### Inflammation and Cytokines  
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When infected cells in your body die, a message triggers inflammation and gets the fighting soldiers (your immune system) to the battle scene. However, in order for this vital communication to occur, special messengers are needed. Cytokines are these key messengers that alert and recruit the immune system. **\*\*Cytokines\*\*** are proteins or glycoproteins (proteins with carbohydrate chains) that enable context-dependent communication in the host<**sup**>3</**sup**>. Immune cells, skin cells, cells that line blood and lymphatic vessels, and even smooth muscle cells can all secrete cytokines to communicate within the host body<**sup**>3</**sup**>. Inflammation spreads beyond the initial damaged site to the rest of the host by systemic circulation of cytokines<**sup**>4</**sup**>. Picture cytokines acting like drummer boys on the battlefield. In the same way the drum rolls signal command to the troops, cytokine signaling recruits immune cells (like T cells) to the site and activate them to fight pathogens.   
There are **\*\*\*\***five**\*\*\*\*** major types of cytokines<**sup**>4</**sup**>:  
  
 1. Interferons  
 2. Interleukins  
 3. Chemokines  
 4. Colony-stimulating factors  
 5. Tumor necrosis factors (TNF)  
  
Interferons are involved in controlling cell proliferation,the innate immune system, and the activation of defenses against viruses<**sup**>4</**sup**>. They are used to treat hepatitis B and C<**sup**>4</**sup**>. Interleukins were named as such since they communicate or “interact” with “leukocytes” or immune cells. They communicate to regulate leukocytes division, growth, and differentiation<**sup**>4</**sup**>. Interleukins also kick off inflammation and guide immune cells to infected sites and increase cytokine production<**sup**>4</**sup**>. Chemokines form the largest cytokine type and are also involved in promoting inflammation<**sup**>4</**sup**>. Chemokines work by selectively attracting specific immune cells to control their overall migration<**sup**>4</**sup**>. Colony-stimulating factors are appropriately named in that they promote the proliferation and differentiation of immune cells<**sup**>4</**sup**>. TNF’s encourage inflammation and activate T cells to kill virally infected cells, especially for viral diseases like dengue, Ebola, and the flu<**sup**>4</**sup**>.   
###Cytokine Storm   
The immune system is your body’s way of defending itself from threats. You have defense mechanisms set in place in case bacteria,viruses or some pathogen invades. When a breach occurs and the pathogen begins infecting and subsequently killing cells, the death of cells sets off local alarms about the damage and triggers an inflammatory response<**sup**>5</**sup**>. Cytokines, or the drummer boys of the immune system, spread the alarm to promote inflammation. ![enter image description here](https://www.dropbox.com/s/45eoymoiuoopmga/cytokine\_stormImagessingle.jpeg?dl=0) Inflammation has four components: rubor (redness), tumor (swelling), calor (heat), and “function laesa” (loss of function)<**sup**>4</**sup**>. These four components work to increase blood flow to enable the immune cells (your soldiers) to reach the inflammation site more quickly and in greater numbers. As part of the inflammatory defense mechanisms, the local temperature of the inflammation site increases to impair the invaders, and pain is generated in the area to further warn the host of danger<**sup**>4</**sup**>. This inflammatory response protects the host and fights off the infection. Cytokine storms happen when the danger signal never shuts off, a phenomenon that can be **\*\*\*deadly\*\***\* to the host.   
During the course of an infection, the **\*\*pathogen’s virulence\*\*** and the **\*\*host resistance\*\*** fight for dominance. A third factor also influences the dynamic within the host, **\*\*host healing mechanisms\*\***<**sup**>4</**sup**>.![enter image description here](https://www.dropbox.com/s/nai5qhvh2tl7f0b/cytokine\_stormImagesscale.jpeg?dl=0) Compensatory repair or healing processes are initiated very once the drummer boys have sounded the alarm<**sup**>4</**sup**>. Think of these healing responses as army medics, treating the wounded soldiers and clearing the battlefield. As long as the host resistance and host healing are stronger than pathogen virulence, the host will recover from the infection. In a mild infection, the host resistance tapers off once the pathogen is neutralized and the healing processes have taken care of enough of the damage for the threat to be gone<**sup**>5</**sup**>.   
Cytokine storms occur when the host resistance doesn’t slow down but instead continues to wage war within the host <**sup**>5</**sup**>. Though the exact causes are not known, one factor that is recognized is that the damage done by the pathogen and/or the inflammatory process spreads beyond the local area of infection to the rest of the host<**sup**>4,5</**sup**>. When local inflammation turns systemic, a cytokine storm has begun<**sup**>4</**sup**>. In this case, the battle will not stop even as the enemy weakens. The drummer boys will keep pounding out the call to battle and the battlefield size will increase. The soldiers will continue fighting, even as they hurt themselves, propelled by the alarm. The army medics will become overwhelmed and the battlefield will continue to worsen. Cytokine storms majorly end with the death of the host<**sup**>4</**sup**>.  
###Diseases that involve Cytokine Storms   
Some of the diseases that are associated with cytokine storms include influenza, dengue, yellow fever, malaria, severe acute respiratory syndrome coronavirus (SARS), graft versus host disease in transplant rejection and sepsis<**sup**>4,6</**sup**>. The high number of deaths, estimated 50 to 100 million, has made infamous 1918-1919 H1N1 “Spanish Flu” pandemic one of the most **\*\*\*devastating\*\***\* pandemics in history<**sup**>7</**sup**>. One of the reasons this pandemic was so horrible was because of the unusually high number of deaths of 20-40 year olds, a group that usually has a low risk of dying from influenza<**sup**>7</**sup**>. Researchers believe that the cytokine storm component of the 1918 Spanish Flu is responsible for the high mortality rate of the 20-40 year olds and the overall high death rate<**sup**>7</**sup**>. Sepsis is the iconic example of cytokine storm and is responsible for the majority of deaths in intensive care units (ICU) worldwide <**sup**>6</**sup**>.  
###Treatments for Cytokine Storm  
  
Though cytokine storms result in death most of the time, there are a few treatments. Most of the treatments target the immune system to try to limit the host resistance<**sup**>4</**sup**>. These type of drugs are known as immunomodulatory drugs and they limit inflammation during infections<**sup**>4</**sup**>. When used along with antiviral drugs, they improve the effectiveness of the antiviral drugs in treating the infection<**sup**>4</**sup**>. Anti-TNF therapy is one example of this type of drug<**sup**>5</**sup**>. Since TNF is viewed as one of the key cytokines involved in the formation of cytokine storms, inhibiting it may prevent a storm from forming or gaining strength <**sup**>5</**sup**>. The effectiveness of this therapy is being evaluated in different viral infections<**sup**>4</**sup**>. Another more recent therapy involves sphingosine-1-phosphate receptor 1 agonists (S1P1 receptor agonists)<**sup**>5</**sup**>. This drug inhibits cytokines and their subsequent recruitment of immune cells, effectively shutting down the drummer boys and the alarm signals<**sup**>5</**sup**>. S1P1 receptor agonists were highly effective in treating the 2009 influenza strain in mice and may work in humans as well<**sup**>5</**sup**>.   
The main difficulty involved in treating cytokine storms is limiting the inflammation while still enabling the host to clear the infection. Studying the time course of cytokine storms may provide some answers as to when to give the inflammation inhibitors and when to give the anti-viral drugs. Moreover, a time course study could enable doctors to detect when a cytokine storm is likely to begin so that they could treat it before it grows too strong. One other component that should be explored includes the host healing mechanisms. If the host can heal from injury or infection faster then the cytokines may shut down before reaching the systemic level needed for a storm.   
###Concluding Remarks   
Your immune system is your body’s way of defending itself. It has many different components, including its drummer boys, cytokines. Cytokines function as messengers for the immune system and when the host is able to balance resistance with healing and fighting virulent pathogens, they are a great help in keeping you alive. Much like instabilities in the atmosphere (humidity and pressure differences) result in thunderstorms, tornados and hurricanes, imbalances in your body can result in dangerous cytokine storms.   
  
  
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