

INFLAMMATION: FUNCTION & PROCESSES

So many diseases have at their roots inflammation - allergies are an obvious example, arthritis, auto-immune diseases, and so on. We need to keep in mind that in fact inflammation is a natural process and one designed to protect and heal the body. Without inflammation, damage to our tissue wouldn't heal and foreign invaders may not be eradicated, so don't be tempted to fall into the trap of believing inflammation, under normal circumstances, is bad for us. While there are times it is beneficial to reduce inflammation, there are other times where it is best to let it take its natural course. It's only when inflammation goes on for too long, or when its root cause is not addressed, or overwhelms the body's defense systems, that it becomes deleterious to health. Ongoing inflammation however can lead to a range of diseases and disease states, potentially cancer, forms of arthritis, damage to blood vessels even those servicing your gums, and allergy. It is likely that as we learn more about the processes and implications, particularly of long-term unaddressed inflammation, that we will uncover more connections to other diseases.

The inflammatory processes are referred to as **innate immunity**; that is, natural immunity derived from our body itself. **Adaptive immunity** is a type of immunity we can gain from infections (where our immune system gains a memory of the pathogen and can fight it better next time) or via vaccination (which was designed to 'arm' the immune system with a passive memory of pathogens, though it's somewhat used differently today, rather it's aimed to be immunity itself, perhaps controversially).

WHAT IS INFLAMMATION?

Simply, inflammation is a response of our vascular tissue (blood vessels) to infection or damage. The blood supply allows our body to secrete substances to cope with pathogenic invasion or damage to tissue. Immune and inflammatory substances migrate to the site to eliminate pathogens or to begin the wound healing process. In some cases, inflammation can be self-perpetuating. This is when intervention is required, for example RICE in First Aid (Rest, Ice, Compression, Elevation). When inflammation is misdirected, an autoimmune challenge can occur, or allergic reaction, or chronic inflammatory disease such as rheumatoid arthritis (RA).

The main components of inflammation include **white blood cells** called leukocytes, plus other immune cells such as neutrophils, lymphocytes, monocytes and others which can ingest or destroy unwanted invaders. The other important component is the **blood vessels** which tend to dilate causing stasis (pooling) of blood; we see this as swelling and oedema. These two aspects are critical in the inflammatory response.

The aim of the inflammatory process is to:

1. Remove invaders or toxins that would do damage and
2. Remove the consequences of tissue injury, for example when we experience a burn or cut

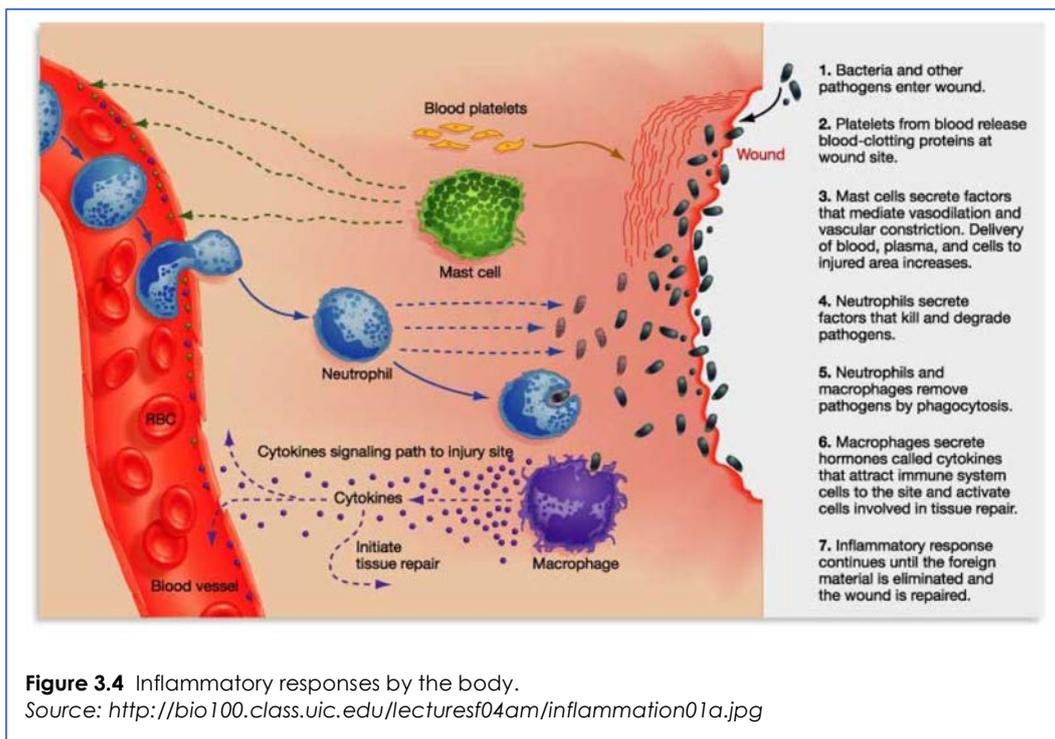
There are five typical signs of inflammation. If you think about a time where you have damaged tissue such as in a major bruise, or an infection in your skin, you will be able to relate to most of these.

1. Redness
2. Heat
3. Swelling
4. Pain
5. Loss of function

The main causes of inflammation include:

1. Infection, for example bacterial, viral, fungal and parasitic
2. Tissue death, also referred to as necrosis, for example after a trauma. Injury to tissue causes a loss of blood supply and such damage can't be repaired
3. Foreign bodies, such as transplants, splinters, dirt, stitches and so on
4. Immune reactions, from allergens in food or the environment, including medications
5. Tissue damage, as in the case of sprains, breaks and strains

The immune system uses chemical mediators to send messages to target cells to get to work, or it stimulates the release of metabolites and compounds that help. Refer Figure 3.4 below.



There are two types of inflammation, acute and chronic.

Acute inflammation is characterised by the following:

- An initial rapid response lasting a few minutes to a few days
- Exudation of fluid and plasma protein, as we see in weeping or pus
- Immigration of leukocytes such as neutrophils, basophils, eosinophils (in the case of parasite and worms) and mononuclear cells such as macrophages and monocytes into the region to mount an immune response. The type of cells that appear in a blood test is one way doctors can narrow down the cause of an infection.
- Tending to subside reasonably quickly, however if it goes on this leads to chronic inflammation

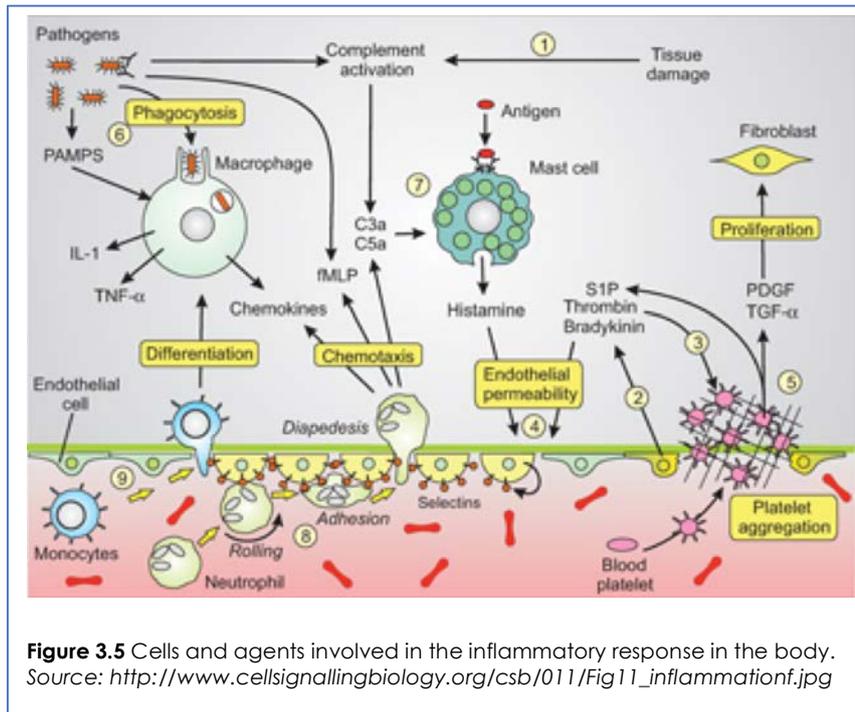
The three components to acute inflammation involve:

1. An alteration of blood vessel integrity
2. An alteration of the permeability of blood vessels (that is, how easily fluid moves in and out of the vessels), and
3. Migration of leukocytes to the site

Examples of acute inflammation that you may have experienced, or been exposed to, might include acute bronchitis, a sore throat from a cold, a scald or burn, acute tonsillitis, acute sinusitis or a blow or sprain.

An alteration of the vascular calibre is one of the earliest signs of inflammation, leading to increased blood flow. Vessels dilate (vasodilation) as a result of a release of chemicals (for example nitric oxide and histamine from injured cells). We can view this process in the redness and heat that occurs in the affected area. One of the benefits of this process is that when healing occurs new capillary beds can be created.

Alteration in vascular permeability (that is, the permeability is increased), allows protein-rich fluid to move to the outside of the tissue (out of the cells), referred to as extravascular tissue. The fluid causes swelling and oedema, which in turn slows blood flow to the area. As fluid leaves the vessels, it thickens the blood (increased blood viscosity) which causes the blood to pool in the affected area (referred to as stasis or congestion). As this occurs, immune cells called neutrophils gather; this vascular permeability is the hallmark of inflammation. To explain it a little more, the cells that line our vessels called endothelial cells contract (shrink) as a reaction to substances produced during inflammation, such as histamine. This then 'opens' up gaps between the cell lining allowing 'leakage' of fluid and cell components to flow into the area out of the blood vessels.



And, lastly we have **immigration** of leukocytes and other immune cells into the area. For example, neutrophils (a type of white blood cell) gather in the area and can release substances to digest invaders, while macrophages, again a type of white blood cell ingest foreign material.

The whole process begins to make sense when you view it from this angle. Clearly inflammation has a role and purpose in healing, we shouldn't entirely fear it.

VIDEO: Super quick video on inflammations

Here's a super quick view of inflammation and swelling. Take note of the cells making up the tissue around the injury site, and then the cells flowing through the vessel. Note how vessel permeability occurs and how cells can move into the tissue.

<https://www.youtube.com/watch?v=vQzbTxnjjl>

YOUR NOTES TO SELF

Chronic inflammation on the other hand is of prolonged duration, weeks or months, while tissue injury and ongoing attempts to repair is also occurring. The predominant cells in this process are monocytes, macrophages, lymphocytes and fibroblasts, we also see fibrosis (thickening and scarring of the tissue). The signs are less prominent and more elusive visually. Chronic inflammation may occur from a failure to eliminate a pathogen, an auto-immune response to a component of the immune system, or the immune system can attack itself in error, or from a long-lasting attack to the immune system. Examples might include asthma, peptic ulcer of long duration, RA, chronic gum disease, Crohn's disease, and hepatitis.

SLEEP APNOEA & HEALTH

Here's something you might like to consider: the effect of sleep on the risk of stroke. Did you know that chronic obstructive sleep apnoea (OSA) appears to increase our risk of premature death, heart disease, and stroke (Hermann et al., 2016; Marshall et al., 2014). It seems that the intermittent lack of oxygen (yes that holding of the breath in your sleep, referred to as intermittent hypoxia), waking over and over and the changes all of this can cause in the pressure in your chest and your blood pressure during the night appear to be the most likely reasons (Marshall, et al., 2014). Studies also suggest that increased inflammatory markers in the body were a risk factor in adverse effects from sleep disturbances.

PRACTICAL: Set of resources on inflammation to enhance your learning

Below is a great little site with quizzes and video tutorials on aspects of inflammation.

<http://www.nottingham.ac.uk/nmp/sonet/rlos/bioproc/inflam/3.html>

Have some fun, take the quizzes, listen to the audio and expand on your learning.

YOUR NOTES