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**

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

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

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

Source: http://www2.nau.edu/~fpm/immunology/spleen.html
Lymph Nodes

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

Supravcavicular 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 f'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

Production of Lymph

| Blood in Capillary Fluid from post-capillary venule | Interstitial Fluid O2, nutrients Ag in tissues | Lymph Collected in Lymphatics |
| Blood Arteries & Arterioles | T lymphocytes | Lymph Node Filtration Removal of Ag Release of Abs and cells |
| Heart | L Subclavian Vein to Blood | Lymph into Thoracic Duct |

Lymphatic System & Flow

Lymphatic 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 plaque 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 or 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?