# Defensive properties of neutrophils and monocyte-macrophages

- Once produced, neutrophils spend 4-8 hours in blood, then enter tissue & survive for 4-5 days
- Once produced, monocytes spend 10-20 hours in blood, then enter tissue, swell up and mature into macrophages – survive for months
- Both neutrophils and monocytes phagocytoze foreign and unwanted material. They can exit blood and enter tissue via diapedesis. They move to the site of infection by chemotaxis, which is caused by chemical substances, e.g. bacterial/viral toxins, tissue debris from inflamed tissue etc.

## Macrophage and Neutrophil response during inflammation:

- **1st line of defense**: within minutes after inflammation begins, tissue macrophages begin their phagocytic actions. Many of them break loose from their site of attachments and become mobile in response to chemotactic factors
- **2nd line of defense**: large numbers of neutrophils move to inflamed area as a result of chemotaxis caused by products in inflamed tissues. Number of neutrophils increases rapidly after a few hours (neutrophilia); this is caused by inflammatory products that are transported through blood to bone marrow, causing neutrophils to be mobilized and moved into circulating blood
- **3rd line of defense**: a second macrophage invasion of inflamed tissue. Along with neutrophils, monocytes enter inflamed tissue and enlarge to become macrophages. Build-up of MPs in inflamed tissue is much slower than that of neutrophils because number of monocytes in blood is low and storage pool in bone marrow is much less than that of neutrophils
- **4th line of defense**: stimulation of granulocytic and monocytic progenitor cells of bone marrow. This takes 3-4 days for newly formed granulocytes & monocytes to leave the bone marrow

## Factors that control the macrophage-neutrophil response to inflammation:

The following 5 factors are formed by activated macrophages and T cells in inflamed tissue:

1. Tumor necrosis factor (TNF)
2. Interleukin-1 (IL-1)
3. Granulocyte-monocyte colony-stimulating factor (GM-CSF)
4. Granulocyte colony-stimulating factor (G-CSF)
5. Monocyte colony-stimulating factor (M-CSF)

The 3 colony-stimulating factors cause increased production of granulocytes and monocytes by bone marrow.

Combination of all 5 factors provides a powerful feedback mechanism that begins with tissue inflammation and proceeds to the formation of defensive WBCs and removal of the cause as well as the inflammation.

## Phagocytosis:

Phagocytosis is the cellular ingestion of foreign/offending agents.

**Factors that influence phagocytosis:**

1. Roughness of surface (most natural substances of tissues have smooth surface, which resist phagocytosis)
2. Most natural substances have a protective protein coat that repels phagocytes (dead tissue and most foreign particles do not!)
3. Antibodies bind to bacteria making them susceptible to phagocytosis (opsonization = the process by which bacteria are altered by opsonins (binding enhancers) so as to become more readily and more efficiently engulfed by phagocytes)

**Phagocytosis by neutrophils:**

- Neutrophils can attack bacteria even in blood (macrophages cannot because they are not mature)
- They attach to particles via pseudopodia, which fuse forming a chamber containing the particle; this chamber becomes engulfed forming phagosome (phagocytic vesicle)

**Phagocytosis by MPs:**

- Much more powerful phagocytes
- Engulf much larger particles
- Can survive/function for many months

Phagosome becomes digested by lysosomal enzymes e.g. proteolyases (in both MPs & NPs), lipases (only in MPs) etc. In case of bacteria having protective coat, they are digested by oxidizing agents or in peroxisomes (containing hydrogen peroxide)

Note: formation of pus: when neutrophils & macrophages engulf large numbers of bacteria and necrotic tissue, they eventually die; the combination of necrotic tissue, dead neutrophils, dead macrophages and tissue fluid is known as PUS! When the infection has been suppressed, the dead cells and necrotic tissue in pus gradually autolyze over a period of days and are absorbed into the surrounding tissues