WHAT IS INFLAMMATION?

Inflammation is the body's immune response to injury or foreign invaders (infections). Inflammation is involved in both self-protection and repair. It can be acute and chronic. As the body's natural response to any kind of infection or germs, signs and symptoms can include redness, swelling, heat, pain, itchiness, or any other forms of malfunctions in the body.

Normal levels of inflammation are good for the body for many reasons. First, inflammatory cytokines and mediators (e.g. histamines, leukotrienes, prostaglandins, nitric oxides) are necessary for communication within the immune system. Second, inflammation is also necessary for deep quality sleep.

Inflammation only becomes bad when it is chronically elevated, when it can't resolve itself.

Now, before you assume inflammation is bad – just like anything else we look at here - we've got to consider its natural role. Your body's ability to produce inflammation is very important for health and survival because without it, you wouldn't be able to heal wounds or protect yourself from germs.

Most people will be aware of obvious symptoms of "bad" inflammation, including

- Aches and pain
- Skin problems of any kind
- Digestive problems
- Swelling

There are also many conditions that are less obviously related to inflammation, although most people or even medical doctors may not associate these with inflammation, including:

- Brain fog or cognitive dysfunction
- Mood problems
- Anxiety, depression, or both
- Digestive problems
- Insomnia (chicken and egg)
- Poor quality sleep or too much sleep
- Neurodegenerative disorders like Alzheimer's
- Cancers

It is possible to have inflammation without any detectable or visible damage in any organ system. In addition, some types of inflammation cannot be detected through a blood test, because the inflammation is localized to a specific area.

DIFFERENT WAYS TO TEST FOR INFLAMMATION (TECHNICAL)

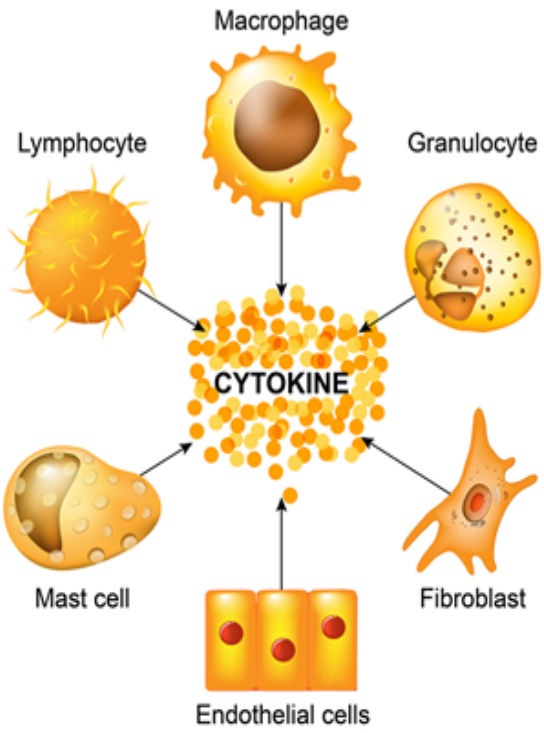
MAINSTREAM BLOOD TESTS FOR INFLAMMATION

Inflammation is detectable in the blood through various types of tests and testing, including:

- C-reactive protein (CRP)
- Erythrocyte Sedimentation Rate (ESR)
- Increased or decreased ferritin
- High white blood cells
- High monocytes
- Antibodies
- Autoimmunity
- Lower albumin
- Increased triglycerides, VLDL, small dense LDL
- High blood glucose (linked to insulin resistance)

In the US, these tests are usually covered by insurance if your doctor orders it.

ALTERNATIVE WAYS TO DETECT INFLAMMATION



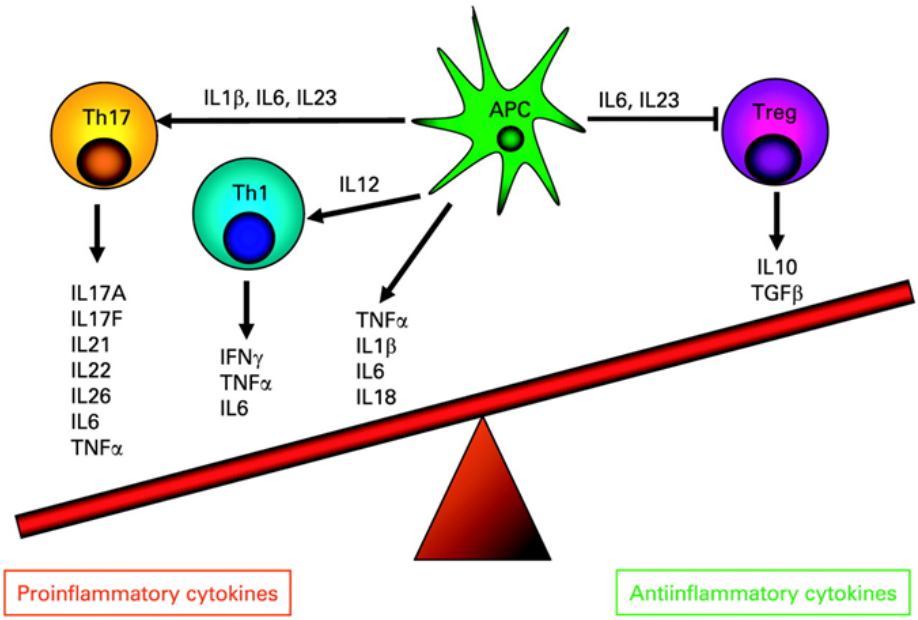
There are alternative ways to detect inflammation, which are available in some commercial labs. Note: this is not a comprehensive list.

- Cytokines – TGF-beta, IL-6, TNF-a
- High MMP-9
- High complement C4a
- High histamine
- Increased oxidative stress
- Increased VEGF
- Secretory IgA (SIgA) in the stool

Multiple cytokines, including interleukin (IL)-4, transforming growth factor-β, IL-5, IL-6, and IL-10 are instrumental in intestinal stimulation of SIgA production. Note: IL-4, 5, and 10 are Th2-dominant cytokines **[1].**

Caveat: if these markers are not high, it doesn't mean that you don't have inflammation. It really depends on the person and situation.

WHAT ARE CYTOKINES?



Cytokines are the proteins that cells use to communicate with each other. They tell other immune cells to attack or ramp up activity, or sometimes to reduce activity.

Here, we are most concerned about cytokines from Helper T cells, including Th1, Th2, Th17, and regulatory T cells (Tregs), as they are most relevant to our understanding of autoimmunity and inflammation. The Th2 cells, which are not pictured here, are responsible for fighting germs that infect outside of cells, such as parasites.

The natural roles of Th17 cells are to protect against pathogens, including at the mucosal barrier.

Regulatory T cells have the same origins as the Helper T cells, but their job is to make sure that Th1, Th2, and Th17 cells only perform their natural functions and are not overactivated. If your Tregs function normally, then you should not have autoimmune or allergic diseases, and you should have no reaction to foods.

The ability of the immune system to ignore harmless proteins is called tolerance. Naturally, your body should have tolerance to food proteins, proteins in the environment (e.g. dust and pollen), and the proteins that are made inside your body. Loss of tolerance can result in inflammation, allergies, and autoimmunity.

Infections and proteins from food that the gut immune system sees as foreign can tip the balance towards inflammatory. That means increased Th17 and reduced T regulatory cells.
Then we also have Th1 cells, whose role is to help fight germs that infect inside the cells, such as bacteria and viruses.

Th1 cells secrete cytokines, including IFN-gamma, IL-2, TNF-beta, TNF-alpha **[2].**

Th2 cells secrete IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13 **[2].**

Th17 cells secretes IL-17, IL-21, IL-22, IL-6, and TNF-alpha. IL-23 is a cytokine that determines if these Th17 will cause diseases **[3].** IL-1β can also increase the production of Th17 cells **[4].** IL-23 is a cytokine that determines if these Th17 will cause disease **[3].** IL-1β can also increase the production of Th17 cells **[4]**.

HORMONES AS PROXIES FOR INFLAMMATION

Hormones can also be used as proxies in order to detect inflammation. Also through the blood, inflammation can be detected if the following signs are present:

- High cortisol
- Increased leptin
- Increased vasopressin
- Increased calcitrol
- Low T3
- High aldosterone
- High prolactin
- Low testosterone
- Low SHBG
- Low insulin
- High or low adiponectin
- Low MSH (Melanocyte Stimulating Hormone)
- Low VIP (Vasoactive Intestinal Peptide)

ACUTE PHASE REACTANTS

Acute phase reactants (proteins that quickly increase or decrease drastically when inflammation is present) include:

- Orosomucoid/α-1-acid glycoprotein (AGP)
- Fibrinogen
- Ceruloplasmin
- Serum amyloid A (can be elevated in mild levels, correlated with BMI)
- Plasminogen activator inhibitor-1 (PAI-1)
- Haptoglobin
- Mannose-binding lectin
- Von Willebrand Factor, Prothrombin, Factor VIII

These proteins have important roles in immune responses. Some act to destroy or inhibit growth of microbes, e.g., C-reactive protein, mannose-binding protein, complement factors, ferritin, ceruloplasmin, serum amyloid A, and haptoglobin. Others work to prevent excessive inflammatory response, e.g. serpins. Alpha 2-macroglobulin, and coagulation factors, which stimulate coagulation, keeping

infections localized. Also, some coagulation proteins may increase permeability of the blood vessels and attract white blood cells to the area.

The acute phase reactants will have a half-life of approximately one week. However, if there are perpetual inflammatory stimuli, these proteins may remain higher for longer.

One exception to these is that C-reactive protein (with a half-life of 6–8 hours) rises rapidly and can quickly return to within the normal range if treatment is employed. For example, in active systemic lupus erythematosus, one may find a raised ESR but normal C-reactive protein.

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