INFLAMMATION

The reaction of **vascular tissue** to local injury.

Injury: micro-organisms, trauma, surgery, chemicals, heat / cold, ischemia.

While thought of as a protection against disease, it is also known to be involved in the genesis of disease: asthma, R.A., atherosclerosis.

GOAL: remove the injurious agent and limit the extent of tissue damage.
5 CARDINAL SIGNS OF INFLAMMATION

1) REDNESS- “rubor”
2) HEAT- “calor”
3) SWELLING- “tumor”
4) PAIN- “dolor”
5) LOSS OF FUNCTION- “functio laesa”
TYPES OF INFLAMMATION

1) ACUTE - immediate, non-specific, short duration; minutes to days.

2) CHRONIC - delayed, longer lasting; days, weeks, years.
ACUTE INFLAMMATION

**2 STAGES:**

1) VASCULAR STAGE.

2) CELLULAR STAGE.
VASCULAR STAGE

✿ VASODILATATION - via histamine.

✿ 1) \( \uparrow \) capillary permeability \( \rightarrow \) fluid leaks into the area.

✿ 2) Dilutes the offending agent.

✿ Causes redness, warmth, swelling, and pain.
CELLULAR STAGE

Phagocytic cells move into the area.

INVOLVES:

1) GRANULOCYTES - primarily the neutrophil, but also eosinophils and basophils.

2) MONOCYTES.
THE NEUTROPHIL

- Granules that do not stain- “neutral.”
- Nucleus- 3-5 lobes- polymorphonuclear leukocyte- the “PMN,” the “poly,” or the “seg” ie the segmented neutrophil.
- Arrives within 90 minutes of injury.
- Is phagocytic- granules contain enzymes (peroxisomes, lysosomes) that destroy the engulfed particle.
THE NEUTROPHIL

Life span of 10 hours → ↑ demand → release of immature forms known as “bands” → horseshoe-shaped nucleus (rather than polymorphonuclear).

When we see these immature forms, we call this a “shift to the left,” or a “left shift.”
THE EOSINOPHIL

- Granules stain red (eosin stain).
- Allergies, parasitic infections.
- Granules → toxic proteins, toxic to parasites that can’t be phagocytized.
- Release chemical mediators that regulate inflammation and allergies.
THE BASOPHIL

✿ Stain blue w/ a “basic” dye.
✿ Release histamine.
✿ Involved in inflammation and allergies.
MONOCYTES

- An agranulocyte (ain’t got no granules).
- Live 3-4X longer than granulocytes.
- Also are phagocytic.
- Release cytokines to stimulate specific/adaptive/acquired immunity.
- Migrate into tissues → macrophages.
- At 48 hrs. → monocytes and macrophages are the predominate cell at the site of inflammation.
MONOCYTES

- Bigger than neutrophils → can engulf bigger stuff.
- Migrate to lymph nodes → stimulate specific/adaptive/acquired immunity.
- Involved in chronic inflammation → wall-off foreign material which can’t be ingested.
MAST CELLS

- Prevalent along mucosal surfaces.
- Release histamine.
- Release IgE in allergies and hypersensitivity reactions.
THE LEUKOCYTE RESPONSE

INVOLVES:

1) MARGINATION.
2) EMIGRATION.
3) CHEMOTAXIS.
4) PHAGOCYTOSIS.
Leukocytes slow their migration and move along the periphery of the blood vessels. 

Affected by the release of chemical mediators and cytokines → affect the endothelial cells of the capillaries → leukocytes increase their expression of adhesion molecules.
Leukocytes migrate through the capillary walls as they become more permeable = diapedesis. Develop “pseudopodia.”

Drawn to the area of inflammation (chemotaxis) by mediators such as cytokines, complement, etc.
PHAGOCYTOSIS

- Neutrophils & macrophages.
- Engulf and destroy bacteria and cellular debris.

3 PHASES

1) Opsonization-enhanced binding of an Ag due to Ab or complement.
2) Engulfment.
3) Killing.
INFLAMMATORY MEDIATORS

1) Vasoactive and smooth muscle constricting properties: histamine, prostaglandins, leukotrienes, platelet-activating actor.

2) Chemotactic Factors: complement, cytokines.

3) Plasma Proteases: activate complement and components of the clotting mechanism.

4) Reactive molecules and cytokines: released by leukocytes → can damage the surrounding tissue.
PLASMA PROTEASES

1) The kinins—e.g., bradykinin—increase capillary permeability, cause pain.
2) Activated complement proteins.
3) Clotting factors.
A “cascade” of proteins involved in inflammation and immunity.

Complement causes:
1) Vasodilatation, increased permeability.
2) Leukocyte activation, adhesion, & chemotaxis
3) Augmentation of phagocytosis.
ARACHIDONIC ACID METABOLITES

- Lead to production of prostaglandins and leukotrienes.
  - Cyclo-oxygenase pathway → PG’s.
  - Lipo-oxygenase pathway → leukotrienes.
PROSTAGLANDINS

- PGE₁, PGE₂ → induce inflammation, potentiate the effect of histamine.
- THROMBOXANE A₂ (a PG) → platelet aggregation and vasoconstriction.
- Aspirin and NSAID’s block cyclooxygenase, ↓ PGE₁ synthesis.
LEUKOTRIENES

✿ Function similar to histamine.
✿ Histamine released while leukotrienes being synthesized.
✿ → Chemotaxis, increased capillary permeability, & extravasation of neutrophils, eosinophils, and monocytes.
✿ Bronchoconstriction.
✿ Asthma, anaphylaxis.
PLATELET ACTIVATING FACTOR

- P.A.F.
- Produced by cell membranes.
- Induces platelet aggregation.
- Activates neutrophils.
- Chemotaxis for eosinophils.
CYTOKINES

- Produced primarily by lymphocytes and monocytes.
- Modulate the function of many kinds of cells.
- Interleukins (IL’s).
- Interferons (INF’s).
- Tumor necrosis factor (TNF).
- Colony stimulating factor (CSF).
CHRONIC INFLAMMATION
CHRONIC INFLAMMATION

✿ Cells of acute inflammation: neutrophils.

✿ Cells of chronic inflammation:
- Lymphocytes, Monocytes.
- Fibroblasts- produce collagen → scar, healing.
PERPETRATORS OF CHRONIC INFLAMMATION

- Low-grade, persistent irritants that are unable to penetrate deeply or spread rapidly:
  - Foreign Bodies: talc, silica, asbestos, suture.
  - Viruses.
  - Certain bacteria: TB, syphilis, actinomyces.
  - Fungi.
  - Parasites.
CHRONIC INFLAMMATION

2 FLAVORS OF CHRONIC INFLAMMATION:

1) NON-SPECIFIC CHRONIC INFLAMMATION.

2) GRANULOMATOUS INFLAMMATION.
NON-SPECIFIC CHRONIC INFLAMMATION

- Lymphocytes and Monocytes (macrophages).
- Macrophages - prolonged survival.
- Fibroblasts → replace normal tissue or parenchyma.
- Examples: inflammatory bowel disease, rheumatoid arthritis, lupus.
GRANULOMATOUS INFLAMMATION

✿ GRANULOMA: A 1-2mm collection of macrophages and lymphocytes.
✿ Macrophages $\rightarrow$ evolve into the “epithelioid” cell.
✿ Elicited By:
✿ Foreign body.
✿ TB, syphilis, fungi.
✿ Sarcoidosis.
✿ All are poorly digested and not controlled by other inflammatory mechanisms.
GRANULOMATOUS INFLAMMATION

THE MULTINUCLEATED GIANT CELL: A coalescence of epithelioid cells around the foreign agent.


CASEOUS (CHEESY) NECROSIS: Found at the center of a tubercle.

“CAVITARY” TB- Cavitary lesions in the lung, due to caseous necrosis in TB.
LOCAL MANIFESTATIONS OF INFLAMMATION

- **DEPENDS ON:**
  1) The cause.
  2) The tissue involved.

- **INVOLVES 5 KINDS OF “EXUDATES”**
  1) SEROUS EXUDATE.
  2) HEMORRHAGIC EXUDATE.
  3) FIBRINOUS EXUDATE.
  4) MEMBRANOUS EXUDATE.
  5) PURULENT EXUDATE.
SEROUS EXUDATE

- Lots of watery fluid.
- Little protein.
HEMORRHAGIC EXUDATE

Injury involves damage to vessels, or leakage of RBC’s into the tissue.
FIBRINOUS EXUDATE

 Lots of fibrinogen → forms a mesh, similar to a clot.
MEMBRANOUS EXUDATE

- Develops a mucous membrane.

- Necrotic cells in a mucopurulent exudate.
**PURULENT / SUPPURATIVE EXUDATE**

- Contains pus - tissue debris, protein, WBC’s.
- Abscess - localized collection of pus.
1) ACUTE PHASE RESPONSE.
   Immune trying to fight infection. IgM goes up, IgG takes over and goes up as you overcome infection.

2) CHANGE IN WBC COUNTS- \( \uparrow \) OR \( \downarrow \).
   2 things can happen: overwhelming = WBC down, if system fighting = WBC up.

3) SEPSIS / SEPTIC SHOCK.
ACUTE PHASE RESPONSE

- **INCLUDES:**
  1. Change in concentration of plasma proteins.
  2. Increase in ESR.
  3. Fever.
  4. Increase in WBC’s.
  5. Skeletal catabolism.
  6. Negative nitrogen balance
ACUTE PHASE RESPONSE

CAUSED BY CYTOKINES:
- Affect the thermoregulatory center in the hypothalamus.
- ↑ production of bone marrow WBC’s → released into the circulation → ↑ numbers, ↓ maturity.
- Skeletal muscle catabolism → amino acids available to produce Ab’s and repair tissue.
ACUTE PHASE PROTEINS

- **LIVER** → CRP, Fibrinogen → ↑ ESR.
- **CRP** → Binds to micro-organisms → tags them for destruction by complement & phagocytosis.
- **ESR** - Acute phase proteins dampen the repulsive effects of like charges on WBC’s → clumping, aggregation (rouleau / rouleaux formation.)
WBC RESPONSE

- **BACTERIA** - ↑ neutrophils.
- **PARASITES** - ↑ eosinophils.
- **VIRUSES** - ↓ neutrophils (neutropenia), ↑ lymphocytes (lymphocytosis).
LYMPHADENITIS

- Tenderness / swelling of nodes in the area draining an inflamed / infected area.

- A response to mediators released by injured tissue, OR an immune response to a specific antigen.
1) REGENERATION.

2) DEVELOPMENT OF SCAR, REPLACEMENT BY CONNECTIVE TISSUE, WHICH RETRACTS WITH TIME
TISSUE REGENERATION

TISSUES MADE UP OF:

1) PARENCHYMA - the functioning cells of an organ or tissue; hepatocytes, etc.

2) STROMA - the supporting connective tissue, blood vessels, nerves, extra-cellular matrix.

Dependent on cellular proliferation.

Forget about labile, stable, and permanent cells.
**DO KNOW**

- **GRANULATION TISSUE** - Highly vascularized tissue w/ newly-formed capillaries, fibroblasts, & residual inflammation.
- **ANGIOGENESIS** - “Sprouting” of new vessels.
- **FIBROGENESIS** - The product of activated fibroblasts - production of fibronectin, hyaluronic acid, proteoglycans, and collagen → scar tissue formation.
WOUND HEALING

HEALING BY:

1) PRIMARY INTENTION.

2) SECONDARY INTENTION.
WOUND HEALING

擞 PHASES OF WOUND HEALING:

擞 1) INFLAMMATORY PHASE.

 eSports 2) PROLIFERATIVE PHASE.

擞 3) REMODELING PHASE.
INFLAMMATORY PHASE

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WHAT YOU LEARNED ABOUT INFLAMMATION.
PROLIFERATIVE PHASE

Within 2-3 days.
Granulation Tissue.
Fibroblasts.
Collagen.
Neovascularity.
REMODELING PHASE

- Week 3 → 6 months.
- Continued production of collagen.
- Lysis of collagen.
- Scar retraction.
1) MALNUTRITION.
2) BLOOD FLOW, OXYGEN.
3) IMPAIRED INFLAMMATORY AND IMMUNE RESPONSE.
4) INFECTION.
5) INFECTION, WOUND SEPARATION, FOREIGN BODIES.
6) AGE.
FACTORS AFFECTING HEALING

MALNUTRITION

» TO HEAL, WE NEED:
» PROTEIN- for synthesis of new cells, enzymes, antibodies, etc.
» CARBS- for cellular energy (ATP).
FACTORS AFFECTING HEALING

BLOOD FLOW, OXYGEN

Both to (arterial) and from (venous).
IMPAIRED INFLAMMATION AND IMMUNITY

INFLAMMATION
- 1st phase of healing.

IMMUNITY
- Prevent infections that impair wound healing.

IMPAIRED BY
- 1) DISORDERS OF PHAGOCYTOSIS.
- 2) DIABETES.
- 3) CORTICOSTEROIDS
DISORDERS OF PHAGOCYTOSIS

★ EXTRINSIC AND INTRINSIC.
★ SEE TEXT.
★ IMPAIRMENTS OF ENGULFMENT, DESTRUCTION OF FOREIGN MATERIAL.
SEE TEXT.

SMALL VESSEL DISEASE (MICROANGIOPATHY).
CORTICOSTEROIDS

✿↓ CAPILLARY PERMEABILITY.
✿↓ PHAGOCYTOSIS.
✿↓ FIBROBLAST PROLIFERATION.
INFECTION, WOUND SEPARATION, FOREIGN BODIES

**INFECTION** - impairs all dimensions of healing.

**FOREIGN BODIES** - invite bacterial contamination, can prolong the inflammatory reaction.

**WOUND SEPARATION** - dehiscence, see text.
• Decreased immunity, decreased healing.
• ↓ collagen & fibroblast synthesis.
• They heal, but more slowly.
• Have coexisting diabetes, vascular disease, etc.