ab

<table>
<thead>
<tr>
<th>[How the Antigen or Antibody entered the body]</th>
<th>ACTIVE NATURAL</th>
<th>PASSIVE NATURAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NATURAL</td>
<td>Ex: exposure to chicken pox</td>
<td>Ex: maternal antibodies crossing the placenta</td>
</tr>
<tr>
<td>ARTIFICIAL</td>
<td>Ex: immunization against polio</td>
<td>Ex: vaccination against the effects of a snake bite</td>
</tr>
</tbody>
</table>
Antibody

- Five classes (isotypes) of antibodies
- Each Ab consists of four proteins connected in a Y-type arrangement
  - Constant region (Fc) – region of the Ab that unique to each isotype
  - Variable region (Fab) – amino acid sequence varies and produce the specificity to each Ab

**Antibody Isotypes and their properties**

<table>
<thead>
<tr>
<th></th>
<th>IgA</th>
<th>IgD</th>
<th>IgE</th>
<th>IgG</th>
<th>IgM</th>
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</thead>
<tbody>
<tr>
<td>Molecular forms</td>
<td>Monomer or dimer</td>
<td>Monomer</td>
<td>Monomer</td>
<td>Monomer</td>
<td>Penta/mer</td>
</tr>
<tr>
<td>% total Ig in serum</td>
<td>10-20</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>70-85</td>
<td>10</td>
</tr>
<tr>
<td>Where found in body</td>
<td>Found in body secretions</td>
<td>Found on B-cell surface</td>
<td>Attach to basophils and mast cells</td>
<td>Blood &amp; extracellular fluid</td>
<td>Blood &amp; extracellular fluid</td>
</tr>
<tr>
<td>Functions</td>
<td>Protect external openings</td>
<td>Unknown; maybe antigen detection</td>
<td>Allergy response and defend infection by large parasite</td>
<td>Long term Ab that protect the body</td>
<td>Appear earlier in the infection and offer valuable defense during critical stage of the infection</td>
</tr>
<tr>
<td>Transferrable to offsprings?</td>
<td>Via colostrum &amp; breast milk</td>
<td>No</td>
<td>No</td>
<td>Via placenta</td>
<td>No</td>
</tr>
</tbody>
</table>

**Typical Humoral response**

1. An Ag is phagocytosed and digested by a macrophage (APC).
2. Ag is presented on APC’s cell surface along with MHCII molecules.
3. A Tc cells recognize the Ag-MHC complex and secret lymphokines.
4. A specific B cell recognizes the chemical signals & Ag, undergoes clonal expansion.
5. Some B cells further differentiated into Ab-secreting plasma cells & others become memory B-cells.
### Effects of humoral response (i.e. antibodies production)

- Neutralizing a toxin if the antigen was on a toxin
- Deactivating a virus if the antigen was on a virus
- Activating the complement system; antibody and complement together can lyse bacteria and kill them
- Opsonization - making the antigen (and what it is attached to) more appealing to phagocytes.

### Cell-mediated response

- Can be Ag-specific
  - Cytotoxic T-cell response
  - Delayed-type hypersensitivity response
- Or nonspecific
  - Natural killer cells – somehow able to recognize and attach to abnormal cells. They kill these cells by secreting certain enzymes that cause lysis.

### Typical Cytotoxic T-cell response

1. APC engulfs Ag and presents on its cell surface or infected cells display abnormal proteins on cell surface
2. Tₘ recognizes Ag-MHC complexes
3. Through lymphokines communication, there is clonal expansion of these T cells
4. Tₖ circulate the body and encounter infected cells. Tₖ secrete various compounds that cause lysis of the targeted cells.
5. Tₛ cells eventually suppresses the immune response

- Some T cells are long-lived and become memory cells (what is the importance?)
Memory cells

- Whether the body's response is primarily humoral (through antibodies) or cell-mediated, certain T and B cells become 'memory cells.' These cells remember their exposure to the specific antigens. This is the mechanism by which vaccination helps protect the body from disease.
- 'Prime' the body in case of a subsequent exposure to the antigen.

Abnormality of the immune system

- **Hypersensitivity** – immune system overreacts to a stimulus. There are four major types of hypersensitivity. The most common is type I which involves immediate allergic response resulting from the production of IgE and stimulation of mast cells to release histamine.
- **Autoimmunity** - the immune system mistakenly sees some part of the body as foreign and starts to attack it. Both the T cells and B cells may be involved in autoimmunity.
- **Immunodeficiency**
- **Immunosuppression** - Certain drugs and disease-causing organisms can suppress the immune system. e.g. organ transplants (to prevent rejection)