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Inflammation

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Learning Outcomes

- Define inflammation.
- Describe characteristics of inflammation.
- Describe the causes, sequence of events and cardinal signs of inflammation.
- Explain macrophage and neutrophil responses during inflammation.
- Describe the feedback control of inflammation.

Definition

Complex biological response of body tissues to harmful stimuli such as pathogens, damaged cells and irritants

It’s a protective response involving

- Immune cells
- Blood vessels
- Molecular mediators

Characteristics of Inflammation

1. **Vasodilation**

2. **Increased capillary permeability**

3. **Clotting of fluid in interstitial spaces(fibrinogen)**

4. **Migration of large number of white cells into tissues**

5. **Swelling of tissue cells**

Products Involved In Inflammation

- Histamine
- Bradykinin
- Serotonin
- Prostaglandins
- Lymphokines (released by the sensitized T-cells)
- Reaction products of complement system
- Reaction products of clotting system

→ Strongly activate macrophages → devour destroyed tissues but can also cause injury to living cells

A Historical Perspective

- comes from the Latin word inflammare

(to set on fire)

- The Roman Celsus documented (1st century AD) the 4 cardinal signs

rubor, tumor, calore, dolore

(redness and swelling with heat and pain)

- a "classical" acute inflammatory response—for example, following a traumatic event such as a macroscopic tear of ligament or muscle

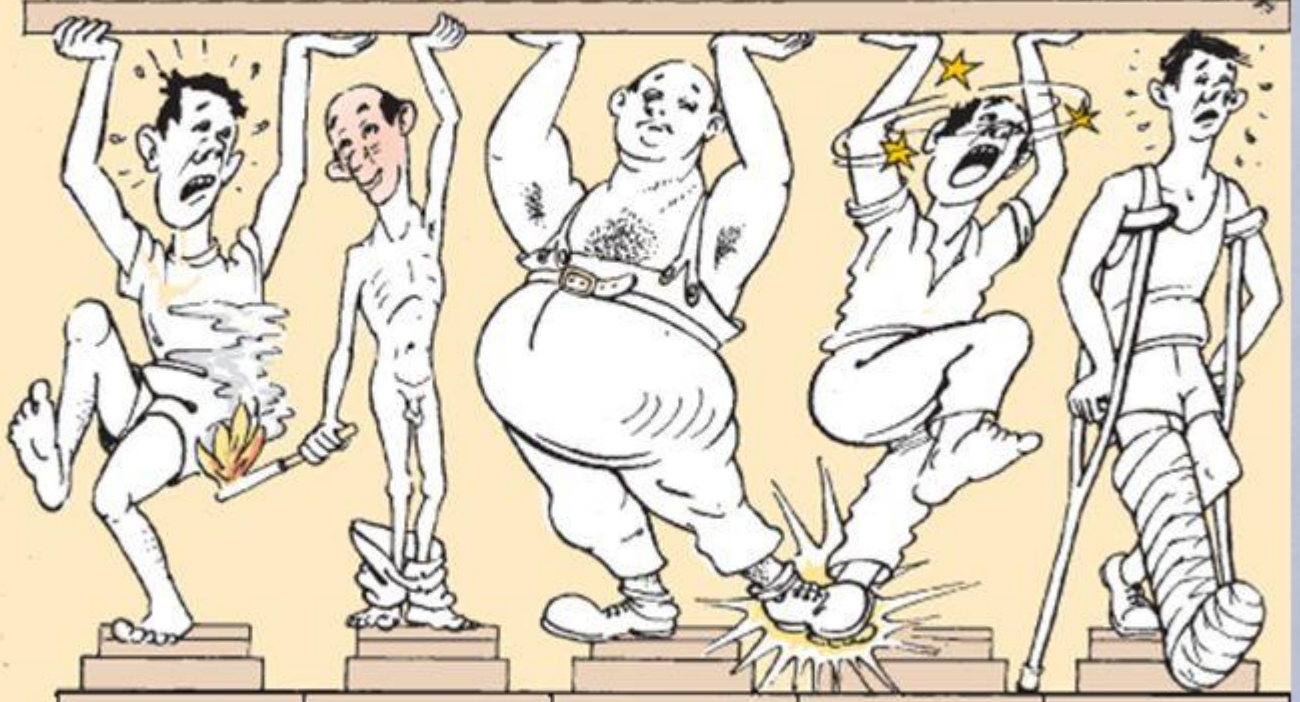
A Historical Perspective….

- Extensive involvement in many disorders
- **Bronchial asthma** – as an inflammatory disorder, followed by various allergies
- Then **diabetes I**, **Alzheimer's**, various **cancers**, **heart** diseases and even **ageing** have been identified as either acute or chronic inflammatory disorders (Glynn, 2013)

Causes of Inflammation

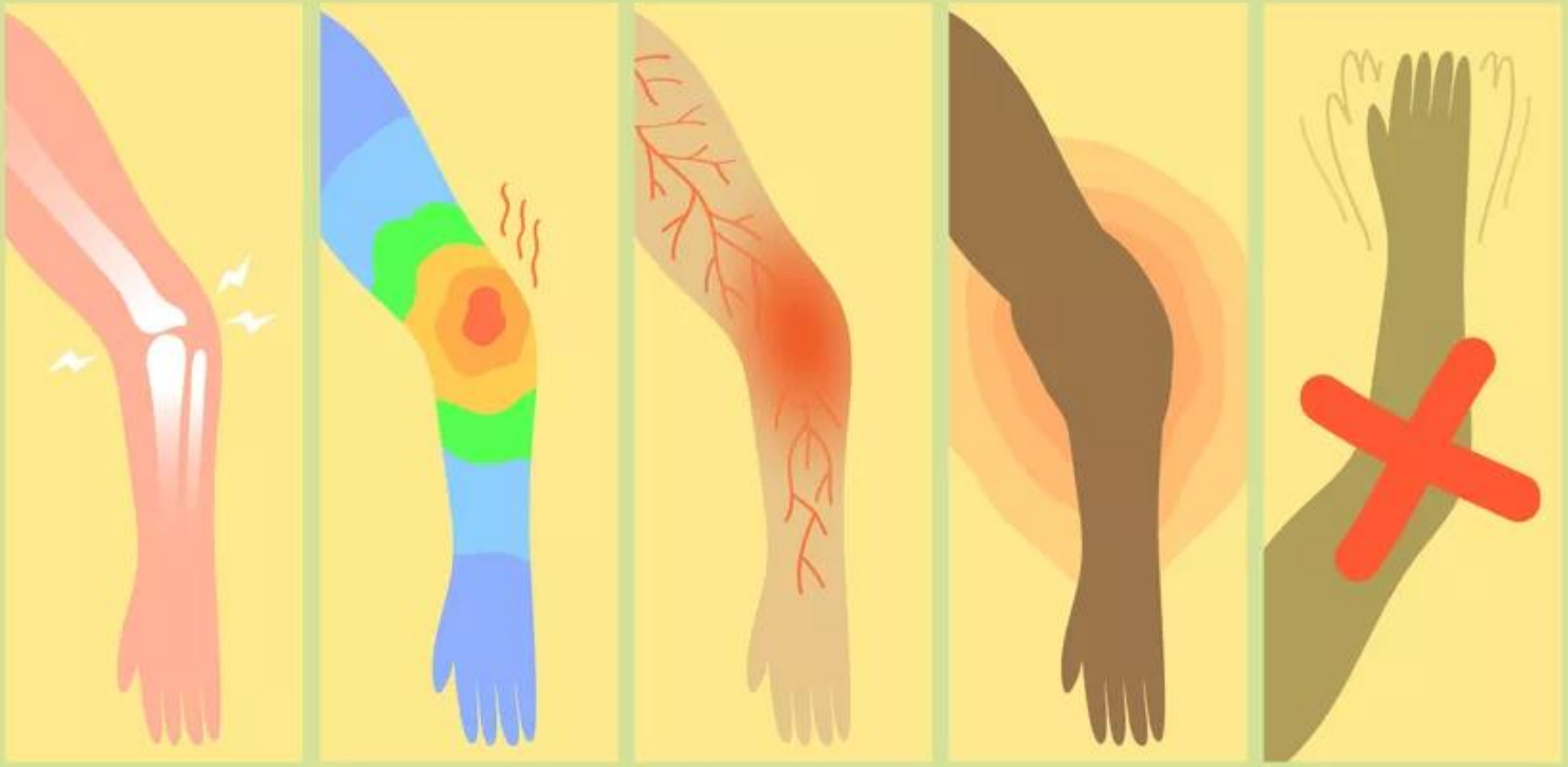
1. Thermal injury
2. Mechanical injury
3. Chemical injury
4. Injury by radiations
5. Infections
6. Autoimmune conditions

INFLAMMATION



Calor	Rubor	Tumor	Dolor	Functio laesa
Local heat, fever	Hyperemia (redness)	Tissue swelling (inflammatory tumor)	Burning pain	Functional impairment

5 Cardinal Signs of Inflammation



Pain | Heat | Redness | Swelling | Loss of Function

verywell

Cardinal signs of inflammation & Its Physiological rationale

Cardinal Signs	Physiological rationale
1. Rubor (Redness)	Increased Blood flow
2. Tumor (Swelling)	Exudation of fluid
3. Calor (Heat)	Increased Blood flow , Exudation of fluid, Release of inflammatory mediators
4. Dolor (Pain)	Stretching of pain receptors and nerves by inflammatory exudates , chemical mediators
5. Functio laesa (Loss of function)	Pain, Disruption of tissue structure, Fibroplasia and metaplasia

“Walling –Off” Effect

The tissue spaces and lymphatics in the injured areas are blocked by fibrinogen clot as a result of inflammation

Significance

- It **delays** the spread of bacteria or toxic products.

Intensity of inflammatory response is **proportional** to the degree of tissue injury

Staphylococci → lethal toxins → quick walling off

Streptococci → slow walling off

Macrophage And Neutrophil Responses During Inflammation

4 lines of defense

- First line of dense
- Second line of dense
- Third line of dense
- Fourth line of dense

Tissue Macrophages As A First Line Of Defense

- **Within minutes** after inflammation begins →

Tissues macrophages

(histiocytes, alveolar macrophages, microglia or others start phagocytosis and

- **Rapidly enlarge**

- Sessile macrophages break loose and **become mobile** in first hour and are **life saving**

Second Line Of Defense

Neutrophil Invasion of the Inflamed Area

Acute increase in the number of neutrophils in the blood by products of inflammation

1. **Inflammatory Cytokines** (tumor necrosis factor and interleukin-1)
2. **Biochemical products** of inflammation

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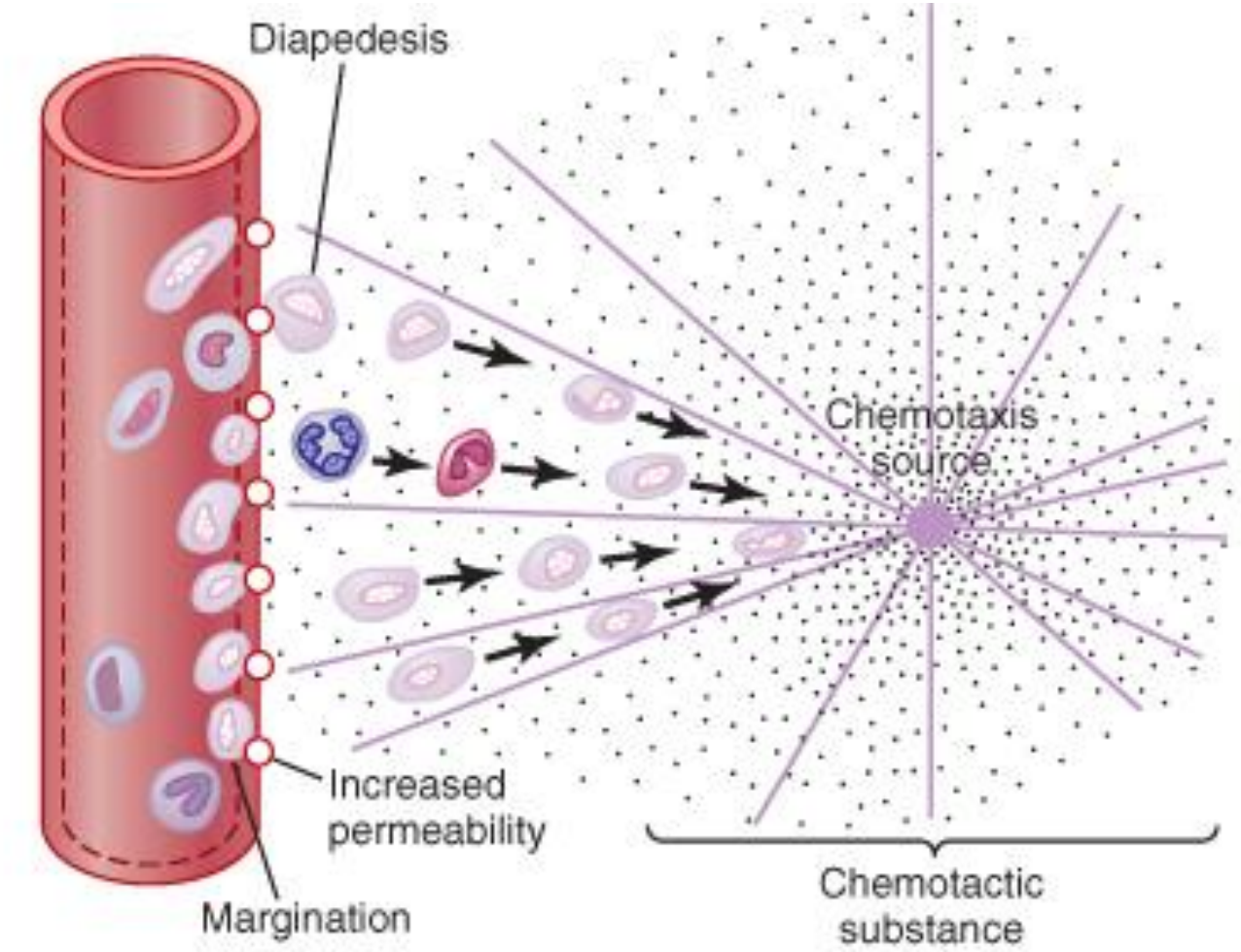
Margination (Selectins, ICAM-I & Integrins)

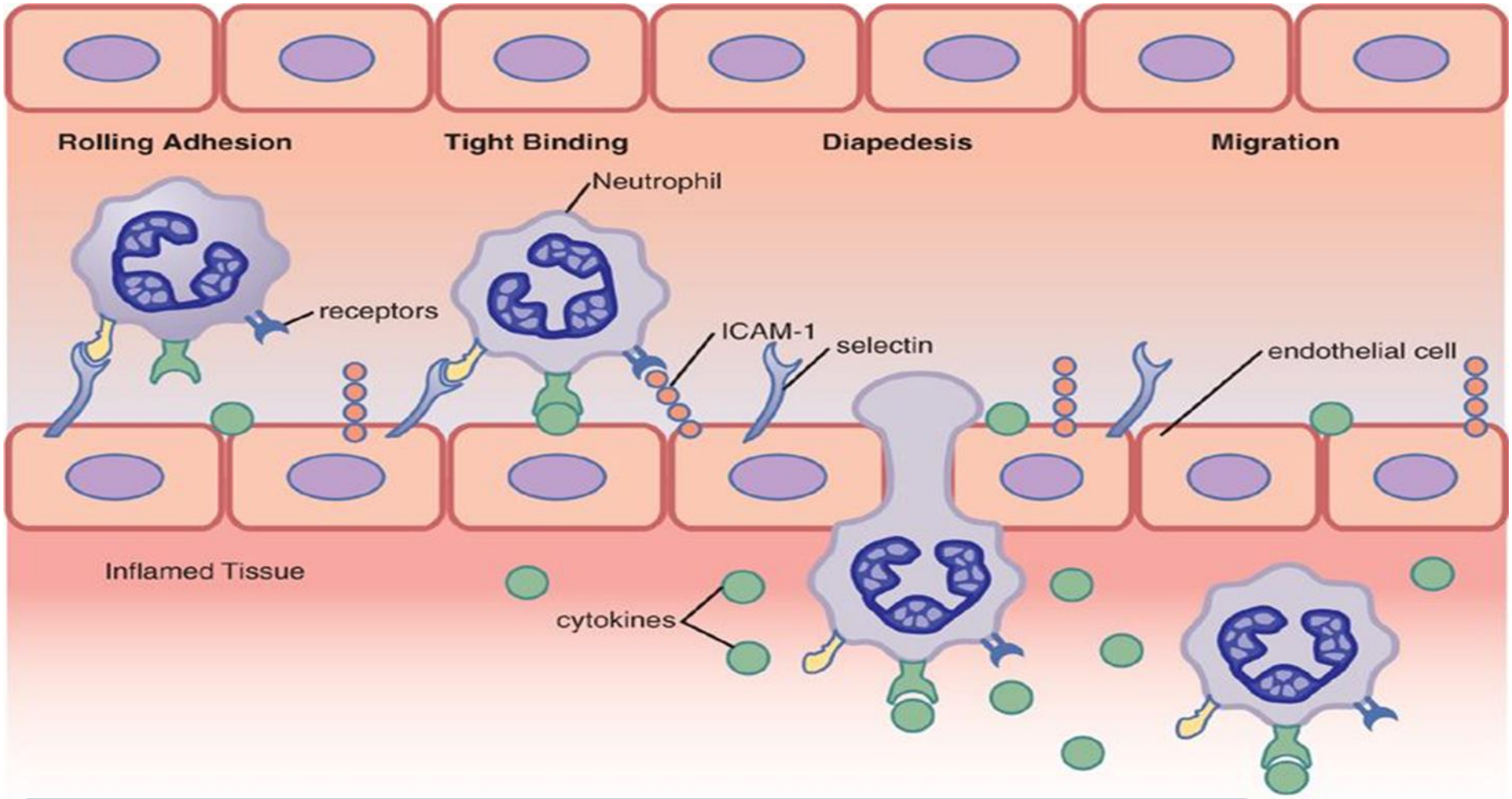
Diapedesis (gaps in endothelial cells)

Chemotaxis

Neutrophil Diapedesis And Chemotaxis



Migration of Neutrophils



Neutophilia → Neutrophils perform SCAVANGER function for killing bacteria and removing foreign matter

Third Line Of Defense

- **Monocytes (immature)** from blood → inflamed tissue and enlarge to become **Macrophages**

- **several days** to become effective as monocytes are less in number

- Tissue Macrophages (**8 hours or more)** phagocytize about **five times more bacteria, larger particles** and role in initiating antibodies production

- Macrophages become dominant due to increased production by bone marrow

Fourth Line Of Defense

- **Increased production of granulocytes and monocytes by the bone marrow**

- Results from stimulation of the granulocyte and monocytes progenitor cells of marrow

- **3 to 4 days**

- Persistent stimulus from the inflamed tissue → cells in tremendous quantities for months and even years, sometimes at a rate **20 to 50 times normal**

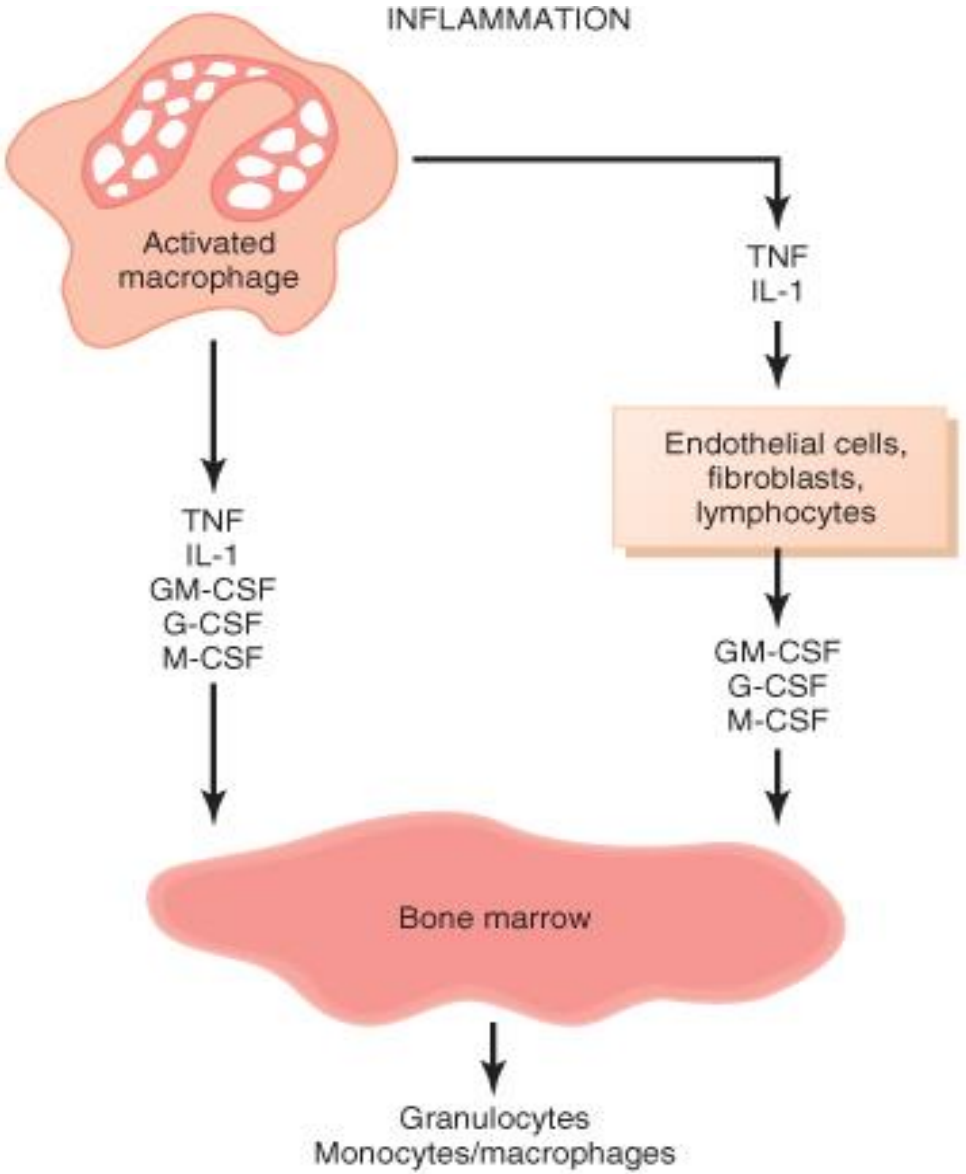
Feed Back Control

Activated macrophage cells in the inflamed tissues and less by other inflamed tissue cells secrete

More than 2 dozen factors but 5 have dominant role

1. Tumor necrosis factor (TNF)
2. Interleukin-I(IL-1)
3. Granulocyte- monocyte colony- stimulating factors(GM-CSF)
4. Granulocyte colony- stimulating factors.(G-CSF)
5. Monocytes colony -stimulating factors(M-CSF)

Feed Back Control

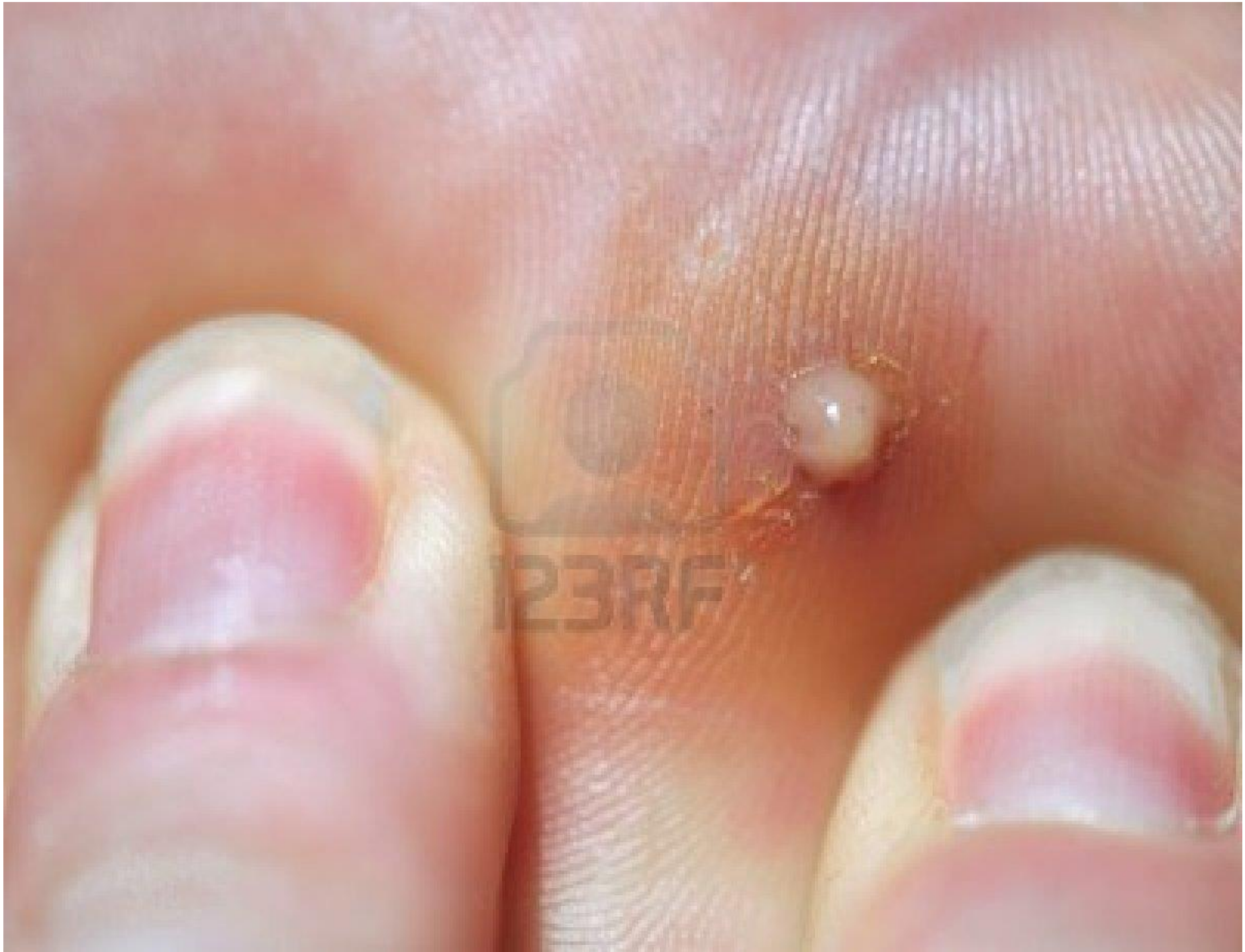


Formation of Pus

- Neutrophils and macrophages **engulf large numbers of bacteria and necrotic tissue** → neutrophils and many macrophages die

- A **cavity is excavated** in inflamed tissues containing necrotic tissues, dead neutrophils, dead macrophages and tissue fluid - **PUS**

- Dead cells and necrotic tissue in the pus gradually **autolyze** over days and are absorbed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Acute Inflammation

- helps the body to attack bacteria and other foreign substances in the body
- Once healing occurs, inflammation subsides

Conditions causing acute inflammation

Acute bronchitis → inflammation of the airways
Infected ingrown toenail
Sore throat
Skin cuts and scratches
Dermatitis
Sinusitis
Physical trauma

Chronic Inflammation

- continue to attack healthy areas if it doesn't turn off
- can occur anywhere in the body

Conditions causing chronic inflammation include

- **Inflammatory arthritis**
  (rheumatoid arthritis, lupus, and psoriatic arthritis)
- **Asthma** inflammation of the air passages
- **Periodontitis** inflammation of gums
- **inflammatory bowel disease (IBD)**
  Crohn’s disease and ulcerative colitis

ACUTE INFLAMMATION
VERSUS
CHRONIC INFLAMMATION

ACUTE INFLAMMATION	CHRONIC INFLAMMATION
Initial short term response of the body to adverse stimuli.	Long term inflammatory reaction that lasts for months or years.
Not specific.	Specific, involves acquired immunity.
Response to physical and chemical damages, pathogen invasion, tissue necrosis, etc.	Response to prolonged irritation of chemicals, foreign particles, infection that cannot be overcome for a long time.
Involved immune cells: dendritic cells, Kupffer cells, histiocytes, resistant macrophages, mast cells.	Involved immune cells: macrophages, neutrophils, lymphocytes.
Response: (1) redness, (2) increased blood flow, and (3) edema.	Response: fibrosis and angiogenesis.
Cardinal signs: pain, heat, redness, and swelling.	No cardinal signs.

Summary

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thank you!