Inflammatoin part 2

Several types of inflammation are recognized, which vary in their morphology and clinical correlates.

***Serous inflammation*** is characterized by the outpouring of a thin fluid that is derived from either the plasma or the secretions of mesothelial cells lining the peritoneal, pleural, and pericardial cavities. In these serous cavities the accumulated fluid is called ***effusion***.

***Fibrinous inflammation***

A fibrinous exudate is characteristic of inflammation in the lining of body cavities, such as the meninges, pericardium, and pleura. With more severe injuries and the resulting greater vascular permeability, larger molecules such as fibrinogen pass the vascular barrier, and fibrin is formed and deposited in the extracellular space and on serosal surfaces. ***Microscopically,*** fibrin appears as an eosinophilic meshwork of threads or amorphous coagulated mass.

***Suppurative (purulent) inflammation***

This is characterized by the production of large amounts of pus or purulent exudate consisting of neutrophils, necrotic cells, and edema fluid. Certain bacteria (e.g., staph. aureus, Str. pyogenes, Pneumococci, gonococci, meningococci and E. coli) produce this localized suppuration and are therefore called pyogenic (pus-producing) bacteria. A common example of an acute suppurative inflammation is **acute (suppurative) appendicitis**. Pus is a thick creamy yellow or blood-stained fluid.

An **abscess** is a localized collection of purulent inflammatory exudate caused by suppuration buried in a tissue, an organ, or a confined space. Abscesses have a central mass of necrotic leukocytes and tissue debris, surrounded by a zone of preserved neutrophils, and outside this region vascular dilation and fibroblastic proliferation occur, indicating the beginning of repair. In time, the abscess may become walled off and replaced by connective tissue. A common example of an abscess is the skin furuncle.

***Ulcers***

Inflammatoin part 2

An ulcer is a local defect, or excavation of the surface of an organ or tissue that is produced by the sloughing (shedding) of inflammatory necrotic tissue. Ulceration occurs only when tissue necrosis and resultant inflammation exist on or near a surface. ***It is most commonly encountered in:***

*1. Inflammatory necrosis of mucosa-lined cavities* e.g. mouth, larynx, stomach, intestines, or genitourinary tract.

*2. Subcutaneous inflammation* of the lower extremities in older persons who have circulatory disturbances that predispose to extensive necrosis.

Ulcerations are best exemplified by peptic ulcer of the stomach or duodenum, in which acute and chronic inflammation coexist.

***Pseudomembranous inflammation of mucous membranes***

Severe injury may be associated with extensive epithelial necrosis and sloughing. This creates large shallow ulcers covered by a mixture of fibrin, dead epithelium, neutrophils, red cells and bacteria forming a white or cream-colored pseudo-membrane. Diphtheria and pseudo-membranous colitis are typical examples.

## EFFECTS OF ACUTE INFLAMMATION

### *Beneficial Effects*

*1. Dilution of Toxins by the edema fluid*

*2. Production of protective Antibodies & promotion of immunity*

*3. Fibrin meshwork formation that forms a scaffold for inflammatory cell migration & also limits the spread of infections*

*4. Cell Nutrition.*

### *Harmful Effects*

*1. Swelling & edema that can be detrimental* for e.g. acute epiglottitis that may be life threatening.

*2. Rise in tissue pressure that contributes to tissue necrosis*

*3. Digestion of adjacent viable tissue*

*4. Sever damaging allergic reaction*

*5. Generalized increase in vascular permeability can cause shock as seen in anaphylactic reactions.*

## OUTCOMES OF ACUTE INFLAMMATION

In general, acute inflammation may have one of three outcomes

### *1. Complete resolution*

The battle between the injurious agent and the host may end with restoration of the site of acute inflammation to normal. This is called resolution and is the usual outcome when

a. the injury is limited or short-lived
b. there has been little tissue destruction
c. the damaged parenchymal cells can regenerate

***The sequence of events in resolution involves:***

- Vasodilatation will subside
- Vascular permeability return to normal
- Excess fluid and soluble substances will be drained by lymphatics, and some return to blood vessels.
- Neutrophils will by their enzymes digest dead tissue and dead neutrophils.
- Dead tissue will be removed by macrophages.
- Fibrin will be lysed by fibrinolytic enzymes or cleared by macrophages..

### *2. Healing by fibrosis*

This occurs

a. after extensive tissue destruction
b. when the inflammatory injury involves tissues that are incapable of regeneration
c. when there is abundant fibrin exudation.

When the fibrinous exudate in tissue or serous cavities (pericardial, pleural, peritoneal, synovial) cannot be adequately cleared by fibrinolysis and macrophages, connective tissue grows into the area of exudate, converting it into a mass of fibrous tissue—a process

also called ***organization.*** When this occurs within the pericardial sac it leads either to fibrous thickening of the pericardium and often to fibrous adhesions that reduce and may even obliterate the pericardial space.

***3. Progression to chronic inflammation***

*Acute to chronic transition occurs when the acute inflammatory response persists,* owing either to the persistence of the injurious agent or to some interference with the normal process of healing. For example, failure of acute bacterial pneumonia to resolve may lead to extensive tissue destruction and formation of a cavity in which the inflammation continues to smolder, leading eventually to a chronic lung abscess.

# CHRONIC INFLAMMATION

Although it may complicate acute inflammation, it frequently begins from the outset as a chronic, insidious and smoldering response- (Chronic inflammation ab initio).

**Chronic Inflammation complicating acute inflammation** is almost always a suppurative type of inflammation that presents as a purulent discharge (pus) as seen in abscess. The cause is either a delay in the evacuation of an abscess, or presence of foreign-body within inflamed area (dirt, wood, metal or a sequestrated bone).

***Causes of chronic inflammation ab initio include***

***1. Persistent infections by certain microorganisms*** such as tubercle bacilli, Treponema pallidum, certain viruses, fungi, and parasites. These organisms are of low toxicity and evoke delayed type hypersensitivity reaction.

***2. Prolonged exposure to toxic agents*** either exogenous as inhaled silica particles, or endogenous such as toxic plasma lipids deposited in arterial wall initiating chronic inflammation that is thought to be responsible for atherosclerosis.

***3. Autoimmunity***

Under certain conditions, immune reactions develop against the individual's own tissues, leading to autoimmune diseases. In these diseases, autoantigens activate a self-perpetuating immune reaction that results in chronic inflammation with associated tissue damage. Examples of this type include several common chronic inflammatory diseases, such as rheumatoid arthritis and lupus erythematosus.

**Morphologic features of chronic inflammation**

In contrast to acute inflammation, which is manifested by vascular changes, edema, and predominantly neutrophilic infiltration, ***chronic inflammation is characterized by:***

*1. Infiltration with mononuclear cells* including macrophages, lymphocytes, and plasma cells.

*2. Tissue destruction*, induced by the persistent offending agent or by the inflammatory cells.

*3. Attempts at healing by fibrosis* of the damaged tissue, achieved by proliferation of small blood vessels (angiogenesis) & fibroblasts.

***Mononuclear inflammatory cell infiltration***

***The macrophage is the dominant cells in chronic inflammation***.

In chronic inflammation, macrophage accumulation persists, and this is mediated by the following:

*1. Recruitment* from circulating monocytes;

*2. Local proliferation* of macrophages after their emigration from the bloodstream. This is prominent in some chronic inflammatory lesions, such as atheromatous plaques.

*3. Immobilization* of macrophages within the site of inflammation by certain cytokines (migration inhibiting factors).

The products of activated macrophages serve to eliminate injurious agents such as microbes and to initiate the process of repair, but are

also responsible for much of the tissue injury in chronic inflammation; these products include

*1. Toxic substances* to microbes and host cells (e.g., toxic O2 species, NO, and proteases)

*2. Chemoattractants* to other inflammatory cells

*3. Growth factors* the cause of fibroblast proliferation, collagen deposition, and angiogenesis.

## GRANULOMATOUS INFLAMMATION

*This is a distinctive pattern of chronic inflammation characterized by focal accumulations of activated macrophages, which often develop an epithelioid (epithelial-like) appearance.*

**Causes**

Granulomatous inflammation is seen in a number of immunologically mediated infectious and some noninfectious conditions, incuding

1. Tuberculosis
2. Sarcoidosis
3. Cat-scratch disease
4. Lymphogranuloma inguinale.
5. Leprosy.
6- Brucellosis.
7- Syphilis.
8- Some fungal infections
9- Berylliosis
10- Reactions to irritant lipids.

A granuloma is a focus of chronic inflammation consisting of a microscopic aggregation of macrophages that are transformed into epithelioid cells surrounded by a collar of mononuclear leukocytes, principally lymphocytes and occasionally plasma cells. The epithelioid cells have a pale pink granular cytoplasm with indistinct cell borders and a vesicular nucleus that is oval or elongate. Older granulomas develop an enclosing rim of fibroblasts and connective tissue. Frequently, epithelioid cells fuse to form giant cells in the periphery or sometimes in the center of granulomas. These **giant cells** may attain diameters of 40 to 50 μm. They have a large mass of cytoplasm containing 20 or more small nuclei arranged either peripherally (Langhan's-type giant cell) or haphazardly (foreign body-type giant cell).

***There are two types of granulomas, which differ in their pathogenesis.***

***1. Foreign body granulomas*** which form when material such as talc (associated with intravenous drug abuse), sutures, or other foreign bodies are large enough to prevent phagocytosis by a single macrophage and do not incite any specific inflammatory or immune response. Epithelioid cells and giant cells form and are apposed to the surface of the foreign body and/or actually include it. The foreign material can usually be identified in the center of the granuloma, particularly if viewed with polarized light, in which it appears refractile.

***2. Immune granulomas;*** these are caused by insoluble, poorly degradable or particulate particles, typically microbes that are capable of inducing a cell-mediated immune response. In these responses, macrophages engulf the inciting agent, process it, and present some of it to appropriate T lymphocytes, causing them to become activated. The responding T cells produce cytokines, such as IL-2, which activates other T cells, perpetuating the response, and *IFN-γ, which is important in activating macrophages and transforming them into epithelioid cells and multinucleate giant cells.*

The typical example of an immune granuloma is that caused *tuberculosis*. Tuberculosis, is classically characterized by granulomas with central caseous necrosis, whereas caseation is rare in other granulomatous diseases. It is always necessary to identify the specific etiologic agent by special stains for organisms (e.g., acid-fast stains for tubercle bacilli), by culture methods (e.g., in tuberculosis and fungal diseases), by molecular techniques (e.g., the polymerase chain reaction in tuberculosis), and by serologic studies (e.g., in syphilis). *In sarcoidosis, the etiologic agent is unknown and the diagnosis is that of exclusion.*

## SYSTEMIC EFFECTS OF INFLAMMATION

Inflammatoin part 2

The systemic changes associated with inflammation, especially infections, are collectively called the ***acute phase response*** (Systemic inflammatory response syndrome [***SIRS***]). These changes are reactions to cytokines produced in response to bacterial infections and other inflammatory stimuli.

***The acute phase response consists of several clinical and pathologic changes:***

**1. Fever** is a prominent manifestation; it is produced in response to pyrogens that act by stimulating PG synthesis in the vascular and perivascular cells of the hypothalamus.

**2. Acute-phase proteins** are plasma proteins, mostly synthesized in the liver, and whose plasma concentrations may increase several hundred times in inflammation. The best-known of these are

***a. C-reactive protein (CRP)***

***b. Fibrinogen***

***c. Serum amyloid A protein (SAA).***

CRP and SAA, bind to microbial cell walls acting as opsonins and fixing complement. The rise in fibrinogen causes erythrocytes to form stacks (rouleaux) that sediment more rapidly than individual erythrocytes. This is the basis for the elevation of the (***erythrocyte sedimentation rate- ESR).***

Prolonged production of SAA causes *secondary amyloidosis* in destructive chronic inflammations (e.g. rheumatoid arthritis).

Elevated serum levels of CRP are now used as a marker for increased risk of myocardial infarction in patients with atherosclerotic coronary artery disease. The inflammation involving atherosclerotic plaques in the coronary arteries may predispose to thrombosis and subsequent infarction,

**3. Leukocytosis** is a common feature of the acute phase response, especially those induced by bacterial infection. The leukocyte count usually rises to 15,000 or 20,000 cells/µl, or even higher. The leukocytosis occurs initially because of accelerated release of cells from the bone marrow reserve pool (induced by cytokines, including IL-1 and TNF). *Neutrophilia* refers to an increase in the blood

neutrophil count. Most bacterial infections induce neutrophilia. Viral infections such as infectious mononucleosis, mumps, and German measles produce a leukocytosis due to *absolute lymphocytosis*. In bronchial asthma, hay fever, and parasitic infestations, there is an absolute increase in the number of eosinophils, creating an *eosinophilia*.

Certain infections (typhoid fever and infections caused by viruses, rickettsia, and certain protozoa) are associated with a decreased number of circulating white cells (*leukopenia*). *Leukopenia is also encountered in infections that overwhelm patients debilitated by disseminated cancer or uncontrolled tuberculosis.*

**4. Other manifestations** of the acute phase response include increased pulse and blood pressure; decreased sweating; rigors, and anorexia.

***5. Disseminated intravascular coagulation (DIC) & septic shock can occur*** in severe bacterial infections (sepsis).