Questions for today:

1. What are non-immune host defenses against infections?

2. What are the visible immune responses to infection?

3. What are the major types of host cells involved in immune responses?

4. What is non-specific immunity and how does it work?

5. How does specific immunity work? (2 types: antibody-mediated vs. cell-mediated immunity)

Non-immune host defense against infections

Resistance to microbial infections is highly variable and depends on the overall health of the host.
- Factors affecting host resistance include age, diet, stress, etc.
- Physical anatomical barriers to infections.
  - epidermis
  - mucus to trap microbes
  - secretions containing anti-microbial compounds (e.g., lysozyme)
  - low pH
  - natural, non-pathogenic microbial populations
Compromised host: one or more of the infection resistance mechanisms is not functioning properly.

- illness
- drug therapy
- AIDS
- injury

- compromised host is often encountered in a hospital situation.
  - proximity to other disease carriers
  - invasive procedures
  - *nosocomial infections*: infections that occur in a hospital setting.
Visible Immune Responses

*Inflammation*: redness and swelling around an infection site.

- designed to localize an invasion site and prevent further spread, often by producing a clot of fibrin around the infection site.
- induced by cytokines from WBCs (leukocytes)
- in some cases, inflammation aids infection because of the tissue damage that can result.
- extreme case = septic shock

*Fever*: increase in body temperature, usually as the result of an infection.

- induced by endogenous pyrogens from infecting agent.
- can be beneficial to host by increasing certain immune functions.
- Strong fever (> 104°F, 40°C) benefits pathogen
  - continuous (e.g., typhoid fever)
  - remittent (varies, but always high, as in TB)
  - intermittent (most common)
Host cell types involved in the immune response

Note: stem cells are used for cloning because they can differentiate into a wide variety of cell types.

Cells produce peptide signaling molecules = chemokines.

About 0.1% of cells in the blood are WBCs or leukocytes. WBCs (not RBCs) are also found in lymph. Cell free component of blood or lymph is called serum.
## Cytokines/chemokines released by leukocytes

<table>
<thead>
<tr>
<th>What</th>
<th>Producer</th>
<th>Target</th>
<th>Effect</th>
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<tr>
<td>IL-1</td>
<td>monocytes</td>
<td>$T_H$</td>
<td>activate</td>
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<td>IL-2</td>
<td>T cells</td>
<td>T cells</td>
<td>growth, diff.</td>
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<td>IL-3</td>
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<tr>
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<td>IKN-gamma</td>
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<td>GM-CSF</td>
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<td>myeloid stem cells</td>
<td>differentiate</td>
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<tr>
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<td>$T_H^{21}$ &amp; $T_H^2$</td>
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<td>inhibit</td>
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<tr>
<td>TNF-alpha</td>
<td>$T_H^1$</td>
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<td>$T_H^1$</td>
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<td>IL-8</td>
<td>macrophage</td>
<td>neutrophiles &amp; T cells</td>
<td>attract and activate</td>
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<tr>
<td>MCP-1</td>
<td>macrophage</td>
<td>macrophage &amp; T cells</td>
<td>attract and activate</td>
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</tbody>
</table>

IL = Interleukin, IFN = interferon, GM-CSF = granulocyte, monocyte-colony stim. factor, TGF = T cell growth factor, TNF = tumor necrosis factor, MCP = macrophage chemoattractant protein.
Non-specific Immunity
The infecting pathogen (or toxin) is eliminated by a phagocyte (i.e., “cell that eats”).
• phagocyte cells include polynuclear leukocytes (neutrophiles), macrophages, and monocytes.
• move by ameboid motion.
• contain lysosomes that possess digestive enzymes (lysozyme, proteases, nucleases, lipases) and noxious chemicals.
• engulf pathogens within vesicles that fuse with lysosome to become phagolysosome.

Some pathogens avoid this type of death:
• kill phagocytes using leukocidins (Streptococcus).
• avoid phagocytosis using a capsule or M-protein (”).
• neutralize toxicity and grow inside phagocyte (e.g., Mycobacterium tuberculosis)
Specific Immunity: Antibody-Mediated (also called Humoral Immunity)

- Phagocytes digest pathogens to create small pieces.
- The phagocyte “presents” these pieces (usually peptides called antigens, Ag) to receptors on T cells.
- A subset of T cells (T-helper or $T_H$) that recognize the Ag stimulate B cells to make antibodies (Ab) specific to this Ag.
- The Ab are released into solution where they bind to the pathogen (carrying the Ag). (Not to scale)
- A series of host complement proteins bind to the Ab attached to the pathogen.
- The final complex of proteins punches a hole through the pathogen wall (opsonization).
- In addition, Ab-exposed cells are more readily phagocytosized.
The Ab produced by an individual B cell is highly specific to one epitope (portion of a cell or macromolecule).

How can a pathogen circumvent this fate?
- synthesize proteases to destroy Ab.
- change surface proteins so Ab does not bind.

B cells producing the specific Ab can live for years. Subsequent exposure to the same Ag can:
- stimulate clonal growth of specific host B cells
- each cell in this clone produces this specific Ab
- results in rapid burst in Ab level
- process termed “immunological memory”
- we use this phenomenon during vaccination
Primary response involves Ab production (as IgM in this case) when first exposed to the Ag. Secondary response involves burst of Ab produced (as IgG in this case) after later exposure. Some vaccines require such a periodic “booster shot”.

**Specific Immunity: Cell Mediated**
- This process also begins with phagocytosis and Ag presentation to T cells.
- T-cytotoxic ($T_C$) cells directly attack Ag-bearing cells
- Thus, host cells containing the pathogen can be killed (through a process called *apoptosis*).
Immunological responses provide a finely balanced protection system that is vastly oversimplified here (consider enrolling in MMG 451 for more details). As examples of additional complexities involving this system, four other issues are mentioned:

*Immediate hypersensitivity* involves an inappropriate immune response after exposure to an Ag (e.g., pollen, peanuts) that rapidly damages the host. Mild cases result in *allergies*; death is possible from *anaphylactic shock*.

*Delayed-type hypersensitivity* is slower to arise and operated by a distinct mechanism, such as the case for contact dermititis (e.g., poison ivy).

*Autoimmune diseases* involve T and B cells reacting against host Ag (e.g., systemic lupus erythromatosis).

Some pathogens produce superantigens that overstimulate immune cells so as to cause severe tissue damage (e.g., toxic shock syndrome and scarlet fever).