MMG 301 Lec 33 Host Defenses

Questions for today:

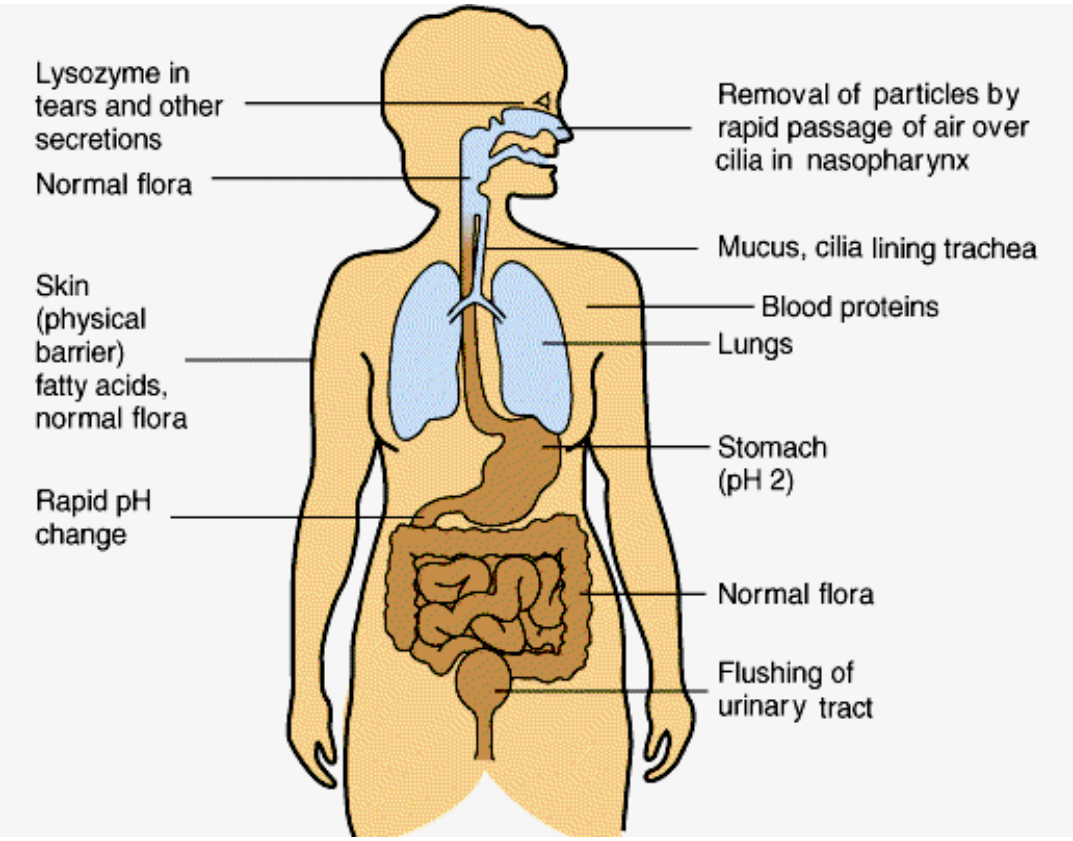
1. What are non-immune host defenses against infections?
2. What are the visible immune responses to infection?
3. What are the major types of host cells involved in immune responses?
4. What is *non-specific immunity* and how does it work?
5. How does *specific immunity work?* (2 types: *antibody-mediated* 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

Changes seen:
Infants?
>65?
Famine?
Smoking?
Alcohol?
Lack of sleep?
Stress?



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 (> 104ºF, 40ºC) benefits pathogen

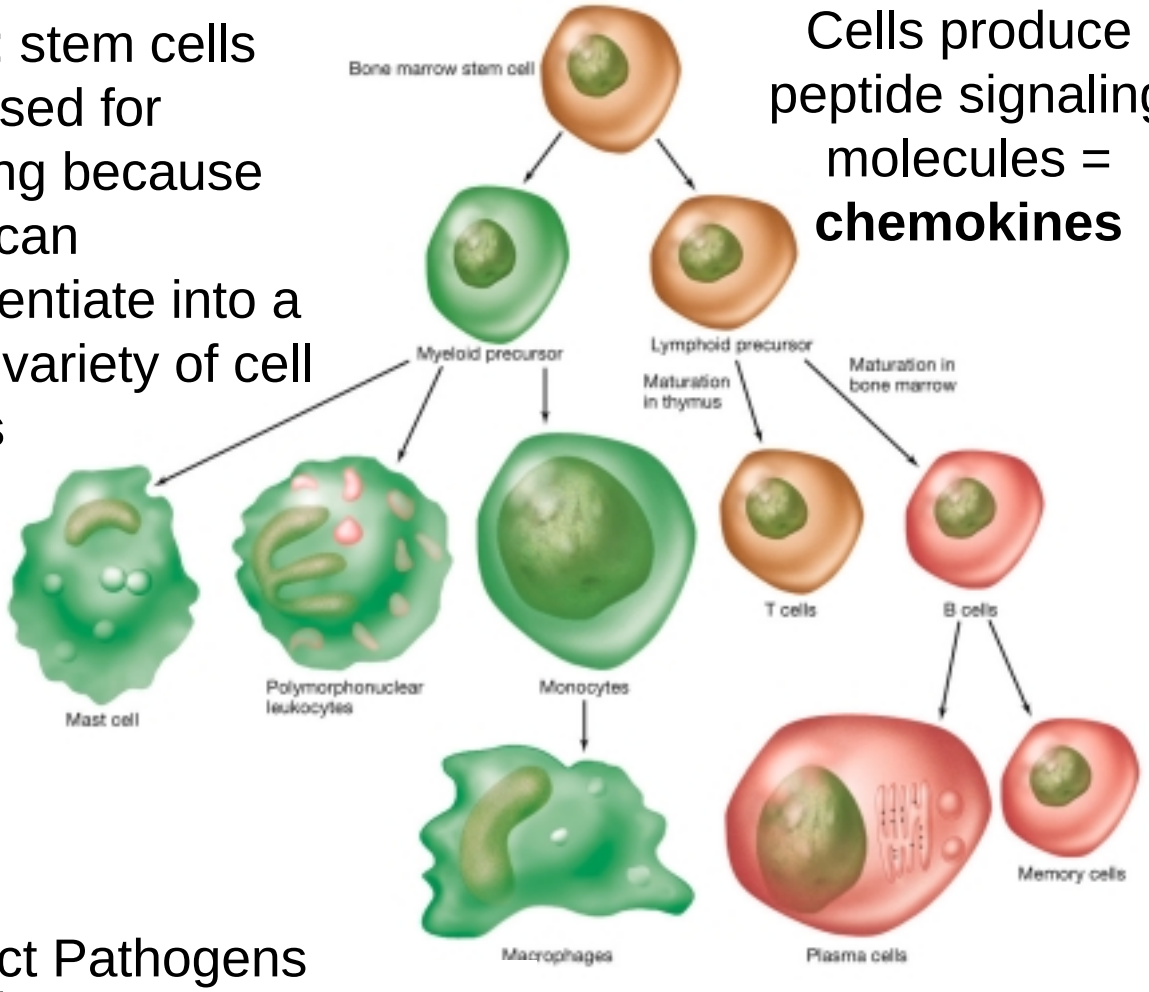
    • continuous (e.g., thyphoid fever)

    • remittent (varies, but always high, as in TB)

    • intermittent (most common)

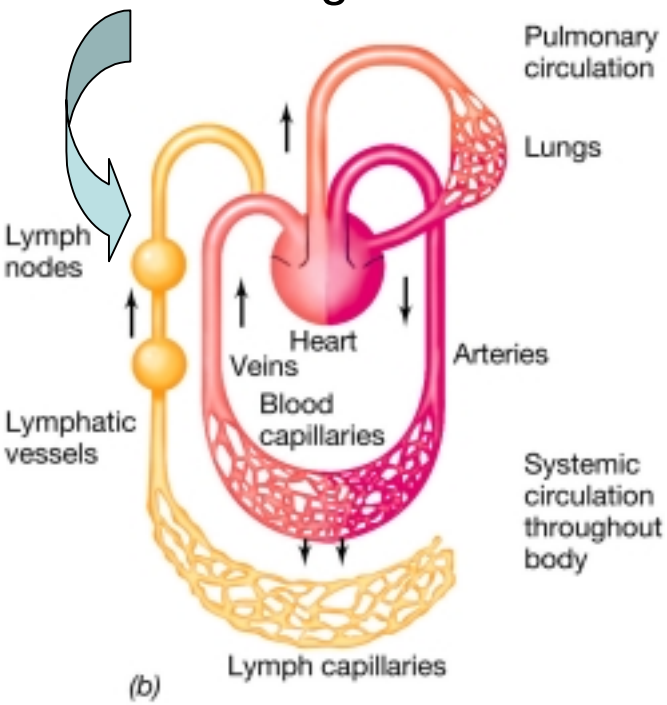
Host cell types involved in the immune response

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



Cells produce peptide signaling molecules = **chemokines**

Collect Pathogens



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

What	Producer	Target	Effect
IL-1	monocytes	T_H	activate
IL-2	T cells	T cells	growth, diff.
IL-3	T_H1	Hematop. stem cells	growth factor
IL-4	T_H2	B cells	Ab synth.
IL5	T_H2	B cells	Ab synth.
IL-10	T_H2	T_H1	inhibit
IL-12	macrophage	T_H1	activate, diff.
IFN-alpha	leukocytes	normal cells	anti-viral
IKN-gamma	T_H1	macrophage	activate
GM-CSF	T_H1	myeloid stem cells	differentiate
TGF-beta	T_H21 & T_H2	macrophage	inhibit
TNF-alpha	T_H1	macrophage	activate
TNF-beta	T_H1	macrophage	activate
IL-8	macrophage	neutrophiles & T cells	attract and activate
MCP-1	macrophage	macrophage & T cells	attract and activate

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

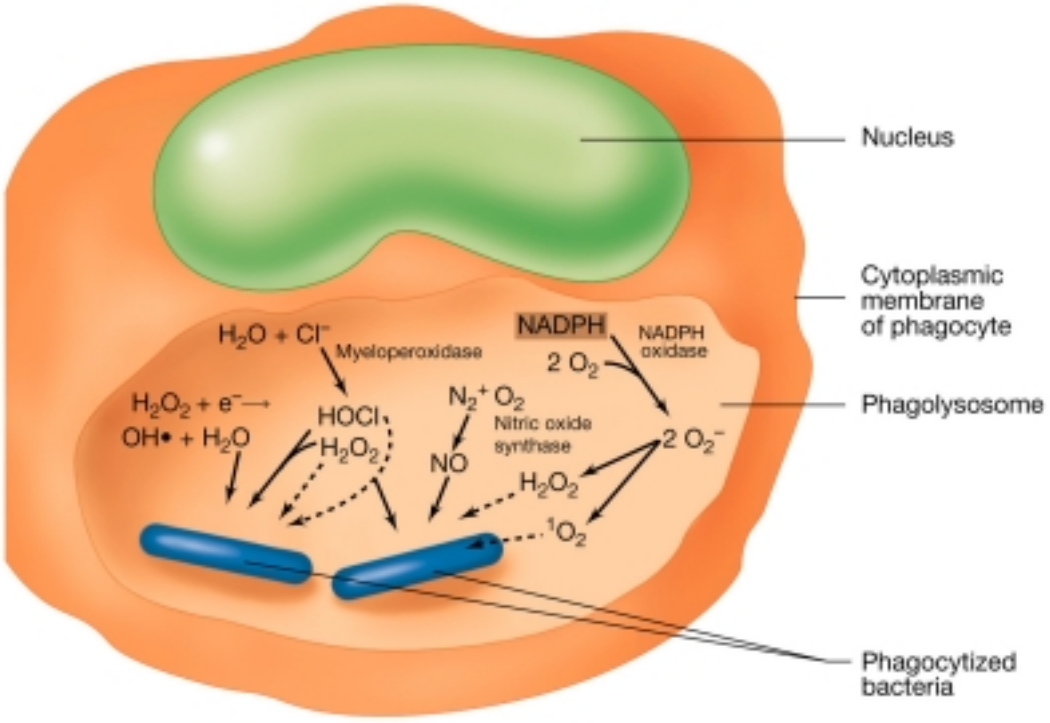
The infecting pathogen (or toxin) is eliminated by a *phagocyte* (i.e., “cell that eats”).

• 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*)

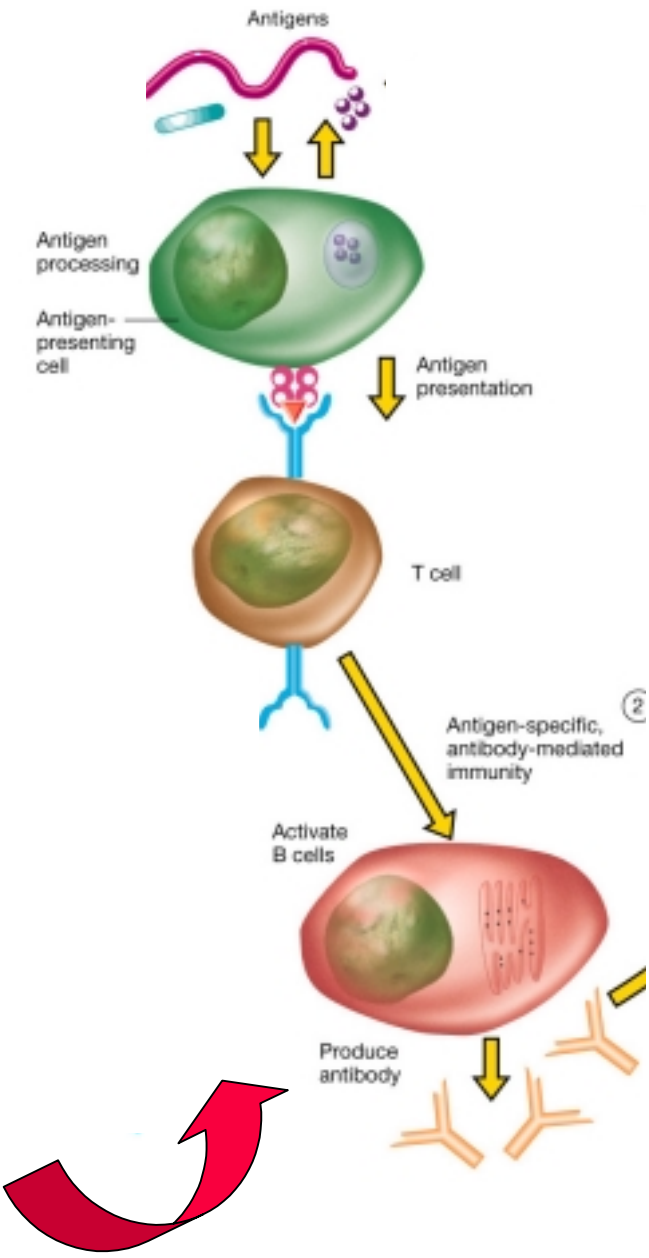
Specific Immunity: Antibody-Mediated (also called Humoral Immunity)

- 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.

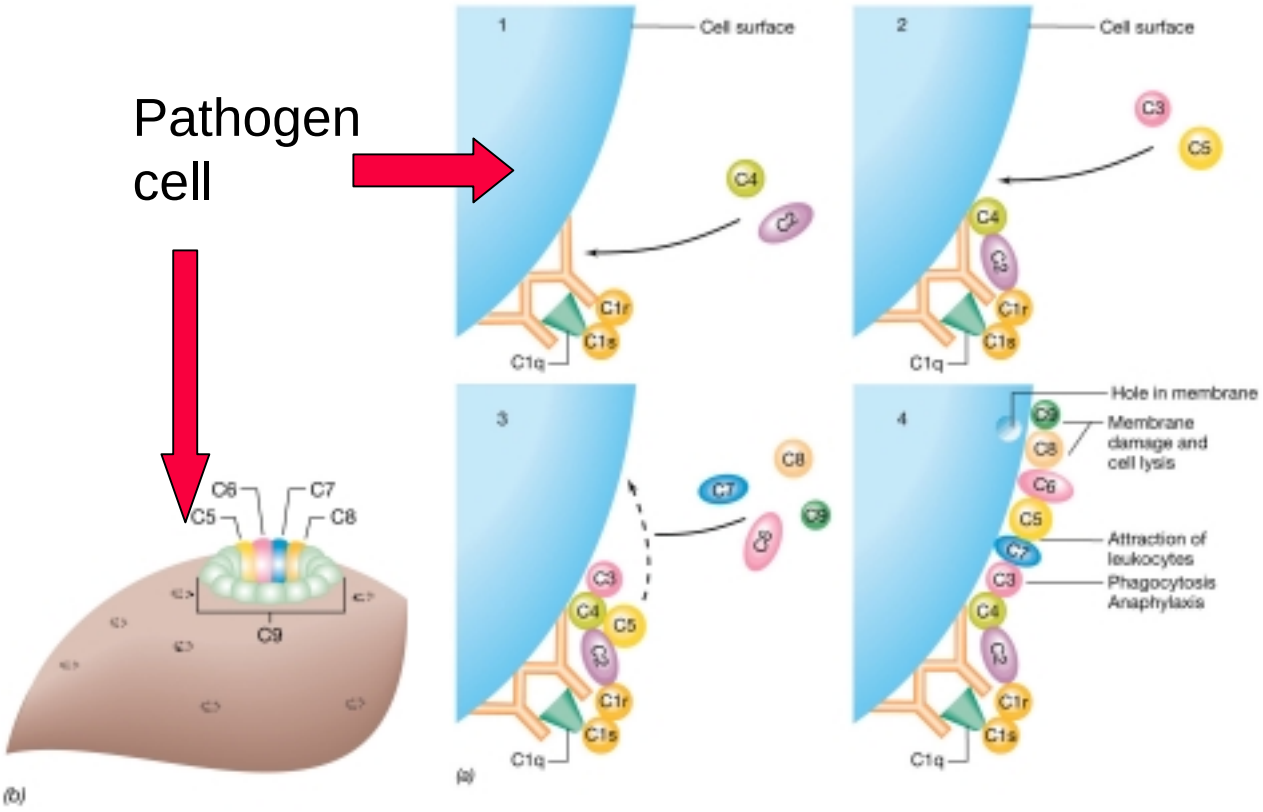
- The Ab are released into solution where they bind to the pathogen (carrying the Ag). **(Not to scale)**



- 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)

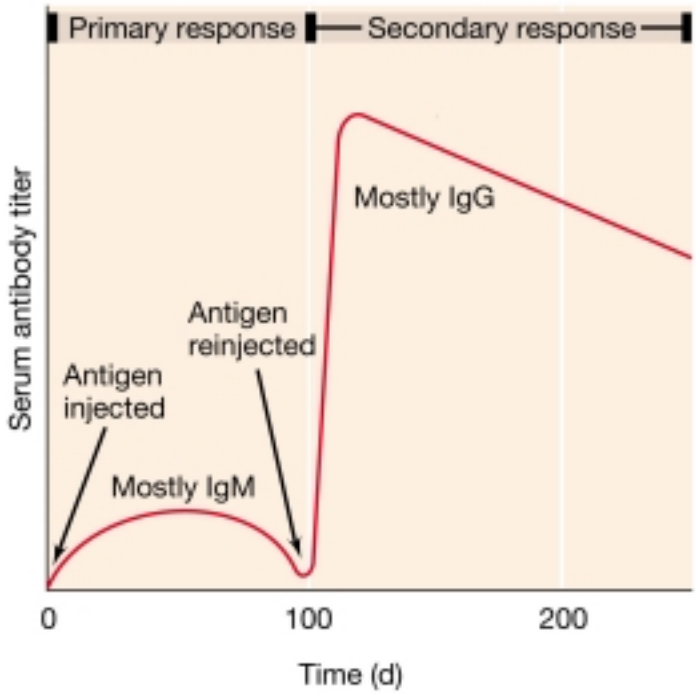
How can a pathogen circumvent this fate?

- 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:

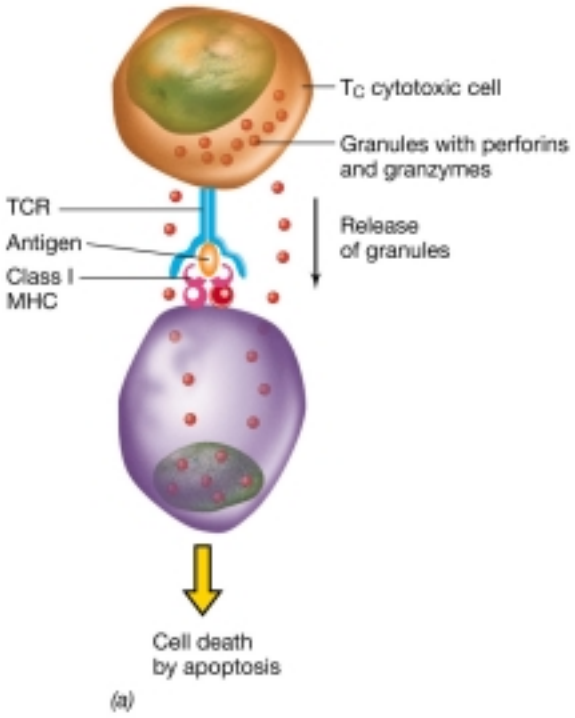
- stimulate clonal growth of specific host B cells
- each cell in this clone produces this specific Ab
- results in rapid burst in Ab level
- process termed “immunological memory”
- we use this phenomenon during vaccination

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).