Cells and Tissues of the Immune System

HST.035 Spring 2003
The origin of immunology is usually attributed to Edward Jenner, who in 1796 discovered that cowpox induced protection against human smallpox. Jenner called his procedure vaccination (after vaccinia, the alternative name for smallpox). Disease prevention through vaccinations have been of the triumphs of modern medicine.
## Effectiveness of Vaccinations

<table>
<thead>
<tr>
<th>Disease</th>
<th>Max. No. (year)</th>
<th>No. in 1999</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>206,939 (1921)</td>
<td>1</td>
<td>~100</td>
</tr>
<tr>
<td>Measles</td>
<td>894,134 (1941)</td>
<td>60</td>
<td>~100</td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209 (1968)</td>
<td>352</td>
<td>99.8</td>
</tr>
<tr>
<td>Polio</td>
<td>21,269 (1952)</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Rubella</td>
<td>57,686 (1969)</td>
<td>238</td>
<td>99.6</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>26,611 (1985)</td>
<td>6,495</td>
<td>75.6</td>
</tr>
</tbody>
</table>

The origin of immunology is usually attributed to Edward Jenner, who in 1796 discovered that cowpox induced protection against human smallpox. Jenner called his procedure vaccination (after vaccinia, the alternative name for smallpox). Disease prevention through vaccinations have been of the triumphs of modern medicine.
When Jenner introduced vaccination he knew nothing of the infectious agents that cause disease: it was not until late in the 19th century that Robert Koch proved that infectious diseases are caused by microorganisms, each one responsible for a particular disease, or pathology. We now recognize four broad categories of disease-causing microorganisms, or pathogens: these are viruses, bacteria, pathogenic fungi, and other relatively large and complex eukaryotic organisms collectively termed parasites.

http://www2.niaid.nih.gov/newsroom/focuson/tb02/optimism.htm
The discoveries of Koch and other great 19th century microbiologists stimulated the extension of Jenner's strategy of vaccination to other diseases. In the 1880s, Louis Pasteur devised a vaccine against cholera in chickens, and developed a rabies vaccine that proved a spectacular success upon its first trial in a boy bitten by a rabid dog. These practical triumphs led to a search for the mechanism of protection and to the development of the science of immunology.
Emil von Behring

In 1890, Emil von Behring and Shibasaburo Kitasato discovered that the serum of vaccinated individuals contained substances—which they called antibodies—that specifically bound to the relevant pathogen.
# Nobel Prizes for Immunological Research

<table>
<thead>
<tr>
<th>Year</th>
<th>Recipient</th>
<th>Country</th>
<th>Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>1901</td>
<td>Emil von Behring</td>
<td>Germany</td>
<td>Serum antitoxins</td>
</tr>
<tr>
<td>1905</td>
<td>Robert Koch</td>
<td>Germany</td>
<td>Cellular immunity to tuberculosis</td>
</tr>
<tr>
<td>1908</td>
<td>Elie Metchnikoff</td>
<td>Russia</td>
<td>Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity</td>
</tr>
<tr>
<td>1913</td>
<td>Paul Ehrlich</td>
<td>Germany</td>
<td></td>
</tr>
<tr>
<td>1913</td>
<td>Charles Richet</td>
<td>France</td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td>1919</td>
<td>Jules Bordet</td>
<td>Belgium</td>
<td>Complement-mediated bacteriolysis</td>
</tr>
<tr>
<td>1930</td>
<td>Karl Landsteiner</td>
<td>United States</td>
<td>Discovery of human blood groups</td>
</tr>
<tr>
<td>1951</td>
<td>Max Theiler</td>
<td>South Africa</td>
<td>Development of yellow fever vaccine</td>
</tr>
<tr>
<td>1957</td>
<td>Daniel Bovet</td>
<td>Switzerland</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>1960</td>
<td>F. Macfarlane Burnet</td>
<td>Australia</td>
<td>Discovery of acquired immunological tolerance</td>
</tr>
<tr>
<td>1960</td>
<td>Peter Medawar</td>
<td>Great Britain</td>
<td></td>
</tr>
<tr>
<td>1972</td>
<td>Rodney R. Porter</td>
<td>Great Britain</td>
<td>Chemical structure of antibodies</td>
</tr>
<tr>
<td>1972</td>
<td>Gerald M. Edelman</td>
<td>United States</td>
<td></td>
</tr>
<tr>
<td>1977</td>
<td>Rosalyn R. Yalow</td>
<td>United States</td>
<td>Development of radioimmunoassay</td>
</tr>
<tr>
<td>1980</td>
<td>George Snell</td>
<td>United States</td>
<td>Major histocompatibility complex</td>
</tr>
<tr>
<td>1980</td>
<td>Jean Daussct</td>
<td>France</td>
<td></td>
</tr>
<tr>
<td>1980</td>
<td>Baruj Benacerraf</td>
<td>United States</td>
<td></td>
</tr>
<tr>
<td>1984</td>
<td>Cesar Milstein</td>
<td>Great Britain</td>
<td>Monoclonal antibody</td>
</tr>
<tr>
<td>1984</td>
<td>Georges E. Köhler</td>
<td>Germany</td>
<td></td>
</tr>
<tr>
<td>1984</td>
<td>Niels K. Jerne</td>
<td>Denmark</td>
<td>Immune regulatory theories</td>
</tr>
<tr>
<td>1987</td>
<td>Susumu Tonegawa</td>
<td>Japan</td>
<td>Gene rearrangement in antibody production</td>
</tr>
<tr>
<td>1991</td>
<td>E. Donnall Thomas</td>
<td>United States</td>
<td>Transplantation immunology</td>
</tr>
<tr>
<td>1991</td>
<td>Joseph Murray</td>
<td>United States</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>Peter C. Doherty</td>
<td>Australia</td>
<td>Role of major histocompatibility complex in antigen recognition by T cells</td>
</tr>
<tr>
<td>1996</td>
<td>Rolf M. Zinkernagel</td>
<td>Switzerland</td>
<td></td>
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Physiological function of the immune system is to prevent infections and to eradicate infections that have escaped prevention.
A specific immune response, such as the production of antibodies against a particular pathogen, is known as an adaptive immune response, because it occurs during the lifetime of an individual as an adaptation to infection with that pathogen. In many cases, an adaptive immune response confers lifelong protective immunity to reinfection with the same pathogen. This distinguishes such responses from innate immunity, which is immediately available to combat a wide range of pathogens without requiring prior exposure.
How is it done?

1. Prevent Entry of Microbes
How is it done?

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Numerous bacteria are present on many epithelial surfaces, but "infections" are rare.
How is it done?

2. Search and Destroy Intruders by Phagocytosis

1. Bacterium becomes attached to membrane evaginations called pseudopodia

2. Bacterium is ingested, forming phagosome

3. Phagosome fuses with lysosome

4. Lysosomal enzymes digest captured material

5. Digestion products are released from cell
Professional Phagocytes: 
*Macrophages and Neutrophils*

Neutrophils, also known as polymorphonuclear leukocytes or PMNs, are the most abundant leukocytes in blood, and the first cell type to respond to most infections.

Monocytes are less abundant than neutrophils in the blood, and differentiate into macrophages in the tissue. Unlike neutrophils which survive only a few hours, macrophages can live for long periods of time in the tissue.
Components of the Mononuclear Phagocytic System

- Peripheral Blood Monocyte
- Tissue Macrophage
Phagocytosis in Action
How is it done?

3. The Natural Killer (NK) Cells

• Histologically, just a lymphocyte (!) with cytoplasmic granules containing pore-forming proteins such as perforin, as well as other proteins that induce target cell apoptosis.

• NK cells respond to intracellular microbes by killing infected cells and by producing the macrophage-activating cytokine, interferon-\(\gamma\) (IFN-\(\gamma\)).

• In turn, macrophages that have encountered a microbe can activated NK cells by the production of interleukin-12 (IL-12).

• NK cells are prevented from destroying host cells by the expression of “killer inhibitory receptors” that are specific for the host class I MHC molecules.
How is it done?

4. The Complement System

- The complement system is a collection of circulating and membrane-associated proteins that lead to an inflammatory and lytic response against microbes.

- In the **alternative pathway** the system is triggered directly by the microbes because of the absence of host regulatory proteins on the microbial surface.

- In the **classical pathway** the system is triggered after antibody bindings to microbes.

- In the **lectin pathway** the system is triggered by binding of mannose-binding lectin to terminal mannose residues on the bacterial surface glycoproteins.
How is it done?

5. The Adaptive Immune System
Cells of Adaptive Immunity:

1. Antigen-Presenting Cells (APCs)

- All potential portal of entry for microbes, as well as most other tissues, contain specialized cells such as *dendritic cells* for antigen processing and MHC-II presentation.

- Dendritic cells have different names according to their location, and are generally characterized by their long branching cytoplasmic processes.

Cells of Adaptive Immunity:  
2. Lymphocytes

- In spite of their diverse and complex functional roles, lymphocytes are simple round cells measuring ~8 to ~15µm in diameter and containing relatively little cytoplasm.

- Mature antibody-producing B-cells or Plasma cells have a characteristic appearance because of their prominent Golgi and RER.

- Otherwise, sub-classification of lymphocytes is difficult to nearly impossible by routine staining, but is easily done by immunohistochemical staining.

- Although isolated lymphocytes are pervasive, organized populations are present in peripheral lymphoid organs: lymph nodes, spleen and the Mucosa-Associated Lymphoid Tissue (MALT).
Peripheral Lymphoid Organs

- The peripheral lymphoid organs are organized to concentrate antigens, antigen-presenting cells, and lymphocytes in a way that optimizes interaction among these cells and the development of adaptive immunity.

- The primary lymphoid organs are:
  - Lymph nodes (numerous and scattered throughout the lymphatic system)
  - Spleen (single abdominal organ)
  - Mucosa-Associated Lymphoid Tissue (diffusely present in the internal and external lining mucosa)
Lymph Nodes

• Encapsulated, small aggregates (typically 0.5-1 cm³) of lymphoid tissues located along the lymphatic channels.

• Lymph nodes screen the entire collection of fluids and fluid-borne particles returning or entering from tissues into the central circulatory system.

(Why do surgeons often take out lymph nodes when they resect cancerous tissues?)
Lymph Nodes

- Lymphoid Follicle (B Cell Zone)
- Germinal Center
- Medullary Sinus
- Medullary Cord
- Efferent Lymphatic Vessel
- Afferent Lymphatic Vessel
- Parafollicular Cortex (T Cell Zone)
- Capsule
- Trabecula
- Artery
- Vein
B and T Cell Zones in the Lymph Node
The Lymph Node
The Lymph Node

by Immunohistochemistry

B cells (CD20)       T cells (CD3)
The Spleen

• A large abdominal organ that serves the same function for blood as lymph nodes do for the lymph.

• The spleen also contains abundant macrophages that actively ingest and destroy blood-borne organisms and particles.
MALT

*No so insignificant!*

- The intestines contain 70% of immunoglobulin-producing cells in the human body.

- There is 1 intraepithelial lymphocyte (IEL) for every 10-20 lining epithelial cells.

- Pharyngeal tonsils, nasal adenoids and ileal Peyer patches are prominent mucosal lymphoid tissues.
MALT in the Normal Terminal Ileum
Supplementary Slides
Review of Lung Structure