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Inflammation

Before you proceed try out the pre-quiz:
https://medicine.nus.edu.sg/pathweb/pathology-demystified/inflammation/quiz/

What is Inflammation?

Definition: Inflammation is a **response of vascularised tissues** to **infection and damaged tissues** that brings cells and molecules of host defence **from the circulation to the sites** where they are needed, in order to **eliminate** the offending agents

Let's break this down:

- **Response of vascularised tissue** – tissues need to be living (i.e. vascularised): vessels and blood components are key players
- **…to infection and damaged tissues… –** some of the causes of inflammation
- **…from the circulation…** – key events start from
- within the blood vessels (that's where the cells and chemical mediators come from)
- **…to the sites…** – cells travel to the site of injury – think about how they do that
- **…to eliminate…** – this is the ultimate goal of inflammation: to get rid of the agent that is causing injury, as well as the dead tissue that accumulated during the event

In summary, Inflammation:

- Is a *protective* mechanism
- It leads to *healing* of tissues

Mindmap: Big picture of acute inflammation:
https://medicine.nus.edu.sg/pathweb/pathology-demystified/inflammation/what-is-inflammation/

Causes of Inflammation

1. Biological agents

- Infectious agents, e.g. viral, bacterial, fungal organisms, etc.
- Necrotic tissue, e.g. post-myocardial infarction – inflammatory response to dead cardiomyocytes

2. Chemical agents

- Toxins, poisons

3. Physical agents

- e.g. heat, cold, radiation, foreign bodies like suture

Characteristics of Acute Inflammation

Acute inflammation
Mechanisms of innate immunity
Initial rapid response – within in minutes, hours → lasts a few days
Main cell: Neutrophil (polymorphonuclear leukocyte)
Clinical signs obvious (especially at a superficial site) ▪ Redness + Warmth ← Vasodilation ▪ Swelling ← Oedema (exudates, due to increased vascular permeability) ▪ Pain ← Chemical mediators stimulate nerve endings ▪ Loss of function ← Tissue damage or lack of use due to pain ▪ Fever ← Chemical mediators (endogenous or exogenous – eg. from bacteria)
Sequelae / Outcomes: ▪ Complete resolution – limited tissue damage, cells at site able to regenerate, causative agent removed early ▪ Suppuration/ purulent inflammation – marked acute inflammatory response with liquefactive necrosis of tissue ← caused by specific types of organisms like pyogenic bacteria • Pus – neutrophils, liquefied necrotic tissue ▪ Healing by scarring / fibrosis – greater extent of tissue destruction, or native tissue unable to regenerate (eg heart muscle in myocardial infarction) ▪ Progression to Chronic inflammation – causative agent cannot be removed
Morphologic patterns: - Suppurative or purulent inflammation; abscess (caused by pyogenic bacteria – characterised by purulent exudates or collections – neutrophils, liquefactive necrosis, tissue fluid) - Ulcers - local defect of the epithelial-lined surface produced by sloughing of inflamed necrotic tissue - Serous inflammation - exudates of serous fluid, eg, body cavity effusions - Fibrinous inflammation – fibrin deposits in extravascular space eg. meningitis, pericarditis

material

4. Immune reactions

- Abnormal inflammatory responses to normal tissue (e.g. autoimmune diseases) or foreign tissue (e.g. allergens like pollen)
- Usually seen in chronic inflammation

Causes of Inflammation

Type of Agent	Examples	Remarks
Biological	- Viruses, bacteria, fungal organisms etc - Necrotic tissue eg. dead heart muscle in myocardial infarction	Different types of micro-organisms incite different types of inflammatory responses eg. bacteria – acute inflammation; viruses chronic inflammation etc.
Chemical	Poisons, toxins	
Physical	Trauma causing tissue injury; Foreign body (eg. splinter)	
Immune reactions	- Autoimmune diseases – immune response to self-antigens - Immune response to foreign tissue like allergens	Seen more in chronic inflammation

Types of Inflammation

Acute Inflammation

Robbins: "Acute inflammation is a rapid host response that serves to deliver leukocytes and plasma proteins, such as antibodies, to sites of infection or tissue injury."
e.g. Appendicitis, abscess

Chronic inflammation

Robbins: "Chronic inflammation is inflammation of prolonged duration (weeks or months) in which **inflammation**, **tissue injury** and attempts at **repair** co-exist, in varying combinations."
E.g. Autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus), tuberculosis infection

Characteristics of Chronic Inflammation

Chronic inflammation
Occurs more by adaptive immunity
Over days → Lasts for weeks to months
Causes: - Persistent infection – eg. viral or parasitic infections; tuberculosis - Immune mediated – eg. autoimmune disease – self-antigens trigger inflammatory response - Persistent exposure to injurious agents – eg. silicosis in the lung; atherosclerosis in vessels
Main cells: Macrophages, Lymphocytes, Plasma cells
Main effects: More tissue destruction; Cellular infiltrates; Blood vessel proliferation and connective tissue deposition
Morphologic patterns: - Infiltration with mononuclear cells (**macrophages**, lymphocytes, plasma cells) + tissue destruction + granulation tissue and fibrosis - Granulomatous inflammation – distinctive pattern of chronic inflammation where the cells fail to eradicate an offending agent. Activation of T lymphocytes and macrophage activation are important events here. Egs. Tuberculosis, foreign body reaction [Granuloma = collection of activated (epithelioid) histiocytes often surrounded by a collar of mononuclear cells (eg. lymphocytes, plasma cells)]

Main Events in Inflammation

1. Acute Inflammation

Main events:

1. **Vascular events**
   - Vasodilation and Increased vascular permeability
     - Think about how this leads to the warmth, redness, swelling …
2. **Cellular events**
   - Neutrophil recruitment -> emigration out of circulation -> chemotaxis to site of injury -> activation -> phagocytosis and clearance

- Think about how the neutrophils get from the blood to the site of injury, and what they do there

2. Chronic inflammation

Main events:

1. **Inflammation and tissue injury**
2. **Attempts at repair**
3. **Immune response**

Mindmap: Overview of acute inflammation:
https://medicine.nus.edu.sg/pathweb/pathology-demystified/inflammation/what-are-the-main-events-in-inflammation/

What brings about the main events in inflammation?

→ **Mediators of inflammation**

There are 2 main types of mediators:

1. Cells – neutrophils and macrophages; endothelial cells; and other leukocytes (platelets, mast cells, basophils)

Tip: Create a table or mindmap for cellular players – What they are, main actions, main products. This is the beginning of a sample table. Fill it up!

Cellular Mediators of Inflammation (sample table)

	Acute inflammation	Chronic inflammation	
Cell	Neutrophil	Macrophage	Lymphocyte
Does?	Eliminate microbes (phagocytosis)	Destroy foreign invaders (phagocytosis) Activate other cells eg, lymphocytes Modulate inflammatory response – Amplify, limit	Amplify and propagate chronic inflammation (cytokines)
Produces?	Reactive oxygen species, nitric oxide	Cytokines - TNF- α, IL-1	Cytokines – TNF- α, IFN- γ

2. Chemical mediators

4 main types:

- Arachidonic acid metabolites
- Cytokines
- Vasoactive amines
- Kinins

Sources: Cells and Plasma

- From **cells** (cell-derived) – endothelial cells, leukocytes, platelets
  1. Pre-made (eg. histamine – vasoactive amine)
  2. **Newly synthesised** (eg. prostaglandins, cytokines) – some anti-inflammatory drugs (e.g. steroids, COX inhibitors) work on these pathways to curb the inflammatory response (Robbins has a great diagram on this)
- From **plasma –** bradykinin, complement, clotting system proteins

Effects of mediators are easy to recall if you know the **main events** (Section **IV**). You can also figure out why **abnormal leukocyte function** or numbers results in susceptibility to infections.

Here is a "sample' table for the cell-derived mediators. Fill this up, and create one for plasma-derived mediators.

Chemical Mediators of Inflammation: Cell derived (Sample table)

Mediator	Source	Effects on inflammatory cells	Effects on endothelial cells	Other effects
TNF- α	**Macrophages** Lymphocytes, Mast cells	Leukocyte activation – promote secretion of other cytokines	Endothelial activation (increased adhesion molecule expression)	Systemic effects – fever, hypotension, decreased appetite
Histamine	Mast cells, basophils, platelets	-	Vasodilation, increased vascular permeability, endothelial activation	-

Talking POTS and slides
https://medicine.nus.edu.sg/pathweb/pathology-demystified/inflammation/talking-pots-and-slides/

Quiz (Post)
https://medicine.nus.edu.sg/pathweb/pathology-demystified/inflammation/quiz/