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**: Mucousal 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

Fig. 2. T cell development occurs primarily in the thymus gland, where immature cells turn into either a killer cell, a helper cell or a suppressor cell.

Thymic Lobule
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
Spleen

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

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

- White pulp
- Periarterial lymphatic sheath (cross-section)
- Follicle
- Splenic sinuses
- Splenic cords (of red pulp)
- Capsule
- Trabecular vein
- Pulp vein
- Splenic cords
- Trabecular artery
- Central artery
- Marginal zone
- Periarterial lymphatic sheath (longitudinal section)
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
Lymph Node
## Production of Lymph

<table>
<thead>
<tr>
<th>Blood in Capillary Fluid from post-capillary venule</th>
<th>Interstitial Fluid $O_2$, nutrients Ag in tissues</th>
<th>Lymph Collected in Lymphatics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Arteries &amp; Arterioles</td>
<td><img src="#" alt="Arrows" /> T lymphocytes <img src="#" alt="Arrows" /></td>
<td>Lymph Node Filtration Removal of Ag Release of Abs and cells</td>
</tr>
<tr>
<td>Heart</td>
<td><img src="#" alt="Arrows" /> L Subclavian Vein to Blood <img src="#" alt="Arrows" /></td>
<td>Lymph into Thoracic Duct</td>
</tr>
</tbody>
</table>
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
Plaque & 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

Fear of an epidemic: Plague outbreak in India reported in Newsweek, 1996
**Lymphatic Filariasis**

- Parasitic filarial worms *Wuchereria bancrofti* and *Brugia malayi* cause Lymphatic Filariasis
- Infected 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

Filarial worms *W. bancrofti* (shown here) are found in tropical & subtropical countries.

Orphan disease – elephantiasis cased by LF.
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?