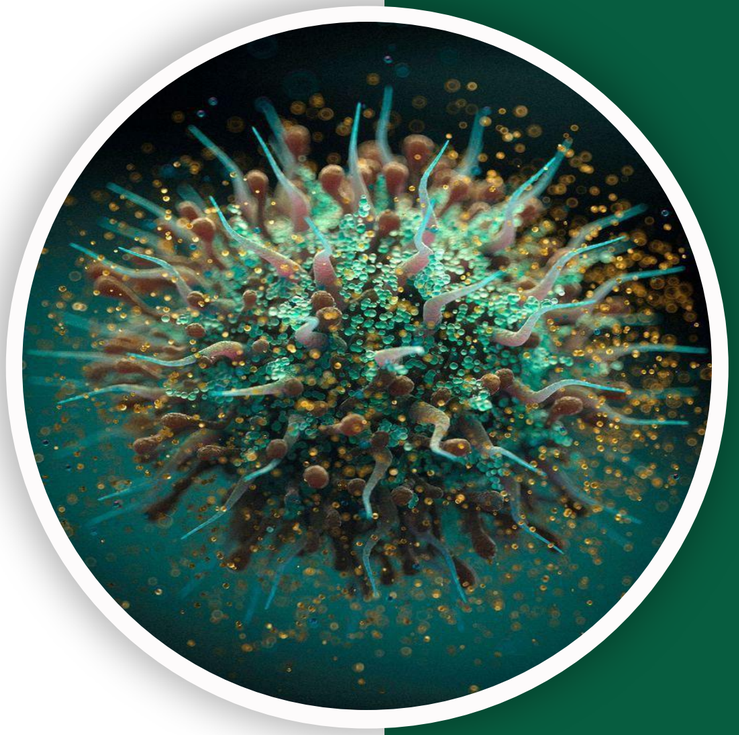
بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Pathology | Lecture 6

Inflammation Pt.1



Written by : Maram Darweesh
Rawan Okour

Reviewed by : Rama Ejueidi

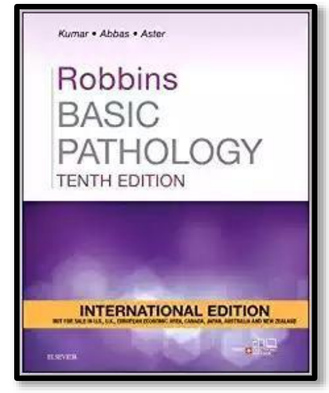
Inflammation and Repair

Mousa Al-Abbadi, MD, FCAP,CPE, CPHQ,FIAC
Professor of Pathology & Cytopathology
University of Jordan
College of Medicine
2024

Lecture 1

Introduction

- **6 lectures inflammation**
- **3 lectures repair; revision lecture**
- **Robbins Basic Pathology 10th Edition + lecture contents**



My duties

- **Simplify**
- **Concepts of pathology**
- **Help U all**
  Understand…understand…
  understand <u>then memorize</u>
- **Answer questions & inquiries**
- **Respect**

UR duties (my advice)

- **<u>On time</u> attending**
- **Plz…plz…plz…NO CHATTING during lecture**
- **Understand first then memorize and recall**
- **Respect to the process**
- **NO MOBILE**

TIPS

- ***"You don't have to be smart to be a good physician; but you need to be thorough"*** ***Thomas Eskin***
- ***"My interest is in the future…bcz Um going to spend all my time there"***

  Charles Kettering

BIG NO

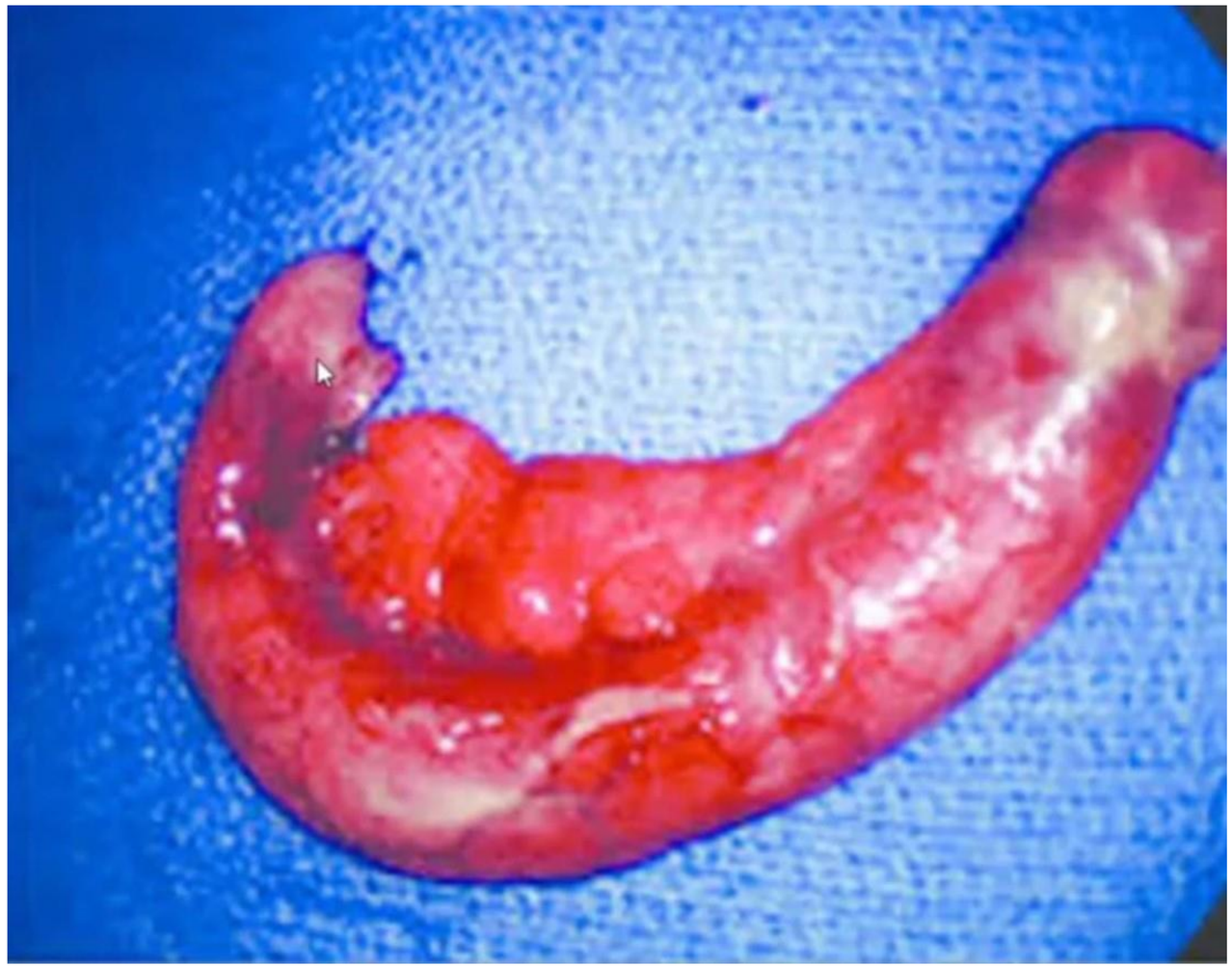
- **I DONNOT answer exam questions to any one before or after the exam**
- **Don’t ask these UNHEALTHY questions:**
  - **Is this important?**
  - **Should I study this?**
  - **How difficult are exam questions?**

E learning 2022 inflammation & Repair Al-Abbadi

1.General review	https://www.youtube.com/wat`ch?v=HrFb0axflGY&ab_channel=MedToday
2. Transudate vs exudate	https://www.youtube.com/watch?v=RE0sT0DYB6k&ab_channel=MEDSCHOOLRADIO
3. Outcomes of A Inflam	https://www.youtube.com/watch?v=Y-xcUN4u_F8&ab_channel=Dr.JohnCampbell
4. AA mediators	https://www.youtube.com/watch?v=PE_D3Os7oWY&t=627s&ab_channel=Dr.JohnCampbell
5. Complement system	https://www.youtube.com/watch?v=BSypUV6QUNw&ab_channel=Kurzgesagt%E2%80%93InaNutshell
6. Granulomatous inflammation	https://www.youtube.com/watch?v=rVaek7-RO0w&ab_channel=MedToday
7. Sarcoidosis	https://www.youtube.com/watch?v=zAq22bbWrNg&ab_channel=DrbeenMedicalLectures
8. Wound healing	https://www.youtube.com/watch?v=TLVwELDMDWs&t=43s&ab_channel=TED-Ed
Tissue repair	https://www.youtube.com/watch?v=KvBt2G4yMx4&t=409s&ab_channel=AnatomyandPhysiologyforParamedics
9. Keloid and HT scars	https://www.youtube.com/watch?v=-VUbBK3K4Ns&ab_channel=djverret
10. Local factors affecting healing	https://www.youtube.com/watch?v=pxOrHRcmeU4&t=22s&ab_channel=Dr.JohnCampbell

This is an appendix. This is not a normal appendix; it is a red, enlarged, congested appendix .This is an inflamed appendix, a condition called acute appendicitis

This appearance shows the major cardinal signs of inflammation



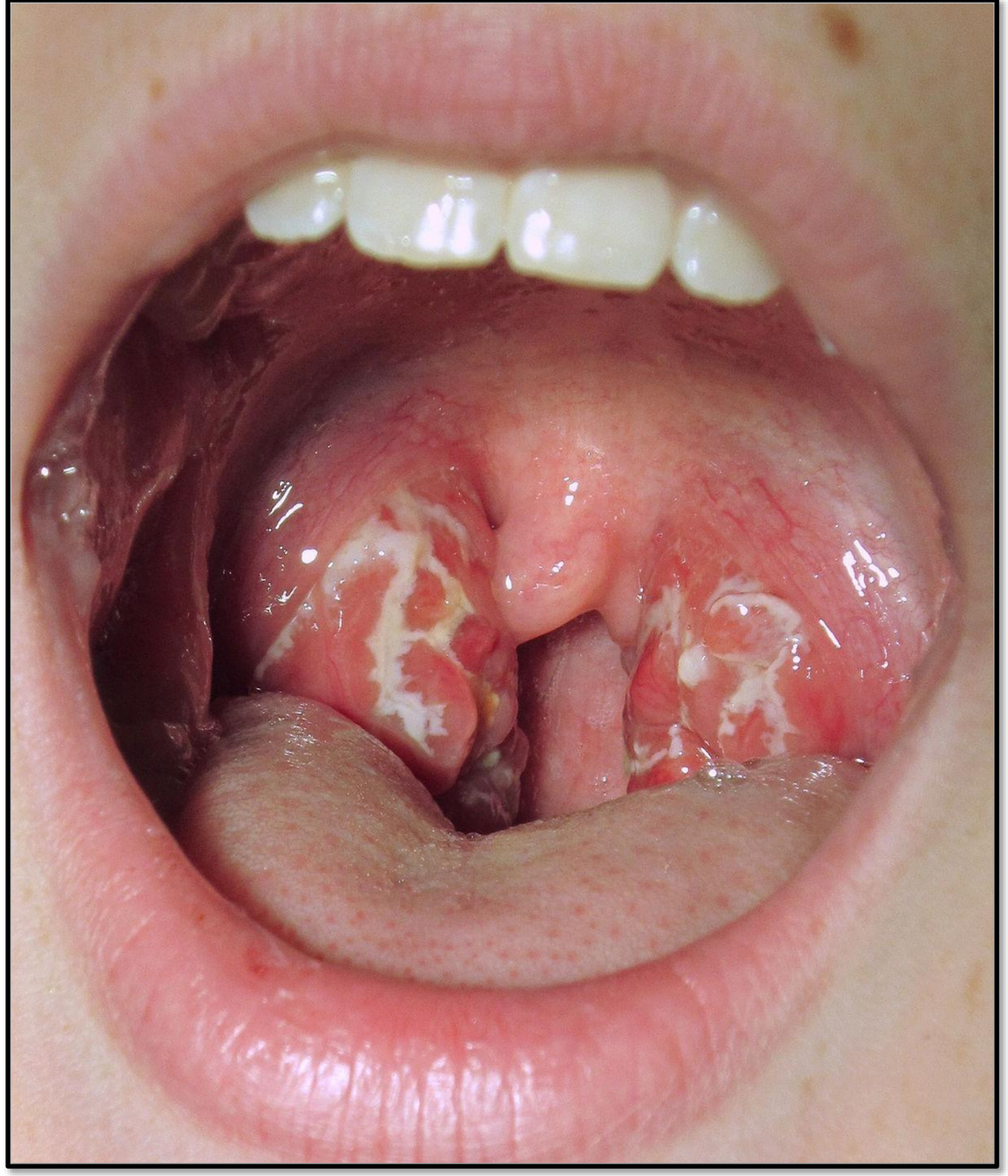
INFLAMMATION

"Response of an alive tissue or vascularized tissue to injury (infections or tissue damage)

Virus or bacteria

This process works by the recruitment of cells and molecules from circulation to the sites of need to Eliminate the offending agent"

For example, with viral tonsillitis, your tonsils will have a response to this virus . You will experience swelling, congestion, and a lot of cells infiltrating the tonsils to get rid of the virus . After a couple of days, you will be back to normal



Inflammation:

- Protective….It bothers you and is not a normal condition, but it protects you from the bad consequences of these offending agents.
- With no inflammation: infections can be fatal, wounds would never heal and injured tissue may sustain permanent damage

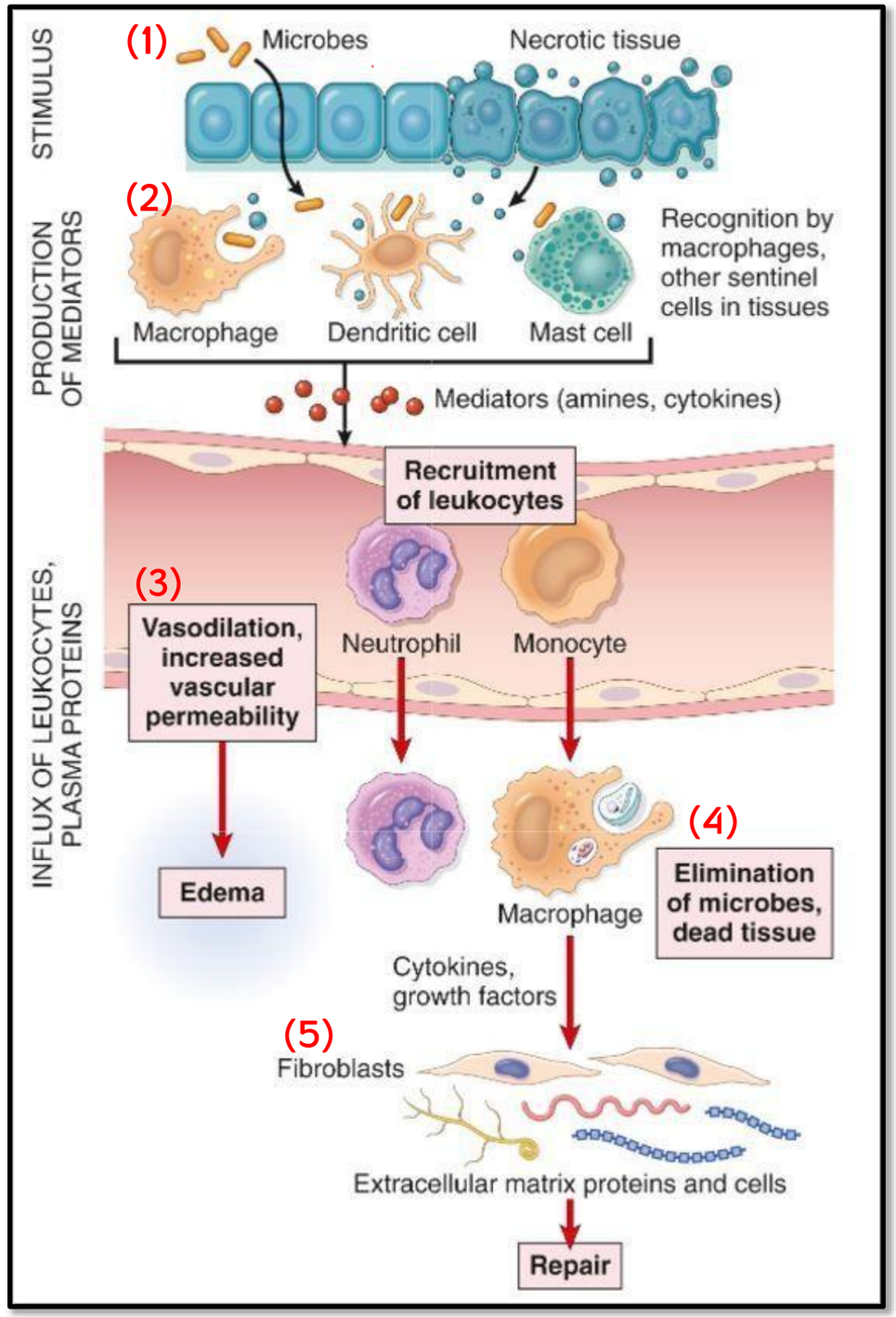
Inflammation helps us fight those fatal consequences and helps our body heal

In the 1920s and 30s, before antibiotics, simple tonsillitis or appendicitis used to be fatal

This image is a summary of all 5 steps of inflammation.

Each step will be explained in a separate lecture

It begins with (1) recognition of an offending agent, such as a microbe or bacteria, as stimulus which causes initial tissue damage. This recognition (either microbes or damaged tissue) (2) stimulates inflammatory cells like macrophages and mast cells to secrete various chemical mediators of inflammation. These mediators (e.g. amines) initiate the vascular phase, leading to (3) vasodilation and increased vascular permeability, where also recruitment of inflammatory cells like neutrophils and monocytes into the tissue. Once they leave from blood vessel into the tissue, these cells (particularly monocytes which become macrophages) and neutrophils or micky mouse cells(c3 three lobe nuclei)(4) attempt to eliminate the microbe by secreting further mediators like cytokines and growth factors and through mechanisms like intracellular killing. Finally, the process concludes with (5) the reparative phase, involving the recruitment of fibroblasts and the deposition of extracellular matrix proteins to heal the damaged tissue.

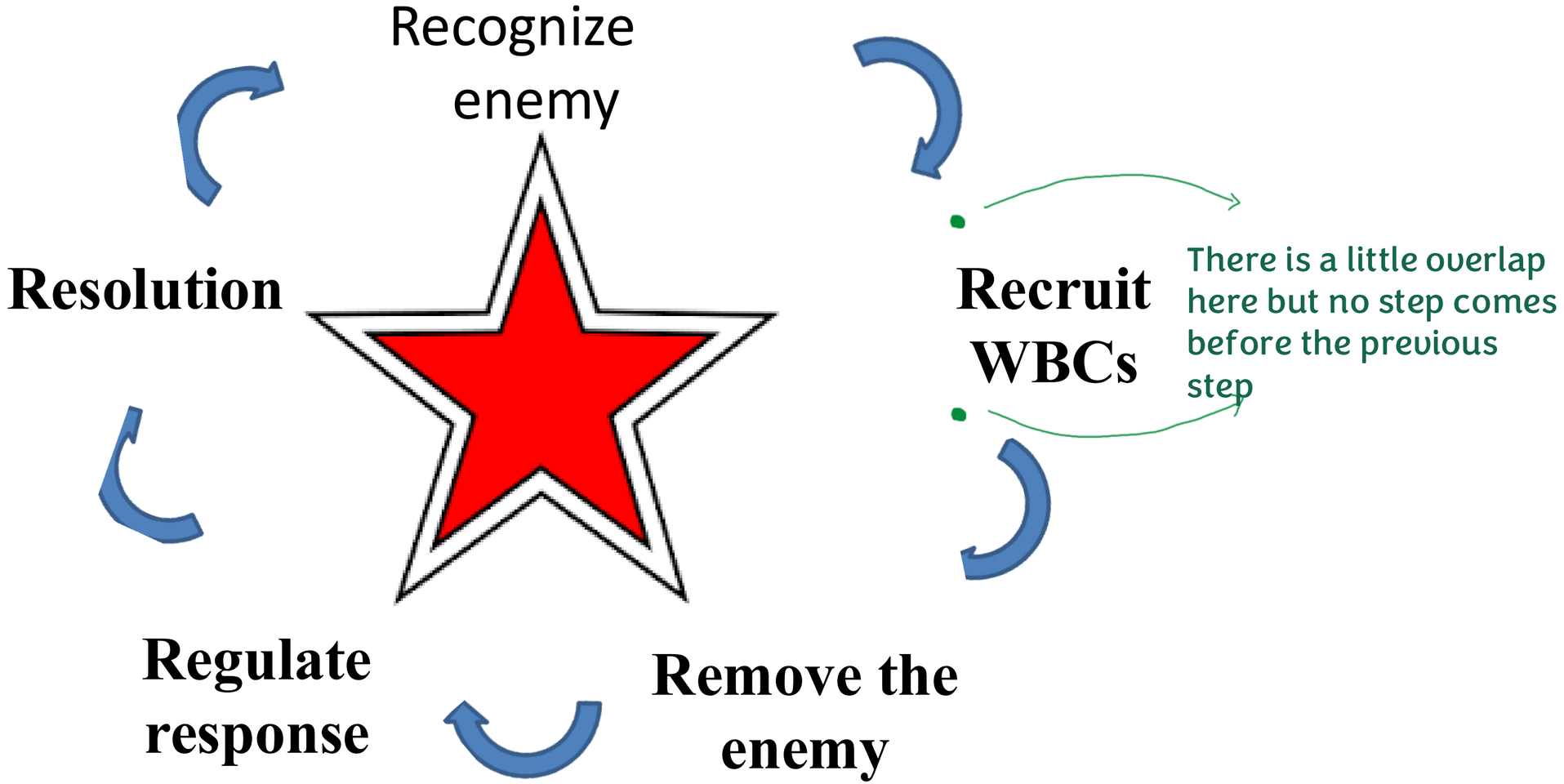


Typical inflamm. Rx. steps:

1. **Offending agent recognized by cells and molecules** → Recognition of the offending agent and the changes it causes like change in the structures, proteins or cells
2. **WBCs & Pl. proteins recruited to injury site** → Recruitment of white blood cells (inflammatory cells) and plasma proteins to the site of injury weather it's tonsils or appendix or liver
3. **WBCs and Pl. proteins work together to destroy and eliminate the enemy** → Removal (elimination) of the injurious agent (e.g., by phagocytosis, intracellular killing)
4. **Rx. Is then controlled and terminated** → Regulation (control) of the inflammatory response. Once the enemy is eliminated, we don't need all these soldiers (WBCs, proteins, mediators) to stay, as they might cause collateral damage. Your body is equipped to control and decrease this response
5. **Repair of damaged tissue (regeneration & fibrosis)** → Resolution and Repair. The tissue that has been lost will be replaced, either by regeneration (if the cells have this ability) or by scar formation

These steps are consequential, meaning one comes after the other, though some overlap can exist between the end of one step and the beginning of the next step but nothing comes before (ordered)

The 5 Rs:



Clinically, this table offers insights for understanding inflammation when seeing patients in the clinic, emergency room or operating room

TABLE 3.1 Features of Acute and Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: minutes or hours	Slow: days
Cellular infiltrate	Mainly neutrophils	Monocytes/macrophages and lymphocytes /Plasma proteins
Tissue injury, fibrosis	Usually mild and self-limited	May be severe and progressive
Local and systemic signs	Prominent	Less

When macrophages are circulating in the blood they are called monocytes (one nucleus – mononuclear cell) , when they are activated and delivered to the tissue they will have more cytoplasmic organelles to secrete the needed substances and proteins and last longer

The best outcome of acute inflammation is to complete resolution of the process and get rid of the offending agent

Feature	Acute (التهاب حاد)	Chronic (التهاب مزمن)
Onset	Rapid onset — symptoms appear **within minutes to a few hours** (e.g., in **acute bronchial asthma** or **encephalitis**). The quick development of symptoms usually pushes the patient to **seek medical advice**.	Slow and gradual onset – develops over days, weeks, or months. In many cases, symptoms are absent until significant tissue or organ damage has already occurred. Chronic inflammation is **insidious**, meaning it progresses **silently** without clear signs or discomfort. 
Cellular infiltrate	Dominated by neutrophils (polymorphonuclear leukocytes) – the hallmark of acute inflammation. These cells have 3–5 lobed nuclei and appear abundantly in tissues such as acutely inflamed appendix.	
Tissue injury, fibrosis	When you get common cold for example you will have fever/ pain for couple of days. The given treatment is supportive treatment antipyretic for fever, Panadol for pain, antihistamines for congestion.	
Local and systemic signs	If somebody has severe acute tonsillitis in 1-2 days will feel pain, sore throat, fever etc.	Both are usually less marked than in acute inflammation. Because of this, chronic inflammation can continue unnoticed for long periods. Its silent progression makes it dangerous, as ongoing tissue damage and fibrosis may lead to irreversible organ dysfunction before diagnosis.

They are major differences but there are more

TABLE 3.1 Features of Acute and Chronic Inflammation

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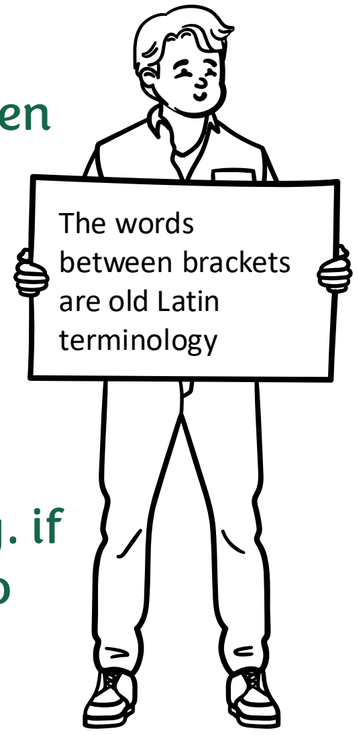
Sometimes, we encounter a condition where both processes are present — a **baseline of chronic inflammation** with an **acute attack** superimposed on it.
This is referred to as **"acute on top of chronic inflammation."**
For example, in the **stomach**, this can be seen in **chronic active gastritis** caused by *Helicobacter pylori* infection, where **neutrophils** (acute inflammatory cells) are present **alongside plasma cells, lymphocytes, and macrophages** (chronic inflammatory cells).

Cardinal signs of inflammation

Those are the major signs of inflammation

each one of them is explained by certain mechanism or pathogenesis

- **HEAT (*calor*)** → If the patient has inflamed tonsils, you would find them warm (feel heat)
- **REDNESS (*rubor*)** → Congested with blood
- **SWELLING (*tumor*)** → Usually, tonsils aren't swollen but if they are inflamed, they will be swollen and have difficulty with swallowing
- **PAIN (*dolor*)** → The organ (the inflamed one) will stimulate the pain receptors
- **LOSS OF FUNCTION (*functio laesa*)** → The inflamed organ will lose its function . E.g. if you have inflamed ankle, you won't be able to walk on , or if you have inflamed big toe, you can't move it



Can inflammation be bad?

The four mechanisms of bad consequences of inflammation

- **Too much…damage**

  Excessive inflammatory response can lead to tissue damage and destruction of healthy cells.
  Example: Severe inflammation in infections or allergic reactions can injure surrounding tissues.

- **Too little… damage**

  Inadequate inflammatory response allows the offending agent (such as bacteria or viruses) to cause further harm.
  Individuals with weak immune systems become vulnerable to opportunistic infections.
  → **Both too much and too little inflammation are damaging.**

- **Misdirected inflammation…autoimmune diseases and allergies**
- **Chronic inflammation…chronic diseases**

Can inflammation be bad?

- **Misdirected inflammation…autoimmune diseases and allergies**

The immune response may become misdirected and attack the body's own tissues instead of the harmful agent.
This leads to autoimmune diseases or allergic reactions.
Example: In some cases, the immune system targets kidneys (glomerulonephritis) or alveolar membranes in the lungs.
→ The immune system damages self-tissues instead of pathogens

- **Chronic inflammation…chronic diseases**

Acute inflammation is more favorable than the chronic inflammation because it leads to complete resolution

→ Continuous inflammation leads to **irreversible organ damage**
Persistent or **long-term inflammation** can cause **progressive tissue damage and fibrosis**.
Examples include:
Chronic hepatitis → chronic liver disease
Chronic glomerulonephritis → end-stage renal disease
Chronic lung inflammation → pulmonary fibrosis

➢Some disorders present as acute on top of chronic – meaning a background of mild chronic disease is followed by an acute episode.
For example, acute relapsing pancreatitis represents a case where chronic pancreatitis is periodically interrupted by acute attacks.

TABLE 3.2 Disorders Caused by Inflammatory Reactions

Disorders	Cells and Molecules Involved in Injury
Acute	
Acute respiratory distress syndrome ARDS (clinical syndrome)	Neutrophils The main mechanism of injury in the 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 And sometimes platelets
Pulmonary fibrosis	Macrophages; fibroblasts

Listed are selected examples of diseases in which the inflammatory response plays a significant role in tissue injury. Some, such as asthma, can present with acute inflammation or a chronic illness with repeated bouts of acute exacerbation. These diseases and their pathogenesis are discussed in relevant chapters.

➢ This table gives you examples of acute and chronic illnesses

Syndrome	Main Mechanism of Injury	Extra Information
Acute Respiratory Distress Syndrome (ARDS)	Neutrophil-mediated injury	A clinical syndrome seen in critically ill or ICU patients with multiple organ failure. The pathologic term is diffuse alveolar damage.
Bronchial Asthma (Acute Attack)	Eosinophils and IgE antibodies	Patients often have atopy and allergies. Symptoms include nasal congestion, severe bronchospasm, wheezing, and difficulty swallowing.
Acute Glomerulonephritis	Antibodies and complement system involving monocytes	Causes tissue injury in the kidneys (and sometimes neurons) due to immune complex deposition and inflammation.
Septic Shock (Septicemia)	Cytokine-mediated injury	Represents blood poisoning from severe bacterial overgrowth in the blood, affecting vital organ functions. Gram-negative septicemia is particularly lethal.

Syndrome	Main Mechanism of Injury	Extra Information
Arthritis (Rheumatoid, Osteoarthritis, Septic, Gouty)	**Chronic immune or inflammatory response** in joints	Affects the **musculoskeletal system**. Different types involve **autoimmune, infectious, or metabolic mechanisms**.
Bronchial Asthma (Chronic Stage)	**Persistent eosinophilic inflammation** and **airway remodeling**	Requires **long-term maintenance therapy**, not just treatment of acute attacks, to prevent **chronic airway obstruction**.
Atherosclerosis	**Chronic inflammatory response** in the arterial wall	Leads to **chronic ischemia** and complications such as **acute myocardial infarction** and **stroke in the brain**
Pulmonary Fibrosis	**Chronic interstitial inflammation and fibroblast activation**	Can result from various lung diseases, progressing to **idiopathic or end-stage pulmonary fibrosis**. Patients may require **long-term oxygen therapy**, and the condition evolves over **months to years**.

Causes of inflammation:

INFECTIONS	**Bacteria, fungi, viruses, parasites And their toxins**
NECROSIS Cell death	**Ischemia, trauma, physical and chemical injuries, burns, frostbite, irradiation like heart attack and brain stroke**
FOREIGN BODIES	**Splinters, dirt, urate crystals (gout), Cholesterol crystals (atherosclerosis)**
IMMUNE REACTIONS	**Allergies and autoimmune diseases** Misdirected inflammatory responses

•specially bacteria are capable of secreting **toxins, endotoxins, and exotoxins.**

•**Trauma** can cut your artery, resulting in **necrosis** and physical and **chemical injury** such as **sunburn.**

•**Urate crystals** will deposit in your joints, especially the **big toe**, causing **gouty arthritis** (النقرس)

•The **position of cholesterol clusters** is the main underlying **pathogenesis** of **atherosclerosis**, which can cause **many fatal diseases.**

•Some people are **allergic to certain medications or pollens**, resulting in an **exaggerated immune response** where **severe reactions** occur.

Recognition of microbes and damaged cells:

- Toll is the scientist who discovered TLRs

- **First step in inflamm. response**
  - **Cellular receptors : Toll-like R (TLRs); on membranes and endosomes. Recognize Pathogen Associated Molecular Patterns (PAMPs)**
  - **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)**
  - **Circulating proteins: complement system, mannose-binding lectins and collectins**

From outside your body

From inside your body

TLRs recognize something strange, foreign or weird happening by a virus or a microbe

There are sensors that recognize damaged tissues when there is necrosis or radiation or ischemia or dead tissues

Complement system and some body proteins have the ability to recognize those microbes or damaged cells

Additional Resources:

رسالة من الفريق العلمي:

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			