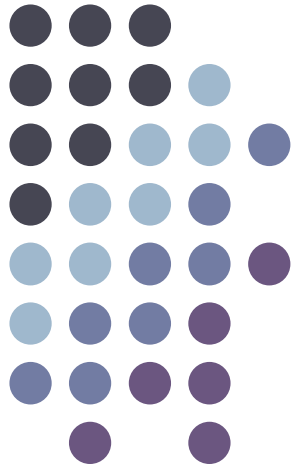
Inflammation



INFLAMMATION

SEQUENCE OF SPECIFIC PHYSIOLOGICAL BEHAVIORS THAT OCCUR IN RESPONSE TO A NONSPECIFIC AGENT.

ACTS TO:

1) **NEUTRALIZE OR DESTROY OF FENDING AGENT**
2) **RESTRICTS TISSUE DAMAGE TO SMALLEST POSSIBLE AREA**
3) **ALERTS BODY TO THREAT OF TISSUE INJURY**
4) **PREPARES INJURED AREA FOR HEALING**

CAUSES: EXOGENOUS OR ENDOGENOUS

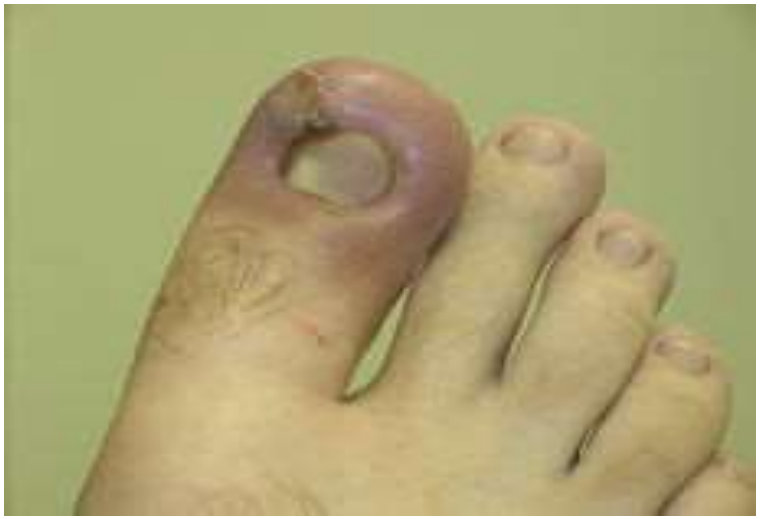
TRAUMA, SURGERY, INFECTION, CAUSTIC CHEMICALS, EXTREMES OF HEAT OR COLD, IMMUNE RESPONSES, ISCHEMIC DAMAGE

- Inflammation is a non specific, localized immune reaction of the organism, which tries to localized the pathogen agent. Many consider the syndrome a self-defense mechanism.

- It consist in vascular, metabolic, cellular changes, triggered by the entering of pathogen agent in healthy tissues of the body.

Cardinal Signs

- Celsius described the local reaction of injury in terms that have come to be known as the *cardinal signs* of inflammation.
- These signs are:
  - *rubor* (redness)
  - *tumor* (swelling)
  - *calor* (heat)
  - *dolor* (pain)
  - *functio laesa,* or loss of function (In the second century AD, the Greek physician Galen added this fifth cardinal sign)



CARDINAL SIGNS OF ACUTE INFLAMMATION

Heat **Redness** **Swelling** **Pain** **Loss of function**

Celsius (30 BC) Virchow (1902)

Acute Inflammation Components

Physiological Responses

Release of soluble mediators

Vasodilation

Increased blood flow

Extravasation of fluid (permeability)

Cellular influx (chemotaxis)

Elevated cellular metabolism

Symptoms

Heat (calor)

Redness (rubor)

Swelling (tumor)

Pain (dolor)

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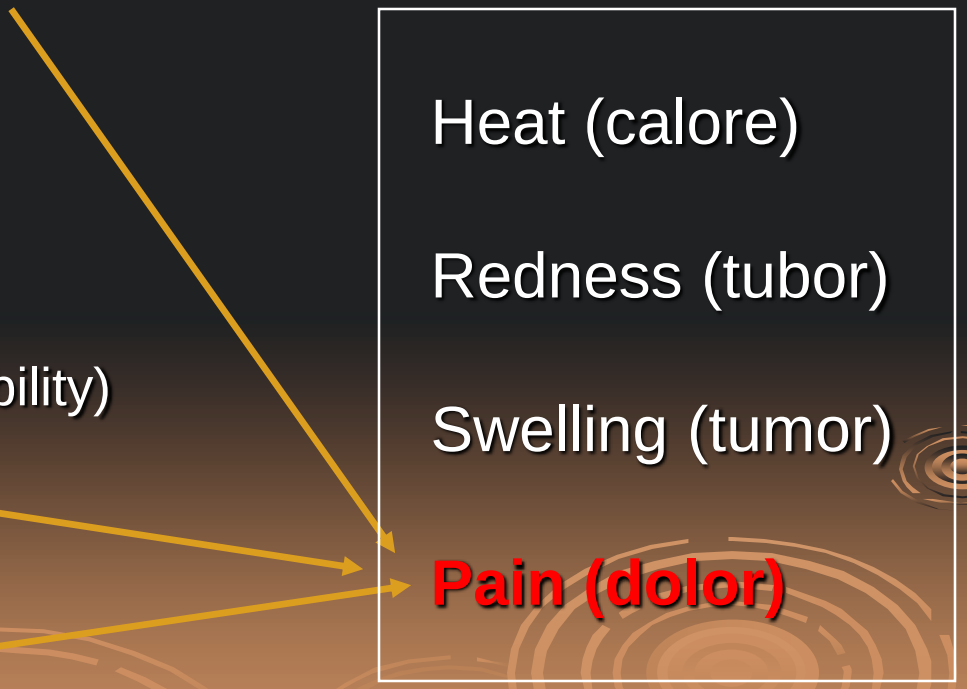


Etiology

- The causes of inflammation are many and varied:
  - Exogenous causes:
    - Physical agents
      - Mechanic agents: fractures, foreign corps, sand, etc.
      - Thermal agents: burns, freezing
    - Chemical agents: toxic gases, acids, bases
    - Biological agents: bacteria, viruses, parasites
  - Endogenous causes:
    - Circulation disorders: thrombosis, infarction, hemorrhage
    - Enzymes activation – e.g. acute pancreatitis

Inflammation

- The inflammatory reaction takes place at the microcirculation level and it is composed by the following changes:
  - Tissue damage
  - Cellular – vascular - cellular response
  - Metabolic changes
  - Tissue repair

Tissue damage

- Changes begin almost immediately after injury:
  - Because of the pathogen agent action, in the affected tissue are released mediators responsible for the following events of inflammation.
  - Tissue macrophages, monocytes, mast cells, platelets, and endothelial cells are able to produce a multitude of cytokines. The cytokines tissue necrosis factor-a (TNF-a) and interleukin (IL)–1 are released first and initiate several cascades.

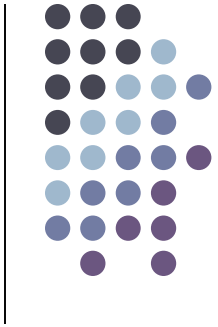
The Vascular Response

- *Faze I = vasoconstriction* (momentary constriction of small blood vessels in the area).
  - Vascular spasm begins very quickly (30 sec.) after the injury at it last a few minutes.
  - The mechanism of spasm is nervous – through catecholamine liberated from sympatic nerves endings.
- *Faze II = active vasodilation* (through catabolism products that act through receptors and directly stimulates vascular dilation – nervous mechanism).
  - Dilation of arterioles and capillaries (***redness = rubor***);
  - Blood flow increases and gives pulsate sensation;
  - Active hyperemia in skin territory and increased metabolism leads to higher local temperature (***heat = calor***).

The Vascular Response

- *Faze III = passive vasodilation*
  - Blood vessels in the affected area loose their reactivity to nervous and humoral stimuli and passive vasodilation occurs.
  - Progressively fluid move into the tissues (increased vascular permeability and structural alteration of blood vessels) and cause swelling (***tumor***), pain, and impaired function.
  - The exudation or movement of the fluid out of the capillaries and into the tissue spaces dilutes the offending agent. As fluid moves out of the capillaries, stagnation of flow and clotting of blood in the small capillaries occurs at the site of injury.
  - This aids in localizing the spread of infectious microorganisms, if case.

Cellular Response



- The cellular response of acute inflammation is marked by movement of phagocytic white blood cells (leukocytes) into the area of injury.
- Two types of leukocytes participate in the acute inflammatory response - the granulocytes and monocytes.
- The sequence of events in the cellular response to inflammation includes:
  - pavementing
  - emigration
  - chemotaxis
  - phagocytosis

Inflammation

- Stage I:
  - Following an insult, local cytokine is produced with the goal of inciting an inflammatory response, promoting wound repair and recruitment of the reticular endothelial system.
- Stage II:
  - Small quantities of local cytokines are released into circulation to improve the local response. This leads to growth factor stimulation and the recruitment of macrophages and platelets. This acute phase response is typically well controlled by a decrease in the proinflammatory mediators and by the release of endogenous antagonists. **The goal is homeostasis**.
- Stage III:
  - If homeostasis is not restored, a significant systemic reaction occurs. The cytokine release leads to destruction rather than protection. A consequence of this is the activation of numerous humoral cascades and the activation of the reticular endothelial system and subsequent loss of circulatory integrity. This leads to organ dysfunction.

Factors That Affect Wound Healing

- Malnutrition
  - Protein deficiencies prolong the inflammatory phase of healing and impair fibroblast proliferation, collagen and protein matrix synthesis, angiogenesis, and wound remodeling.
  - Carbohydrates are needed as an energy source for white blood cells.
  - Fats are essential constituents of cell membranes and are needed for the synthesis of new cells.
  - Vitamins A and C have been shown to play an essential role in the healing process.
    - Vitamin C is needed for collagen synthesis.
    - Vitamin A functions in stimulating and supporting epithelialization, capillary formation, and collagen synthesis. The B vitamins are important cofactors in enzymatic reactions that contribute to the wound-healing process.
    - Vitamin K plays an indirect role in wound healing by preventing bleeding disorders.

Factors That Affect Wound Healing

- **Blood Flow and Oxygen Delivery**
  - Pre-existing health problems
  - Arterial disease and venous pathology

  - Molecular oxygen is required for collagen synthesis.
    - It has been shown that even a temporary lack of oxygen can result in the formation of less stable collagen.
  - Wounds in ischemic tissue become infected more frequently.
  - PMNs and macrophages require oxygen for destruction of microorganisms.

Outcomes

- **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.
- **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.

Outcomes

- **Abscess formation**
  - A cavity is formed containing pus, an opaque liquid containing dead white blood cells and bacteria with general debris from destroyed cells.
- **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.

Comparison between acute and chronic inflammation:

	Acute	Chronic
Causative agent	Bacterial pathogens, injured tissues	Persistent acute inflammation due to non-degradable pathogens, viral infection, persistent foreign bodies, or autoimmune reactions
Major cells involved	neutrophils (primarily), basophils (inflammatory response), and eosinophils (response to helminth worms and parasites), mononuclear cells (monocytes, macrophages)	Mononuclear cells (monocytes, macrophages, lymphocytes, plasma cells), fibroblasts
Outcomes	Resolution, abscess formation, chronic inflammation	Tissue destruction, fibrosis, necrosis
Onset	Immediate	Delayed
Duration	Few days	Up to many months, or years