## Acute inflamation

**Vascular response**

1. increase blood flow by vasodilation (histamine)+ vascular congestion

-> redness, heat

2. increase permeability of vessel by retraction and injury

-> edema

3. Lymph flow increase to drain extravascular fluid + secondary inflammation

## Terminations

1. Mediator bursts rapidly due to short half lives e.g. neutrophil

2. Trigger stop signals

- proinflammatory leukotriene to anti-inflammatory lipoxins

- release anti-inflammatory cytokines

## Chemical mediators

| Cell-derived | Plasma-derived |
|---|---|
| **1. Vasoactive amines** | **1.Complement system** |
| - Histamine by mast cell | - Inflammation |
| - Serotonin by platelet aggregation | - Opsonisation & Phagocytosis |
| _____ | - Cell lysis |
| **2. Arachidonic acid metabolites** | _____ |
| Both by leukocyte in lipoxygenagse pathway | **2.Clotting system** |
| **Leukotrienes** | - Clotting system: induce thrombin formation |

## Chemical mediators (cont)

| | |
|---|---|
| - LTC4,D4,E4: Vasoconstriction, increase vascular permeability | - Kinin system: vasoactive |
| - Inhibit by LT receptor antagonist | - Complement system |
| **Lipoxins** | - Fibrinolytic system |
| - Suppress inflammation | _____- _____ |
| **Prostacyclin** | **3.Kinins** |
| - PGI2, PDI2, PEI2: Vasodilation | - form bradykinin |
| _____ | a. increase vascular permeability |
| **3.Cytokines& chemokines** | b. non-vascular smooth muscle contraction |
| **Cytokines** | c. pain |
| - Tumor necrosis factor (TNF) & interleukin-1 (IL-1) | 4. rapidly inactivated |

a. Increase endothelial cell adhesion molecule expression

b. Activation and aggregation of PMN

c. Systemic acute-phase response:Fever

**Chemokines**

- Attract WBC

## Chronic inflammation

**Causes**

1. Prolonged inflammation

2. Prolonged toxic substance exposure

3. Autoimmune disease



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## Morphological change

1. Mononuclear cell infiltration (e.g. macrophage, lymphocyte, plasma cell)
2. Cell destruction by inflammatory cells
3. Repair attempts by fibrosis & angiogenesis

## Types of inflammation

| Granulomatus inflammation | Defective inflammation |
|---|---|
| - Produce granuloma containing an difficult offending agent | -delayed wound healing |
| - squamous>epitheloid | **Excessive inflammation** |
| - fuse> multinuclear giant cell | - Abnormal reaction of body e.g. allergy |
| | - Fibrosis & tissue injuries |

## Scar formation steps(Connective tissue deposition)

1. Angiogenesis
2. Granulation tissue formation
3. Connective tissue remodelling'

## Cutaneous wound healing(1)

- Clean wound, only epithelial layer

**Inflammatory phase**

1. Formation of blood clot
- Neutrophil appears after 24hrs
- Proteolytic enzyme to clean out debris and invading bacteria

**Proliferative phase**

**1. Formation of granulation tissue**

- Induction of fibroblast and endothelial cell proliferation
- Composed of newly formed thin capillaries & loose ECM also
- Peak at day5

## Cutaneous wound healing(1) (cont)

- To cover the wound

**2. Angiogenesis**

i. **VEGF** >Vasodilation& I+permeability

ii. Proteolytic degradation of parent vessel BM>> capillary sprout

iii. Migration of endothelial cells toward angiogenetic stimulus

iv. Proliferation of endothelial cell behind leading edge of migrating cells

v.Maturation of end. cells into capillary tubes

vi. Recruitment of periendothelial cells for mature vessel

**3.Cell proliferation and collagen deposition**

- Macrophage replace neutrophils after 48hrs (key cellular constitue-nts> main resource for chemokines & GF)
- Migration and proliferation of fibroblast at injury site > secrete and deposit collagen
- Epithelial cells proliferate to centre of wound

**Remodeling phase**

**4. Scar formation**

- Granulation tissue>Scar
- Composed of inactive spindle-shaped fibroblasts, dense collagen, fragments of elastic tissue, ECM
- Pale, avascular

**5. Connective tissue remodeling**

-Balance between ECM synthesis & degradation

- Degradation of collagen & MMPs > smaller & softer scar



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## Defective

**1.Defective scar formation**

- Ulceration

**2.Excessive sf** (keloid)

**3.Contracture**

## Cellular response

important leukocyte; neutrophil and macrophages

**1. Adhesion to endothelium**

**a. Margination**

- stasis of blood >settle out the central flow and marginate along endothelium surface

**b. Rolling**

- complementary surface adhesion molecules sticks and release > rolling along

- mediated by selectins, regulated by cytokines

**c. Adhesion**

- mediated by intergrins

---

**2.Migration thru endo**

-secrete collagenase thru basement membrane

- migrate toward chemotactic gradient

---

**3.Chemotaxi**

-neutrophil>monocyte>macrophage

---

**4.Phagocytosis**

a. Recognition by receptors to sd signals

b. Activation by cytosolic Ca2+ and enzymes

c. Engulf & Degradation

d. anti-inflammatory effects and wound repair

## Morphologic patterns and systemic effects

| Morphologic patterns | Cytokine-induced systemic reaction aka Acute--phase responses |
|---|---|
| **1.Serous** | 1.Fever by pyrogens |
| **2. Fibrinous** | 2. Leukocytosis |
| - Increase cell fibrin | 3.Phase proteins |
| - risk of scar formation | - CRP, Fibrinogen,SAA |

**3.Purulent**

-Pus, leukocyte and debris

**4. Ulcer**

- Open lesion

## Possible outcomes

**1.Complete resolution**

**2. Fibrosis/scarring**

**3.Chronic inflammation**

## Cells and mediators

**Macrophage**

- dominant, from monocyte

**Activated by:**

1. Classical pathway (microbicidal action)

2. Alternative pathway

**Functions**

1. Phagocytosis and destruction

2. Initiate tissue repair & scar formation and fibrosis involvement

3. Secrete inflammation mediators (e.g. cytokines, clotting factors)

4. Processing and presentation of Ag to immune system



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## Tissue repair -- Regeneration (Cell proliferation)

**Depend on:**

1. Cell types (Ability to repair)
2. Degree of injury

**Proliferative potential**

1. Labile (continuo)
- e.g. epithelial cell, xxx tract
2. Stable
- e.g. salivary gland
3. Permanent
- e.g. neuron, myocardium

**Regulation mechanism**

**1. Growth factors** (+population,size,mitosis,survival)

-VEGF

**2. ECM**

**Cell-matrix interactions**

總之講緊growth同 differentiation要用at least 2 types of signal 一個就用soluble(growth factor) 另一個就用insoluble(ECM)

## Secondary intention

- Cell loss more extensive

**Features**

1. More intense inflammatory tissue
2. Abundant granulation tissue
3. ECM accumulation
4. Formation of large scar
- Destroyed appendage are permanently lost

**5. Wound contraction**

- Reduce gap between dermal edge and wound area to close wound
- Myofibroblast for mediator

**6. Fibrosis**

## Secondary intention (cont)

- Excessive collagen deposit
- Pathologic process by persistent stimuli
- Associated with loss of tissue
- Long-lasting

## Healing Factors

**Systemic**

1. Overall nutrition e.g. VitC
2. Metabolic status > Vascular supply
3. Circulatory status
4. Hormones > Cortico :(
5. Age

**Local**

1. Infection
2. Movement
3. Type, size, location
4. Foreign bodies



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