# SHEET NO. 6

# PATHOLOGY

## DOCTOR 2019 | MEDICINE | JU


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## Introduction ...

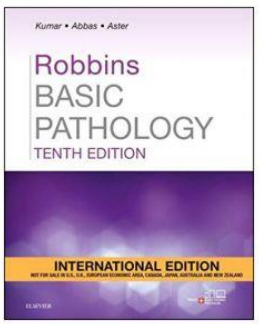
10 lectures will be represented by Dr. Mousa

- 6 lectures → inflammation
- 3 lectures → repair
- One for general revision

Study material:

Robbins Basic Pathology 10th Edition (The book is required for this course; he won't cover all the details in the lecture )

+ lecture contents

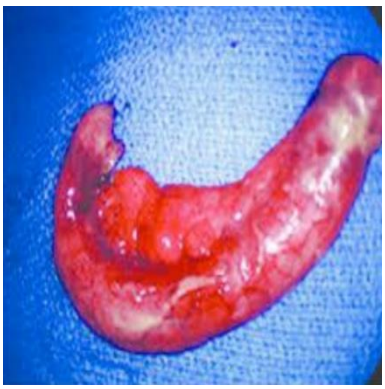



Pages of this lecture in the pdf form of the book *: 67-70 ~ chapter 3*

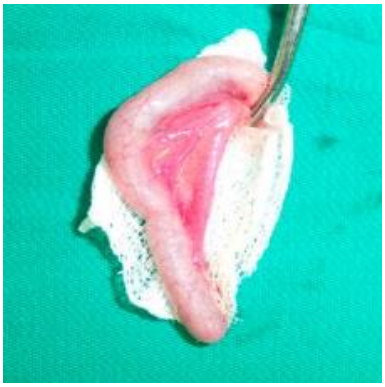
# Inflammation and Repair

## Overview of inflammation: Definitions and general features

*Before we define inflammation, look at the pictures demonstrating the difference between inflamed and normal appendix (الزائدة الدودية)*



**acute appendicitis (inflamed appendix)**
appears red, congested (محتقن), swollen
**abnormal appendix**



**Normal appendix**
Small and white

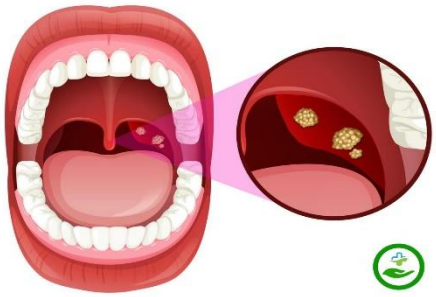
**The 3 major cardinal signs of inflammation of any organ**:

1. Enlarged
2. Swollen
3. Red and congested

## What is inflammation ?

*Best definition* → **Response** of vascularized (viable or alive) tissue to injury (infections or tissue damage) by the **recruitment** of cells and molecules from circulation to the sites of need to eliminate the offending agent.

**Tonsilitis (viral infection)**



**e.g.** *Viral Tonsillitis* → the response of tonsils to try eliminating the virus in couple of days ,so you will have swelling and congestion occur and a lot of cells infiltrating the tonsils .

**It's important to know that inflammation is**

- **Protective**→ fights fatal consequences, help body heal wounds and prevent/decrease/eliminate tissue damage
- With no inflammation: infections can be fatal; wounds would never heal and injured tissue may sustain permanent damage .

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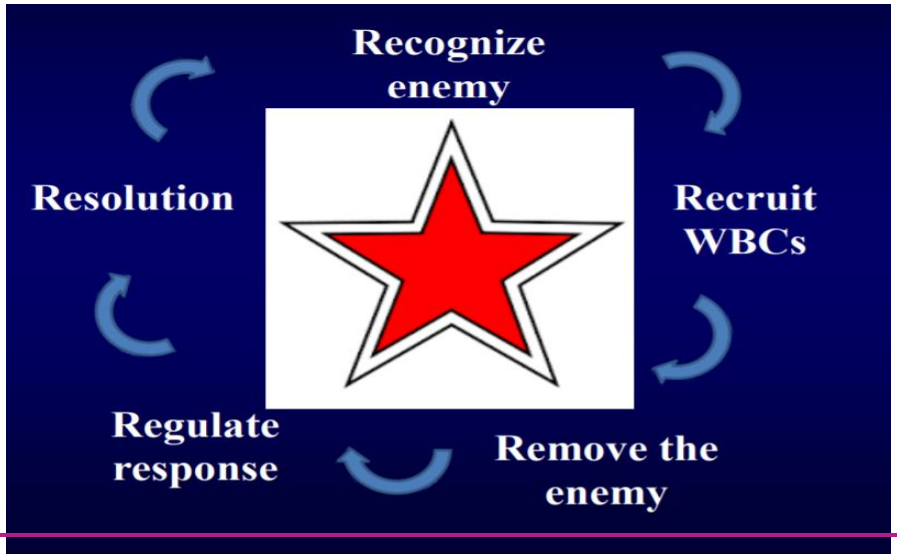
## Typical inflammation Rx. Steps ( 5 R's)

1. **Recognize enemy**: Offending agent recognized by cells and molecules
2. **Recruit WBCs**: WBCs & Plasma proteins recruited to injury site
3. **Remove the enemy:** WBCs and Pl. proteins work together to destroy and eliminate the enemy
4. **Regulate response**: Rx. Is then controlled and terminated → the body will control and decrease the inflammatory response because it's not needed anymore and to avoid collateral damage
5. **Resolution**: Repair of damaged tissue → either by regeneration & fibrosis (scar formation)

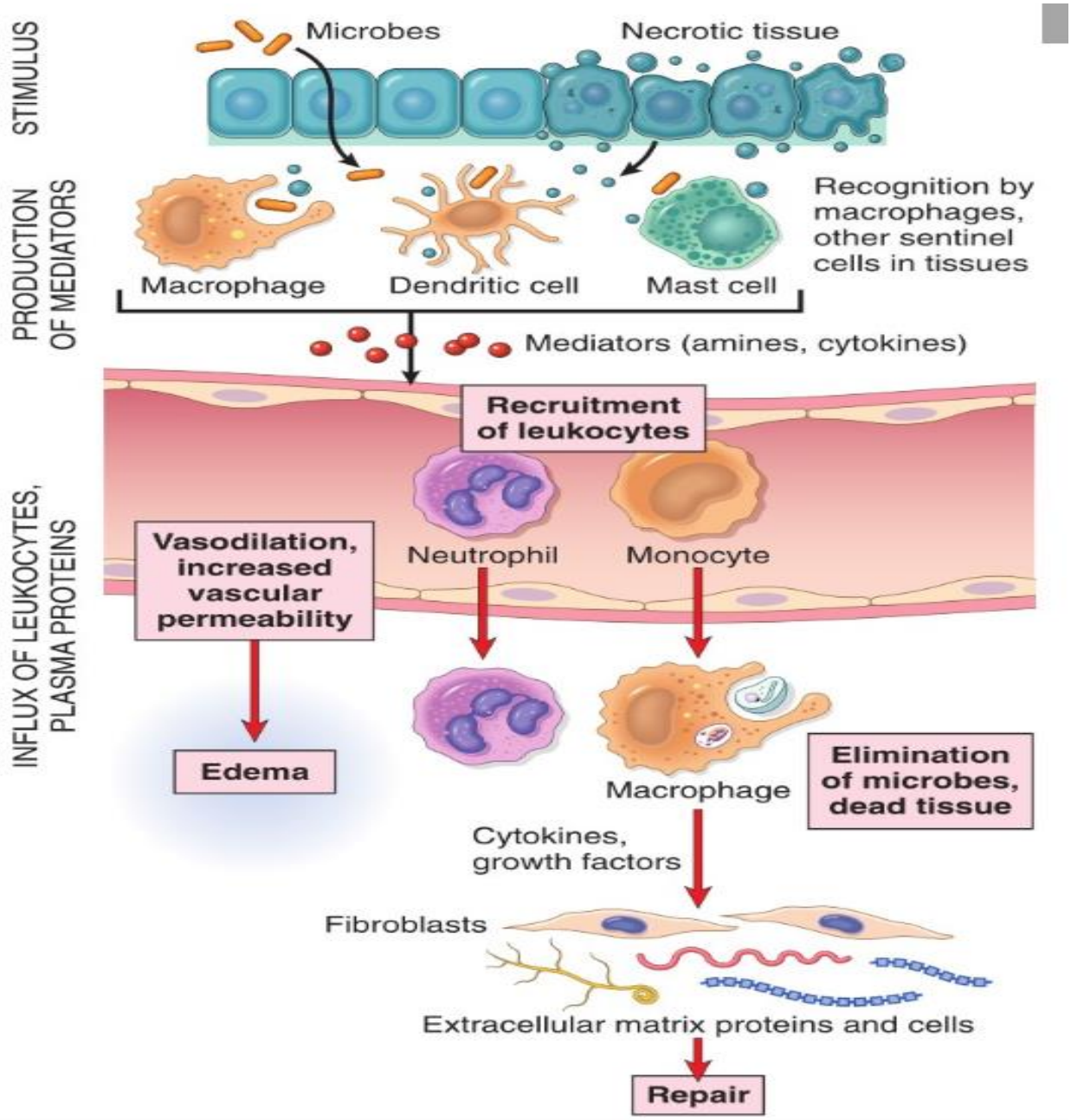
**The 5 R's**

These steps are sequential

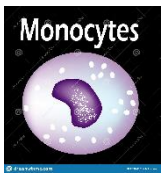
There might be some overlap between the steps



**Summary of all 5 steps of inflamm.** ( each will be discussed in details later on )




NEUTROPHIL




عشان تضلوا متذكرين اشكالهم حبة فاصوليا وميكي ماوس

**Inflammation is divided into 2 major categories: acute and chronic inflammations** it's important to distinguish between them …

| Feature | Acute حادة | Chronic مزمنة |
|---|---|---|
| Onset<br>The first time to notice change (symptoms ) | Fast: minutes or hours | Slow: days |
| Cellular infiltrate | Mainly neutrophils | Monocytes/macrophages and lymphocytes |
| Tissue injury, fibrosis | Usually mild and self-limited | May be severe and progressive |
| Local and systemic signs | Prominent | Less |

- Acute Inflammations symptoms and signs will appear quickly, and local and systemic signs are prominent that's a good thing because the symptoms will drive the patient to seek medical advice
  Chronic Inflammations are insidious (خبيثة) sometimes it doesn't show symptoms until severe damage happen to the organ

- The hallmark of acute inflammation is predominance of NEUTROPHILS (mickey mouse cells 😊)
  Hallmark of chronic inflammation are MONOCYTE/MACROPHAGES+ LYMPHOCYTE + PLASMA CELLS

- **Acute inflammations** usually result in mild tissue injuries that are self-limited and the treatment in this case is supportive e.g. antibiotics, Panadol, antihistamine for congestion**.**
- **Chronic inflammation** Cause a lot of tissue damage.

***Sometimes both acute and chronic inflamm. Appear in the same case.****

They do exist together in what we call **acute on top of chronic inflammations** ( an acute attack on the top of a baseline of a chronic inflammation ) e.g : **chronic active gastritis**, chronic gastritis

Accompanied by acute attack ( in this case we can observe neutrophils in addition to macrophages,
Lymphocytes, and plasma cells ) .

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# 5 Cardinal signs of inflammation

- **HEAT (calor)**
- **REDNESS (rubor)**
- **SWELLING (tumor)**
- **PAIN (dolor)**
- **LOSS OF FUNCTION (functio laesa)** → **e**.g. if you have an inflamed big toe in gout you won't be able to move it … another example a swollen ankle because of severe arthritism would also be hard to move

# Can inflammation be bad?

Although normally protective, in some situations, the inflammatory reaction becomes the cause of disease, and the damage it produces is its dominant feature.

What are these situations?

- Too little inflammation → the immune system is not well equipped and the body will be exposed to infection
- Too much inflammation can damage the tissue

- **Misdirected inflammation…autoimmune diseases and allergies**→ where your immune response will damage your own tissue. For example, if the immune system attack the kidney instead of the virus of bacteria in sore throat
- **Chronic inflammation…chronic diseases** → most chronic diseases, like chronic hepatitis and chronic glomerulitis will damage the kidney, heart, lung or liver, causing chronic liver disease, end stage renal disease, end stage pulmonary fibrosis etc.

# Disorders Caused By Inflammatory Reactions

| Disorders | Cells and Molecules Involved in Injury |
|---|---|
| **Acute** | |
| Acute respiratory distress syndrome | Neutrophils in lungs |
| Asthma | Eosinophils; IgE antibodies |
| Glomerulonephritis | Antibodies and complement; neutrophils, monocytes |
| Septic shock | Cytokines |
| **Chronic** | |
| Arthritis | Lymphocytes, macrophages; antibodies? |
| Asthma | Eosinophils; IgE antibodies |
| Atherosclerosis | Macrophages; lymphocytes |
| Pulmonary fibrosis | Macrophages; fibroblasts |

## ACUTE DISORDERS:

1. **Acute respiratory distress syndrome (ARDS)**

→ clinical syndrome seen in patients with multiple organ failures in ICUs.

n

in autopsy of somebody who recently ended up dying from ARDS we see diffuse alveolar damage (DAD), which is the pathologic term.

2. **Acute bronchial Asthma** → *severe* symptoms such as allergy, infection , severe Bronchospasm, wheezing ,difficulty in swallowing .
3. **Glomerulonephritis** → involves tissue injury in kidneys and sometimes in neurons .

4. **Septic shock (septicemia)** تسمم في الدم→is caused by severe bacterial growth in the blood (specifically gram negative bacteria is lethal ) causing tissue and vital organ damage due to the release of too many cytokines.

## CHRONIC DISORDERS

1. **Arthritis** → e.g. **Osteoarthritis**.,Rheumatoid **arthritis**, gout , **septic arthritis, etc.**
2. **Bronchial asthma** → Notice that bronchial asthma might also be chronic, so we need maintenance of treatment to prevent it.
3. **Atherosclerosis** → Chronic ischemia can cause complications in the heart and CNS in the form of acute myocardial infraction or major strokes in the brain.
4. **Pulmonary fibrosis** تكيس في الرئة … Many lung diseases will end up in geopathic or end stage pulmonary fibrosis, which propagate over months and years, and patients might need oxygen supply at home.

## Causes of inflammation

1. INFECTIONS **Bacteria**, **fungi**, **viruses**, **parasites** And the **toxins** they secrete, especially bacteria[endotoxins, exotoxins].
2. NECROSIS **Ischemia**[ blood vascular compromised], **trauma**[may cut your artery ], **physical and chemical injuries**, **burns**, **frostbite**, **irradiation** .**[**all of them mainly lead to damage of blood vessels**]**.
3. FOREIGN BODIES **Splinters**, **dirt**, **urate crystals** [will be deposited in joints, especially the big toe, causing acute gout arthritis], **Cholesterol crystals** [deposition of which is the main cause of atherosclerosis ,which can cause fatal disease].
4. IMMUNE REACTIONS **Allergies** to medications or pollens, causing exaggerated immune responses and reaction that can cause damage and sometimes, **Autoimmune diseases** [ your immune respose will damage your tissue which called misdirected inflammatory response]

# Recognition of microbes and damaged cells:

## *First step in inflamm. Response:*

- Cellular receptors: Toll-like R (TLRs) on membranes and endosomes recognize Pathogen Associated Molecular Patterns (PAMPs)(they recognize foreign microbes by the changes these microbes cause to our molecules).
- Sensors of cell damage: recognize Damage Associated Molecular Patterns (DAMPs) such as uric acid, ATP, K, & DNA. Consequently, multiple cytoplasmic proteins gets activated (called inflammasomes) – These sensors will also recruit circulating proteins: complement system, mannose- binding lectins and collectins (some of them also have the ability to recognize the microbes or damaged cells).

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## ACUTE INFLAMMATION

The first phase of acute inflammation is the vascular phase, its composed of 3 major component:

some people say that the first response in an injury is transient vasoconstriction, but this continues for just a few seconds and then the vascular dilation will occur.

1. B V dilatation : (have certain mechanisms, so we will take it in details in the next lecture).
2. Emigration of WBCs(from the intervascular compartment to the interstitium)
3. Increased V permeability(the cells, proteins and fluids will escape from the intravascular compartment to the interstitium).

*swelling happened due to leakage out of a lot of cells and fluids which is called Edema*

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From the book .. Required after every lecture

### Summary: General Features and Causes of Inflammation

- Inflammation is a beneficial host response to foreign invaders and necrotic tissue, but also may cause tissue damage.
- The main components of inflammation are a vascular reaction and a cellular response; both are activated by mediators that are derived from plasma proteins and various cells.

- The steps of the inflammatory response can be remembered as the five Rs: (1) recognition of the injurious agent, (2) recruitment of leukocytes, (3) removal of the agent, (4) regulation (control) of the response, and (5) resolution (repair). .
- The causes of inflammation include infections, tissue necrosis, foreign bodies, trauma, and immune responses.
- Epithelial cells, tissue macrophages and dendritic cells, leukocytes, and other cell types express receptors that sense the presence of microbes and necrotic cells. Circulating proteins recognize microbes that have entered the blood.
- The outcome of acute inflammation is either elimination of the noxious stimulus followed by decline of the reaction and repair of the damaged tissue, or persistent injury resulting in chronic inflammation

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**FIN**

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"Do what you have to do until you can do what you want to do." – Oprah Winfrey.