# Pathology sheet

**DONE BY:**

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Inflammation

(1 of 5)

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Overview

Inflammation:
Is a protective response of the body to get rid of invaders and necrotic tissues and to start the process of repair and healing of a tissue

**A protective response**

...involving host cells, blood vessels, and molecules

repair بالإضافة إلى الdefect

...for the elimination of:

- the cause of cell injury
  
  and

- necrotic cells and tissues that resulted from injury

...and to initiate the process of repair

*A component of the innate immune system*
Immune system comprises of:
- Innate immune system
- Adaptive immune system

Inflammation is a component of the innate immune system. It involves blood vessels, cells, chemicals or mediators.
Inflammation can be harmful sometimes

if the reaction is very strong ...e.g., severe infection •

if the reaction is prolonged (e.g., when the causative agent resists eradication) •

When the reaction is inappropriate...mention 2 examples •

Chronic hepatitis B disease :

Occupational disease :

harmful inflammation
Acute inflammation VS chronic inflammation

<table>
<thead>
<tr>
<th>Feature</th>
<th>Acute</th>
<th>Chronic</th>
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</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Fast: minutes or hours</td>
<td>Slow: days</td>
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<tr>
<td>Cellular infiltrate</td>
<td>Mainly neutrophils</td>
<td>Monocytes/macrophages and lymphocytes</td>
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<tr>
<td>Tissue injury, fibrosis</td>
<td>Usually mild and self-limited</td>
<td>Often severe and progressive</td>
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<tr>
<td>Local and systemic signs</td>
<td>Prominent</td>
<td>Less prominent; may be subtle</td>
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The repair process could be regeneration or fibrosis
Sources of chemical mediators

- WBCs
- Plasma
- Endothelial cells
- Injured cells
- Extracellular matrix
- Microbes
Local manifestations of inflammation like an insect bite

• Heat (calor)

• Redness (rubor)

• Swelling (tumor)

• Pain (dolor)

• Loss of function (functio laesa)
Progress of inflammation

• The reaction is initially short-lived
  …the injurious agent is eliminated
  …the mediators and cells of inflammation are degraded or inactivated
  …various anti-inflammatory mechanisms become active

*If the injurious agent cannot be quickly eliminated, the result may be chronic inflammation
Steps of the inflammatory response

1. Recognition of the injurious agent
2. Recruitment of leukocytes and secretion of chemicals
3. Removal of the agent
4. Regulation (control) of the response
5. Resolution and repair
Acute inflammation

2 major components:

- Vascular changes
  - vasodilation
  - vascular permeability
  - endothelial cells are activated for migration of WBCs to the tissue

- Cellular events

WBCs: adhesion to WBCs

migration of WBCs to the tissue
Acute inflammation: cellular events

• Migration of WBCs from the circulation

• Recruitment of WBCs into the tissue

• Activation of WBCs to fight the invaders
Stimuli for acute inflammation

- Infections
- Trauma
- Tissue necrosis...due to any noxious stimulus
- Foreign bodies
- Immune reactions
Recognition of stimulus on the stimulus by ligand to its receptor

By macrophages, dendritic cells, epithelial cells...etc.

...These cells use receptors called: pattern recognition receptors (PRRs)

specific immune reaction is the recognition of foreign bodies by the innate immune system by matching the antigen.

Antigen

The antibody is released by the B lymphocyte. In the adaptive immunity, each antigen has a specific receptor on the B lymphocyte surface, which is synthesized upon stimulation and specific PRRs.

AMA 36
Pattern recognition receptors

**Toll-like receptors (TLRs)** •
...recognize microbial components
...10 types
...on membrane and in endosome, so recognize extracellular and phagocytosed microbial components
(...phagocytosis خاصة في الخلايا التي تعمل) endosomes
...signal transduction of them: release of mediators (cytokines...etc.)
**Pattern recognition receptors, cont’d**

- *Inflammasome*
  - a multi-protein cytoplasmic complex موجودة في السيتو بلازم
  - recognizes - products of dead cells, e.g., uric acid and extracellular ATP
    - crystals
    - some microbial products
  - activates *caspase-1*

  cleaves precursor of interleukin-1beta (an inflammatory cytokine) into active form

*Gout disease: deposition of urate crystals ➞ ingested by phagocytes ➞ activation of inflammasome ➞ IL-1 production ➞ acute inflammation*
Vascular changes in acute inflammation

• Vasodilation...after seconds of vasoconstriction
  ...the cause of erythema and warmth

• Increased vascular permeability
vascular permeability

...extravasation of protein-rich fluid into the tissue

...local concentration of RBCs in the vessel → more viscosity (slowing)

Followed by margination of WBCs (mainly neutrophils)
vascular permeability, cont’d

• Protein-rich fluid in the interstitium = exudate

...different from transudate
Mechanisms of increased permeability

**Endothelial cell contraction**

- **gaps in post-capillary venules**

...short-lived: 15-30 minutes

...due to -histamine
- bradykinin
- leukotrienes
- others

or ...slower and more prolonged: 4-6 hours after trigger and persist

>=24 hours

...due to changes in cytoskeleton in endothelial cells due to TNF (tumor necrosis factor) and IL-1

**cytoskeleton** لمدة اطول شوي بسبب تغيرات على ال**permeability**
Mechanisms of increased permeability, cont’d

• Direct injury of endothelial cells…due to
  -burns
  -microbial toxins
  -radiation
  -mediators of inflammation
  -...etc

• Transcytosis of proteins: 
  -in venules
  -induced by VEGF (vascular endothelial growth factor)
and in repair: permeability may also due to:

leakage from newly formed blood vessels

*new vessel formation = angiogenesis ...role of VEGF
...in addition, these vessels have more receptors for vasoactive mediators
About lymphatic vessels in inflammation

• Lymph flow ↑ to drain - edema fluid
  - WBCs
  - cell debris
• In severe infections: may disseminate the microbe
• If the inflammation involves lymphatic vessels → lymphangitis
• If the inflammation involves the draining lymph node → lymphadenitis
  ...the L.N. is enlarged due to - hyperplasia of lymphoid follicles
  - ↑ # of lymphocytes
  - ↑ # of phagocytes that line sinuses

Reactive (inflammatory) lymphadenitis
Lymphangitis

Red streak
موجود في مسار الymphatic vessels