1.1.1

The First Line of Defense

The first line of defense is the external non-specific defenses. The three main categories of our external non-specific line are intact skin, mucous membranes and normal flora.

The skin has several characteristics that make it a good barrier to defend our body from infection. Our epidermis has a natural resistance to bacteria due to keratin, which is a waterproof matrix made by keratinocytes. These cells make up most of the epidermis and are held together by desmosomes. The sebum created by our sebaceous glands provides additional protection due to its low pH and bacteriostatic properties. Other characteristics of skin that make it a good barrier of defense include closely packed cells, high salt content (which can cause osmotic damage to microbes), antibacterial proteins (like defensins) and continual shedding of skin cells.

Mucous membranes are another important part of our external non-specific defense. Mucus is produced by goblet cells which are located at strategic points of entry to our body. One mucous membrane that is vital to the immune system is the mucociliary escalator system. The goblet cells in this system line the respiratory tract and prevent pathogens from invading the body. The mucus these goblet cells produce collect pathogens which are then removed from the respiratory tract through ciliary movement of the pulmonary epithelium. While smoking causes many negative effects in our body, it is specifically destructive to our mucociliary escalator system because it paralyzes and ultimately destroys it.

Watch Mucociliary Escalator System (from 25 sec - 3:30)

Another major player in our first line of defense is our normal flora. **Normal flora** is the “good bacteria” that prevents the growth of “bad bacteria.” An example of this is *Lactobacillus acidophilus*, a normal flora found in the vagina. The epithelial cells of the vaginal canal will produce glycogen which *Lactobacillus acidophilus* uses as a fuel. A byproduct of this catabolism is lactic acid, which keeps the pH of the vaginal canal low. This low pH as well as the fact that *Lactobacillus acidophilus* competes for glucose results in an inhibitory effect on the growth of *Candida albicans*, a fungus species that can lead to yeast infection. Another example of normal flora is the *E. coli* in our gut. This *E. coli* releases bacteriocins that inhibit growth of *Salmonella* and *Shigella*. *Pseudomonas aeruginosa* found on human skin produces a substance called pseudomonic acid which can kill staphylococcus and streptococcus species of bacteria. Sometimes, large wounds like a burn can become infected with a “staph” infection in part because of the loss of pseudomonic acid. Pseudomonic acid can be produced commercially and is available in a common antibiotic for topical use called Mupirocin.

A note on antibiotics: While broad spectrum antibiotics kill bacteria, these medications do not differentiate between normal flora and harmful bacteria. Prolonged treatment with antibiotics can kill normal flora in the gut, skin, vagina, and other places. If this happens in the gut, a species of bacteria called *Clostridium difficile* can overrun the tissue and cause a “C. Diff” infection. *Clostridium Difficile* causes pseudomembranous colitis (death of a part of the bowels) which can only be fixed by a bowel resection.

While intact skin, mucous membranes, and normal flora make up the three main categories of our external first line of defense, there are several other physical factors that also contribute to our defense. The lacrimal apparatus of our eyes produces tears that contain lysozymes, which are also present in our saliva. Lysozymes are an important part of prohibiting bacterial growth because they cleave peptidoglycan, the structure that forms the gram-positive bacterial wall. Another substance in our saliva that helps us get rid of pathogens is the antibody IgA. IgA is part of the adaptive immune system and acts as a barrier to help prevent the attachment of bacteria to mucous membranes. IgA is the antibody that is passed from mother to baby through the breast milk. Without this antibody, the infant could be at risk for infection. **Defensins** are "defense" peptides that are produced by many cells including circulating white blood cells, epithelial cells of the gastrointestinal tract, mammary glands for breast milk and mucus membranes in general. Defensins are amphipathic molecules with a net (+) charge that are attracted to the (-) charges on the phospholipid membranes of pathogens. When these defensin peptides insert into the pathogen membrane, it can form pores or holes that will disrupt the intracellular compartment and kill the pathogen. Other physical defense factors include hair (lining the ears to prevent bacterial entry), epiglottis (covers larynx to prevent entry of food and bacteria into lungs), urine (low pH that is bacteriostatic), gastric juices (low pH), peristalsis, defecation, vomiting, coughing and sneezing. The purposes of these physical factors are to prevent a pathogen from ever entering the body or to expel them afterwards.

Anticholinergic drugs can greatly affect the first line of defense. If given to a patient, they would cause decreased saliva production and decreased stomach acid, which would ultimately cause the patient to be more prone to bacterial infections.