

Acute & Chronic Inflammation

Dr Adel Abdel-Azim

Professor & Chairman of Oral Pathology
Department, Faculty of Dentistry, Ain-Shams
University, Cairo, Egypt

Acute & Chronic Inflammation

General Introduction

1. Inflammation (Preamble)
 2. Acute Inflammation
 3. Chronic Inflammation
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Acute & Chronic Inflammation

General Introduction

- Definition
 - Terminology
 - Main Types of Inflammation
 - Types of Inflammatory Cells
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Acute Inflammation - Outline

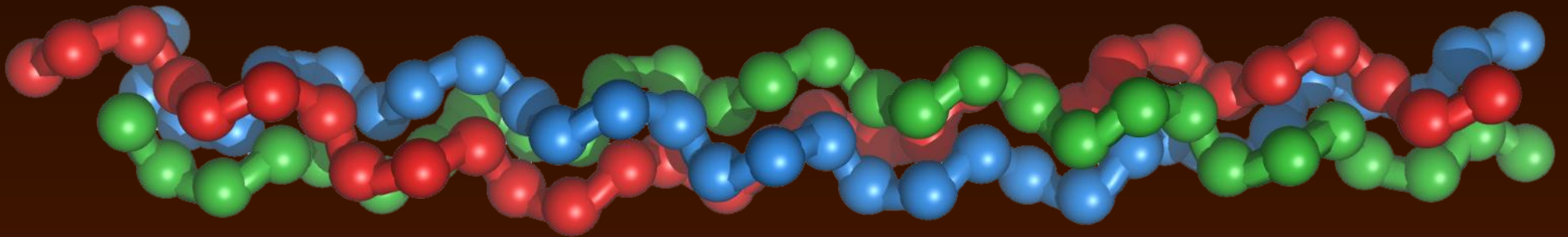
- Definition
 - Cardinal Signs of Inflammation
 - Causes of Acute Inflammation
 - Aims of Inflammation
 - Classification (Other Types of Inflammation)
 - Types of Inflammation Based on Exudate:
 - Types of Inflammation Based on Histological Features
 - Types of Inflammation Based on Causative Agent
 - Stages of Acute Inflammation
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Chronic Inflammation - Outline

- Definition
- Causes
- Mechanisms
- Classification
- General Features
- Cells of Chronic Inflammation
- Mixed Acute & Chronic Inflammation
 - Chronic Suppurative Inflammation
 - Recurrent Acute Inflammation
- Granulomatous Inflammation
 - Definition
 - What is a Granuloma
 - Causes of Granulomatous Inflammation
 - Mechanism of Granuloma Formation

Inflammation

Preamble



Definition

- Inflammation is the body reaction against injury or irritant
 - Is not synonym for infection
 - Only affects living tissue
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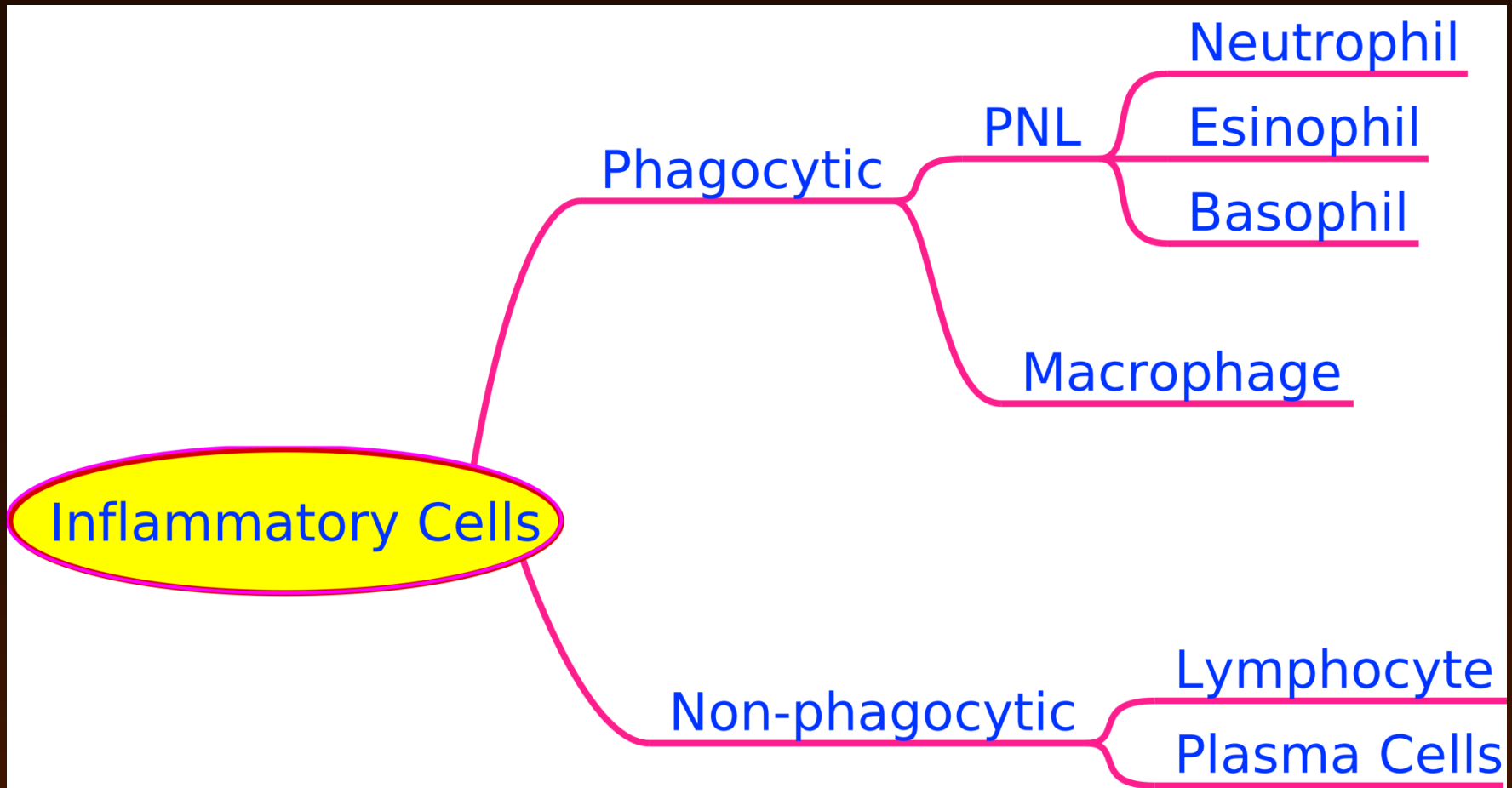
Terminology

- Greek or English prefix + -itis
 - gingivitis, metritis, pulpitis, nephritis
and son on
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Main Types of Inflammation

- Peracute: Very rapid onset and fulminating
 - Acute: Rapid onset and of shorter duration
 - Subacute: Slower onset with longer duration than acute
 - Chronic: Slowest onset with protracted duration
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Types of Inflammatory Cells



Types of Inflammatory Cells

1. Function (phagocytosis)

- Phagocytic cells
 - Monocytes (histiocytes, macrophages)
 - PNL (particularly neutrophils)
 - Non-phagocytic cells
 - Lymphocytes
 - Plasma cells
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Types of Inflammatory Cells

2. Presence of absence of cytoplasmic granules:

1. Granulocytes

- ◆ Polymorph nuclear leukocytes (PNL)
 - Neutrophils
 - Eosinophils
 - Basophils

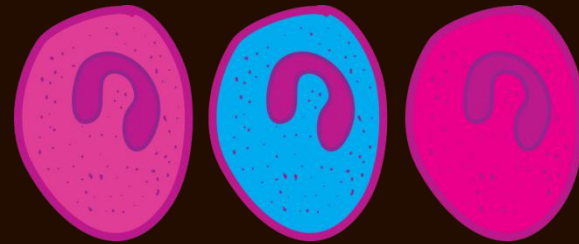
2. Agranulocytes

- Monocytes (histiocytes, macrophages)
 - Lymphocytes
 - Plasma cells
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Inflammatory Cells

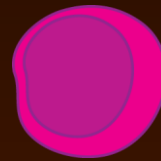
Acute Inflammatory Cells

- PNL – Microphages



Chronic Inflammatory Cells

- Macrophages – Histiocytes – Monocytes
- Lymphocytes
- Plasma cells



Phagocytic Cells

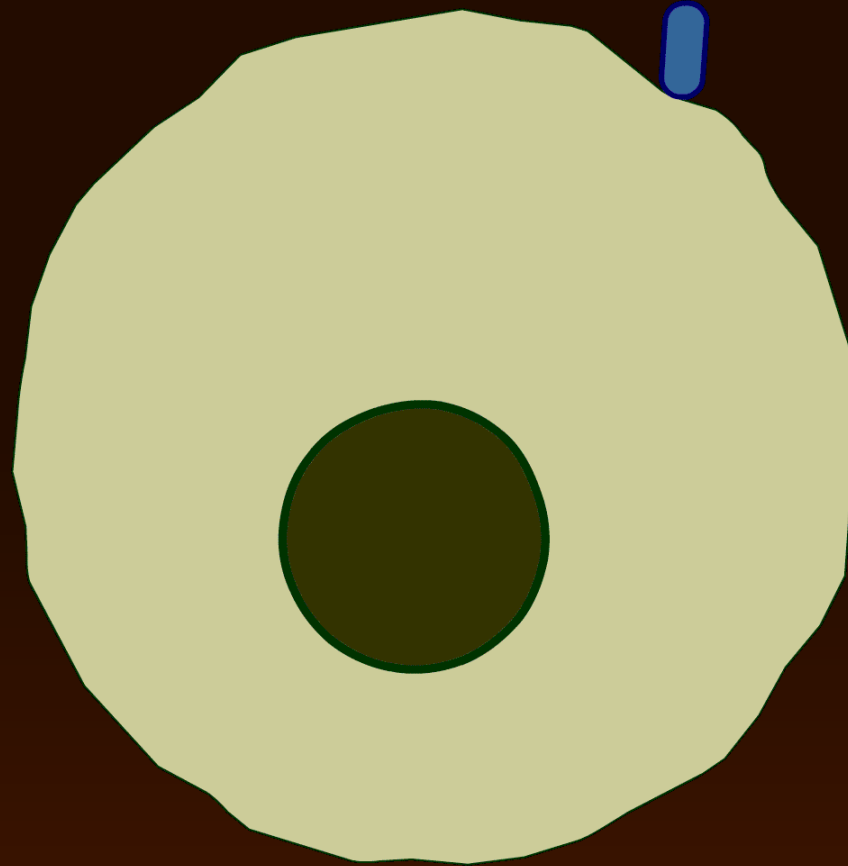
1. Professional Phagocytic Cells

- PNL, macrophages, osteoclasts, odontoclasts, cementoclasts, other giant cells

2. Non-Professional Phagocytic Cells

- Many as fibroblasts, osteoblasts
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Phagocytosis



Acute Inflammation

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- Aims of Inflammation
- Classification (Other Types of Inflammation)
 - Types of Inflammation Based on Exudate:
 - Types of Inflammation Based on Histological Features
 - Types of Inflammation Based on Causative Agent
- Stages of Acute Inflammation
 - Transient Vasoconstriction
 - Persistent Vasodilatation and Stasis
 - Increased Permeability of Vessel Walls
 - Fluid Exudate and Formation of Edema
 - Cellular Exudate (Neutrophil Emigration & Accumulation)
 - Resolution or progression
 - Chemical Mediators of Inflammation
 - Factors Involved in the Termination of Acute Inflammation
 - Outcomes (Consequences) of acute inflammation
 - Systemic Manifestations of Inflammation

Definition

A **rapid** and transient
response to injury or
irritant

Cardinal Signs of Inflammation

- **Calor** - heat, resulting from vasodilation of blood vessels
 - **Rubor** - redness, resulting from vasodilation of blood vessels
 - **Tumor** - swelling, resulting from edema
 - **Dolor** - pain. resulting from local release of prostaglandin and kinins
 - **Functio laesa** - loss (or impairment) of function
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Cardinal Signs of Inflammation

1. Heat (calor)
2. Redness (rubor, erythema)
3. Edema (tumor)
4. Pain (dolor)
5. Loss of function (functio laesa)



Causes of Acute Inflammation

- Infections (e.g., bacterial or viral infection)
 - Immune reactions (e.g., reaction to a bee sting)
 - Other stimuli:
 - Tissue necrosis (e.g., acute myocardial infarction)
 - Trauma, radiation, burns, foreign body (e.g., glass, splinter)
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Aims of Inflammation

- Is the inflammation beneficial ???????
 - **Yes**, inflammation aims at elimination of the noxious agents and restoration of tissue integrity.
 - But sometimes, one has to pay for this benefit. This payment may be represented in a form of residual scarring or other forms of inflammatory complications.
 - Inflammation may be **harmful** as in hypersensitivity, rheumatoid arthritis, anaphylactic reaction and atherosclerosis.
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Classification (Other Types of Inflammation)

- Based on Exudate
 - Based on Histological Features
 - Based on Causative Agent
-

Types of Inflammation Based on Exudate:

1. Suppurative (purulent) inflammation: pus

- Localized proliferation of pus-forming organisms, such as *Staphylococcus aureus* (e.g., skin abscess).
 - *S. aureus* contains coagulase, which cleaves fibrinogen into fibrin and traps bacteria and neutrophils.
 - Pyogenic bacteria, eg, staphylococci, streptococci, gram-negative bacilli, anaerobes.
-

Types of Inflammation Based on Exudate:

2. Serous inflammation: effusion

- Thin, watery exudate
 - Insufficient amount of fibrinogen to produce fibrin
 - Example - blister in second-degree burns, viral pleuritis
-

Types of Inflammation Based on Exudate:

3. Catarrhal inflammation (inflammation of mucous membranes)

- Marked secretion of mucus.
 - Infections, eg, common cold (rhinovirus); allergy (e.g. hay fever).
-

Types of Inflammation Based on Exudate:

4. **Fibrinous inflammation: fibrinogen - fibrin**
 - Due to increased vessel permeability.
with deposition of a fibrin-rich exudate
 - Often occurs on the serosal lining of the pericardium, peritoneum, or pleura
 - Danger of adhesions
 - Example: fibrinous pericarditis
-

Types of Inflammation Based on Exudate:

5. Pseudomembranous inflammation: surface necrosis

- Bacterial toxins damage mucosal lining, producing a membrane composed of necrotic tissue
- Example — pseudomembranes associated with *Corynebacterium diphtheriae* produces a toxin causing pseudomembrane formation in the pharynx and trachea.

Types of Inflammation Based on Exudate:

6. Necrotizing inflammation:

- Marked tissue necrosis
 - Highly virulent organisms (bacterial, viral, fungal), eg, plague (*Yersinia pestis*), anthrax (*Bacillus anthracis*), mucormycosis, maxillofacial gangrene (noma).
-

Types of Inflammation Based on Exudate:

7. Hemorrhagic inflammation:

- Destruction of blood vessel walls resulting in leakage of a large number of red blood cells resulting in the red coloration of inflammatory exudate.
 - Example — Epidemic hemorrhagic fever, Leptospirosis and Plague.
-

Types of Inflammation Based on Exudate:

8. Ulcerative inflammation:

- Necrosis on or near the surface leads to loss of tissue and creation of a local defect (ulcer)
 - Example — Ulcerative colitis
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Types of Inflammation Based on Exudate:

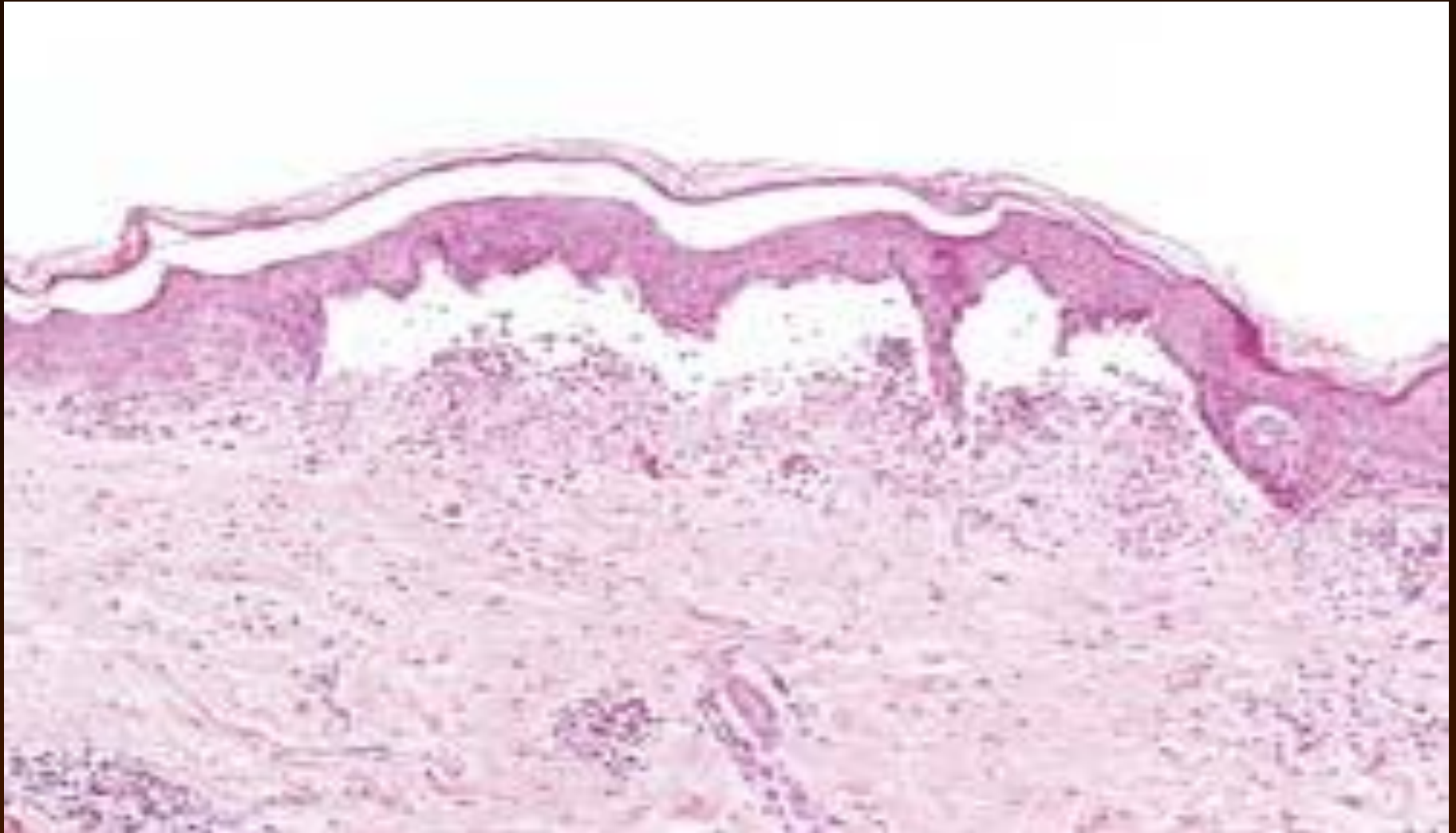
9. Granulomatous inflammation:

- Is a distinct type of chronic inflammation characterized by formation of granuloma
 - Example — TB, syphilis, actinomycosis and leprosy
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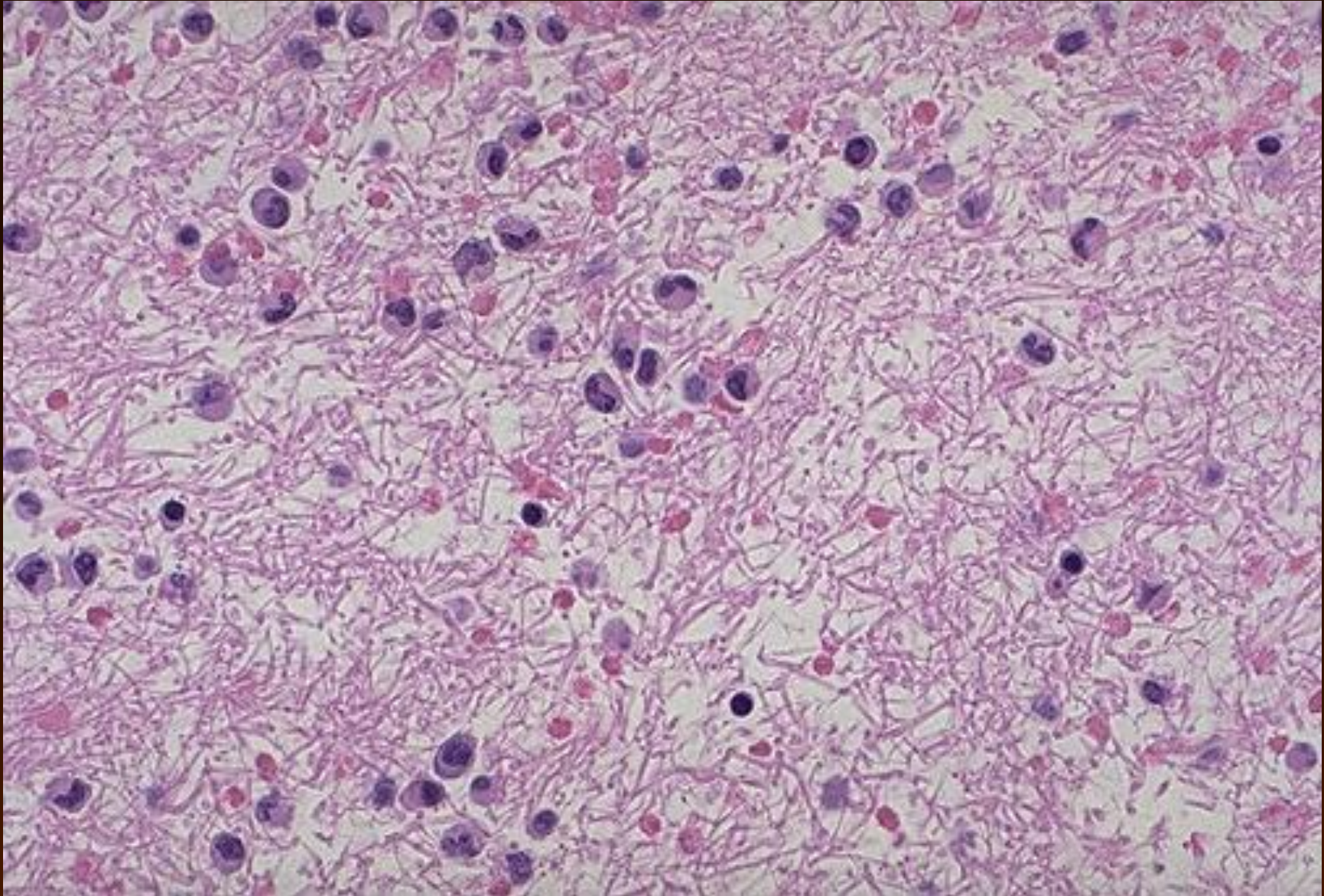
Serous Exudate



Serous Inflammation



Fibrinous Exudate



Purulent Exudate



Types of Inflammation Based on Histological Features

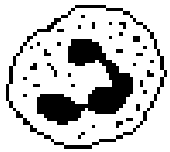
- **Nonspecific:** Produce non-specific histologic picture
 - **Specific:** Produce a specific histologic picture that is peculiar to that type of infection e.g. TB.
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Types of Inflammation Based on Causative Agent

- **Aseptic** (sterile) - chemical substances, radiation
 - **Septic** (caused by living organisms)
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Stages of Inflammation

MARGINATION

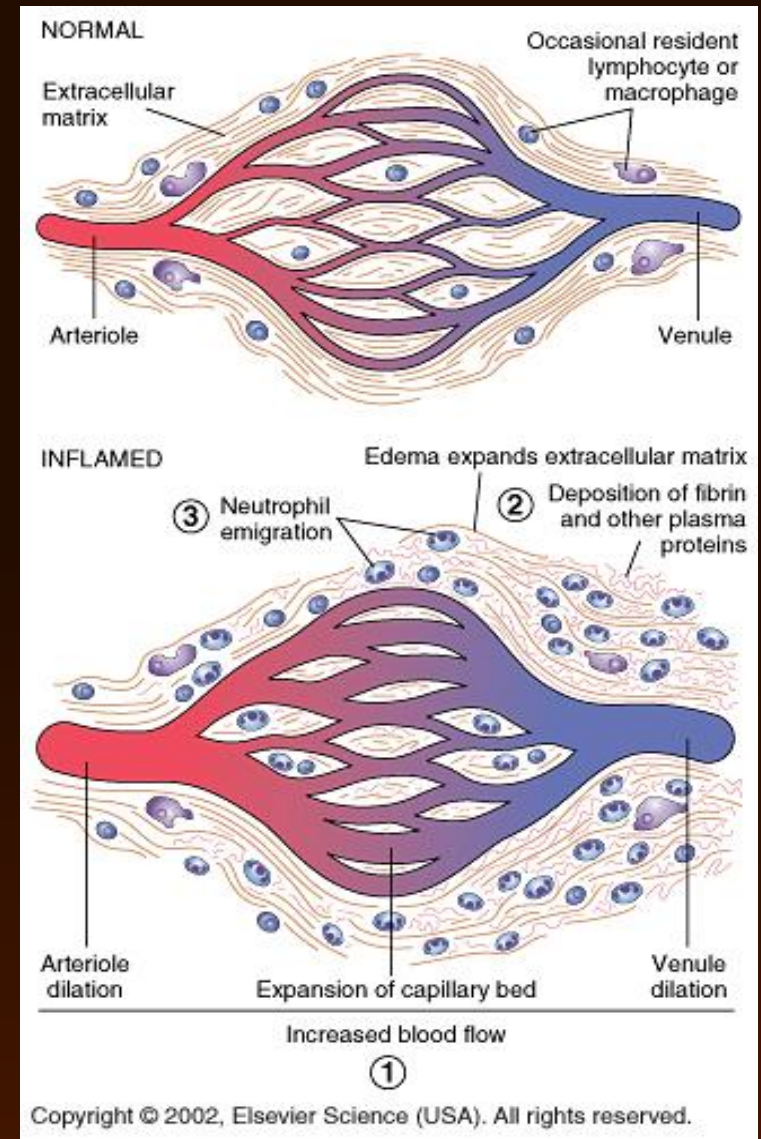


Stages of Acute Inflammation

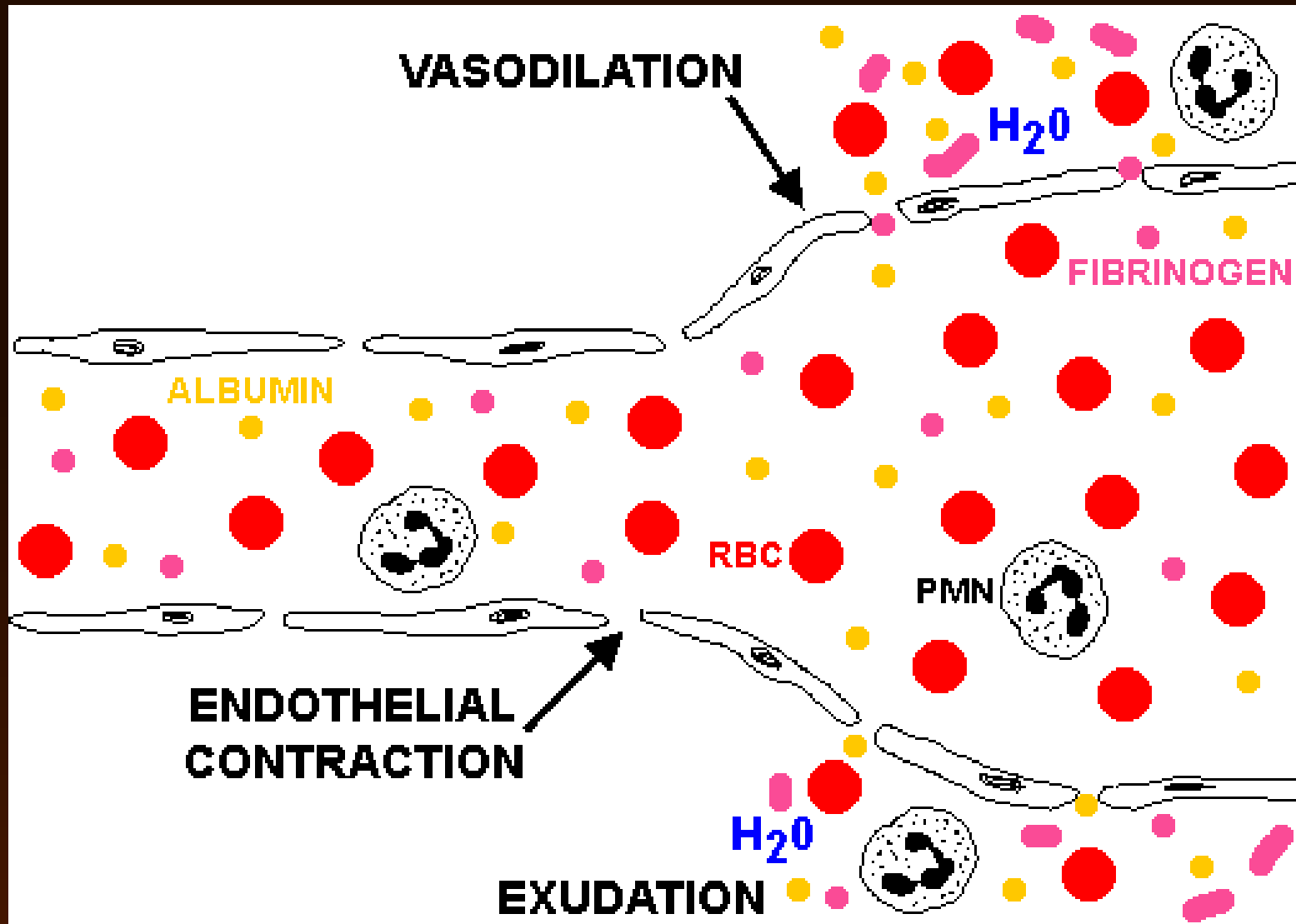
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 2. Persistent Vasodilatation and Stasis
 3. Increased Permeability of Vessel Walls
 4. Fluid Exudate and Formation of Edema
 5. Cellular Exudate (Neutrophil Emigration & Accumulation)
 6. Resolution or progression
-

Stages of Inflammation

1. Transient vasoconstriction
2. Persistent vasodilatation
3. Increased Permeability
4. Fluid exudate (edema)
5. Cellular exudate (Neutrophil emigration & accumulation)
6. Resolution or progression



Mechanism of Inflammation



Acute Inflammation – Continue

- Chemical Mediators of Inflammation
 - Factors Involved in the Termination of Acute Inflammation
 - Outcomes (Consequences) of acute inflammation
 - Systemic Manifestations of Inflammation
-

Chemical Mediators of Inflammation

- ◆ Derived from plasma, leukocytes, local tissue, bacterial products.
 - ◆ Example — arachidonic acid mediators are released from membrane phospholipids in macrophages, endothelial cells, and platelets).
 - ◆ They have short half-lives (e.g., seconds to minutes).
 - ◆ They may have local and systemic effects.
 - ◆ Example — histamine may produce local signs of itching or systemic signs of anaphylaxis.
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Functions of Chemical Mediators of Inflammation

- Vasodilation; Examples — histamine, nitric oxide.
 - Vasoconstriction; Example — thromboxane.
 - Increase vessel permeability; Example — histamine, bradykinin.
 - Produce pain; Example — bradykinin
 - Produce fever; Examples — IL-1, T N F
 - Chemotactic; Examples — IL8
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Factors Involved in the Termination of Acute Inflammation

- **Short** half-life of inflammatory mediators
 - **Lipoxins**
 - Anti-inflammatory mediators
 - Derive from arachidonic acid metabolites
 - Inhibit transmigration and chemotaxis
 - **Resolvins**
 - Synthesized from omega-3 fatty acids
 - Inhibit production and recruitment of inflammatory cells to the site of inflammation
 - Clearance of neutrophils by **apoptosis**
-

Outcomes (Consequences) of acute inflammation

- Resolution
 - Healing by repair or regeneration
 - Progression into chronic inflammation.
 - Spread
 - Direct-e.g. cellulitis
 - Lymphatic
 - Blood vessels: Pyaemia - Septicaemia
 - Death
-

Systemic Manifestations of Inflammation

- Pyrexia (fever)
 - Negative nitrogen balance
 - Increased erythrocyte sedimentation rate
 - Anemia
 - Leucocytosis
-

Chronic Inflammation - Outline

- Definition
 - Causes
 - Mechanisms
 - Classification
 - General Features
 - Cells of Chronic Inflammation
 - Lymphocytes and plasma cells
 - Macrophages
 - Eosinophils
 - Basophils
-

Chronic Inflammation - Definition

Is the persistence of inflammation with attempts of repair resulting from persistence of the injurious agent.

Chronic Inflammation - Causes

- Persisting infection or prolonged exposure to irritants (intracellular surviving of agents - TB)
 - Repeated acute inflammations (otitis, rhinitis)
 - Primary chronic inflammation - low virulence, sterile inflammations (silicosis)
 - Autoimmune reactions (rheumatoid arthritis, glomerulonephritis, multiple sclerosis)
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Chronic Inflammation - Mechanisms -1

- Defective acute inflammatory response
 - Poor blood supply
 - Poor general nutrition
 - Abnormal neutrophil function
 - Anti-inflammatory drugs, especially corticosteroids
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Chronic Inflammation - Mechanisms - 2

- Agent is resistant to phagocytosis and/or intracellular destruction
 - Intracellular infectious agents, e.g. tuberculosis, salmonellosis, brucellosis, viral infections
 - Foreign-body reactions.
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Chronic Inflammation - Mechanisms - 3

- The provoking agent is a body constituent as in:
 - Auto-immune diseases, e.g. diffuse lymphocytic thyroiditis (Hashimoto's disease), auto-immune atrophic gastritis, adrenal atrophy, etc.
 - Reactions to altered self-antigens, e.g. contact dermatitis to rubber, nickel, etc.
-

Chronic Inflammation - Classification

1. Clinical

- Following acute inflammation, e.g. chronic osteomyelitis
- Arising de novo, e.g. brucellosis, tuberculosis

2. Histological

- **Specific** - having a reproducible histological pattern, e.g. tuberculosis, syphilis, leprosy
 - **Non-specific** - showing only the general features of inflammation, e.g. chronic pulpitis
-

General Features

1. Continuing some features of acute inflammation
 - Polymorph infiltration
 - Fibrinous exudation
 - Increased vascularity
 2. Features of healing-repair and/or regeneration
 3. Infiltration by chronic inflammatory cells
 - Lymphocytes
 - Plasma cells
 - Macrophages
 - Eosinophils
-

Cells of Chronic Inflammation

1. Lymphocytes
 2. plasma cells
 3. Macrophages
 4. Eosinophils
 5. Basophils
-

Mixed Acute & Chronic Inflammation

- Features of both types of inflammation may coexist in certain circumstances, as in chronic suppurative inflammation and recurring acute inflammation.
 - Two Types:
 1. Chronic Suppurative Inflammation
 2. Recurrent Acute Inflammation
-

Chronic Suppurative Inflammation

Example: Chronic suppurative osteomyelitis

Recurrent Acute Inflammation

- Repeated attacks of acute inflammation may occur if there is a predisposing cause, eg, in the gallbladder when there are **gallstones**.
 - Each attack of acute inflammation is followed by incomplete resolution.
 - Depending on the time of examination, the picture may be mainly that of chronic inflammation or of acute superimposed on chronic inflammation.
 - The terms **subacute** inflammation and acute-on-chronic inflammation are also used to denote this pattern.
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Granulomatous Inflammation - Outline

- Definition
 - What is a Granuloma
 - Causes of Granulomatous Inflammation
 - Mechanism of Granuloma Formation
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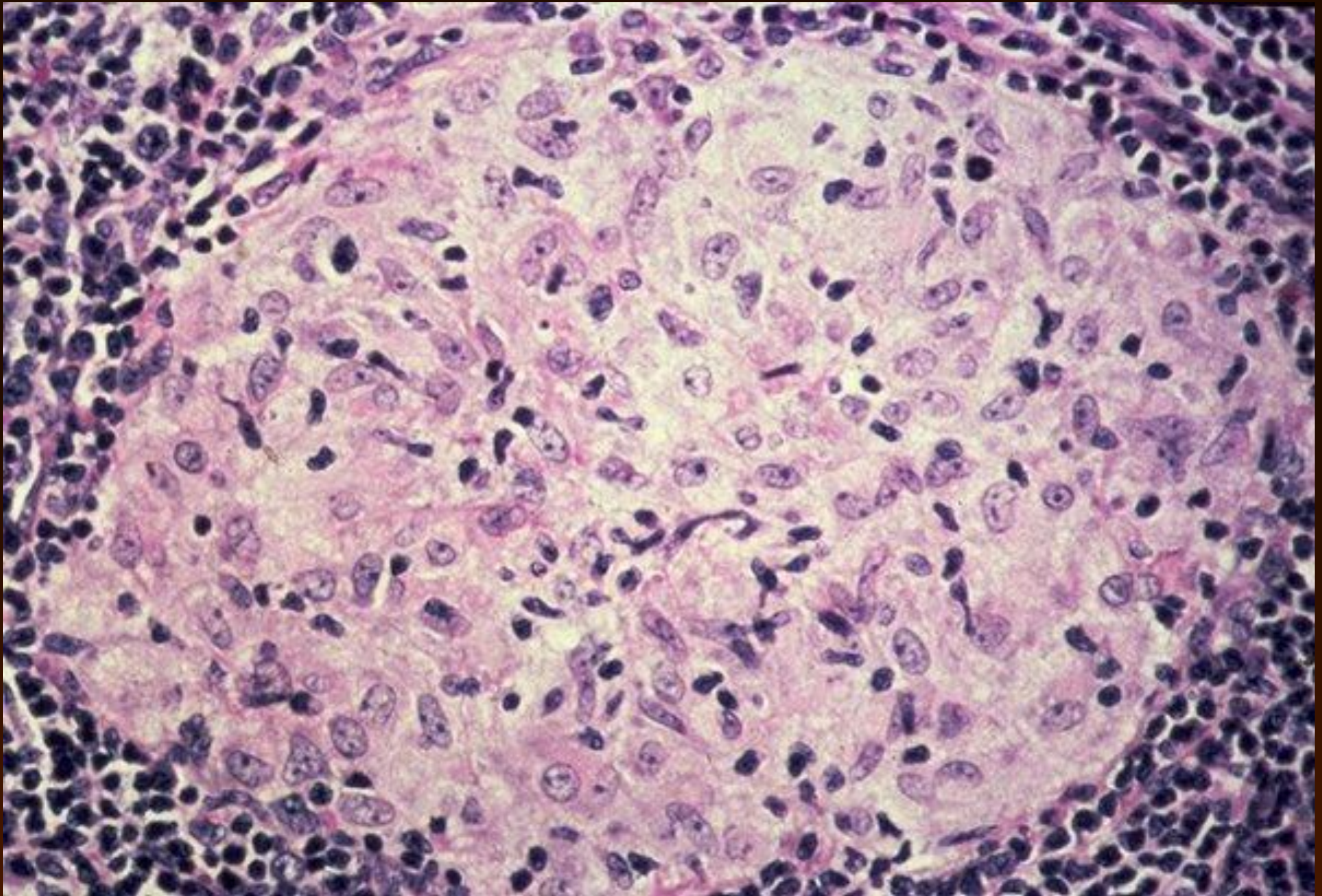
Granulomatous Inflammation - Definition

- A distinct pattern of chronic inflammation characterized by formation of granulation tissue.
 - It is a protective response to chronic infection or foreign material, preventing dissemination and restricting inflammation.
 - Some autoimmune diseases such as rheumatoid arthritis and Crohn's disease are also associated with granulomas.
-

What is a Granuloma

A granuloma is a localized mass of granulation tissue with aggregations of chronic inflammatory cells.

Granuloma



Causes of Granulomatous Inflammation

- **Bacteria:** Tuberculosis, Leprosy, Syphilis, Actinomycosis
 - **Parasites:** Schistosomiasis
 - **Fungi:** Histoplasmosis, Blastomycosis
 - **Foreign body Granulomas**
 - Endogenous (keratin, necrotic bone or adipose tissue uric acid crystals)
 - Exogenous (wood, silica, asbestos, silicone)
 - **Unknown** cause such as sarcoidosis
-

Mechanism of Granuloma Formation

- The classic example for the immune granuloma is that caused by the TB. In this disease, the granuloma is referred to as a tubercle and is characterized by the presence of central caseous necrosis. Caseating necrosis is rare in other granulomatous diseases.
 - There are many atypical presentations that it is always necessary to identify the specific etiologic agent by: special stains for organisms (acid-fast stains for tubercle bacilli), culture methods (tuberculosis, fungal disease), and serologic studies (syphilis). In sarcoidosis, the etiologic agent is unknown.
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Mechanism of Granuloma Formation

1. Bacilli are inhaled by droplets
 2. Then phagocytosed by alveolar macrophages. Macrophages fail to digest the phagocytosed bacteria and accumulate at the site of injury.
 3. A localized inflammatory response recruits more mononuclear cells
 4. The granuloma consists of a kernel of infected macrophages surrounded by foamy macrophages and a ring of lymphocytes and a fibrous cuff.
 5. The granuloma may caseates, ruptures and spills into the airway
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