Why do you need immunity?
Development of the Immune System
ACTIVE IMMUNE DEFENSES

Innate Immunity
- invariant (generalized)
- early, limited specificity
- the first line of defense

1. Barriers - skin, tears
2. Phagocytes - neutrophils, macrophages
3. NK cells and mast cells
4. Toll-like receptors TLRs
5. Complement and other proteins

Adaptive Immunity
- variable (custom)
- later, highly specific
- “remembers” infection

1. APC’s present antigen to T cells
2. Activated T cells help B cells and kill abnormal and infected cells
3. B cells - produce antibody specific for antigen
INNATE IMMUNITY

Physical Barriers

– skin
– hair
– mucous
INNATE IMMUNITY

Chemical Barriers

–sweat
–tears
–saliva
–stomach acid
–urine
Innate Immune System

**INNATE IMMUNE SYSTEM**

- Lysozyme in tears kills Gram-positive bacteria
- Removal of particles by turbinates and humidification
- Mucus and cilia capture organisms and remove them
- Skin: physical barrier
- Stomach acid kills ingested pathogens
- Fatty acids inhibit growth of many bacteria
- Competition and toxic products from intestinal flora
- Flushing action of urinary flow removes organisms
- Low vaginal pH from lactobacilli prevents colonization by pathogens
- Whole body:
  - Molecular and cellular defence
  - Pattern recognition molecule e.g. TLRs
  - Neutrophils
  - Macrophages

**NORMAL FLORA**

- **NASOPHARYNX**
  - Streptococci
  - Haemophilus
  - Neisseria
  - Mixed anaerobes
  - Candida
  - Actinomyces
- **SKIN**
  - Staphylococci
  - Streptococci
  - Corynebacteria
  - Propionibacteria
  - Yeasts
- **UPPER BOWEL**
  - Enterobacteriaceae
  - Enterococci
  - Candida
- **LOWER BOWEL**
  - Bacteroides
  - Bifidobacteria
  - Clostridium
  - Peptostreptococci
  - **VAGINA**
  - Lactobacilli
  - Streptococci
  - Corynebacteria
  - Candida
  - Actinomyces
  - Mycoplasma hominis
The Human Toll-like Receptor Family

- Various Membrane/Wall Components
- LPS
- Flagellin
- TLR4
- TLR5
- TLR1
- TLR2
- TLR6
- TLR10

TLRs

- Endosome
  - dsRNA
  - ssRNA
  - Viral and Bacterial Nucleic Acids

INNATE IMMUNE RESPONSE
TLRs in Treatment

Imiquimod (Aldara) activates immune cells through the toll-like receptor 7 (TLR7), commonly involved in pathogen recognition. Cells activated by imiquimod via TLR-7 secrete cytokines (primarily interferon-α (INF-α), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). There is evidence that imiquimod, when applied to skin, can lead to the activation of Langerhans cells, which subsequently migrate to local lymph nodes to activate the adaptive immune system.[9] Other cell types activated by imiquimod include natural killer cells, macrophages and B-lymphocytes
Toll-like receptors chemistry
The Immune System

Innate
- physical barriers
- natural killer cells
- macrophages
- Toll-like receptors

Cell-mediated
- T & B cells

Acquired

Humoral
- antibody-mediated
1. **Innate immunity**
Components of microorganisms bind to Toll-like receptors located on many cells in the body. This activates innate immunity, which leads to inflammation and to the destruction of invading microorganisms.

2. **Adaptive immunity**
Dendritic cells activate T lymphocytes, which initiates adaptive immunity. A cascade of immune reactions follows, with formation of antibodies and killer cells.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Innate</th>
<th>Adaptive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>For structures shared by groups of related microbes</td>
<td>For antigens of microbes and for nonmicrobial antigens</td>
</tr>
<tr>
<td>Diversity</td>
<td>Limited; germline-encoded</td>
<td>Very large; receptors are produced by somatic recombination of gene segments</td>
</tr>
<tr>
<td>Memory</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>Nonreactivity to self</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Components</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical and chemical barriers</td>
<td>Skin, mucosal epithelia; antimicrobial chemicals</td>
<td>Lymphocytes in epithelia; antibodies secreted at epithelial surfaces</td>
</tr>
<tr>
<td>Blood proteins</td>
<td>Complement</td>
<td>Antibodies</td>
</tr>
<tr>
<td>Cells</td>
<td>Phagocytes (macrophages, neutrophils), natural killer cells</td>
<td>Lymphocytes</td>
</tr>
</tbody>
</table>
**Except for IgE allergic reactions**
Model of Immune Responses: Speed and Specificity

response

Innate immune responses

Adaptive responses

time after infection
23

**Host**
- Age
- Genetics
- Immune status

**Environment**
- Lifestyle
- Exposure

**Stimulus**
- Microbial
- Non-Microbial

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**Chronic inflammation**

**Acute inflammation**

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**Innate Immunity**
- Toll-like receptors (TLRs)
- NOD-like receptors (NLRs)
- RIG-like receptors (RLRs)

**Adaptive Immunity**
- CD4 and CD8 T cells
- Antigen-specific B cells

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- DEFICIENT innate immune signaling: Death due to infection
- Host recovery and protection from reinfection
- EXCESSIVE innate immune signaling: Death due to inflammation
<table>
<thead>
<tr>
<th>Innate Immunity</th>
<th>Adaptive Immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen independent</td>
<td>Antigen dependent (except IgE)</td>
</tr>
<tr>
<td>No time lag</td>
<td>A lag period</td>
</tr>
<tr>
<td>Not antigen specific</td>
<td>Antigen specific</td>
</tr>
<tr>
<td>No Immunologic memory</td>
<td>Development of memory</td>
</tr>
</tbody>
</table>
Primary Function of the Adaptive Immune System

• Protect self from non-self;

and …

• Remember it!
T and B Lymphocytes

• T cells originate from the Thymus and may be Helper (CD4), Suppressor (CD8) or Cytotoxic.

• B cells originate from the “Bursa”. Their major function is to produce antibodies in response to foreign proteins including bacteria, viruses, and tumor cells.
Bursa of Fabricus
B CELL CLONAL EXPANSION

1. B cells encounter and bind to antigen.

2. B cell c responds to antigen by proliferating.

3. Some B cells differentiate into long-lived memory cells.

4. Other B cells differentiate into plasma cells.

5. Plasma cells secrete antibodies into circulation.

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Function of the Immune System (Self / Non-self Discrimination)

• To protect from pathogens
  • Intracellular (e.g. viruses and some bacteria and parasites)
  • Extracellular (e.g. most bacteria, fungi and parasites)

• To eliminate modified or altered self
Hypersensitivity

There are four different responses of the immune system:

**Type I: Immediate hypersensitivity**
- onset within minutes of antigen challenge
- examples are allergies to molds, insect bites

**Type II: Cytotoxic hypersensitivity**
- onset within minutes or a few hours of antigen challenge
- examples are adult hemolytic anemia and drug allergies

**Type III: Immune complex-mediated hypersensitivity**
- onset usually within 2 - 6 hours
- examples include serum sickness and systemic lupus erythematosus

**Type IV: Delayed hypersensitivity**
- inflammation by 2- 6 hours; peaks by 24 - 48 hours
- examples include poison ivy and chronic asthma