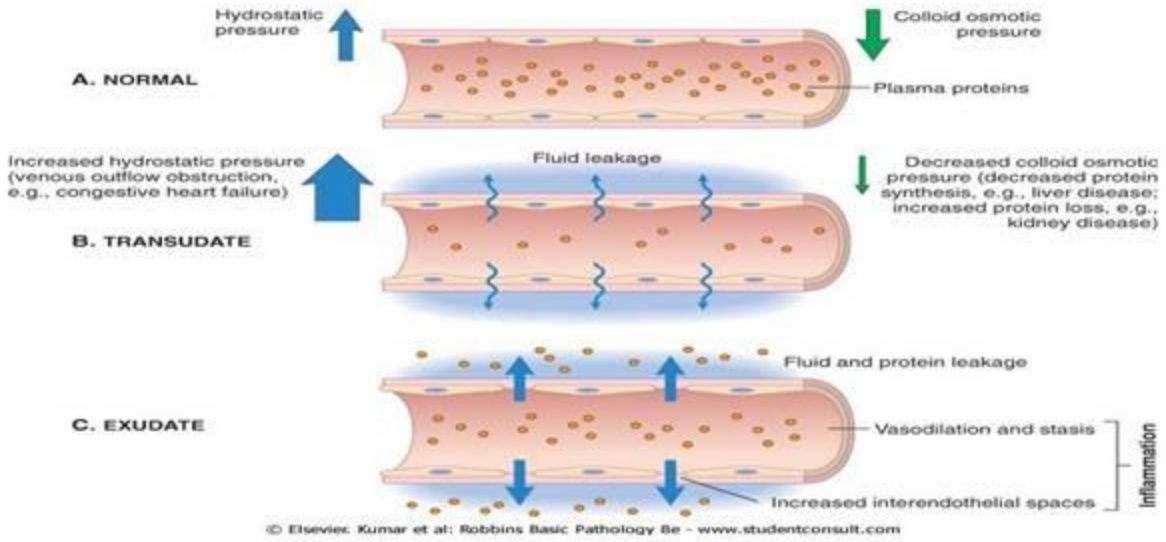
-2Increased vascular permeability:

-1Vasodilation is induced by inflammatory mediators such as histamine, and is the cause of erythema and stasis of blood flow.

-2Increased vascular permeability is induced by histamine, kinins, and other mediators that produce gaps between endothelial cells, by direct or leukocyte-induced endothelial injury, and by increased passage of fluids through the endothelium. This fluid, called a Transudate. .

-3Increased vascular permeability allows plasma proteins and leukocytes, the mediators of host defense, to enter sites of infection or tissue damage. Fluid leak from blood vessels (exudation) results in edema.

-4Lymph flow is increased to help drain edema fluid that accumulates because of increased vascular permeability. In addition to fluid, leukocytes and cell debris, as well as microbes, may find their way into lymph. The lymphatics may become secondarily inflamed (lymphangitis),as may the draining lymph nodes)lymphadenitis). Inflamed lymph nodes are often enlarged because of increased cellularity.



Inflammation causes endothelial cells to separate, thus allowing fluid + protein)exudate) to enter tissue bed.

Characteristics	Transudate	Exudate
Protein contents	Low	high

Mechanism	Increase hydrostatic pressure	Increase permeability of capillaries
Specific gravity	Low	high
Example	Heart failure	Inflammation

Cellular changes of acute inflammations

Movements of leukocytes from vascular lumen to the extravascular space controlled by cytokines, "are secreted by cells in tissues in response to microbes and other injurious agents, thus ensuring that leukocytes are recruited to the tissues where these stimuli are present. The two major families of molecules involved in leukocyte adhesion and migration are the selectins and integrins. These molecules are expressed on leukocytes and endothelial cells, as are their ligands. leukocyte are activated to perform their functions.

.1Migration & Rolling:

Leukocyte recruitment is a multistep process consisting of loose attachment to and rolling on endothelium (mediated by selectins); firm attachment to endothelium)mediated by integrins); and migration through interendothelial gaps.

.2Adhesion transmigrations

Various cytokines promote the expression of selectins and integrin ligands on endothelium (TNF, IL-1), increase the avidity of integrins for their ligands)chemokines), and promote directional migration of leukocytes (also chemokines .(Tissue macrophages and other cells responding to the pathogens or damaged tissues produce many of these cytokines.

•Neutrophils predominate in the early inflammatory infiltrate and are later replaced by monocytes and macrophages. divided into

.3Chemotaxis & Activation

Chemotaxis means WBC migrate toward sites of injury along a chemical gradient (by amebic like movement & under control of Chemotactics.(

i. Chemical gradient is more at the site of injury.
ii. Chemotactics : proteins present at the site of injury attract WBC to this site like Soluble bacterial proteins, Cytokines, leukotriene

iii. Activation of WBC is achieved by Chemotactics.

.4Phagocytosis & Degranulation of Leukocytes which include three steps:

Recognition of microbes or dead cells induces leukocyte activation caused:

(1)attachment of the particle to be ingested by the leukocyte.

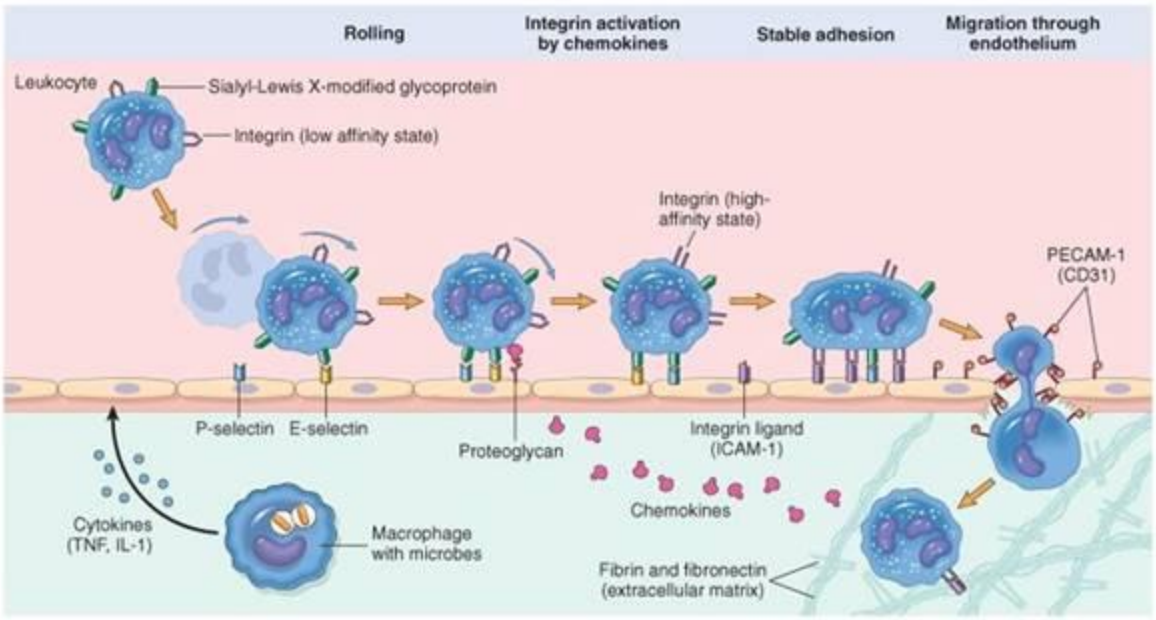
(2)engulfment, with subsequent formation of a phagocytic vacuole.

(3)killing or degradation of the ingested material are accomplished by reactive oxygen species (ROS, also called reactive oxygen intermediates), reactive nitrogen species, mainly derived from nitric oxide (NO),and lysosomal enzymes.

Cells of acute inflammation:

.1Neutrophils: reach site of inflammation within first 12 hours

.2Macrophages (mast cell): reach site of inflammation after 24 hours.



Chemical Mediators of acute inflammation:

These are substances that regulate the vascular & cellular changes of acute inflammation. Two types of Mediators

.1Tissue Mediators (present in the tissue & at site of acute inflammation)Examples of tissue mediators

TYPE MEDIATOR	Source	Action
Histamine	Mast cells, basophils	Vascular changes of inflammation
Serotonin	Platelets	Vascular changes of inflammation
Prostaglandins	WBC, Platelets	Vascular changes of inflammation also fever pain
Substances P	Nerve fibers	Pain
Nitric oxide	Macrophages	Free radical action

.1Plasma Mediators (proteases)Include three circulating systems in the plasma of blood.

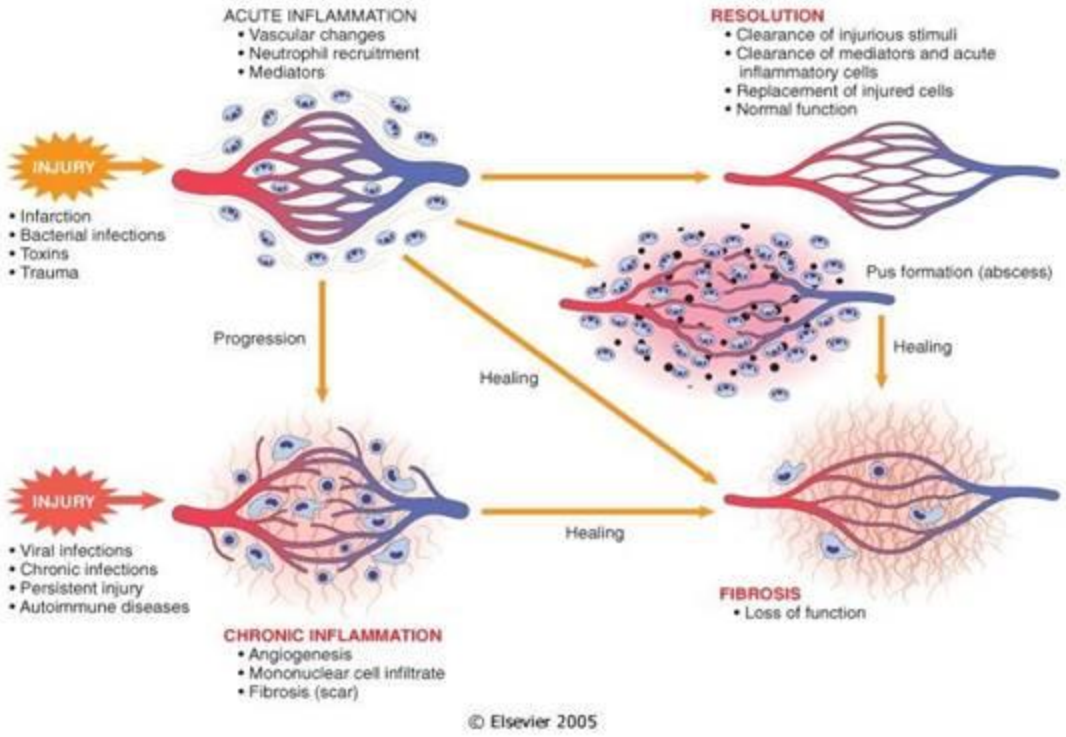
Type of plasma system	Active substances	action
Kinin system	Bradykinin	Like histamine &pain
Clotting system	Xlla, xa, Like histamine firinopeptides, fibrin degradation products	Like histamine, also cause Chemotaxis, fibrin formation
Complement system	C5a, C3a	Chemotactics

Outcomes (Fate) of acute inflammation:

.1Resolution: All changes that are occurred in inflammation are subsided resolution occur if there is minimal tissue damage & short lived cell injury.

.2Fibrosis: means scar formation. Fibrosis occured with great tissue damage, severe tissue injury, non dividing tissue.

Types of repair: resolution vs. organization (fibrosis(



.3Suppuration means pus formation:

Pus: yellow thick, creamy inflammatory exudates, contains living & e dead neutrophils, microorganisms, & tissue debris.

Abscess: collection of pus within a cavity & need surgical drainage. Bacteria produces pus is called Pyogenic bacteria

.4Progress to Chronic inflammation

Advantages of acute inflammation:

.1Dilution of toxins at the site of inflammation by Exudate.

.2Provision of immunity by lmmunoglobulins within the Exudate.

.3Delay spread of bacterial infection by formation of fibrin meshwork.

.4nutrients to the site of inflammation by exudate.

Disadvantages of acute inflammation

.1Swelling of inflamed site can cause death like swelling of larynx (dyspnea.(

.2Acute inflammation can result in loss of blood supply (death of tissue), like in osteomyelitis.

.3Impaired function of inflamed tissue like meningitis.

Types of Acute inflammation according to contents of exudates:

.1**Serous inflammation**: Characterized by clear watery, poor protein contents exudate, not infected by destructive organisms and does not contain large numbers of leukocytes, created by injury to surface epithelia or into body cavities lined by the peritoneum, pleura, or pericardium, may be derived from the plasma (as a result of increased vascular permeability) or from the secretions of mesothelial cells (as a result of local irritation); accumulation of fluid in these cavities is called an effusion. e g. pleural effusion, skin blister

.2**Fibrinous effusion**: Characterized by fibrin rich exudate, this fibrin will result in formation of fibrous scar tissue. It accrued when the vascular leaks are large or there is a local procoagulant stimulus. With a large increase in vascular permeability ، higher-molecularweight proteins such as fibrinogen pass out of the blood, an fibrin is formed and deposited in the extracellular space. A fibrinous exudate is characteristic of inflammation in the lining of body cavities, such as the meninges, pericardium، and pleura. fibrin appears as an eosinophilic meshwork of threads or sometimes as an amorphous coagulum e.g. acute pericarditis.

.3**Suppurative inflammation:** Characterized by formation of pus. The exudate consisting of neutrophils, the liquefied debris of necrotic cells, and edema fluid. The most frequent cause of purulent (also called suppurative) inflammation is infection with bacteria that cause liquefactive tissue necrosis, such as staphylococci; these pathogens are referred to as pyogenic (pus-producing) bacteria. A. Catarrhal inflammation Mild inflammation of mucous membrane

.5**Hemorrhagic inflammation:** Bloody exudate, e.g. viral pneumonia, meningitis

.6**Pseudomembraneous inflammation**: formation of necrotic membrane at the site of inflammation was characterized by gray-white pseudomembranes composed of densely matted fungal hyphae and inflammatory cells covering the mucosa. e.g. Pseudomembraneous

.7**Necrotizing gangrenous inflammation**: that has lost its blood supply and has undergone coagulative necrosis involving multiple tissue layers. When

bacterial infection is superimposed, the morphologic appearance changes to liquefactive necrosis because of the destructive contents of the bacteria and the attracted leukocytes (vascular inflammation) e.g. acute severe appendicitis.

.8**Ulcerative inflammation**: inflammation associated with ulcer formation) e g. Peptic ulcer.

Chronic inflammation: Chronic inflammation is a response of prolonged duration (weeks or months) in which inflammation, tissue injury, and attempts at repair coexist, in varying combinations. It may follow acute inflammation, sometimes progressive, process without any signs of a preceding acute reaction. **Causes of it:**

- Persistent infections e.g *Treponema pallidum* [syphilis], viruses, fungi, parasites
- Exposure to toxic agents
  - –Exogenous: silica (silicosis(
  - –Endogenous: toxic plasma lipid components (atherosclerosis(
  - –Autoimmunity e.g Rheumatoid arthritis, systemic lupus erythematosus

Histological characterized by:

.1Chronic inflammatory cells (lymphocytes, macrophages & plasma cells) cells

.2Tissue destruction by the products of these cell.

.3Repair by angiogenesis & fibrosis.

Types of Chronic inflammatory cells:

.1Macrophages : in blood called Monocytes, can transform into epitheloid cells, giant cells of granuloma.

.2Lymphocytes: activate macrophages by lymphokines, interferons

.3Plasma cells produce antibodies.

.4Eosinophiles: increase in parasitic of inflammation.

.5Mast cells : produce histamine (mediator inflammation. (

.6Fibroblasts: important in repair process by formation of scar tissue.

Table 3.1 Features of Acute and Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: minutes or hours	Slow: days
Cellular infiltrate	Mainly neutrophils	Monocytes/macrophages and lymphocytes
Tissue injury, fibrosis	Usually mild and self-limited	May be severe and progressive
Local and systemic signs	Prominent	Less

Chronic Granulomatous inflammation:

Specific type of chronic inflammation characterized by collections of activated macrophages, often with T lymphocytes, and sometimes associated with central necrosis. The activated macrophages may develop abundant cytoplasm and begin to resemble epithelial cells, and are called epithelioid cells. Some activated macrophages may fuse, forming multinucleate giant cells to formation of Granuloma.

Granuloma: is a collection of modified macrophages (epitheloid. cells), surrounded by a cuff of lymphocytes, fibroblasts & sometime have central area of caseous necrosis, & in many conditions contain Giant cells (fusion of epitheloid cells(

Causes of granuloma:

.1Bacterial Infections like tuberculosis leprosy syphilis

.2Fungal infection eeg Cryptococcus.

.3Parasitic infection: belharizia.

.4Foreign bodies: silica, suture material.

.5Unknown causes: sarcoidosis

Tissue repair:

Restoration of tissue functions & structure after cell injury, Include two type

.1Repair by regeneration (dividing cells(

.2Repair by scar formation (fibrosis.(

❖ **Repair by regeneration:** According to regenerative capacity, there are three types of body cells.

.1**Labile cells:** Continuous proliferation throughout the life .e.g. blood cells, skin lining of GIT, urinary, respiratory, genital organs.

.2**Stable cells**: Minimal replicative capacity, but increase its replicative capacity in response to injury e.g. liver, kidney, pancreas, endothelial cells fibroblasts, & smooth muscles.

.3**Permanent cells**: include cells cannot divided e a nerve, skeletal muscles& . cardiac muscles.

❖ **Repair by Scar formation: include**

-1Replacement of parenchymal tissue at site of injury by fibroblasts & blood vessels with 24 hours(
-2Formation of granulation tissue (within 3-5days.(

❖ Granulation tissue: characterized by Gross: pink soft tissue. Mic: composed of small blood vessels fibroblasts edematous stroma macrophages.

Healing wound: By two types of healing

.1Healing by first intention: Occur in wounds with opposed edges, clean uninfected wounds without tissue loss (surgical wound.(

.2Healing by second intention occur in with separated edges, with extensive tissue loss like infection, ulceration, & abscess.

It differs from first intention by:

.1Large tissue loss with more inflammation.

2More granulation tissue.

.3wound contraction phenomena within 6 months (by myofibroblasts.(

Factors affect wound healing:

.1Infection (delay healing(

.2Presence of foreign body.

.3Type, site & size of wound, e g wound on the face heal rapidly than wound on the leg (more blood supply in the face(

.4Nutrition lack of proteins, vitamin C& Zinc lack of delay wound healing

.5Diabetes Mellitus and increased steroid hormones delay wound healing.

.6Vascular insufficiency like atherosclerosis will delay wound healing

.7Excess movement at site of wound will delay wound healing

.8Decrease WBC caused arrest wound healing.