Video 1

by Leen Al-kutteb
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Introduction to Inflammation

Inflammation classically describes four key signs, each with a Latin derivation: calor (heat), dolor (pain), rubor (redness), and tumor (swelling). These signs can combine to cause a fifth sign, functional lysa, or temporary loss of function due to pain or swelling.

Causes of Inflammation

Inflammation typically begins with stimuli such as pathogens. While pathogens are common causes leading to inflammation, it can also be triggered by toxins and trauma. For example, sore muscles after an intense workout are due to inflammation trying to repair overused muscle fibers. The goal of inflammation is to respond to stimuli and restore balance, which often includes eliminating the cause of tissue injury, clearing out dead cells, and starting tissue repair.

External and Internal Triggers

Inflammation can be triggered by external and internal factors. External factors include non-microbial (allergens, irritants, toxic compounds) and microbial factors (virulence factors, pathogen-associated molecular patterns or PAMPs). Microbial factors help pathogens colonize tissues and cause infection. PAMPs are molecules shared across many pathogens, including bacterial and fungal wall components. Internal factors include damage-associated molecular patterns or DAMPs, which signal serious cell damage and trigger inflammation.

→ cell dies
injured plasma membrane
Endogenous

Innate Immune Response

Pattern recognition receptors (PRRs) on leukocytes recognize PAMPs and DAMPs, sparking an inflammatory response as part of the innate immune system. This response is non-specific, fast, and lacks memory. Leukocytes are classified as granulocytes (neutrophils, eosinophils, basophils, mast cells) and agranulocytes (lymphocytes, monocytes).

endothelial cells may release NO → vasodilation & ↑ permeability

Inflammatory Process

Extravasation = squeezing

The process usually starts with macrophages or mast cells in tissues responding to PAMPs or DAMPs. Mast cells release inflammatory mediators like histamine, serotonin, cytokines, and prostaglandins. These mediators cause endothelial cells to separate, increasing vascular permeability. Neutrophils are the first leukocytes recruited and start phagocytosing pathogens and damaged cells.

also express adhesion proteins

often kill themselves after pathogens (apoptosis)

cause cells to separate & increase vessel size

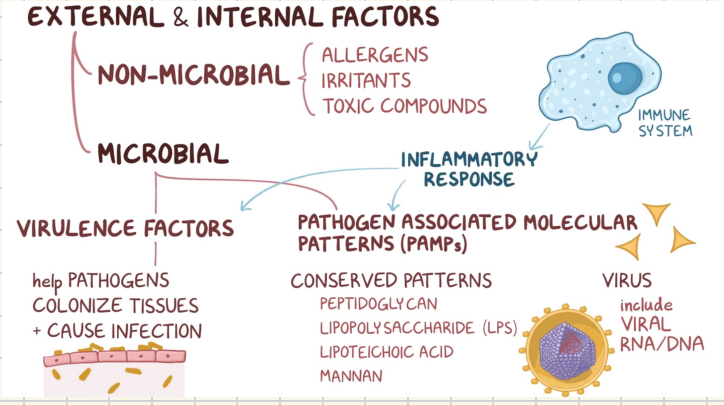
Complement System and Adaptive Immune Response

The complement system, activated by antibodies or pathogen molecules, helps attract leukocytes and enhances phagocytosis. Dendritic cells present pathogen fragments to T lymphocytes, activating the adaptive immune system. In cases of cuts or scrapes, platelets and clotting factors clot the wound, preventing pathogen entry and aiding tissue repair.

Also MAC

Conclusion: Inflammation and Tissue Repair

The inflammatory response concludes with tissue repair. Macrophages clear dead cells to make room for new ones. Angiogenesis forms new blood vessels, which regress once healing is complete. Fibroblasts synthesize collagen for wound healing. Depending on the damage severity, the tissue either regenerates or forms a fibrous scar.

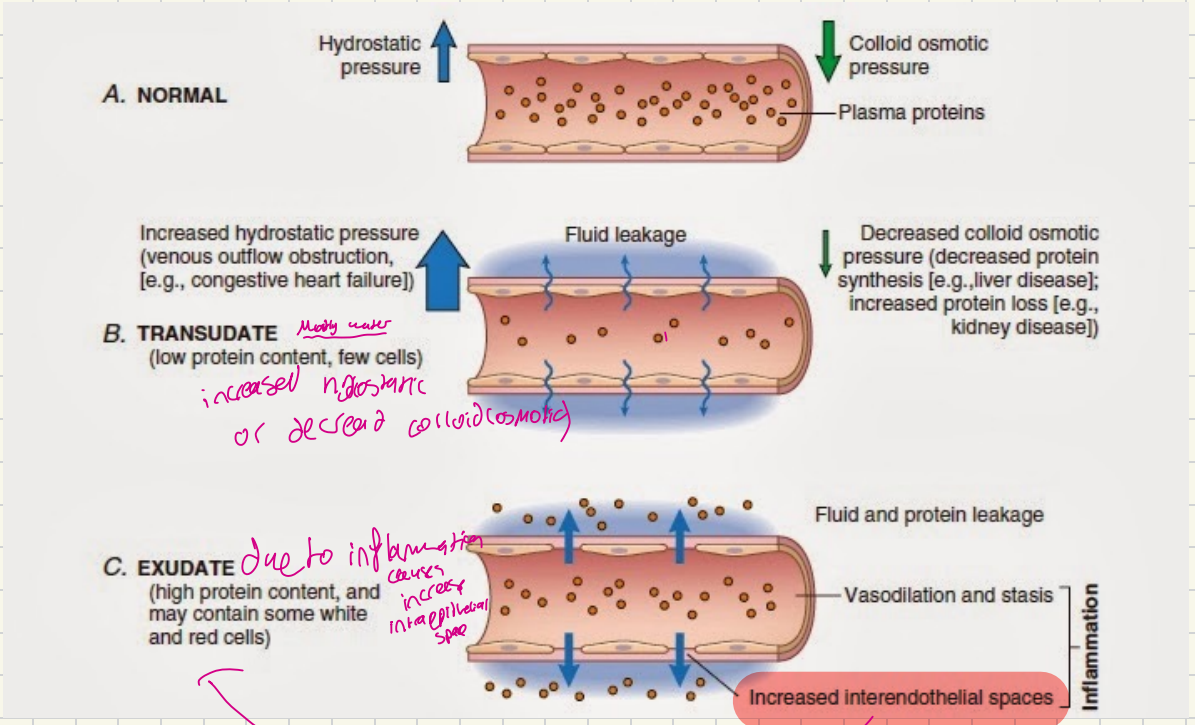


Video 2. exudate vs transudate

protein rich fluid

transudate

exudate



Causes

Video 3 outcomes of inflammation

- short inflammatory response
  - complete resolution
    - normal physiology
- greater response
  - scarring
    - fibrosis

- cell heal by
  - fibrosis
  - regeneration
    - complete healing

or combination maybe with minor scarring

- Inflammation cause not removed → chronic inflammation

- ng cause pus filled abscess, collects on hollowed area

- best to let it out once consolidated

pus → dead PMN, macrophages, maybe live leukocytes.

phagocytosis going on, middle dead cells & phagocytosis products & bacterial cells

↓ treats why its infectious

pus counts as necrotic tissue.

- No healthy cells migrating into the wound we ready to heal.

You also get liquefaction necrosis

when cells necrose they liquify, you get solution of pus.

Suppurative → pus producing

purulent → a lot of pus

empyema → pus filled cavity
↓
severe cholecystitis
↳ empyema of gallbladder

If pus not evacuated in time ⇒ autolyse & absorption to surrounding tissue.

but risk of spread

So much cytokine will cause systemic inflamatory response syndrome

due to large infections,

spread of inflamation from local to systemic.

↓

can cause death

mostly resolution with or without scaring

Video 4 AA mediators

Normally we don't want to inhibit inflammation but inflamatory response itself can become disruptive

(most important things)

inflamations are mediated locally by mediators

Prostacyclin

* phospholipid in cell membrane released to tissue spaces
* phospholipase A is in surrounding tissue, it finds phospholipids & will convert them to Arachidonic acid (AA)
* cyclooxygenase also in tissues it'll convert AA to prostaglandins

will cause inflamation

* steroids abolish inflamation

local vasoactive molecules

* low molecular weight
* macrophages are important but their secretion like (TNF)
* attract neutrophils to marginalise
* can cause constriction of endothelial cells (big gap between)
* systemic absorption → go all over body

remember the systemic pic

cell cyto kines move

by inhibiting PLA

(therefore No inflamation)

* also other anti inflamatory drugs

non steroidal

NSAIDs (like ibuprofen) Aspirin

↓

analgesic Pain reliever (give for 24 hr it'll get anti inflamatory effect)

inhibit COX

bigger area of injury

↓

more likely

to become systemic (more cytokine)

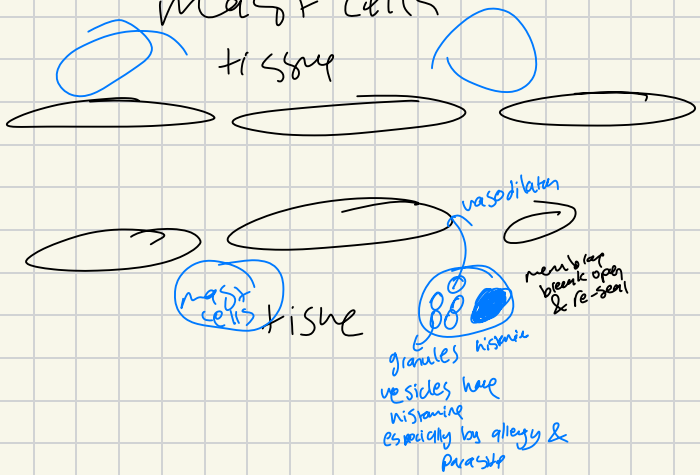
Acute phase Response

systemic No longer local

inflamatory mediators can be derived from plasma (since when tissue is damaged, capillaries might be damaged & plasma will leak thus some mediators are derived from plasma, platelets can aggregate or leak into tissue space)

* complement system can act as inflamatory mediator

* Histamine released from mast cells



source of amines

platelets

plasma

endothelium via complement

histamine

Video 5 complement system

* change shape to activate

- cripples enzymes
- attack immune system
- puts holes in things till they die

C3b has very little time to find victim or iPH1 hydrolysis

or attach to cell & form C3 convertase

also it makes it easy to phagocytose cells.

C3A → chemotaxis

Vaccinia virus

Can cause cells to produce proteins that shut down complement

Video 6

Granulomatous Inflammation

Specialized type of inflammation

- Usual chronic inflammation cannot get rid of the offending agent

Ex :- Tuberculosis

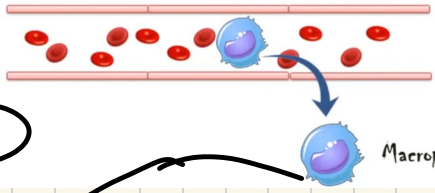
Chronic inflammation → Macrophage

Macrophage

Mononuclear phagocyte system/Reticuloendothelial system

Mononuclear phagocyte system

- Blood monocytes
- Tissue Macrophages



Macrophage

- Kupffer cells – Liver
- Sinus histiocytes – spleen & LN
- Alveolar macrophages – Lungs
- Microglia – CNS

Microbial products
Cytokines
γ IFN

Activated Macrophage

Eliminate the injurious agent

- ROS & RNS
- Proteases
- Cytokines
- Coagulation factors
- Arachidonic acid metabolites

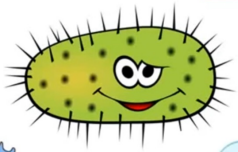
Initiate the repairing process

- Growth factors (PDGF, FGF, TGF β)
- Fibrogenic cytokines
- Angiogenic factors
- collagen Remodelers

ROS & RNS
Proteases
} Damage to the surrounding tissue (Macrophages may)

Tissue destruction → Characteristic feature of chronic

Pathogenesis



Resistant to be killed by Macrophages so macrophages are stimulated to more epithelioid cells and have more ability to kill

Acute :- (Macrophages might disappear by)
- Dying off
- Into lymphatics

Chronic :-

Macrophages accumulate at site due to
- Continuous recruitment from blood
- Local proliferation
- Immobilization – MIF (migration inhibitory factor by lymphocytes)

Macrophage

Epithelioid cell

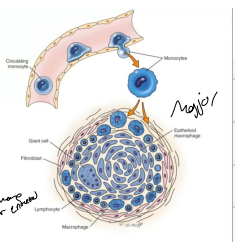
- More microbial killing ability

Granuloma – Collection of epithelioid cells
Rim of lymphocytes
Multinucleated giant cells
Fibroblasts
(Eosinophils – parasitic inf.)

Fusion of epithelioid cells

Granulomatous inflammation

More tissue destruction & fibrosis (due to poor or slow)



2 Types (pathogenesis)

(Can be phagocytosed by a single macrophage)

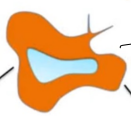
- Foreign body granuloma

Talc, suture material, fibers

No immune response

(agent induced)

(macrophages engulf)



T-lymphocytes

Cytokines

γ IFN

- Immune granuloma
- Digest the foreign agent
- Activate Macrophages
- Activate T cells

Poorly degradable

Cell types

Epithelioid cells :-

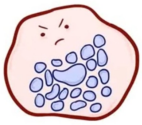
(activated tissue macrophages)

- Pale, eosinophilic cytoplasm
- Dispersed chromatin – Increased synthetic activity
- Elongated nucleus – Footprint shape
- Less phagocytic capability
- Enhanced secretory ability
- More microbial killing ability

Langhan's giant cells :-

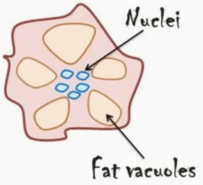
- Nuclei – Periphery of the cell (Horse shoe)
- Tuberculosis

Foreign body type giant cells :-



- Nuclei – Arranged randomly
- Foreign material

Touton giant cells :-



- Foamy macrophages
- Fat necrosis

Morphological patterns of granulomatous inflammation

1. Caseating Granulomata

   Center – Caseous necrosis

   Tuberculosis

2. Non – necrotizing Granulomata

   No central necrosis

   Sarcoidosis, Leprosy, Crohn's disease

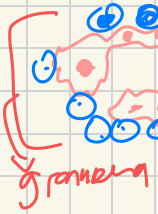
3. Suppurating Granulomata

   Centre – Suppurative necrosis with neutrophils

   Cat scratch disease, Fungal infection, TB (rarely)

Video 7

non caseating granuloma



multinucleated cells (fused)

CD4 will be consumed

anergic cells

Anergy pdd

epithelioid cells (epithelial like)

long elongated but irregular shape

macrophages release (IL-8, TNF, MIP-IX)

recruitment of lymphocytes monocytes

amplification cause

Schaumann bodies (Ca^{++}) + Asteroid bodies

video 8

wound healing

homeostasis

blood clot forms

inflammation & vasodilation

Proliferation by fibroblasts

epidermal cells divide

dermis contracts

Remodeling & wound matures (collagen arranges)

video 9 keloids & HT scars

keloids

* ear keloid
* grows outside incision

* 1) decrease inflammation (steroid)
  2) excise it & administer kenalog
  * if recurrence / silicone sheeting / radiation

* grows on same sides as incision
* No need for surgery
  * use kenalog to decrease collagen
  * dermabrasion to smooth & decrease ability to be seen

video 10

Understanding Factors Affecting Wound Healing

infected wounds can never heal & become chronic

The Impact of Infection on Wound Healing

Infection is a significant hindrance to wound healing. Microorganisms growing in the wound lead to inflammation and prevent healing, turning the wound chronic. Bacterial toxins damage the tissues, disrupting the healing process. Effective wound healing requires eliminating infections through localized wound cleaning, irrigation, culture of exudates, and, in severe cases, systemic antibiotics.

The Role of Local Pressure and Shearing Forces

Reduce blood supply

Pressure and shearing forces can adversely affect wound healing. Pressure, even from a tightly applied dressing, can impede the capillary circulation, thus reducing the blood supply essential for healing. Shearing forces can disrupt the approximation of wound edges, impeding healing. Minimizing these forces is crucial for proper wound recovery.

Necrotic Tissue and its Removal

Necrotic tissue, a result of trauma, hinders healing by providing a habitat and food source for bacteria, thus promoting infection. Living cells cannot migrate over necrotic tissue, which impedes regeneration. Therefore, debridement, the removal of necrotic tissue, is vital for promoting wound healing. In severe cases like burns, this might require anesthesia and thorough cleaning to reach healthy tissue.

Pus is considered necrotic

Foreign Bodies and Wound Nature

Foreign materials within a wound can lead to infection and obstruct cell migration. Removing foreign bodies, such as splinters or glass, is crucial for healing. The nature of the wound, especially in high-energy injuries like road accidents or falls, can complicate healing due to disrupted blood supply and increased infection risk.

The Importance of Maintaining Wound Temperature

Regulating the temperature of the wound area is critical. While initial cooling post-injury can help with hemostasis, maintaining physiological temperatures is crucial for enzymatic activity essential for healing. Enzymes function optimally at around 37 degrees Celsius, and cooling the wound during treatment can significantly slow down the healing process.

In summary, various local factors, including infection, pressure, necrotic tissue, foreign bodies, and temperature, significantly influence wound healing. Understanding and mitigating these factors can enhance healing outcomes, reducing complications and promoting faster recovery.

Video 11 tissue repair

* lots of responses happen in post capillary venules

Overview of Tissue Injury and Healing Process

Introduction to Tissue Types and Cellular Functions
The video begins with a review of various tissue types, cellular structures, and functions, including membrane receptors and transport mechanisms. This introduction sets the stage for a detailed exploration of tissue injury and the healing process.

Scenario: Stepping on a Rusty Nail
The narrator presents a scenario where an individual steps on a rusty nail, leading to pain, bleeding, swelling, and the risk of infection. This example is used to delve into the cellular-level events that occur in response to such an injury.

Anatomy of the Injury: Skin, Blood Vessels, and Connective Tissue
The focus shifts to the anatomical details of the injury, highlighting the layers of the skin, connective tissue, and blood vessels affected by the nail. The narrator explains how the depth of the wound influences the severity of damage and bleeding.

Inflammation Response: Redness, Warmth, Swelling, and Pain
Inflammation is identified as the first response to the injury, characterized by redness (erythema), warmth, swelling, and pain. The role of mast cells in releasing histamine, which increases vascular permeability and leads to swelling, is discussed.

Vasodilation and Its Effects
The process of vasodilation, which is the widening of blood vessels, is explained. Vasodilation results in increased blood flow to the injured area, contributing to the warmth and redness observed in inflammation.

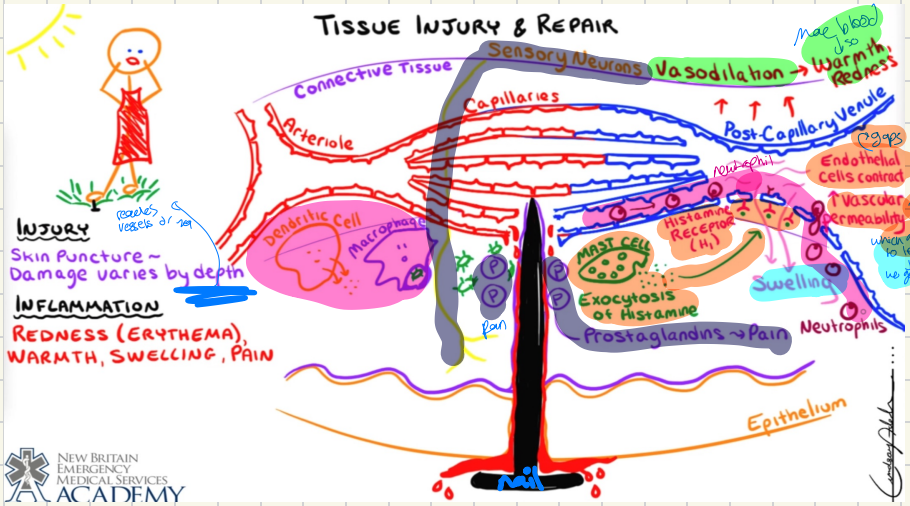
Pain and Prostaglandins
Pain, another key aspect of inflammation, is attributed to the synthesis of prostaglandins, chemicals that signal pain. The narrator links this to common pain relief medications like Tylenol or Advil, which inhibit prostaglandin synthesis.

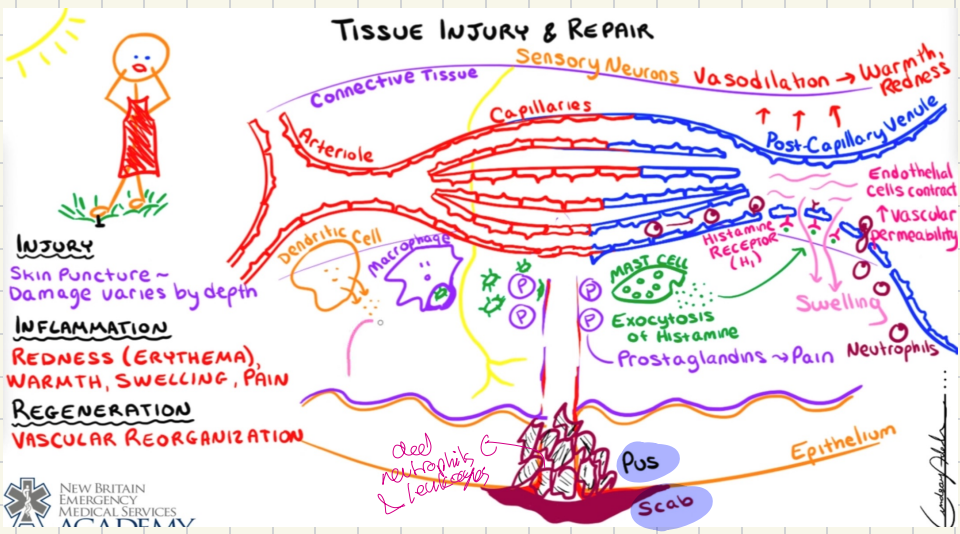
White Blood Cells and Pathogen Defense
The role of macrophages and dendritic cells in the immune response is outlined. These cells engulf pathogens and release cytokines to attract more white blood cells, such as neutrophils, to the site of der the step-by-step nature of tissue injury and healing.

Healing Process: Blood Clotting, Scab Formation, and Pus Accumulation
The video progresses to the healing phase, including blood clotting, scab formation, and the potential accumulation of pus, which is composed of dead cells and pathogens.

Regeneration and Scar Formation
Finally, the process of regeneration is explained, focusing on vascular reorganization and the role of fibroblasts in producing collagen to repair the wound. The formation of scar tissue and its eventual remodeling are discussed as part of the healing process.

Conclusion
The video concludes with a summary, emphasizing the importance of understanding these processes as a synthesis of various biological concepts. The narrator encourages viewers to consi der the step-by-step nature of tissue injury and healing.


TISSUE INJURY & REPAIR
Sensory Neurons
Vasodilation → Warmth, Redness
Connective Tissue
Capillaries
Arteriole
Post-Capillary Venule
Endothelial Cells contract
↑ Vascular Permeability
Dendritic Cell
Macrophage
MAST CELL
Histamine Receptor (H1)
Exocytosis of Histamine
Swelling
Prostaglandins → Pain
Neutrophils
Epithelium
INJURY
Skin Puncture ~ Damage varies by depth
INFLAMMATION
REDNESS (ERYTHEMA), WARMTH, SWELLING, PAIN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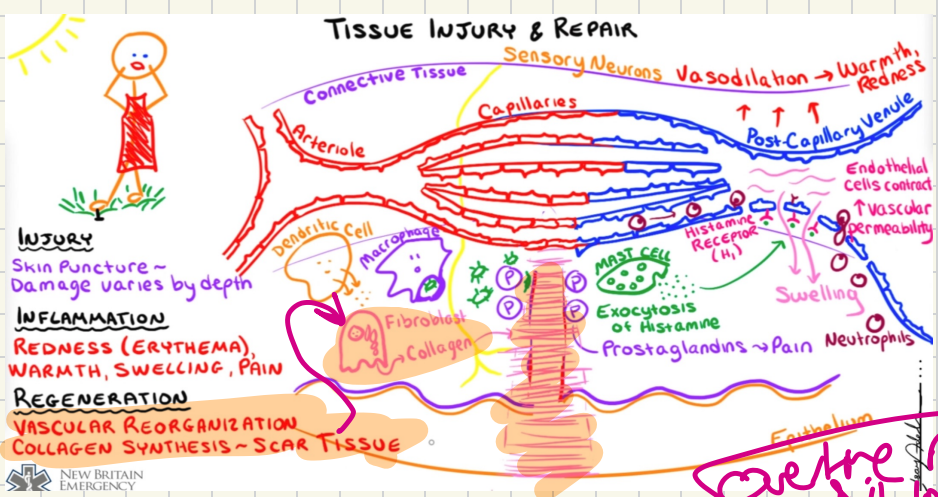
REGENERATION
VASCULAR REORGANIZATION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Fibroblast
Collagen
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INFLAMMATION
REDNESS (ERYTHEMA), WARMTH, SWELLING, PAIN
REGENERATION
VASCULAR REORGANIZATION
COLLAGEN SYNTHESIS ~ SCAR TISSUE

The END

by Leen.AL.Kutub ادعولي

اللهم ارزق أهل فلسطين الثبات والنصر والتمكين، وبارك في إيمانهم وصبرهم.
اللهم احفظ أهل فلسطين والمسجد الأقصى من كيد الظالمين، وأيدهم بنصرك وقوتك.
اللهم إني أستودعك بيت المقدس وأهل القُدس وكُل فلسطين، اللهُم كُن لهم عوناً ونصيراً

"Oh God, grant the people of Palestine steadfastness, victory and empowerment, and bless their faith and patience. Oh God, protect the people of Palestine and Al-Aqsa Mosque from the plots of the oppressors, and support them with your victory and strength. Oh God, I entrust you to Jerusalem, the people of Jerusalem, and all of Palestine. Oh God, be their helper and supporter"