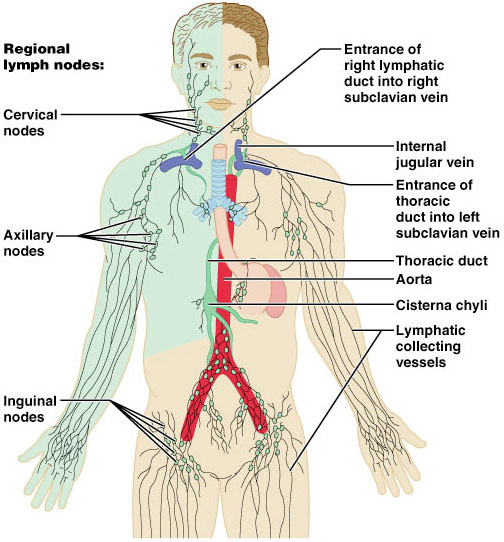
**The Lymphatic System**

**Dr. Gary Mumaugh**

**Lymphatic System: Overview**

* Consists of two semi-independent parts
  + A meandering network of lymphatic vessels
  + Lymphoid tissues and organs scattered throughout the body
* Returns interstitial fluid and leaked plasma proteins back to the blood
* Lymph – interstitial fluid once it has entered lymphatic vessels



**Where is the lymph going?**

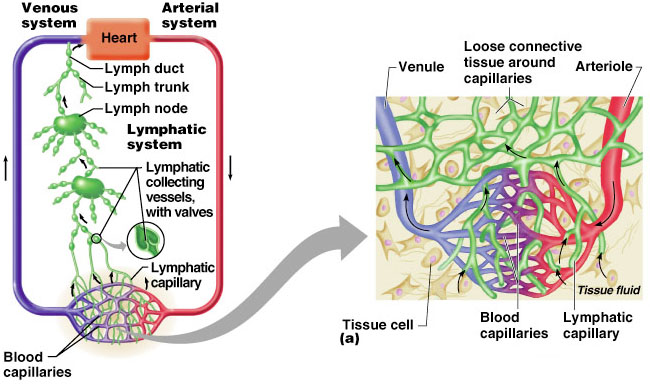
* As blood circulates through the body, nutrients, wastes and gases are exchanged between the blood and interstitial fluid
  + Interstitial fluid – extracellular fluid derived from blood
* The pressure of the capillary beds force fluid out of the blood
* The fluid that remains behind in the tissue spaces becomes interstitial fluid
  + Up to 3 liters per day
  + Once interstitial fluid enters the lymphatic's, it is called lymph

**Lymphatic Vessels**

* A one-way system in which lymph flows toward the heart
* Lymph vessels include:
  + Microscopic, permeable, blind-ended capillaries
  + Lymphatic collecting vessels
  + Trunks and ducts

**Lymphatic Capillaries**

* Similar to blood capillaries, with modifications
  + Remarkably permeable
  + Loosely joined endothelial minivalves
  + The minivalves function as one-way gates
* During inflammation, lymph capillaries can absorb:
  + Cell debris
  + Pathogens
  + Cancer cells
* Cells in the lymph nodes:
  + Cleanse and “examine” this debris
* Lacteals – specialized lymph capillaries present in intestinal mucosa
  + Absorb digested fat and deliver chyle to the blood

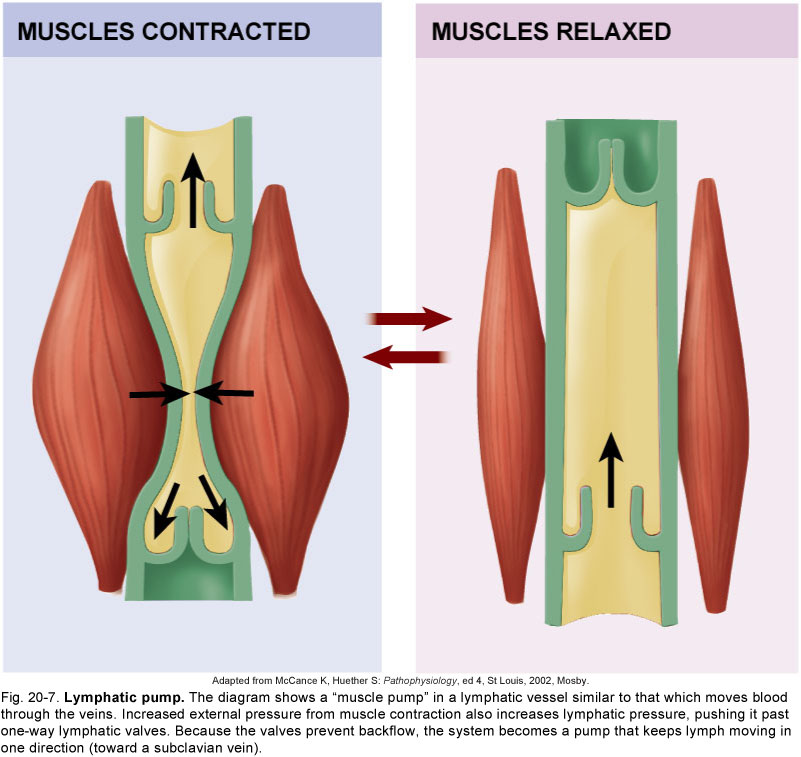
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**Lymphatic Trunks**

* Lymphatic trunks are formed by the union of the largest collecting ducts
* Lymph is delivered into one of two large trunks
  + Right lymphatic duct – drains the right upper arm and the right side of the head and thorax
  + Thoracic duct – arises from the cisterna chyli and drains the rest of the body

**Lymph Transport**

* The lymphatic system lacks an organ that acts as a pump
* Vessels are low-pressure conduits
* Uses the same methods as veins to propel lymph
  + Pulsations of nearby arteries
  + Contractions of smooth muscle in the walls of the lymphatics
  + Respiratory movements



**Lymphoid Cells**

* Lymphocytes are the main cells involved in the immune response
* Infectious microorganisms manage to penetrate the body are encountered by a fight from the phagocytes and the lymphocytes
* The phagoctyic macrophages are crucial in protection

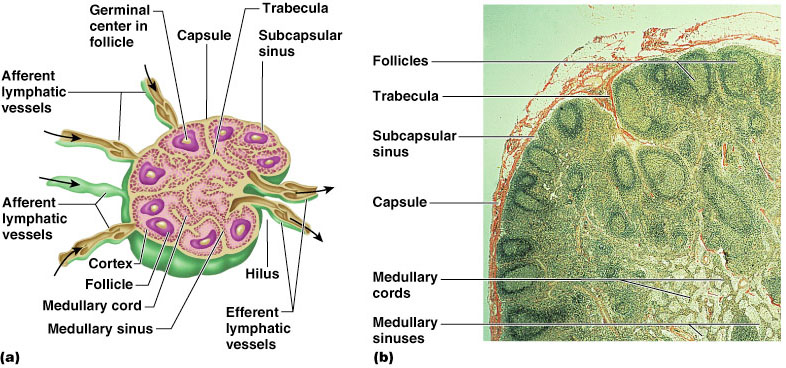
**Lymphoid Tissue**

* Lymphoid (lymphatic tissue) is an important component of the immune system, mainly because it
  + Houses and provides a proliferation site for phagocytes
  + Furnishes a great surveillance point for lymphocytes and macrophages

**Lymph Nodes**

* Lymph nodes are the principal lymphoid organs of the body
* Nodes are imbedded in connective tissue and clustered along lymphatic vessels
* Aggregations of these nodes occur near the body surface in inguinal, axillary, and cervical regions of the body
* Their two basic functions are:
  + Filtration – macrophages destroy microorganisms and debris
  + Immune system activation – monitor for antigens and mount an attack against them

**Structure of a Lymph Node**

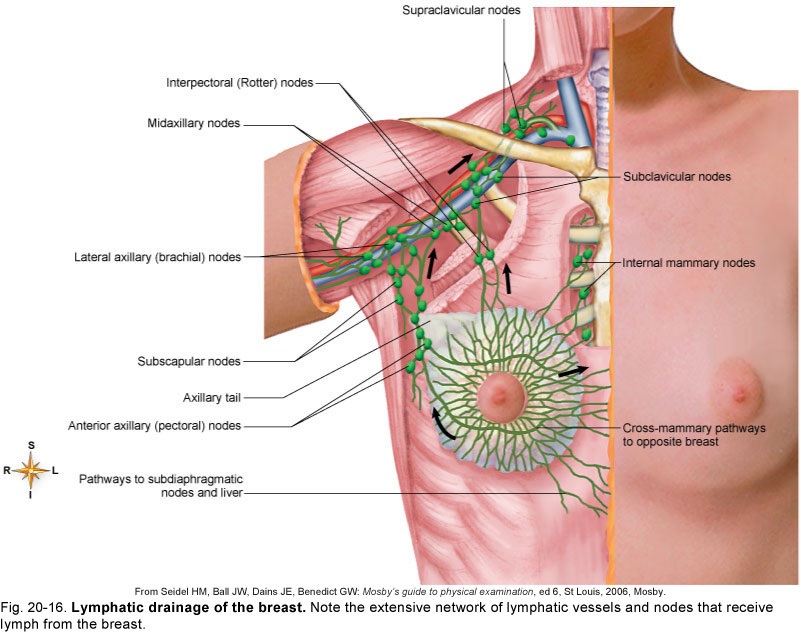
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**Circulation in the Lymph Nodes**

* There are fewer efferent vessels draining the node then afferent vessels feeding it
* Because there are fewer efferent vessels, lymph stagnates and pools somewhat in the node
* This allows lymphocytes and macrophages time to carry out their protective functions
* Nodes often become secondary cancer sites in metastasizing cancers

**Other Lymphoid Organs**

* The spleen, thymus gland, and tonsils
* Peyer’s patches in the small intestines
* Appendix in the large intestine
* Lymphoid tiisue in the walls of the bronchi
* Lymphatic tissue scattered in connective tissue

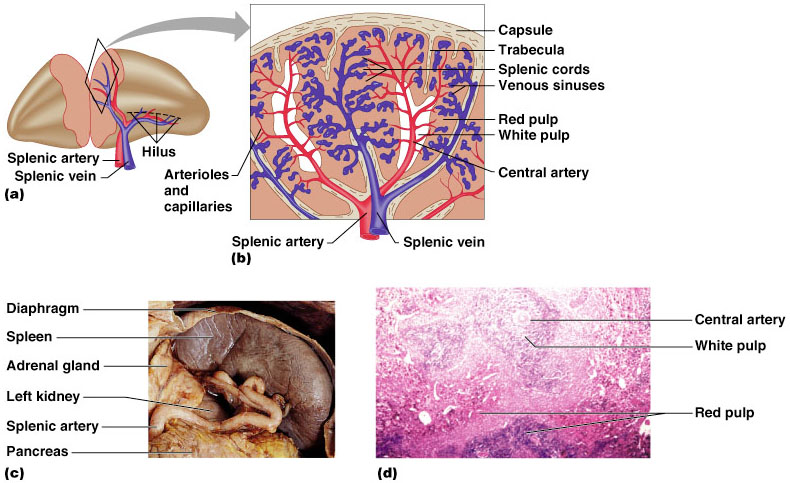
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**Spleen**

* Largest lymphoid organ, located on the left side of the abdominal cavity beneath the diaphragm
* It extends to curl around the anterior aspect of the stomach
* Functions
  + Site of lymphocyte proliferation
  + Immune surveillance and response
  + Contains macrophages
  + Cleanses the blood
  + Produces antibodies
  + Stores platelets
    - Destroys them when they are no longer useful

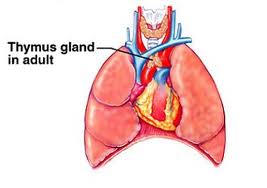
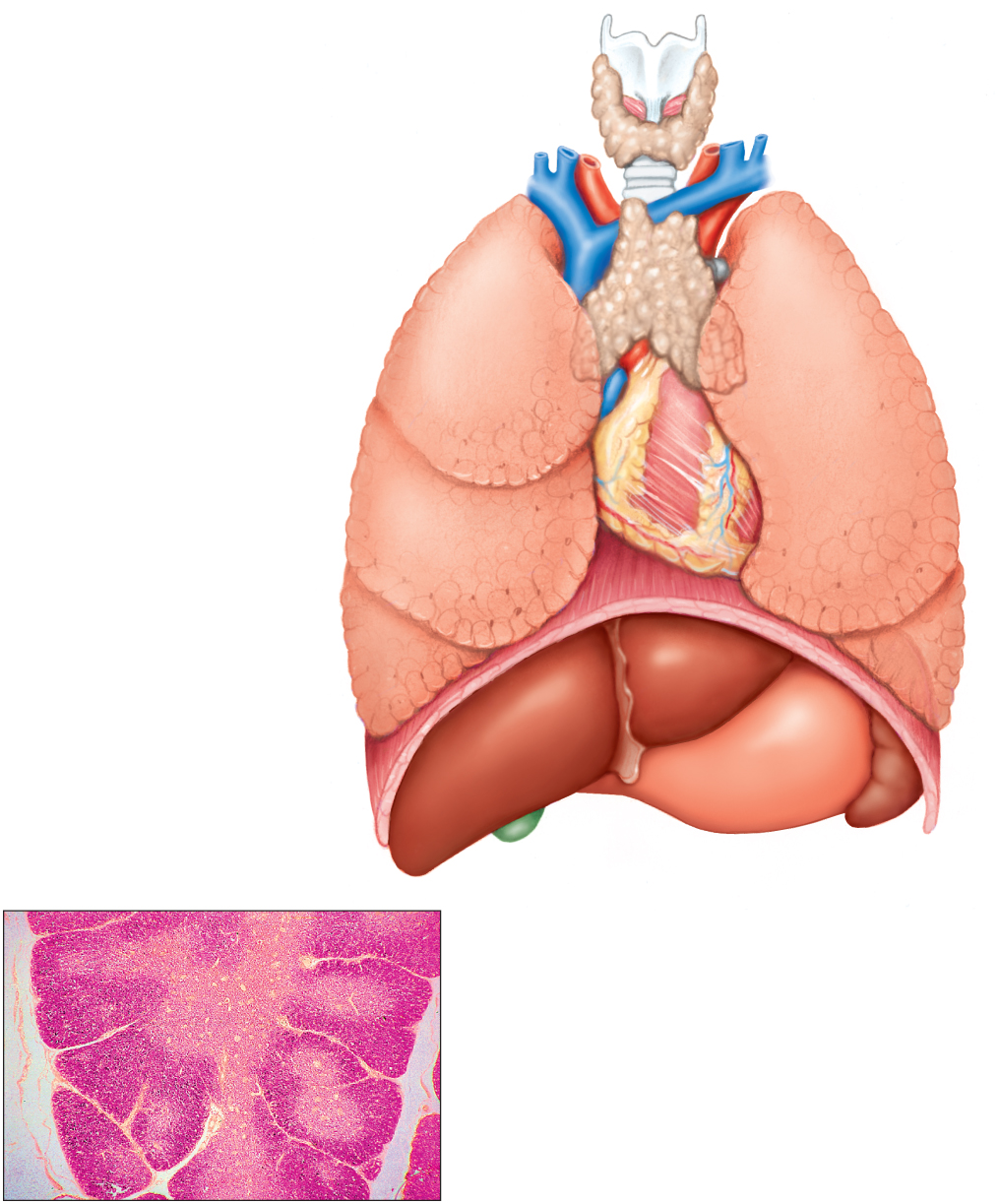
**Spleen Trauma**

* Because the spleen capsule is very thin, a direct blow or infection may cause it to rupture. This rupture spills blood into the peritoneal cavity
* In the past, a splenectomy was performed
* Now, the tendency is to let the spleen regenerate
* If the spleen is removed, the liver and bone marrow will attempt to take over most of it’s functions

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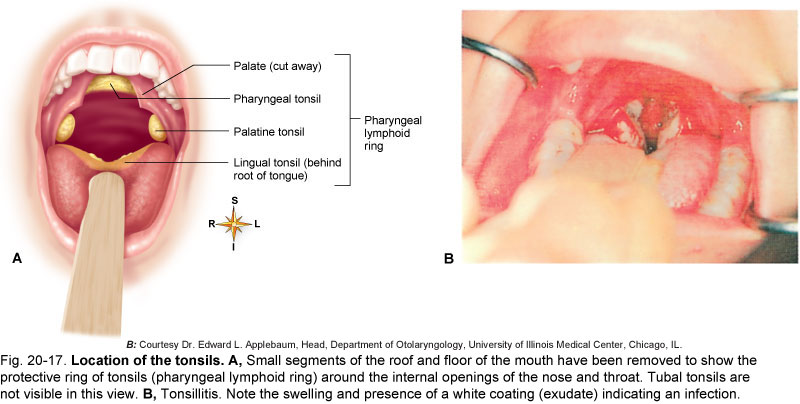
**Thymus**

* A organ that secrets hormones that cause T lymphocytes to become immunocompetent
* The size of the thymus varies with age
  + In infants, it is found in the inferior neck and extends into the mediastinum where it partially overlies the heart
  + It increases in size and is most active during childhood
  + It stops growing during adolescence and then gradually atrophies

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**Tonsils**

* Simplest lymphoid organs; form a ring of lymphatic tissue around the pharynx
* Location of the tonsils
  + Palatine tonsils – either side of the posterior end of the oral cavity
  + Lingual tonsils – lie at the base of the tongue
  + Pharyngeal tonsil – posterior wall of the nasopharynx
  + Tubal tonsils – surround the openings of the auditory tubes into the pharynx



**The Immune System: Innate and Adaptive Body Defenses**

Dr. Gary Mumaugh

**Immunity: Two Intrinsic Defense Systems**

* Nonspecific system responds quickly and consists of:
  + First line of defense – intact skin and mucosae prevent entry of

microorganisms

* + Second line of defense – antimicrobial proteins, phagocytes, and other cells
    - Inhibit spread of invaders throughout the body
    - Inflammation is its hallmark and most important mechanism
* Immunity: Two Intrinsic Defense Systems
* Specific defense system
  + Third line of defense – mounts attack against particular foreign substances
    - Takes longer to react than the innate system
    - Works in conjunction with the innate system

**Surface Barriers**

* Skin, mucous membranes, and their secretions make up the first line of defense
* Keratin in the skin:
  + Presents a formidable physical barrier to most microorganisms
  + Is resistant to weak acids and bases, bacterial enzymes, and toxins
* Mucosa provide similar mechanical barriers

**Epithelial Chemical Barriers**

* Epithelial membranes produce protective chemicals that destroy microorganisms
  + Skin acidity (pH of 3 to 5) inhibits bacterial growth
  + Sebum contains chemicals toxic to bacteria
  + Stomach mucosae secrete concentrated HCl and protein-digesting enzymes
  + Saliva and lacrimal fluid contain lysozyme
  + Mucus traps microorganisms that enter the digestive and respiratory systems

**Respiratory Tract Mucosae**

* Mucus-coated hairs in the nose trap inhaled particles
* Mucosa of the upper respiratory tract is ciliated
  + Cilia sweep dust- and bacteria-laden mucus away from lower respiratory passages

**Internal Defenses: Cells and Chemicals**

* The body uses nonspecific cellular and chemical devices to protect itself
  + Phagocytes and natural killer (NK) cells
  + Antimicrobial proteins in blood and tissue fluid
  + Inflammatory response enlists macrophages, mast cells, WBCs, and chemicals
* Harmful substances are identified by surface carbohydrates unique to infectious organisms

**Phagocytes**

* Macrophages are the chief phagocytic cells
* Free macrophages wander throughout a region in search of cellular debris
* Neutrophils become phagocytic when encountering infectious material
* Eosinophils are weakly phagocytic against parasitic worms
* Microbes adhere to the phagocyte

**Natural Killer (NK) Cells**

* Cells that can lyse and kill cancer cells and virus-infected cells
* Natural killer cells:
  + Are a small, distinct group of large granular lymphocytes
  + React nonspecifically and eliminate cancerous and virus-infected cells
  + Kill their target cells by releasing perforins and other cytolytic chemicals
  + They “police” the blood and lymph and are the “pits bulls” of the defense system

**Inflammation: Tissue Response to Injury**

* The inflammatory response is triggered whenever body tissues are injured
  + Prevents the spread of damaging agents to nearby tissues
  + Disposes of cell debris and pathogens
  + Sets the stage for repair processes
* The four cardinal signs of acute inflammation are redness, heat, swelling, and pain

**Antimicrobial Proteins**

* Enhance the innate defenses by:
  + Attacking microorganisms directly
  + Hindering microorganisms’ ability to reproduce
* The most important antimicrobial proteins are:
  + Interferon
    - blocks viral reproduction
  + Complement proteins
    - Amplifies all aspects of the inflammatory response
    - Kills bacteria and certain other cell types

**C-reactive Protein (CRP)**

* CRP is produced by the liver in response to inflammatory molecules
* CRP is a clinical marker used to assess for:
  + The presence of an acute infection
  + An inflammatory condition and its response to treatment
* Plays a surveillance role in targeting damaged cells for disposal

**Fever**

* Abnormally high body temperature in response to invading microorganisms
* The body’s thermostat is reset upwards in response to pyrogens, chemicals secreted by leukocytes and macrophages exposed to bacteria and other foreign substance
* High fevers are dangerous as they can denature enzymes
* Moderate fever can be beneficial, as it causes:
  + The liver and spleen to sequester iron and zinc (needed by microorganisms)
  + An increase in the metabolic rate, which speeds up tissue repair

**Specific Defenses**

* The adaptive immune system is a functional system that:
  + Recognizes specific foreign substances
  + Acts to immobilize, neutralize, or destroy foreign substances
  + Amplifies inflammatory response and activates complement

**Adaptive Immune Defenses**

* This is the third line of defense called immune response
* It is based on the ability thatto distinguish molecules that are part of the body (“self” from “non-self”)
* Antigens are molecules that can elicit an immune response
* The adaptive immune system is:
  + Specific
  + Systemic
  + Has memory

**Immunological Memory**

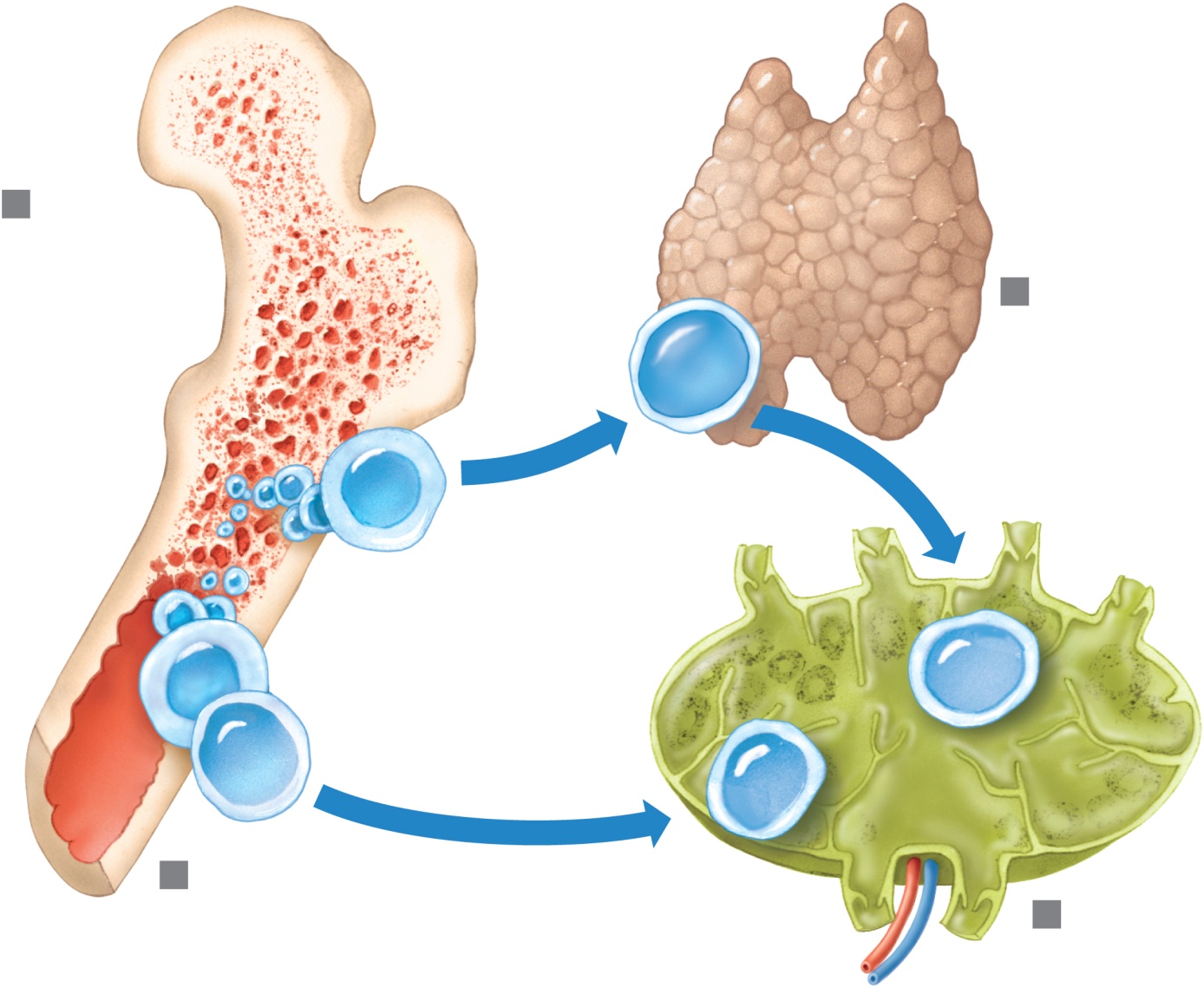
* Primary immune response – cellular differentiation and proliferation, which occurs on the first exposure to a specific antigen
  + Lag period: 3 to 6 days after antigen challenge
  + Peak levels of plasma antibody are achieved in 10 days
  + Antibody levels then decline
* Secondary immune response – re-exposure to the same antigen
  + Sensitized memory cells respond within hours
  + Antibody levels peak in 2 to 3 days at much higher levels than in the primary response
  + Antibodies bind with greater affinity, and their levels in the blood can remain high for weeks to months

**Cells of the Adaptive Immune System**

* Two types of lymphocytes
  + B lymphocytes – oversee humoral immunity
  + T lymphocytes – non-antibody-producing cells that constitute the cell-mediated arm of immunity

**Lymphocytes**

* Whether a lymphocyte matures into a B cell or a T cell depends on where in the body it becomes immunocompetent
  + B cells mature in the bone marrow
  + T cells mature in the thymus

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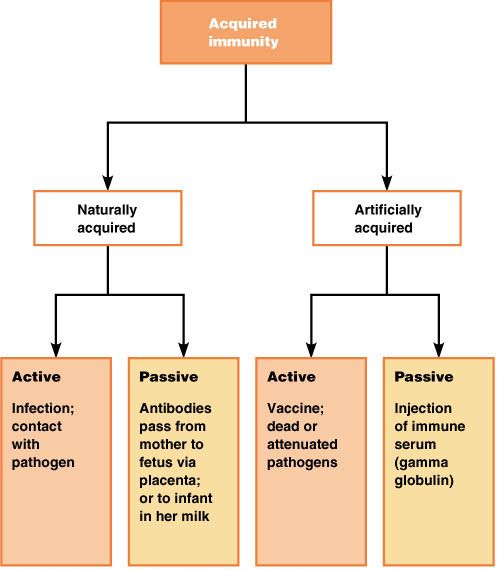
**Active Humoral Immunity**

* B cells encounter antigens and produce antibodies against them
  + Naturally acquired – response to a bacterial or viral infection
  + Artificially acquired – response to a vaccine of dead or attenuated pathogens
* Vaccines – spare us the symptoms of disease, and their weakened antigens provide antigenic determinants that are immunogenic and reactive

**Passive Humoral Immunity**

* Differs from active immunity in the antibody source and the degree of protection
* Naturally acquired – from the mother to her fetus via the placenta
* Artificially acquired – from the injection of serum, such as gamma globulin

**Types of Acquired Immunity**



**T Cell Summary**

* T cells are best suited for cell-to-cell interactions, and target:
  + Cells infected with viruses, bacteria, or intracellular parasites
  + Abnormal or cancerous cells
  + Cells of infused or transplanted foreign tissue
* Each T cell has unique roles to play in the immune response
* Each T cell is heavily involved in interactions with other immune cells and elements
* Without helper T cells, there would be no adaptive immune response
* The helper T cells direct and help complete the activation of other cells
* Their role is evident when they are destroyed in AIDS

**Organ Transplants**

* The four major types of grafts are:
  + Autografts – graft transplanted from one site on the body to another in the same person
  + Isografts – grafts between identical twins
  + Allografts – transplants between individuals that are not identical twins, but belong to same species
  + Xenografts – grafts taken from another animal species

**Prevention of Rejection**

* Prevention of tissue rejection is accomplished by using immunosuppressive drugs
* However, these drugs depress patient’s immune system so it cannot fight off foreign agents

**Immunodeficiencies**

* Congenital and acquired conditions in which the function or production of immune cells, phagocytes, or complement is abnormal

**Acquired Immunodeficiencies**

* Hodgkin’s disease – cancer of the lymph nodes leads to immunodeficiency by depressing lymph node cells
* Acquired immune deficiency syndrome (AIDS) – cripples the immune system by interfering with the activity of helper T (CD4) cells
  + Characterized by severe weight loss, night sweats, and swollen lymph nodes
  + Opportunistic infections occur

**AIDS**

* Caused by human immunodeficiency virus (HIV) transmitted via body fluids – blood, semen, and vaginal secretions
* HIV enters the body via:
  + Blood transfusions
  + Contaminated needles
  + Intimate sexual contact, including oral sex
* HIV:
  + Destroys TH cells
  + Depresses cell-mediated immunity
* HIV multiplies in lymph nodes throughout the asymptomatic period
* Symptoms appear in a few months to 10 years
* Treatments include:
  + Reverse transcriptase inhibitors (AZT)
  + Protease inhibitors (saquinavir and ritonavir)
  + New drugs currently being developed that block HIV’s entry to helper T cells

**Hypersensitivity**

* Immune responses that cause tissue damage
* Different types of hypersensitivity reactions are distinguished by:
  + Their time course
  + Whether antibodies or T cells are the principle immune elements involved
* Antibody-mediated allergies are immediate and subacute hypersensitivities
* The most important cell-mediated allergic condition is delayed hypersensitivity

**Anaphylaxis**

* Reactions include runny nose, itching reddened skin, and watery eyes
* If allergen is inhaled, asthmatic symptoms appear – constriction of bronchioles and restricted airflow
* If allergen is ingested, cramping, vomiting, or diarrhea occur
* Antihistamines counteract these effects

**Anaphylactic Shock**

* Response to allergen that directly enters the blood (e.g., insect bite, injection)
* Basophils and mast cells are enlisted throughout the body
* Systemic histamine releases may result in:
  + Constriction of bronchioles
  + Sudden vasodilation and fluid loss from the bloodstream
  + Hypotensive shock and death
* Treatment – epinephrine is the drug of choice

**Delayed Hypersensitivities**

* Onset is slow (1–3 days)
* Antihistamines are ineffective and corticosteroid drugs are used to provide relief
* Example: allergic contact dermatitis (e.g., poison ivy)
* Involved in protective reactions against viruses, bacteria, fungi, protozoa, cancer, and rejection of foreign grafts or transplants

**Lifespan Changes**

* The immune system declines early in life as the thymus gland shrinks
* There is a higher risk of infection
* Antibody response to antigens become slower
* Elderly may not be candidates for certain medical treatments that suppresses immunity

**Developmental Aspects**

* Immune system stem cells develop in the liver and spleen by the ninth week
* Later, bone marrow becomes the primary source of stem cells
* Lymphocyte development continues in the bone marrow and thymus system begins to wane
* The immune system is impaired by stress and depression
* With age, the immune system begins to wane

