

# MECHANISM OF DISEASE—HOW PATHOGENS MAKE US SICK

Pathogens must be able to accomplish all of the following if they are going to make us feel bad:

1. Adhere to our bodies, either inside or out
2. Avoid being phagocytosed or otherwise attacked by our immune system
  - a. note: our normal flora do steps one and two in order to colonize us.
3. Damage our cells

**Virulence factors:** characteristics of pathogens that increase their ability to make us sick.

**Adherence:** Structures such as fimbriae, flagella, or a glycocalyx (slime layer) help bacteria adhere.

**Avoiding/Inhibiting Phagocytosis:**

- The bacterial capsule is often essential to avoiding phagocytosis. *Staph* and *Strep* both “hide” their surfaces with proteins native to US— using fibrin (via coagulase) and hyaluronic acid (part of our connective tissue ground substance)
- *Mycobacterium* (causes tuberculosis) has a waxy cell wall that makes it hard for WBCs to destroy it.
- **“Sweet-talking” the WBCs into letting them stay:** Worm infections are well-known for “calming” the immune system down so that an attack is not mounted, despite the foreign presence. This may tie in with the interesting inverse relationship between worm infections and allergies (that is, people with a history of worm infections don’t have allergies)
- **Antigenic Variation:** Some pathogens (for example, influenza virus) change the antigens on their surface every so often. Then, even if adaptive immunity recognizes and destroys the pathogen, the next year the memory cells won’t recognize the virus, since it will be displaying different antigens.

**Damage:**

- **Causing systemic inflammation:** Gram negative bacteria have lipid A, an **endotoxin**, as part of their cell wall. Our immune systems react very strongly to this lipid. It triggers inflammation, fever, body aches, clotting, and vascular leakiness. Sometimes all these symptoms are called the “cytokine storm”. Systemically, blood vessel dilation can lead to septic shock (drop in blood pressure and subsequent organ failure).
- **Damaging Cells with Exotoxins:** Exotoxins are products secreted out of pathogens that damage our cells directly, or trigger an immune reaction that causes us to feel very sick.
  - **Cytotoxins (hemolysins/leukocidins/streptolysins, etc):** cause lysis of cells, usually red blood cells
  - **Enterotoxins/Emetics:** cause diarrhea (entero = intestine) or vomiting
  - **Neurotoxins:** Disrupt synaptic transmission—can cause either paralysis or muscle spasms, depending on which neurons are affected.