Chapter 22

The Lymphatic System and Immunity

composed of
1. lymphatic vessels
2. specialized cells called lymphocytes
2. numerous lymphoid tissues and organs

function of the lymphatic system
1. production, maintenance and distribution of lymphocytes
   resist or overcome infection and disease
2. collection of fluid and solutes lost by the capillaries during filtration
3. distribution of hormones, nutrients, and waste products from there
tissues of origin to the general circulation

Lymphatic vessels

purpose
arterial side of the capillaries lose more fluid then venous end
reabsorbs

the excess (3 L/day) is picked up by the lymphatic vessels and
returned to the cardiovascular system

once fluid is in lymph vessel it is called lymph fluid

are one-way system flowing toward heart
contain valves to prevent backflow of fluid

lymphatic capillaries

are the start of the lymphatic network

originate as blind packets
larger diameter then capillaries
have thinner walls
are very permeable

1. endothelial cells are not joined by tight junctions
so edges overlap forming minivalves

2. filament attachments from the endothelial cells to
surrounding cells results in gaps being pulled open
during inflammation, lymph vessels form openings that permit large particles to enter -- even cancer cells

**lymphatic vessels**

formed in the embryo by budding from the veins

larger lymphatic vessels have three tunics which are similar to though of the veins

the tunics are thinner and there are more valves then in veins

**distribution of lymphatic vessels**

wide-spread originating from most capillary beds

absent in bone, teeth, bone marrow, and entire central nervous system

**nervous system**

lymphatic system replaced by cerebralspinal fluid

**plumbing of the lymphatic vessels**

lymphatic capillaries

collecting vessels

lymph node

collecting vessels

six lymphatic trunks

lumbar, intestinal, intercostals, bronchomediastinal, subclavian, jugular

two collecting ducts

1. thoracic duct or
2. right lymphatic duct

**thoracic duct**

drains most of the lymphic system

everything inferior to the diaphragm

left half superior to the diaphragm

empties into the left subclavian vein near where the jugular arises

**right lymphatic duct**

drains right side superior to diaphragm

empties into right subclavian vein
intestinal mucosa have specialized lymph vessels called lacteals that collect much of the digestive product

**movement of lymph fluid**

there is no pump

1. larger lymphatic vessels have smooth muscle cells that contract rhythmically

2. movement is by milking action of skeletal muscles there are valves to prevent backflow

3. lymphatic vessels are packaged closely with arteries pulsating action of arteries help move lymph fluid

4. respiratory pump

blockage of lymph flow results in localized edema exercise increases the rate of lymphatic return

**lymphocytes**

cells that help fight off infectious agents

**types of lymphocytes**

1. **T cells**
   thymus-dependent cells
   
   **cytotoxic T cells**
   attack foreign cells or cells infected by viruses are involved in the production of cell-mediated immunity or cellular immunity

   **helper T cells**
   stimulate the activation and function of T cells and B cells

   **suppressor T cells**
   inhibit the activation and function of both T and B cells

   the balance between suppressor and helper T cells establishes control and sensitivity of the immune response

2. **B cells**
   bone marrow-derived
when stimulated by the presence of a foreign substance (antigen) they differentiate into plasma cells

**plasma cells**
secret antibodies
when antibodies bind to its target antigen a chain of events occurs which destroys the antigen

plasma cells are responsible for antibody-mediated immunity or **humoral immunity**

3. **NK cells**
natural killer cells

will attack foreign cells and normal cells infected with viruses and cancer cells

**lymphoid tissue**
are reticular connective tissue (except thymus) dominated by lymphocytes
also contains numerous macrophages

part of immune system
located in ideal surveillance point for lymphocytes and macrophages to attack infectious materials

**types of lymphoid tissue**

1. **diffuse lymphatic tissue**
loosely scattered lymphocytes found in reticular tissue

is simplest in construction

located under most epithelial tissue
most prevalent in body passages that are open to the exterior such as digestive urinary respiratory and reproductive system is called **MALT**
mucosa-associated lymphoid tissue
are clusters of lymphoid nodules beneath the epithelial lining of the mucosa
removes infectious material introduced in food, during respiration, and reproduction
and produce memory lymphocytes for long-term immunity

diffuse lymphatic tissue may congregate in dense oval masses called **lymphatic nodule or follicles**
also has no fibrous capsule so boundaries are not distinct

central zone called germinal center
site of B cell division to produce plasma cells

located
beneath the epithelia lining the respiratory digestive and urinary tracts
includes
**Peyer’s patches**
nodules in the wall of the appendix

2. **lymphoid organs**
more organized
are an encapsulated collection of lymphoid nodules
include tonsils, lymph nodes, spleen, thymus

1. **tonsils**
form a ring of lymphocyte-rich tissue around the pharynx
are large nodules in the walls of the pharynx
contain crypt that trap bacteria and particulate matter
this allows immune cells with a memory to gain exposure to numerous infectious agents during childhood, producing long-term immunity

if it does not kill you, you will benefit as an adult
three types
lingual tonsil
at base of tongue

pharyngeal tonsil
adenoids- upper back of

palatine tonsil (paired)
back of mouth before pharynx

largest most often infected tonsillectomy

lymph nodes
small oval lymphoid organs from 1 to 25mm
are covered by a capsule of dense connective tissue
called lymph glands where nodes are largest and most numerous
neck, axillary and groin

lymph returning to the bloodstream is filtered through the lymph nodes

only lymphoid tissue that filters the lymph

two functions
1. where macrophages in the nodes remove microorganisms and other debris in the lymph

2. after macrophages destroys the infectious material they present the material to lymphocytes (antigen presentation) so have a role in activating immune system

thymus
important during infant years
in adults it atrophies to fibrous and fatty tissue

function
release two hormones

thymosin and thymopoitin

stimulate the maturation of T lymphocytes

has a blood-thymus barrier to protect immature lymphocytes from antigens

does not directly fight infectious agents

unlike other lymphatic tissue, is not made of reticular connective tissue is made of specialized epithelial cell called thymocytes

spleen

takes the largest collection of lymphoid tissue in the body

functions

1. lymphocyte proliferation and immune surveillance and response
2. extracts old and defective blood cells and platelets from blood
3. stores breakdown products of red blood cells
4. is site of RBC production in fetus
5. stores platelets
6. removes bacteria, foreign matter, toxins, etc. from blood

can live without liver will take over role of spleen

composition:

White pulp

white looking clusters that surround the arteries of the spleen

contains mostly lymphocytes suspended on reticular fibers
Nonspecific Body Defenses and Immunity

overview

two intrinsic defense systems of the body that deal with infectious agents such as bacteria and viruses

1. nonspecific or innate defense system
   is always ready and waiting

   composed of two barriers to infection
   1. first line of defense is a physical barrier
      an intact skin and mucosa
   2. second line of defense (when invaded)
      antimicrobial proteins
      phagocytes
      inflammation

2. specific or adaptive defense system
   also called the immune system

   mounts an attack against particular foreign substances

nonspecific body defenses

1. surface membrane barriers
   results from
   1. continuous unbroken epithelial lining of the skin surface, and linings of the digestive, respiratory, urinary, and reproductive tracts
2. acidity of skin
3. antibacterial sebum or skin section
4. acidity of vagina
5. stomach hydrochloric acid
6. digestive enzymes
7. lysozyme of saliva and lacrimal fluid
8. sticky mucous of digestive and respiratory passageways
9. fluids entering the body (saliva and semen) have iron chelators to deprive bacteria of iron for growth

2. phagocytes
   nonspecific cellular defenses
   perform janitorial and police services
   are the first line of cellular defense

major types are

1. macrophages
   derived from monocytes
   most tissues have resident or visiting macrophages
   destroy by phagocytosis
   engulfing and destroying in a lysosome
   bind to pathogen and weight for help
   release toxic chemicals
   tumor necrosis factor
   nitric oxide
   hydrogen peroxide
   can make you feel bad

2. microphages
   neutrophils and eosinophils
   destroy by phagocytosis

3. NK cells
   are rare type of large granular lymphocytes
   NK cells can spontaneously attach any cancer cell
   or virus infected cells (is not specific like other lymphocytes)
   do not destroy by phagocytosis
   they release cytolytic chemicals on the surface of prey opening up holes

2. antimicrobial proteins
   attach microorganisms directly or hinder their ability to reproduce

1. complement
group of 20 or more plasma proteins which form the complement system
aid nonspecific and specific defenses
named because it complements the action of antibodies

has three effects
1. cytolysis
   creates a pore in cell membranes
2. stimulates inflammation
   stimulates mast cells and basophils
to secrete inflammatory chemicals
3. attracts phagocytes
4. opsonization
   enhances phagocytes
   complement coats the pathogen and makes it an easy target

circulate in inactive form
activated occurs in two ways
1. classical pathway
   antibodies bound to the antigen activate the complement proteins C1,C2,C3,C4
tered complement fixation
   most rapid and effective

2. alternative pathway
   complement activated by presence of polysaccharide molecules on the surface of some microorganisms

2. interferon
   produced from
   1. cells that have been infected with a virus
   2. macrophages
   3. lymphocytes

effects
   1. stimulates neighboring cells to produce antiviral proteins
   2. attracts NK cells
   3. stimulates macrophage activity
3. **pyrogens**
   released from macrophages
   act at the hypothalamus to rise body temp *(fever)*

**effects of fever**
1. high temp impedes most bacterial growth
2. fever increases metabolic rate of tissue speeding up defensive actions and tissue repair

3. **inflammation**
   1. is triggered whenever body tissues are injured
   2. purpose
      1. prevent spread of damaging agents
      2. dispose of cell debris and pathogens
      3. set stage for repair

**first stage** vasodilatation and increased vascular permeability
1. inflammatory chemicals are released into extracellular fluid by injured tissue cells
   - **chemicals** are
     - histamine
     - kinins
     - prostaglandins
     - complement

   these are also release from
   - phagocytes
   - lymphocytes
   - mast cells

   these chemicals promote dilation of small vessels nearby
   thus **hyperemia** = redness and heat

   these chemicals promote increase permeability of capillaries
   thus fluid with clotting factors and antibodies seeps from blood
   permeability and dilation causes local edema
   = pressure on nerves = pain
   pain may be from bacterial toxin

**effect of edema**
1. dilutes harmful substances
2. increase amount of oxygen and nutrients for repair
3. allows clotting proteins in
clot will block bacterial spread

**second step** in inflammation is initiated by phagocytes
inflammatory chemicals act as chemotactic agents
attracting phagocytes and other wbs to the site
neutrophils are the first to combat the antigen
they are later replaced by macrophages

**specific body defenses: immunity**

immunity is provided by the coordinated action of T and B lymphocytes

**immune system**
system that recognizes specific foreign substances and
immobilizes
neutralizes
or destroys them

To parts to immunity
there are two separate but overlapping arms of immunity

1. **cellular or cell-mediated immunity**
   result of the action of the T-lymphocyte cells
   is our defense against abnormal cells in the tissues and
   pathogens found inside living cells
   1. directly kill abnormal cells by lysing them
   2. indirect role by releasing chemical that
      enhance inflammation
      activate other lymphocytes and
      macrophages

2. **humoral immunity** or antibody-mediated immunity
   defense against pathogens in body fluids
   provided by the antibodies produced by a type of B
   lymphocytes called plasma cells
   1. circulate freely in the blood
   2. bind to bacteria and their toxins and free viruses
   3. result in their
      1. temporary inactivation
2. mark for destruction by phagocytes or complement

**Properties of Immunity**
1. is antigen-specific
2. is systemic not restricted
3. has memory
4. tolerance

What does the immune system attack?

**A ntigens**

**What is an antigen**
any substances that can mobilize the immune system and provide an immune response
1. are the ultimate targets of all immune responses
2. are intruders
3. nonself (hopefully)

**Substances recognized as an antigen**
all foreign
1. proteins (strongest effect)
2. nucleic acids
3. some lipids
4. some large polysaccharides

**Haptens**
1. small molecules such as peptides nucleotides, and hormones that are not normally immunogenic
2. will bind to body’s own proteins and become immunogenic
3. this is basis for allergies

**Cell-mediated immunity**
key cell types involved
1. cytotoxic T cells
2. suppressor T cells
3. helper T cells
   - for every antigen there is a specific cytotoxic, suppress, and helper T cell
4. macrophages

**Steps involved in a cell mediated immune response**
**step 1: antigen presentation**

macrophage encounters foreign material (bacteria)
macrophage phagocytosis the material and digests it in a lysosomes

partials (antigens) are combined with **major histocompatibility complex (MHC)** proteins

MHC are proteins produced at the ER of cells that bind to internalized antigens (like a hot dog in a bun) and ships them back out to the cell surface

Once MHC with the antigen is places at the macrophage surface you have completed antigen presentation

**Step 2: T cell recognition**

does all three types of T cell know must encounter and recognize the presented antigen this will start immune response

there must be a specific helper, cytotoxic, and suppressor T for the antigen

**Step 3: T-cell activation**

Following the recognition of the antigen by the T-cells they will become activated

**activated cytotoxic T lymphocytes**

these cells roam through injured tissue looking for antigens that are presented

(bound to MHC proteins)

when activated they are stimulated to divide into more cytotoxic T cells and memory T cells

when activated cytotoxic Ts encounter antigens they kill by

1. releasing perforin (porins)
2. releasing toxic lymphotoxin which fragments cell DNA
3. activating genes in the cell’s nucleus that activates **apoptosis**

    important for virally infected cells and cancer cells
4. tumor necrosis factor mechanism unknown
5. gamma interferon which stimulates macrophages to killer form
once an antigen is encountered 2 or more days are required to mount a large attack

**memory T cells**
- are a reserve of cytotoxic T cells
  - are clones of the original so only recognize that antigen
- once the specific antigen is encountered for the second time the memory cells react much quicker to produce activated cytotoxic T cells
  - requires much less then 2 days to attack
  - will never know you were infected

**activated helper cells**
- secrete necessary cytokines that
  1. stimulate T cell division
  2. attract macrophages
  3. attract and stimulate NK cells
  4. promote B cell division (major role)

there is no immune response without Helper cells
- are destroyed by HIV virus

**activated suppressor T cells**
- depresses the activity of T and B cells
- are activated by the exposure to the same antigen that activated the cytotoxic T cells
- activation of suppressor cells is slow so that the suppression of function is delayed giving time for the T and B cells to defeat the pathogen
- suppressor activity limits and terminates the immune response

**macrophages** are also important for the immune response
- also part of the nonspecific body defenses
- located throughout the lymphoid tissues and in connective tissue
arises from monocytes that have left the blood

major role in immunity is to engulf foreign particles and present fragments of these antigens to the T cells
antigen presenters

also secrete soluble proteins that activate the T cells

activated T cells release chemicals that further activate macrophages
activated macrophages secrete bactericidal chemicals

**humoral immune response**
(antibodies)
starts with antigen being attacked by a specific B lymphocyte

**B lymphocyte**
1. formed in bone marrow but here become immunocompetent
screened to remove cells that recognize own tissues
2. after immunocompetent they migrate to the lymph nodes, spleen, lymphoid organs where they can encounter antigens
immunocompetence process is same as with T lymphocytes

**steps of the humoral immune response**
1. **B cell sensitization**
   when a B cell binds to its specific antigen, the antigen is internalized and bound to MHC proteins
   the antigen bound to MHC returns to the cell surface membrane
cell is now sensitized

2. **B cell activation**
   the B cell next encounters a **helper T cell** which recognizes the antigen bound to the MHC protein
   the helper T cell secretes cytokines that promote B cell activation
   stimulate B cell division
   accelerate plasma cell formation
   enhance antibody production
activated B cells divides producing plasma cells and memory B cells
plasma cell
secret large numbers of antibodies that bind to the same antigen that started it all

memory B cells
do not respond to the first exposure
on second exposure they differentiate into plasma cell and make antibodies

antibody targets and functions
antibodies cannot directly destroy
are involved in

complement fixation
when antibody binds to antigen like on bacteria it exposes a complement binding site on the antibody this allows complement binding and lysis of cell

neutralization
antibodies bind to and block specific sites on virus’ toxins so they can not do harm

agglutination
antibodies have more that one antigen binding site so can bind to several antigens and form large clumps or agglutinations

precipitation
soluble molecules like toxins once bound to antibodies will settle out of solution and are easy prey for phagocytes

attraction of phagocytes

opsonization
coating of antibodies increases the effectiveness of phagocytes

stimulation of inflammation
stimulate basophiles and mast cells to release histamine

primary and secondary responses of B lymphocytes to antigen exposure

primary immune response
immunocompetent B lymphocytes are activated by the binding of a specific antigen to its surface
2. the receptor bound to antigen are endocytosed

3. endocytosis stimulates the cell to multiply and produce 1000s of clones

4. **most** of these clone cells become plasma cells
   rest become memory cells

5. after days to first initial exposure the plasma cells secrete
   specific antibodies against the antigen 2000 per second for
   4 or 5 days then dies

6. the antibodies are the same as the receptor that started it all

7. the primary immune response is a 3 to 6 day lag and peaks after
   8 days

**secondary immune response**

1. occurs when re-exposed to same antigen

2. the memory cells can quickly divide and produce any plasma cells

3. results in
   more antibodies quicker
   better antibodies
   levels remain higher longer

memory cells can live 20 years or more
this is the basic principle behind immunization to prevent disease