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PATHOLOGY

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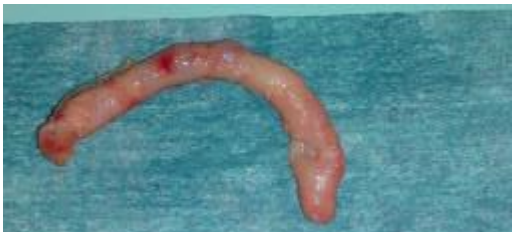
Inflammation

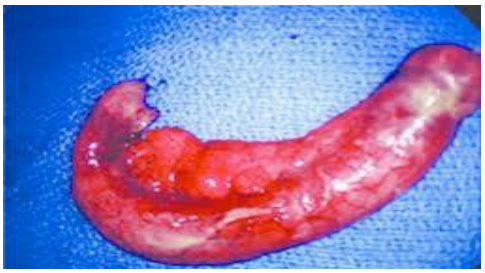
Example: appendix inflammation (notice the difference in shape and color)

Normal Appendix



small, white in color.

Actue **Appendicitis** (abnormal,inflammmed appedix)



red, enlarged, congested appendix

Defintion of inflammation:

A Response of a viable, **alive**, **vascularized** tissue to a certain type of injury (tissue damage or infections like bacetria and viruses) recruitment of cells and molecules from circulation to the sites of need to eliminate the offending, injurious agent.

Example—Viral tonsillitis is an <u>inflammation</u> of the tonsils due to a viral infection inflammation <u>signs</u>: swelling, congestion, and multiple cells infiltrating the tonsils to get rid of the virus in a couple of days.

-Inflammation is 99% **protective** againts the bad consequences of the offending agents, in which inflammation helps the body to fight fatal consequences, eliminate tissue damage and heal its wounds.

Note:
the suffix **(-itis)** denotes to organ inflammation or refer to an inflammatory disease

-without inflammation infections even simple ones (simple tonsilitis, appendicitis) can be fatal, wounds would never heal and injured tissue may sustain permanent damage.

5 Major Steps of a typical Inflammatory rxn:

The 5 Rs: **(recognize→ recruit→ removal→ regulate→ resolution or repair)**

these steps are organized and sequential. However, there might be some overlap between the step.

1- **Recognition** of offending <u>agents</u> and the resulting celluar and structural <u>changes</u> by cells and molecules.

2-**Recuitment** of WBCs and different types of plasma proteins (PL) to concentrate and focus on the injury site (tonsils, appendix, liver, etc…)

3- **Removal**, elimination and destortion of the offending agent by WBCs & PL proteins.

4- **Regulation**, Control, termination of the inflammatory response.
the WBCs, proteins, and chemical mediators are not needed to stay anymore after the termination of the offending agent to prevent collateral damage such as tissue damage.

5-**Repair** of the damaged tissue and replacing it either by ①regeneration if regenrating abilities are present or ②scar formation by fibrosis.

This schematic picture explains the 5 steps:

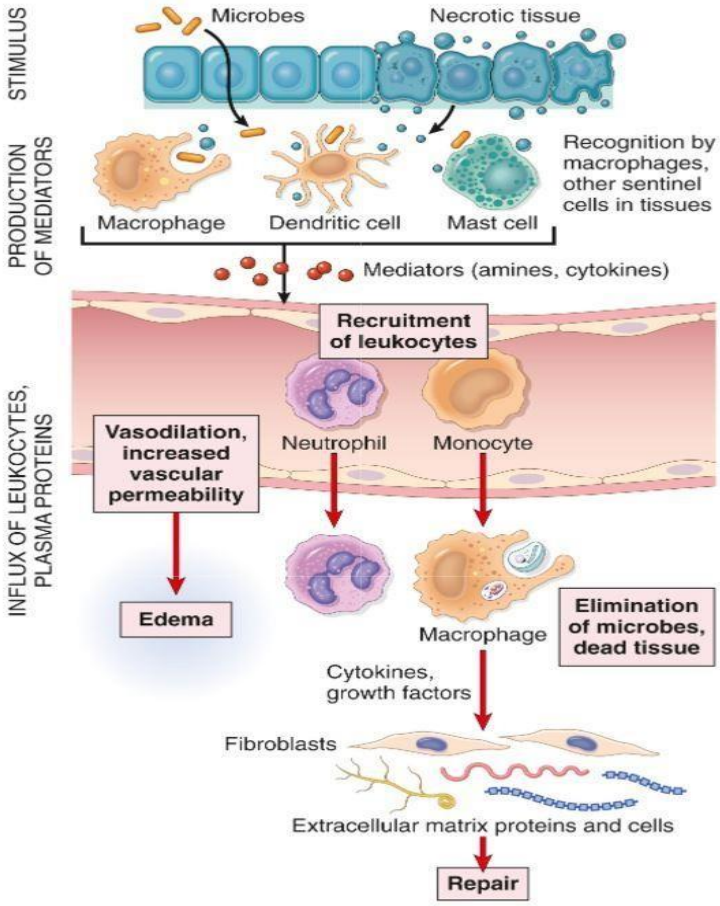
an offending micorbe will act as a stimulus (like bacteria e.g., bacilli), and cause tissue damage, cells of the body will **recgonize** the offending agent by either recognizing the microbe or the damaged tissue.

as a consequnce, many inflammatory cells like macrophages, dendritic cells, mast cells will be stimulated to **secrete** inflammation chemical mediators.

intially there will be a predominance of hormones that will cause vasodialtion to increase vascular permiability which recruits the entry of inflammtory cells into the tissue

neutrophils will stimulate the secretion of multiple mediators like cytokines and growth factors to also **elimenate** the microbe with different mechanisms like intracellular killiing

reparative process will propagate and start the recruitment of fibroblasts and extracellular matrix proteins.



Side Note:

*once the circulating monocytes leave the blood vessel and enter the tissue they'll transform into tissue macrophages also known as activated macrophages.

*neutrophils (mickey mouse cells :) polymorphonuclear cells, nucleus is segmented into 3 connected lobules.

Classification of Inflammation: 1) Acute. 2) Chronic.

Feature	Acute	Chronic
Onset (beginning)	Fast: minutes or hours Example: in acute bronchial asthma or acute tonsillitis symptopms and signs will quickly show up taking only a few minutes to hours.	Slow: days, weeks, months, years Sometimes chronic inflammation doesn't show symptomps until severe damage has occurred to the organ Described as **insidious**
Cellular infiltrate (types of cells that enter the inflammed tissue and can be seen in histological sections)	Mainly **neutrophils** ***hallmark** of acute inflammation	Monocytes/macrophages, lymphocytes, and plasma cells Sometimes eosinophils and mast cells would be present
Tissue injury and fibrosis	Usually mild and self-limited	May be severe and progressive
Presence of local and systemic signs	Prominent (localized inflammation)	Less prominent *this is why they're insidious

- throughout histological sections seen under the microscope of the inflamed organ we can identify the type of inflammation, if neutrophils are present→ acute, macrophgaes + lymphocytes → chronic.
- Regular flu is an acute upper respiratory tract infection that doesn't result in severe tissue injuries, so with supportive therapy the inflammation will be resolved within a couple of days.
- Chronic inflammation causes severe tissue injury causin chronic diseases: chronic renal failure caused by chronic glomerulonephritis in the kidneys or liver cirrhosis (liver failure) caused by chronic hepatitis C that has been ongoing for year
- Acute inflammation pushes the patient to see a doctor because it progresses <u>fast</u> and has <u>prominent</u> local and systemic signs, the diagnosis is early and so is the healing.
- chronic + acute inflammations can occur together and different pathological terms are used to describe such cases.
  →when there is a baseline of chronic inflammation and acute attack would come on top of it.

Examples:
-stomach chronic acitve gastritis; chronic gastritis + an acute attack comes on top. neutrophils would be present on top of plasma cells in histological sections of the stomach along with lymphocytes and macrophages due to methane helicobacter primary bacteria.

Examples on Acute illnesses:

Disorders	Cells and Molecules Involved in Injury
Acute	
Acute respiratory distress syndrome	Neutrophils
Asthma	Eosinophils; IgE antibodies
Glomerulonephritis	Antibodies and complement; neutrophils, monocytes
Septic shock	Cytokines

-ARDS (acute respiratory distress syndrome): terminally ill patients with multiple organ failures in the ICUs, main mechanism of injury is in the lungs where fluids leak.
autopsy performed on a dead ARDS patient will show diffused lung sections due to alveolar damage known as DAD.

-Glomerulonephritis: involves tissue injury on kidneys and sometimes in neurons.

-Acute bronchial asthma: severe bronchospasm, wheezing, difficulty in swallowing

-Septic shock (septicemia)—blood poising due to severe bacterial overgrowth in the blood results in secreting too many cytokines are released which impacts vital functions
gram-negative bacterial septicemia is lethal.

Examples on Chronic illnesses:

Chronic	
Arthritis	Lymphocytes, macrophages; antibodies?
Asthma	Eosinophils; IgE antibodies
Atherosclerosis	Macrophages; lymphocytes
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.

- Types of arthritis: rheumatoid arthritis, osteoarthritis, septic arthritis, gouty arthritis.

- Artherosclerosis (تصلّب الشرايين) : caused by chronic ishemia that can issue complications in the heart and the central nervous system in the form of acute myocardial infarction or major brain strokes.
artherosclerosis causes ischemic heart disease which is no.1 cause of death worldwide

-Pulmonary fibrosis (تليف الرئة) many lung diseases will end up causing geopathic pulmonary fibrosis or end stage formula fibrosis.
patients would need oxygen supply at home

Cardinal signs of inflammation—major signs

any inflamened organ would express:

- **HEAT** (*calor*): sensibly warm tissue.
- **REDNESS** (*rubor*): due to excessive blood flow
- **SWELLING** (*tumor*).
- **PAIN** (*dolor*): by stimulating pain receptors.
- **LOSS OF FUNCTION** (*functio laesa*): loss of function of an inflamed big toe in gout, or in a swollen ankle due to severe arthritis.

Can inflammation be bad?

in the following cases inflammation is bad:

- **Too much** inflammation causes tissue damage.
- **Too little** inflammation: not a proper response and the immune system isn't well equipped leads to exposure to multiple personalistic infections where damage can also happen.
- **Misdirected** inflammation: the inflammatory response will attack the body's own tissues instead of attacking the offending agent and this is what happens in autoimmune diseases and allergies.
  Example: misdirection of tonsilitis inflammtory response as it attacks the kidneys causing glomerulonephritis or attacks alveolar tissue instead of attacking the bacteria or the virus in the throat.

- **Chronic** inflammation will cause chronic diseases; chronic hepatitis, chronic glomerulitis will end up damaging the organs (heart, lungs, kidnyes, liver) and causing diseases like chronic liver disease, end stage renal disease, end stage pulmonary fibrosis…etc

Causes of inflammation whether acute or chronic

①INFECTIONS	**Bacteria, fungi, viruses, parasites <u>And</u> their toxins**
②NECROSIS	**Ischemia (vascular compromise), trauma, physical and chemical injuries, burns, frostbite, irradiation**
③FOREIGN BODIES	**Splinters, dirt, urate crystals that deposit in joints causing acute gouty arthritis, Cholesterol crystals (atherosclerosis)**
④IMMUNE REACTIONS	**Allergies (to certain drugs and pollens) exaggerated immune response and severe rxns that causes damage autoimmune diseases (misdirected immune response)**

First Step in Inflammatory response:

Recognition of microbes and damaged cells

-Cellular receptors: Toll-like R (TLRs); naturally present on cellular membranes and endosomes. Their function is to: 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 (inflammasomes) gets activated and recruit circulating proteins like complement system, mannose- binding lectins and collectins that can also recognize the microbes or damaged cells.

ACUTE INFLAMMATION

1st phase of acute inflammation: vascular/cellular phase composed of 3 major components:
1) blood vessel dilatation (BV dilatation): but in injury sometimes the first response is transient <u>vasoconstriction</u> that continues for a few seconds but then vasodilatation will ensure.

2) Increased vascular permeability:
cells, proteins, fluids from the intravascular compartment will escape to the interstitium leading to edema.
→this is why the appendix was swollen; a lot of cells and fluids leaked out from the blood vessels (intravascular compartment) to the interstitial compartment.

3) Imigration of WBCs: from intravascular compartment to the interstitial compartment as a result of vasodilation.

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.

BEST WISHES 😊

- ***"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 because I'm going to spend all my time there"***
  -Charles Kettering