Foundations of Public Health
Immunology

Anatomy & Physiology of the Lymphoid System

Objectives

- Anatomy & Physiology
  - Identify primary vs. secondary lymphoid organs
  - Identify the function of each organ
  - Identify structures in each organ & location of cell types
  - Describe the lymphatic system & flow of lymph through the nodes, body

Lymphoid System

- Cells: lymphocytes, macrophages, antigen presenting cells (APC), epithelial cells
- Diffuse aggregates of cells: Mucosal associated lymphoid tissue (MALT)
- Encapsulated organs: Primary & secondary
Lymphatic System

- Network of vessels, tissues, organs, and cells
- Lymphatic system carries lymph in only one direction - to the heart
- Lymph carries products of immune responses, as well as cellular waste byproducts

Lymph

- A watery fluid that runs throughout this network
- Lymph contains higher concentrations of white blood cells in the bone marrow, spleen & thymus
- In the intestine, lymph contains fats absorbed during digestion
- In the limbs, more proteins

Lymphedema

- Condition of localized fluid retention
  - Properly functioning lymphatic system is integral to prevent fluid accumulation
  - In US, frequently seen after surgery, cancer treatment, or lymph node dissection resulting in damage to the lymphatic system
  - Often associated with treatment of breast cancer
  - Many patients may not develop symptoms until months or years later
  - May also be associated with accidents or diseases that may impair lymphatic network
  - See parasitic disease of lymphatic filariasis later in this presentation (most common cause of lymphedema)
Primary Lymphoid Organs

- Thymus – T cells
- Bone marrow – B cells
- Cells differentiated from pluripotent hemopoietic stem cells into functional cells
- *Immune responses do not occur here*

The Immune System

**Primary Lymphoid Organs**
- Bone Marrow
- Thymus

**Secondary Lymphoid Organs**
- Spleen
- Lymph Nodes
- Peyer’s Patches
- Tonsils

Bone Marrow

- **Produces hematopoietic cells** – all cells of the immune system are derived from stem cells
- In embryo, B cells differentiate in the fetal liver
  - After birth, this function moves to the bone marrow
- Necessary for the production of B lymphocytes
- **Both negative & positive selection**
- B cells committed to one antigen-binding specificity (1 cell – Ab rule) when synthesizes surfaces immunoglobulin
Thymus

- A gland located under the breastbone, it shrinks with age reducing immunity (elderly have very little thymic function)
- Progenitor cells migrate from bone marrow & then differentiate into T cells here
- T cells mature and learn to be self-tolerant
- Complete their maturation as migrate from cortex to medulla
- Thymocytes which can recognize and respond to self Ag as foreign are eliminated (negative selection), which prevents autoimmunity

Cortex and Medulla of the Thymus

Source: http://wenliang.myweb.uga.edu/mystudy/immunology/ScienceOfImmunology/Tissuesandorgansofimmunesystems.html

Thymus

- Selection for thymocytes with affinity for self MHC recognition (positive selection)
- These T cells can see antigens complexed with self cells (i.e. infected host cells)
- Those not selected die by apoptosis – programmed suicide
- No lymphatic drainage
B cells and T cells migrate to the spleen & lymph nodes

![Diagram](http://www.vrp.com/art/755.asp)

**Secondary Lymphoid Organs**

- Two Main Functions:
  - To *trap & concentrate* foreign substances
  - Primary sites for production of *antibodies* & induction of ag-specific *T cells*
Secondary Lymphoid Organs

- Lymph nodes filter regional lymph flow
- Spleen filters blood
- MALT protects mucosal surfaces
- These encapsulated organs & nonencapsulated tissues (MALT) are where immune responses take place
- Protect different areas of the body

Spleen

- Largest secondary lymphoid organ
- Filters blood to remove Ag & old RBC
- Architecture: encapsulated, red & white pulp (periarteriolar lymphoid sheath – PALS)
- White pulp:
  - PALS (T cells) with B cells embedded in follicles
  - Marginal zone with APCs (macrophages & dendritic cells)
- Red pulp: removal of effete RBC; phagocytes

Source: http://www2.nau.edu/~fpm/immunology/spleen.html
Spleen - Exterior

- Renal surface
- Gastric surface
- Splenic artery
- Hilus
- Splenic vein

Lymph Nodes

- Clusters of nodes at strategic points
- Filter lymph; subcutaneous, visceral & mucosal

- Supraclavical lymph nodes are shown in green.
Lymph Nodes

- Anatomy designed for close interaction
  - Cortex has follicles & germinal centers, location of B cells
  - Paracortex contains T cells and antigen presenting cells
  - Medulla has plasma cells & macrophages
- Blood supply; HEV (high endothelial venues) allow cell traffic
- HEV activation, cuboidal endothelium, "addressins" direct l'cytes to specific tissues

Lymph Nodes

Two directions of lymphatic flow:
- Afferent (contains Ag) lymphatics
  - into node, contains "bad" stuff
- Efferent (contains T cells & Ab) lymphatics
  - out of node, contains "good" stuff to circulate
**Lymph Node**

Blood in Capillary Fluid from post-capillary venule → Interstitial Fluid O2, nutrients Ag in tissues → Lymph Collected in Lymphatics

<table>
<thead>
<tr>
<th>Blood Arteries &amp; Arterioles</th>
<th>T lymphocytes</th>
<th>Lymph Node</th>
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<tbody>
<tr>
<td>Heart</td>
<td>L Subclavian Vein to Blood</td>
<td>Filtration Removal of Ag Release of Abs and cells</td>
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**Lymphatic System & Flow**

Lymphatic Flow → Lymphatic System
Lymph Nodes & Public Health

- **Black Death**
- In 1346, a bubonic plague pandemic killed 20-30 million people (1/3 of the population)
- Caused by G-Bacteria, *Yersinia pestis*, & transmitted by fleas
- Lymph nodes, especially those in the groin, become painful and swollen
- The inflamed nodes, called *buboes* (where the disease gets its name), swell with pus, turn black & split open
- The infection is rampant in the lymphatic system, and quickly spreads throughout the body, and death soon follows
- Early diagnosis can prevent the disease, with antibiotic treatment

Plague & Public Health

- **Ancient disease** that has caused 3 major pandemics (in the 6th, 14th, and 19th centuries), unlikely that it will ever be eradicated
- Each year, 1000 to 3000 cases occur worldwide
- Recent identification of multi-drug resistant strains (& its bioweapon potential) have kept plague as a serious threat to public health

Lymphatic Filariasis

- Parasitic filarial worms *Wuchereria bancrofti* and *Brugia malayi* cause Lymphatic Filariasis
- Infects over 120 million people in 80 countries
- Severe cases called **ELEPHANTIASIS**
- Worms live in lymphatic system and cause repeated attacks of inflammation
  - Lymph vessels become dilated, thickened, fibrosed
  - Fluid collects and causes swelling in the arms, legs, breasts of females, scrotum of males
  - Constant inflammation causes permanent damage to lymphatics
- Lymphatic damage leads also to thickened skin & bacterial or fungal superinfections
**Epstein-Barr Virus: Infectious Mono**

- **EBV** is a herpesvirus & one of the most common human viruses
- **Up to 95% of adults** in the US have been infected (usually as children or adolescents)
- Symptoms of infectious mono include fever, sore throat, and swollen lymph glands & usually resolve within 1-2 months.
- **Virus remains dormant in the body for life**
- No antiviral drugs or vaccines are available

**Mucosal Lymphoid Tissue: MALT**

- Non-encapsulated tissue in mucosa of respiratory, gastrointestinal & genitourinary tract; makes up > 50% of the lymphoid tissue
- Protect mucosal surfaces; specialized functions (secretory IgA)
- Nodules containing germinal centers
- Mucosal lymphocytes; LPL & IEL (T memory cells), PC
- Local circulation of cells; homing molecules
- Tonsils, Peyer’s patches, etc.

**Stress & Immunity**

- **Stress can have a significant impact on immune response**
- **Short-term stressors boost** immune system
  - “Fight of flight” response prompts immune system to ready itself for possible attack (infectious)
  - Examples: public speaking or mental math challenges in a lab, or those in the real world such as academic tests
- **Chronic stressors suppress** immune system
  - Shifts immune system from adaptive changes of “fight or flight” to negative changes at both cellular level & overall function
  - Decreases nearly all measures of immune system function
  - Examples: injury leading to permanent disability, caring for spouse with dementia, or refugee forced from native country by war
  - Elderly or those already ill more susceptible to stress-related changes
In Summary

• Primary vs. secondary lymphoid organs
• Know specific anatomic structures of the spleen, lymph node, and thymus
• Understand the function of each organ
• Recognize the close relationship between structure & function necessary of enhancement of immune response

Self-Test Questions: Anatomy

• Name the 2 primary lymphoid organs. How do they function?
• Name the secondary lymphoid organs. How do they function?
• Where are T cells located in the spleen?
• Where are B cells located in the lymph nodes?
• What is an afferent lymph?