

Immunity

Stem cells can form:

- lymphocytes (T, B and large granular lymphocytes). 30% of WBC are lymphocytes
 - Cytotoxic T cells fight off viruses and cancer
 - Helper T cells coordinate the immune response
 - B cells make antibodies
- polymorphonuclear cells (neutrophils, basophils and eosinophils)
- mast cells
- megakaryocytes that produce platelets

B-Cells: Trained in the bone marrow
Make antibodies
Each B Lymphocyte makes only one shape of antibody
Plasma cell is a type of B-Cell that secretes antibodies
Memory cells are long-lived, inactive cells that are activated at subsequent exposure to an antigen. They are a key component of long-term Immunity

PMNs (Polymorphonuclear cells)

When mature, WBCs are PMNs. When immature, the nucleus is just a band, so they are called Band Cells. If you see a lot of bands, then you know the infection is new.

- 60% of all WBCs are neutrophils. They are the first to arrive in bacterial infections and then they call the others to join via chemotaxis. They also activate complement.
- Eosinophils are not very numerous...important in allergic responses and in parasitic infections.
- Basophils and Mast cells. Mast cells release histamine as part of the allergic response. Note that narcotics cause histamine release, but this is not mediated by antibodies...it is a side effect, not an allergic reaction.

CBC Differential

- RCB 4-5 million/cu. Mm (H&H)
- WBC 5000-10,000 cu. Mm
 - Neutrophils 50-60% (range from immature band cells to mature PMNs)
 - Lymphocytes 20-40%
 - Monocytes 2-6%
 - Eosinophils 1-4%
 - Basophils 1%
- Platelets 150,000 to 300,000/cu mm.

What to do about abnormal lab values:

ANC: -Normal absolute neutrophil count is 60% of the total WBC (about 2500-7000 cells/microliter)

-Below 500 there is a great risk for infection, and often few S&S. If your pt is below 500, then they would be on neutropenic precautions, including IV antibiotics for the fever.

-Above 1000, there is not a significant risk for infection (note that the NCLEX still thinks there is)

-So, for example... a week after chemo a pt's ANC is 200/microliter. What interventions will you do?

- Use alcohol-based hand wash
- Prohibit fresh flowers in the room
- Triple wash fruits and veggies
- No fresh unpeeled fruits

Complement has many functions in the inflammatory response.

- Increased vascular permeability causes fluid to leave the vessel travel through the interstitial area and trough the lymphatics. Maybe bacteria will be washed into the lymph system too.
- Smooth muscles contract in blood vessels and airways.
- Mast cells degranulate, releasing substances like histamine.
- Complexes of antigen-ab are trapped in the lymph node. The WBC responding to the antigen is cloned up in the nursery for making new WBC (the germinal center). This causes the lymph node to swell.
- Sticks to the bacteria, making phagocytosis easier.
- Neutrophils are activated and called into the area.
- Holes are poked in the walls of microbes. The microbes being under increased hdrostatic pressure, explode.
- Foreign cells are lysed too.

Platelets

Note that platelets don't just clot. They also release substances that increase permeability and activate complement allowing for chemotaxis of WBC.

Lymph Nodes

When lymph nodes are removed, pts are at higher risk for infection. Pts with mastectomy are at risk for infection on the side of the mastectomy, so you would never start an IV line on that arm. You would also want to watch for edema on that arm as it is very likely. Elevation is helpful and note that this is not an arterial problem, so no need to check pulses. It is a venous problem!

When bad things happen to the 1st line of defense (the epithelium)

Respiratory epithelium are damaged by smoking. It paralyzes the cilia, which means that all that gunk you breathe in gets dumped in the lungs.

Gastrointestinal defenses are designed to keep pathogens at bay. Lysozymes in secretions, rapid pH changes (2 in stomach to 8 in small intestine), normal flora, flow, peristalsis, secretions, exfoliation...all work to keep the microbes from causing harm.

What is the clinical significance of:

- Bypassing the top part of the GI tract with a feeding tube? You want to be sure to change bags out daily and not hang more than about 4 hours of food.
- What if you give an H2 blocker? Stomach not so acidic, more likely to get infection with aspiration? (not just chemical pneumonitis which is bad enough).
- GI Surgery... it is important to decontaminate gut before GI surgery. In emergency with no time, the peritoneal cavity can get contaminated, so you would give antibiotics like Flagyl post op. When you give lots of broad spectrum Abx, you wipe out normal flora and can get overgrowth, for example with *Clostridium difficile*.

Genitourinary defenses

Females are at higher risk for UTI due to a shorter urethra. Males have the benefit of antimicrobial seminal fluid. Both males and females have acidic urine and the bladder mucosa secretes mucus, IgA and lysozymes. Both have peristalsis, valves and macrophages.

The clinical significance of this:

- Inserting a Foley has a high risk of UTI
- Better to do an in-and-out cath multiple times a day.
- Residual urine increases the risk of UTI
- Infections can tract up to the kidneys...very serious!

2nd line of defense, nonspecific defenses:

- Inflammation
 - Can be caused by pathogens (cellulites), thermal (cold test tube on arm), radiation (sunburn) and chemical (aspiration of gastric juices into lungs)
 - The hallmark features of inflammation are:
 - Red (vasodilation)
 - Hot (vasodilation)
 - Swollen (leaky capillaries)
 - Painful (chemical response, also swollen tissue stims nerves)

Oral care every 4 hours on ventilator!

- Pathophysiology of inflammation: When the vessels vasodilate, the neutrophils arrive via chemotaxis. They get into the tissue because the vessels have increased permeability. (see A&P notes for more)
- Therapies include drugs, heat & cold, elevation
 - There are three general classes of drugs commonly used in the treatment of rheumatoid arthritis: non-steroidal anti-inflammatory agents (NSAIDs), corticosteroids, and remittive agents or disease modifying anti-rheumatic drugs (DMARDs). NSAIDs and corticosteroids have a short onset of action while DMARDs can take several weeks or months to demonstrate a clinical effect. DMARDs include methotrexate, leflunomide (Arava™), etanercept (Enbrel™), infliximab (Remicade™), adalimumab (Humira™), anakinra (Kineret™), antimalarials, gold salts, sulfasalazine, d-penicillamine, cyclosporin A, cyclophosphamide and azathioprine. Because cartilage damage and bony erosions frequently occur within the first two years of disease, rheumatologists now move more aggressively to a DMARD agent.
 - Heat & Cold: Heat increases superficial blood flow. Use heat for muscle spasm, stiff joints, superficial thrombophlebitis. Cold vasoconstricts, decreases swelling, decreases metabolism, slows nerve conduction. Use cold after a trauma, either intermittently or continuous (some studies show continuous is better)
- Phagocytosis
 - This is the domain of the neutrophils and macrophages.
 - Pus is basically dead neutrophils that responded to bacterial infection.
 - Pustules are involved in an acne bacterial infection
 - Vesicles are blisters and present in herpes virus.
- Fever
 - Temp is regulated by the thermostat in the hypothalamus
 - Metabolism creates heat
 - Perfusion and diaphoresis dissipate heat
 - Increased temp with pyrogenic factors (infection) or injury to the hypothalamus (head injury or brain attack) or inability to dissipate (heat stroke)
 - 37-degree is normal. We start treating/culturing around 38.5. At 40-degrees, thermoregulation is impaired. 41-degrees is lethal! A slight fever is beneficial because it interferes with bacterial growth.
- Interferon
 - Protects adjacent cells from infection or cancer
 - Improves immune response
 - Is suppressed by high dose steroids.

The 3rd Line of Defense: Acquired Immunity

- B & T Lymphocytes
 - Lymphocytes are “trained” in the bone marrow (B cells) or the thymus (T cells). As lymphocytes mature, the DNA that codes for cell surface receptors is sliced and diced so that (when expressed into RNA and ultimately protein) each cell makes a different shape of receptor. Cells with receptors that will fight off the bad guys and not hurt one’s own tissue are further developed and sent out into the circulation. Those receptors with the potential to interact and destroy native (self) tissue are destroyed. Well, not always. If they get out into the body, later in life they can get activated and will then attack one’s normal tissue (thus causing an autoimmune disease).
- Lymphocyte function
 - B cells make antibodies.
 - Cytotoxic T-cells destroy non-self expressing cells (cancer, transplant, virally infected cells).
 - Helper Ts help!
- Immunizations (see A&P notes for more)

Hypersensitivity

- Allergies (Type I)
- Autoimmune (Type II)
- Immune Complex (Type III)
- Delayed hypersensitivity

Type I Hypersensitivity

This is the allergic response. It is a rapid response to an antigen against which the individual has pre-existing IgE antibodies. IgE is present in very low levels in most people and it has a half life in the serum of only 2-3 days. However, if it is bound to high-affinity receptors, then its half-life is about 3 weeks. The high-affinity receptors are found on mast cells and basophils.

Type II Hypersensitivity (Autoimmunity)

This type is caused by specific antibodies (IgM or IgG) binding to cells or tissue antigens. Except in cases of autoimmunity, the target cell is foreign to the host...so this is usually only seen in blood transfusion pts and people with certain autoimmune diseases.

Some problems with physiology similar to autoimmune disease:

- Transfusion reaction: Normal gut Ab cross react with blood of different type.
- Hemolytic disease of newborn: Rh- mom makes Ab against Rh+ baby
- Transplant graft rejection
- Some drug reactions: drug binds to RBC, Ab binds to drug, RBC lysed.

Type III Hypersensitivity (Immune Complex)

This type is mediated mainly by IgG antibodies. It is now thought that this form of hypersensitivity has a lot in common with Type I, except that the antibody involved is IgG and therefore not bound to mast cells. The IgG soaks up Ag and forms complexes while it waits for mast-cell attachment...these large complexes are not easily cleared by the spleen or liver and they tend to lodge in areas of high BP, blood flow turbulence, and in joints where inflammation is set up.

The Arthus reaction is the name given to a local type III hypersensitivity reaction. It is easy to demonstrate experimentally by subcutaneous injection of any soluble antigen for which the host has a significant IgG titre. Because the Fcγ₃ is a low affinity receptor and because the threshold for activation via this receptor is considerably higher than for the IgE receptor the reaction is slow compared with a type I reaction, typically maximal at 4-8hrs, and consequently more diffuse. The condition extrinsic allergic alveolitis occurs when inhaled antigen complexes with specific IgG in the alveoli, triggering a type III reaction in the lung, for example in 'pigeon fanciers lung' where the antigen is pigeon proteins inhaled via dried faeces. Complement is not required for the Arthus reaction, but may modify the symptoms.

Generalized or systemic reactions

The presence of sufficient quantities of soluble antigen in circulation to produce a condition of antigen excess leads to the formation of small antigen-antibody complexes which are soluble and poorly cleared. In the normal animal these complexes fix complement but experiments in animals genetically deficient in C3 or C4 have shown that complement is not required for pathology to be observed following antibody-antigen complex challenge. The major pathology is due to complex deposition which seems to be exacerbated by increased vascular permeability caused by mast cell activation via Fcγ₃ as above. The deposited immune complexes trigger neutrophils to discharge their granule contents with consequent damage to the surrounding endothelium and basement membranes. The complexes may be deposited in a variety of sites such as skin, kidney and joints. Common examples of generalised type III reactions are post-infection complications such as arthritis and glomerulonephritis.

Delayed Hypersensitivity

Diseases related to delayed hypersensitivity include TB, Rheumatoid Arthritis, Type 1 DM, Multiple Sclerosis, contact dermatitis, sarcoidosis and talc-related disease.

Tx: Avoid the allergen,
suppress the immune
system, stimulate SNS,
desensitize

Talc is difficult for the body to clear and it sets up a granulomatous reaction (similar to delayed hypersensitivity). Talc has thus been replaced with corn starch in many patient care areas (though in my hospital we don't use any talc or corn starch at all...nothing that could potentially be inhaled).