Inflammation A Review for Biofeedback Therapists

The local response to injury, involving small blood vessels, the cells circulating within these vessels, and nearby connective tissue.

The early phases of the inflammatory response are stereotyped: A similar sequence of events occurs in a variety of tissue sites in response to a diversity of injuries. The response characteristically begins with hyperemia, edema, and adherence of the circulating white blood cells to endothelial cells. The white cells then migrate between the endothelial cells of the blood vessel into the tissue. The subsequent development of the inflammatory process is determined by factors such as type and location of injury, immune state of the host, and the use of therapeutic agents. *See also* Circulation; Edema.

A local inflammatory response is usually accompanied by systemic changes: fever, malaise, an increase in circulating leukocytes (leukocytosis), and increases in specific circulating proteins called acute-phase reactants. Such signals and symptoms are often helpful to the physician, first as clues to the presence of **inflammation** and later as an indication of its course.

The process of **inflammation**, both vascular and cellular, is orchestrated by an array of molecules produced locally. These mediators include histamine, leukotrienes, prostaglandins, complement components, kinins, antibodies, and interleukins. Many anti-inflammatory drugs function by preventing the formation of those mediators or by blocking their actions on the target cells whose behavior is modified by the mediators.

Inflammation is basically a protective mechanism. The leakage of water and protein into the injured area brings humoral factors, including antibodies, into the locale and may serve to dilute soluble toxic substances and wash them away. The adherence and migration of leukocytes brings them to the local site to deal with infectious agents. There are also instances in which no causative toxic substance or infectious agent can be found to account for the **inflammation**. This is the case in rheumatoid arthritis and rheumatic fever. Such diseases may be examples in which an uncontrolled or misdirected inflammatory response with an autoimmune component is turned against the host. *See also* Arthritis; Autoimmunity; Infection; Rheumatic fever.

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inflammation

noun

An instance of being irritated, as in a part of the body: irritation, soreness.
See help/harm/harmless.

Britannica Concise Encyclopedia
inflammation
Local reaction of living tissues to injury or illness, including burns, pneumonia, leprosy, tuberculosis, and rheumatoid arthritis. Its major signs are heat, redness, swelling, and pain. The process begins with brief contraction of nearby arterioles (*see* arteries). Dilation follows, flushing

the capillaries with blood, from which fluid, plasma proteins, and leukocytes pass into the injured tissues, causing swelling as they attack the cause of injury. Initial acute **inflammation** can have any of four outcomes: resolution (return to normal), organization (new tissue buildup; *see* scar), suppuration (pus formation; *see* abscess), or chronic **inflammation**. Sometimes treatment — including antibiotics for bacteria, or surgical removal of an irritating foreign body — can eliminate the cause. If not, anti-inflammatory drugs (e.g., cortisone or aspirin) may be given, or simple remedies (e.g., hot or cold compresses) may be applied.

*For more information on **inflammation**, visit Britannica.com.*

Columbia Encyclopedia

inflammation, reaction of the body to injury or to infectious, allergic, or chemical irritation. The symptoms are redness, swelling, heat, and pain resulting from dilation of the blood vessels in the affected part with loss of plasma and leucocytes (white blood cells) into the tissues. White blood cells communicate with each other via cytokines, which are polypeptides released by cells of the immune system that regulate other cells. They are a broad class of soluble compounds that signal one cell type to another, particularly in response to foreign substances. Granulomas are most common in infectious diseases such as tuberculosis, leishmaniasis, and schistosomiasis, in which the body's defenses, unable to destroy the offending organisms, try to enclose them in a mass of inflammatory cells. Certain types of **inflammation** result in pus formation, as in an abscess. The leukocytes destroy harmful microorganisms and dead cells, preventing the spread of the irritation and permitting the injured tissue to repair itself.

Veterinary Dictionary

inflammation

A localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off both the injurious agent and the injured tissue.
The inflammatory response can be provoked by physical, chemical and biological agents, including mechanical trauma, exposure to excessive amounts of sunlight, x-rays and radioactive materials, corrosive chemicals, extremes of heat and cold, and infectious agents such as bacteria, viruses and other pathogenic microorganisms. Although these infectious agents can produce **inflammation**, infection and **inflammation** are not synonymous.
The classic signs of **inflammation** are *heat*, *redness*, *swelling*, *pain* and *loss of function.* These are manifestations of the physiological changes that occur during the inflammatory process. The three major components of this process are: (1) changes in the caliber of blood vessels and the rate of blood flow through them (hemodynamic changes); (2) increased capillary permeability; and (3) leukocytic exudation.

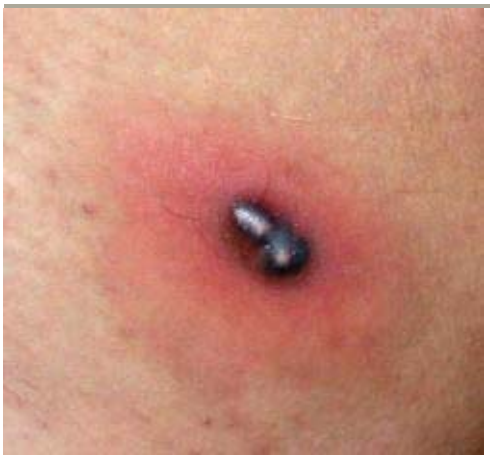
- acute i. — **inflammation**, usually of sudden onset, marked by the classic signs of heat, redness, swelling, pain and loss of function, and in which vascular and exudative processes predominate.
- adhesive i. — promotes adhesion of adjacent surfaces.
- atrophic i. — one that causes atrophy and deformity.
- catarrhal i. — a form affecting mainly a mucous surface, marked by a copious discharge

of mucus and epithelial debris.

- chronic i. — prolonged and persistent **inflammation** marked chiefly by new connective tissue formation; it may be a continuation of an acute form or a prolonged low-grade form.
- chronic i. bowel disease of sheep — a syndrome of unknown etiology, manifest with wasting, ill thrift and mortality or culling for poor production. Reported in England and Canada, it affects both housed and pastured sheep, predominantly in their first year of life, but cases up to three years-of-age have been seen. Affected sheep are dull and anorectic with pale mucous membranes and have fecal staining of the perineum. The rumen fill is reduced and the feces are soft and malodorous. Blood examination shows hypoalbuminemia, an elevated blood urea nitrogen and leukocytosis with neutrophilia. On postmortem there is a lymphocytic enteritis with gross thickening of segments or the entire or distal part of the small intestine. There is no evidence for Johne's disease or parasitic gastroenteritis and the syndrome has similarities to the proliferative enteropathies of swine and horses.
- croupous i. — a homogeneous layer of exudate lying close to but detached from the underlying inflamed tissue, which is comparatively unharmed; may form a fibrinous cast.
- diphtheritic i. — manifested by the development of a fibrinous exudate which is firmly attached to the underlying tissue, such that it cannot be removed except by tearing off a superficial layer.
- exudative i. — one in which the prominent feature is an exudate.
- fibrinous i. — one marked by an exudate of coagulated fibrin.
- fibrous i. — leads to the development of fibrous tissue.
- granulomatous i. — a form, usually chronic, attended by formation of granulomas.
- hyperplastic i. — leads to the development of new connective tissue.
- hypertrophic i. — leading to the enlargement of the affected tissues.
- interstitial i. — **inflammation** affecting chiefly the stroma of an organ.
- obliterative i. — **inflammation** within a vessel or viscus leading to occlusion of the lumen.
- parenchymatous i. — **inflammation** affecting chiefly the essential tissue elements of an organ.
- productive i., proliferative i. — one leading to the production of new connective tissue fibers.
- pseudomembranous i. — an acute inflammatory response to a powerful necrotizing toxin, e.g. *Fusobacterium necrophorum* toxin, characterized by formation on a mucosal surface of a *false* membrane composed of precipitated fibrin, necrotic epithelium and

inflammatory leukocytes. See also diphtheritic **inflammation** (above).

- purulent i. — suppurative **inflammation**.
- serous i. — one producing a serous exudate.
- specific i. — one due to a particular microorganism.
- systemic i. response syndrome (SIRS) — a generalized inflammatory response with vasodilation of capillaries and postcapillary venules, increased permeability of capillaries, and hypovolemia. Depressed cardiac function and decreased organ perfusion follow. The various initiating stimuli include sepsis and septic shock, hyperthermia, pancreatitis, trauma, snake bite and immune-mediated diseases.
- toxic i. — one due to a poison, e.g. a bacterial product.
- traumatic i. — one that follows a wound or injury.
- ulcerative i. — that in which necrosis on or near the surface leads to loss of tissue and creation of a local defect or ulcer.



An abscess on the skin, showing the redness and swelling characteristic of **inflammation**. Black rings of necrotic tissue surround central areas of pus

Inflammation (Latin, *inflammatio*, to set on fire) is the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. It is a protective attempt by the organism to remove the injurious stimuli as well as initiate the healing process for the tissue. **Inflammation** is not a synonym for infection. Even in cases where **inflammation** is caused by infection it is incorrect to use the terms as synonyms: infection is caused by an exogenous pathogen, while **inflammation** is the response of the organism to the pathogen.

In the absence of **inflammation**, wounds and infections would never heal and progressive destruction of the tissue would compromise the survival of the organism. However, **inflammation** which runs unchecked can also lead to a host of diseases, such as hay

fever, atherosclerosis, and rheumatoid arthritis. It is for this reason that **inflammation** is normally tightly regulated by the body.

Inflammation can be classified as either *acute* or *chronic*. *Acute **inflammation*** is the initial response of the body to harmful stimuli and is achieved by the increased movement of plasma and leukocytes from the blood into the injured tissues. A cascade of biochemical events propagates and matures the inflammatory response, involving the local vascular system, the immune system, and various cells within the injured tissue. Prolonged **inflammation**, known as *chronic **inflammation***, leads to a progressive shift in the type of cells which are present at the site of **inflammation** and is characterised by simultaneous destruction and healing of the tissue from the inflammatory process.

Causes

- Burns
- Chemical irritants
- Frostbite
- Toxins
- Infection by pathogens
- Necrosis
- Physical injury, blunt or penetrating
- Immune reactions due to hypersensitivity
- Ionizing radiation
- Foreign bodies, including splinters and dirt

Types

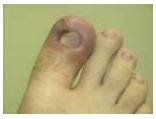
Comparison between acute and chronic **inflammation**:

	Acute	**Chronic**
Causative agent	Pathogens, injured tissues	Persistent acute **inflammation** due to non-degradable pathogens, persistent foreign bodies, or autoimmune reactions
Major cells involved	Neutrophils	Mononuclear cells (monocytes, macrophages, lymphocytes, plasma cells), fibroblasts
Primary mediators	Vasoactive amines, eicosanoids	IFN-γ and other cytokines, growth factors, reactive oxygen species, hydrolytic enzymes
Onset	Immediate	Delayed
Duration	Few days	Up to many months, or years
Outcomes	Healing, abscess formation, chronic **inflammation**	Tissue destruction, fibrosis

Acute inflammation

The classic signs and symptoms of acute **inflammation**:

English	**Latin**
Redness	*Rubor*
Heat	*Calor*
Swelling	*Tumor*
Pain	*Dolor*
Loss of function	*Functio laesa*



Infected ingrown toenail showing the characteristic redness and swelling associated with acute **inflammation**

Acute **inflammation** is a short-term process which is characterised by the classic signs of **inflammation** - swelling, redness, pain, heat, and loss of function - due to the infiltration of the tissues by plasma and leukocytes. It occurs as long as the injurious stimulus is present and ceases once the stimulus has been removed, broken down, or walled off by scarring (fibrosis). The first four characteristics have been known since ancient times and are attributed to Celsus. *Loss of function* was added to the definition of **inflammation** by Rudolf Virchow in the 19th century[1].

The process of acute **inflammation** is initiated by the blood vessels local to the injured tissue, which alter to allow the exudation of plasma proteins and leukocytes into the surrounding tissue. The increased flow of fluid into the tissue causes the characteristic swelling associated with **inflammation**, and the increased blood flow to the area causes the reddened colour and increased heat. The blood vessels also alter to permit the extravasation of leukocytes through the endothelium and basement membrane constituting the blood vessel. Once in the tissue, the cells migrate along a chemotactic gradient to reach the site of injury, where they can attempt to remove the stimulus and repair the tissue.

Meanwhile, several biochemical cascade systems, consisting of chemicals known as plasma-derived inflammatory mediators, act in parallel to propagate and mature the inflammatory response. These include the complement system, coagulation system and fibrinolysis system.

Finally, down-regulation of the inflammatory response concludes acute **inflammation**. Removal of the injurious stimuli halts the response of the inflammatory mechanisms, which require constant stimulation to propagate the process. Additionally, many inflammatory mediators have short half lives and are quickly degraded in the tissue, helping to quickly cease the inflammatory response once the stimulus has been removed[1].

Chronic inflammation

*Main article: Chronic **inflammation***

Chronic **inflammation** is a pathological condition characterised by concurrent active **inflammation**, tissue destruction, and attempts at repair. Chronic **inflammation** is not characterised by the classic signs of acute **inflammation** listed above. Instead, chronically inflammed tissue is characterised by the infiltration of mononuclear immune cells (monocytes, macrophages, lymphocytes, and plasma cells), tissue destruction, and attempts at

healing, which include angiogenesis and fibrosis.

Endogenous causes include persistent acute **inflammation**. Exogenous causes are varied and include bacterial infection, especially by *Mycobacterium tuberculosis*, prolonged exposure to chemical agents such as silica, or autoimmune reactions such as rheumatoid arthritis.

In acute **inflammation**, removal of the stimulus halts the recruitment of monocytes (which become macrophages under appropriate activation) into the inflamed tissue, and existing macrophages exit the tissue via lymphatics. However in chronically inflamed tissue the stimulus is persistent, and therefore recruitment of monocytes is maintained, existing macrophages are tethered in place, and proliferation of macrophages is stimulated (especially in atheromatous plaques).[1]

Exudative component

The *exudative component* involves the movement of plasma fluid, containing important proteins such as fibrin and immunoglobulins (antibodies), into inflamed tissue. This movement is achieved via the chemically-induced dilation and increased permeability of blood vessels, which results in a net loss of blood plasma. The increased collection of fluid into the tissue causes it to swell (edema).

Vascular changes

Acute **inflammation** is characterised by marked vascular changes, including vasodilation, increased permeability, and the slowing of blood flow, which are induced by the actions of various inflammatory mediators. Vasodilation occurs first at the arteriole level, progressing to the capillary level, and brings about a net increase in the amount of blood present, causing the redness and heat of **inflammation**. Increased permeability of the vessels results in the movement of plasma into the tissues, with resultant *stasis* due to the increase in the concentration of the cells within blood - a condition characterised by enlarged vessels packed with cells. Stasis allows leukocytes to marginate along the endothelium, a process critical to their recruitment into the tissues. Normal flowing blood prevents this, as the shearing force along the periphery of the vessels moves cells in the blood into the middle of the vessel.

Plasma cascade systems

- The complement system, when activated, results in the increased removal of pathogens via opsonisation and phagocytosis.
- The kinin system generates proteins capable of sustaining vasodilation and other physical inflammatory effects.
- The coagulation system or *clotting cascade* which forms a protective protein mesh over sites of injury.
- The fibrinolysis system, which acts in opposition to the *coagulation system*, to counterbalance clotting and generate several other inflammatory mediators.

Plasma derived mediators

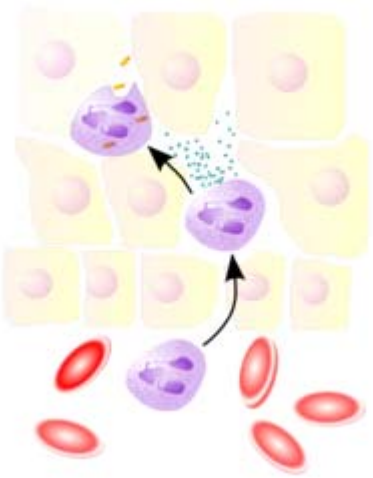
** non-exhaustive list*

Name	Produced by	Description
Bradykinin	*Kinin system*	A vasoactive protein which is able to induce vasodilation, increase vascular permeability, cause smooth muscle contraction, and induce pain.
C3	*Complement system*	Cleaves to produce *C3a* and *C3b*. C3a stimulates histamine release by mast cells, thereby producing vasodilation. C3b is able to bind to bacterial cell walls and act as an opsonin, which marks the invader as a target for phagocytosis.
C5a	*Complement system*	Stimulates histamine release by mast cells, thereby producing vasodilation. It is also able to act as a chemoattractant to direct cells via chemotaxis to the site of **inflammation**.
Factor XII (*Hageman Factor*)	*Liver*	A protein which circulates inactively, until activated by collagen, platelets, or exposed basement membranes via conformational change. When activated, it in turn is able to activate three plasma systems involved in **inflammation**: the kinin system, fibrinolysis system, and coagulation system.
Membrane attack complex	*Complement system*	A complex of the complement proteins C5b, C6, C7, C8, and multiple units of C9. The combination and activation of this range of complement proteins forms the *membrane attack complex*, which is able to insert into bacterial cell walls and causes cell lysis with ensuing death.
Plasmin	*Fibrinolysis system*	Able to break down fibrin clots, cleave complement protein C3, and activate Factor XII.
Thrombin	*Coagulation system*	Cleaves the soluble plasma protein fibrinogen to produce insoluble fibrin, which aggregates to form a blood clot. Thrombin can also bind to cells via the PAR1 receptor to trigger several other inflammatory responses, such as production of chemokines and nitric oxide.

Cellular component

The *cellular component* involves leukocytes, which normally reside in blood and must move into the inflamed tissue via *extravasation* to aid in **inflammation**. Some act as phagocytes, ingesting bacteria, viruses, and cellular debris. Others release enzymatic granules which damage pathogenic invaders. Leukocytes also release inflammatory mediators which develop and maintain the inflammatory response. Generally speaking, acute **inflammation** is mediated by granulocytes, while chronic **inflammation** is mediated by mononuclear cells such as monocytes and lymphocytes.

Leukocyte extravasation



Neutrophils migrate from blood vessels to the inflamed tissue via chemotaxis, where they remove pathogens through phagocytosis and degranulation

Main article: Leukocyte extravasation

Various leukocytes are critically involved in the initiation and maintenance of **inflammation**. These cells must be able to get to the site of injury from their usual location in the blood, therefore mechanisms exist to recruit and direct leukocytes to the appropriate place. The process of leukocyte movement from the blood to the tissues through the blood vessels is known as *extravasation*, and can be divided up into a number of broad steps:

1. **Leukocyte localisation and recruitment to the endothelium local to the site of inflammation – involving margination and adhesion to the endothelial cells:** Recruitment of leukocytes is receptor-mediated. The products of **inflammation**, such as histamine, promote the immediate expression of P-selectin on endothelial cell surfaces. This receptor binds weakly to carbohydrate ligands on leukocyte surfaces and causes them to "roll" along the endothelial surface as bonds are made and broken. Cytokines from injured cells induce the expression of E-selectin on endothelial cells, which functions similarly to P-selectin. Cytokines also induce the expression of integrin ligands on endothelial cells, which further slow leukocytes down. These weakly bound leukocytes are free to detach if not activated by chemokines produced in injured tissue. Activation increases the affinity of bound integrin receptors for ligands on the endothelial cell surface, firmly binding the leukocytes to the endothelium.

2. **Migration across the endothelium, known as *transmigration,* via the process of diapedesis:** Chemokine gradients stimulate the adhered leukocytes to move between endothelial cells and pass the basement membrane into the tissues.

3. **Movement of leukocytes within the tissue via chemotaxis:** Leukocytes reaching the tissue interstitium bind to extracellular matrix proteins via expressed integrins and CD44 to prevent their loss from the site. Chemoattractants cause the leukocytes to move along a chemotactic gradient towards the source of **inflammation**.

Cell derived mediators

** non-exhaustive list*

Name	Type	Source	Description
Lysosome granules	*Enzymes*	Granulocytes	These cells contain a large variety of enzymes which perform a number of functions. Granules can be classified as either *specific* or *azurophilic* depending upon the contents, and are able to break down a number of substances, some of which may be plasma-derived proteins which allow these enzymes to act as inflammatory mediators.
Histamine	*Vasoactive amine*	Mast cells, basophils, platelets	Stored in preformed granules, histamine is released in response to a number of stimuli. It causes arteriole dilation and increased venous permeability.
IFN-γ	*Cytokine*	T-cells, NK cells	Antiviral, immunoregulatory, and anti-tumour properties. This interferon was originally called macrophage-activating factor, and is especially important in the maintenance of chronic **inflammation**.
IL-8	*Chemokine*	Primarily macrophages	Activation and chemoattraction of neutrophils, with a weak effect on monocytes and eosinophils.
Leukotriene B4	*Eicosanoid*	Leukocytes	Able to mediate leukocyte adhesion and activation, allowing them to bind to the endothelium and migrate across it. In neutrophils, it is also a potent chemoattractant, and is able to induce the formation of reactive oxygen species and the release of lysosome enzymes by these cells.
Nitric oxide	*Soluble gas*	Macrophages, endothelial cells, some neurons	Potent vasodilator, relaxes smooth muscle, reduces platelet aggregation, aids in leukocyte recruitment, direct antimicrobial activity in high concentrations.
Prostaglandins	*Eicosanoid*	Mast cells	A group of lipids which can cause vasodilation, fever, and pain.
TNF-α and IL-1	*Cytokines*	Primarily macrophages	Both affect a wide variety of cells to induce many similar inflammatory reactions: fever, production of cytokines, endothelial gene regulation, chemotaxis, leukocyte adherence, activation of fibroblasts. Responsible for the systemic effects of **inflammation**, such as loss of appetite and increased heart rate.

Morphologic patterns

A skin ulcer resulting from infection with *Corynebacterium diphtheriae*

Specific patterns of acute and chronic **inflammation** are seen during particular situations that arise in the body, such as when **inflammation** occurs on an epithelial surface, or pyogenic bacteria are involved.

- **Granulomatous inflammation:** characterised by the formation of granulomas, they are the result of a limited but diverse number of diseases, which include among others tuberculosis, leprosy, and syphilis.
- **Fibrinous inflammation: Inflammation** resulting in a large increase in vascular permeability allows the blood vessels to pass through fibrin. If an appropriate *procoagulative* stimulus is present, such as cancer cells[1], a fibrinous exudate is deposited. This is commonly seen in serous cavities, where the conversion of fibrinous exudate into a scar can occur between serous membranes, limiting their function.
- **Purulent inflammation: Inflammation** resulting in large amount of pus, which consists of neutrophils, dead cells, and fluid. Infection by pyogenic bacteria such as staphylococci is characteristic of this kind of **inflammation**. Large, localised collections of pus enclosed by surrounding tissues are called abscesses.
- **Serous inflammation:** Characterised by the copious effusion of non-viscous serous fluid, commonly produced by mesothelial cells of serous membranes, but may which also be derived from blood plasma. Skin blisters exemplify this pattern of **inflammation**.
- **Ulcerative inflammation: Inflammation** occurring near an epithelium can result in the necrotic loss of tissue from the surface, exposing lower layers. The subsequent excavation in the epithelium is known as an ulcer.

Inflammatory disorders

Abnormalities associated with **inflammation** comprise a large, unrelated group of disorders which underly a variety of human diseases. The immune system is often involved with inflammatory disorders, demonstrated in both allergic reactions and some myopathies, with many immune system disorders resulting in abnormal **inflammation**. Non-immune diseases with aetiological origins in inflammatory processes are thought to include cancer, atherosclerosis, and ischaemic heart disease.[1]

A large variety of proteins are involved in **inflammation**, and any one of them is open to a genetic mutation which impairs or otherwise dysregulates the normal function and expression of that protein.

Examples of disorders associated with **inflammation** include:

- Asthma
- Autoimmune diseases

- Chronic **inflammation**
- Chronic prostatitis
- Glomerulonephritis
- Hypersensitivities
- Inflammatory bowel diseases
- Pelvic inflammatory disease
- Reperfusion injury
- Rheumatoid arthritis
- Transplant rejection
- Vasculitis

Allergies

An allergic reaction, formally known as type 1 hypersensitivity, is the result of an inappropriate immune response triggering **inflammation**. A common example is hay fever, which is caused by a hypersensitive response by skin mast cells to allergens. Pre-sensitised mast cells respond by degranulating, releasing vasoactive chemicals such as histamine. These chemicals propagate an excessive inflammatory response characterised by blood vessel dilation, production of pro-inflammatory molecules, cytokine release, and recruitment of leukocytes.[1] Severe inflammatory response may mature into a systemic response known as anaphylaxis.

Other hypersensitivity reactions (*type 2* and *type 3*) are mediated by antibody reactions and induce **inflammation** by attracting leukocytes which damage surrounding tissue.[1]

Myopathies

Inflammatory myopathies are caused by the immune system inappropriately attacking components of muscle, leading to signs of muscle **inflammation**. They may occur in conjunction with other immune disorders, such as systemic sclerosis, and include dermatomyositis, polymyositis, and inclusion body myositis.[1]

Leukocyte defects

Due to the central role of leukocytes in the development and propagation of **inflammation**, defects in leukocyte function often result in a decreased capacity for inflammatory defence with subsequent vulnerability to infection[1]. Dysfunctional leukocytes may be unable to correctly bind to blood vessels due to surface receptor mutations, digest bacteria (Chediak-Higashi syndrome), or produce microbicides (chronic granulomatous disease). Additionally, diseases affecting the bone marrow may result in abnormal or few leukocytes.

Pharmacological

Certain drugs or chemical compounds are known to affect **inflammation**. Vitamin A deficiency causes an increase in inflammatory responses[2], and anti-inflammatory drugs work specifically by inhibiting normal inflammatory components.

Termination

The inflammatory response must be actively terminated when no longer needed to prevent unnecessary "bystander" damage to tissues.[1] Failure to do so results in chronic **inflammation**, cellular destruction, and attempts to heal the inflamed tissue. One intrinsic mechanism employed to terminate **inflammation** is the short half-life of inflammatory mediators *in vivo*. They have a limited time frame to affect their target before breaking down into non-functional components, therefore constant inflammatory stimulation is needed to propagate their effects.

Active mechanisms which serve to terminate **inflammation** include[1]:

- TGF-β from macrophages
- Anti-inflammatory lipoxins
- Inhibition of pro-inflammatory molecules, such as leukotrienes

Systemic effects

An organism can escape the confines of the immediate tissue via the circulatory system or lymphatic system, where it may spread to other parts of the body. If an organism is not contained by the actions of acute **inflammation** it may gain access to the lymphatic system via nearby lymph vessels. An infection of the lymph vessels is known as lymphangitis, and infection of a lymph node is known as lymphadenitis. A pathogen can gain access to the bloodstream through lymphatic drainage into the circularitory system.

When **inflammation** overwhelms the host, systemic inflammatory response syndrome is diagnosed. When it is due to infection, the term sepsis is applied, with bacteremia being applied specifically for bacterial sepsis and viremia specifically to viral sepsis. Vasodilation and organ dysfunction are serious problems associated with widespread infection that may lead to septic shock and death.

Acute-phase proteins

Inflammation also induces high systemic levels of *acute-phase proteins*. In acute **inflammation**, these proteins prove beneficial, however in chronic **inflammation** they can contribute to amyloidosis[1] These proteins include C-reactive protein, serum amyloid A, serum amyloid P, vasopressin, and glucocorticoids, which cause a range of systemic effects including[1]:

- Fever
- Increased blood pressure
- Decreased sweating
- Malaise

- Loss of appetite
- Somnolence

Leukocyte numbers

Inflammation often affects the numbers of leukocytes present in the body:

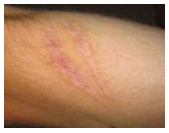
- Leukocytosis is often seen during **inflammation** induced by infection, where it results in a large increase in the amount of leukocytes in the blood, especially immature cells. Leukocyte numbers usually increase to between 15 000 and 20 000 cells per ml, but extreme cases can see it approach 100 000 cells per ml[1]. Bacterial infection usually results in an increase of neutrophils, creating neutrophilia, whereas diseases such as asthma, hay fever, and parasite infestation result in an increase in eosinophils, creating eosinophilia[1].
- Leukopenia can be induced by certain infections and diseases, including viral infection, *Rickettsia* infection, some protozoa, tuberculosis, and some cancers[1].

Systemic inflammation and obesity

With the discovery of interleukins (IL), the concept of *systemic **inflammation*** developed. Although the processes involved are identical to tissue **inflammation**, systemic **inflammation** is not confined to a particular tissue but involves the endothelium and other organ systems.

High levels of several **inflammation**-related markers such as IL-6, IL-8, and TNF-α are associated with obesity.[3][4] During clinical studies, inflammatory-related molecule levels were reduced and increased levels of anti-inflammatory molecules were seen within four weeks after patients began a very low calorie diet.[5] The association of systemic **inflammation** with insulin resistance and atherosclerosis is the subject of intense research.

Outcomes



Scars present on the skin, evidence of fibrosis and healing of a wound

The outcome in a particular circumstance will be determined by the tissue in which the injury has occurred and the injurious agent that is causing it. There are three possible outcomes to **inflammation**:[1]

1. **Resolution**
   The complete restoration of the inflamed tissue back to a normal status. Inflammatory measures such as vasodilation, chemical production, and leukocyte infiltration cease, and damaged parenchymal cells regenerate. In situations where limited or short lived **inflammation** has occurred this is usually the outcome.
2. **Fibrosis**

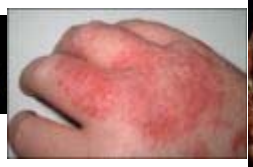
Large amounts of tissue destruction, or damage in tissues unable to regenerate, can not be regenerated completely by the body. Fibrous scarring occurs in these areas of damage, forming a scar composed primarily of collagen. The scar will not contain any specialized structures, such as parenchymal cells, hence functional impairment may occur.

3. **Chronic inflammation**
   In acute **inflammation**, if the injurious agent persists then chronic **inflammation** will ensue. This process, marked by **inflammation** lasting many days, months or even years, may lead to the formation of a chronic wound. Chronic **inflammation** is characterised by the dominating presence of macrophages in the injured tissue. These cells are powerful defensive agents of the body, but the toxins they release (including reactive oxygen species) are injurious to the organism's own tissues as well as invading agents. Consequently, chronic inflammation is almost always accompanied by tissue destruction.

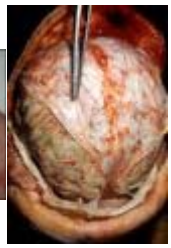
Examples

Inflammation is usually indicated by adding the suffix "-itis", as shown below. However, some conditions such as asthma and pneumonia do not follow this convention. More examples are available at list of types of inflammation.

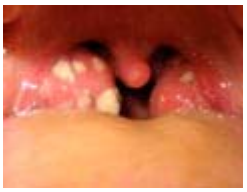
Acute appendicitis



Acute dermatitis



Acute infective meningitis



Acute tonsillitis