

# INFLAMMATION

## L32- HEALING AND REPAIR

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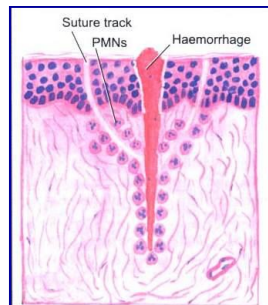
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### Factors favoring Fibrosis over regeneration

- Severe and prolonged tissue injury
- Loss of tissue framework (basement membranes)
- Large amounts of exudate
- Lack of renewable cell populations
- Loss of functional parenchymal tissue
- Skin with scar is more prone to tearing

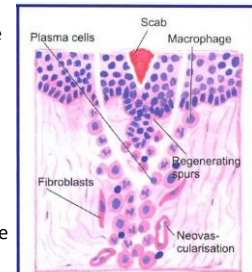
### Healing by First Intention

- Example: **surgical wound**
- Result: **healing with little scar formation (fibrosis)**
- Epithelial regeneration predominates over fibrosis
- **24 hours**
  - Neutrophils migrate into fibrin clot
  - Basal cells at edges
  - Increase mitotic activity



### Healing by First Intention Wound healing

- **24 – 48 hours**
  - Epithelial cells migrate and proliferate
  - Deposition of basement membrane
- **Days 3 - 7**
  - Macrophages replace neutrophils
  - Neovascularization
  - Granulation tissue
  - More collagen bundles
  - Bridging of wound
  - Epithelial cells continue to proliferate



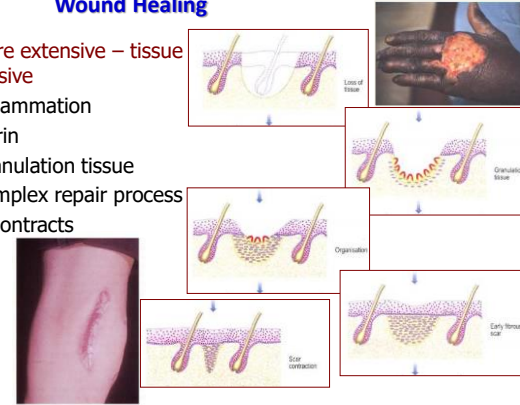
### Healing by First Intention Wound Healing

- **Week 2 ( day 14)**  
Collagen accumulation continues to increase
  - Fibroblast proliferation
  - WBC and edema decreases
  - Vascular channels regress
  - Blanching (pale)
- **4 weeks**
  - scar formed by fibroblasts and collagen
  - Few inflammatory cells
  - Tensile strength increases



### Healing by Second Intention Wound Healing

- **Injury more extensive – tissue loss excessive**
  - More inflammation
  - More fibrin
  - More granulation tissue
  - More complex repair process
  - wound contracts



### Skin Wound Healing

#### By First intention

- Clean cut wound
- Less injury
- Less dead tissue
- Less infection
- Faster healing
- Minimal scar
- Minimal complications

#### By Second intention

- Large rough wound
- More injury
- More dead tissue
- More infection
- Delayed healing
- More scar
- More complications

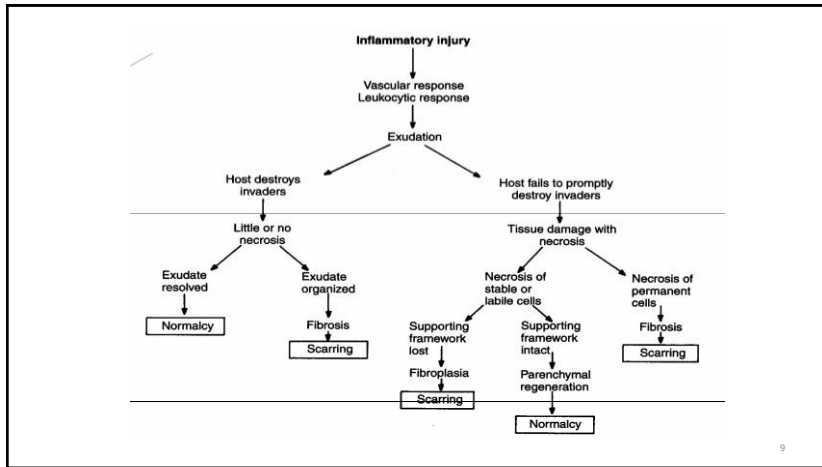
### Factors affecting Healing

#### Systemic

- Nutrition
- Vitamin def.
- Age
- Immune status
- Other diseases

#### Local

- necrosis
- Infection
- apposition
- Blood supply
- Mobility
- Foreign body



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### Complications of wound healing

- Non Healing / delayed healing
- Deficient scar formation
  - Wound dehiscence
  - Ulceration
- Excessive formation of scar tissue
  - Keloid (excessive collagen deposition)
  - Proud flesh- Exuberant granulation (proliferation of fibroblasts that inhibits re-epithelialization)
  - Hypertrophic Scar
- Scar contractures – Burns
- Adhesions – Internal organs

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Wound dehiscence



Wound ulceration



Contracture



Source: Wounds © 2003 Health Management Pl

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**Keloid** - raised scar of the skin due to accumulation of great amount of collagen.

Common in blacks.

Here: **keloid** after vaccination



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## SYSTEMIC EFFECTS OF INFLAMMATION

- ▣ Development of the **fever** (rise in body temperature)
- ▣ **Acute Phase Reactions**
  - Anorexia
  - Accelerated degradation of skeletal muscle proteins
  - Hypotension
  - Hepatic synthesis of acute-phase proteins (e.g., complement and coagulation proteins)
  - Changes in circulating white blood cell count
- ▣ **IL1, IL-6 and TNF** are the most important mediators of acute phase reactions.
  - **fibrinogen** Production. --- Increase in ESR
  - IL-1 and TNF also induce fever — prostaglandin E (**PGE**)
  - **Leukocytosis** in blood – IL1, TNF

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### PATHOGENESIS OF FEVER

- ▣ The body temperature above **37.2 °C**, associated with **sweating**, **hyperventilation**, and **vasodilatation** in the skin (Fever)
- ▣ At the beginning, gradual increase in body temperature is observed together with **muscle shivering**, **vasoconstriction** in the skin, and **piloerection (chills)**.
- ▣ **Increased body temperature** is achieved by lowered loss of heat and increased production of heat.
- ▣ When the **vasodilatation** starts in the skin, the feeling of warmth and sweating occurs.
- ▣ Fever may be **provoked** by bacteria and their endotoxins, viruses, yeasts, spirochetes, protozoa, immune reactions, several hormones, medications, and synthetic polynucleotide — exogenous pyrogens.

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- ▣ **Exogenic pyrogens** cause production of endogenous pyrogens
- ▣ **Endogenous pyrogens** centrally affect the **thermo-sensitive** neurons in the **preoptic** area of the hypothalamus resulting in
  - increased production of heat and
  - decrease in heat loss.
- ▣ The body temperature increases until it reaches the set point.
- ▣ The most important endogenous pyrogens are **IL-1, IL-6 and TNF- $\alpha$** .
- ▣ Also the **interferon** display the pyrogenic activity.
- ▣ **Glucocorticoids and PGE** may display inhibitory effect on the production of IL-1 and TNF- $\alpha$ .
- ▣ In the hypothalamus, IL-1 and TNF- $\alpha$  trigger the synthesis of **PGE** of target cells.
- ▣ TNF and IL-1 activate **immune response**

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### PROGRESS OF FEVER AND SYMPTOMS

- ☐ **First phase** is called **prodromal phase** or pre-report phase that occurs for about **15 to 90 minutes**.
  - In this stage, the release of endogenous pyrogen occurs
  - Endogenous pyrogen mediated through **PGE2** affects the thermo-sensitive neurons of thermoregulatory center in hypothalamus.
  - In this stage, the resetting of thermoregulatory center for a different temperature take place.
- ☐ **Second Phase** is called the **phase of increase**.
  - The impulses from the **sympathetic compartment** that are sent by sympathetic fibers to the whole body causes **vasoconstriction** in cutaneous and subcutaneous vessels
  - On the other hand, muscles, liver, and heart, under the influence of sympathetic compartment, increases production of heat
  - but the person (sick) has a feeling of cold.

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- ☐ **Third Phase** is called the **climax phase**.
  - Body temperature **culminates** (highest point).
  - The **parasympathetic** compartment of the thermoregulatory center is activated.
  - Subsequently, the impulses cause **vasodilatation**
  - These changes are the reason of **decreased blood pressure**
  - The pressure in the pulmonary artery increases because of **vasoconstriction of pulmonary arteriole**.
  - The patient has warm and red skin, sweats, and loses heat by conduction, radiation, and evaporation.
- ☐ **Fourth Phase** is called the **descent phase**.
  - Characterized by the **decrease of the body temperature**.
  - **Expressive decrease of fever, decreased pulse, and peripheral vasodilatation** may cause the **failure of circulation**.
  - This is especially dangerous for persons with cardiovascular disease and for old persons.

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### UTILITY OF FEVER

- ☐ Increases **immune reactions**, increases chemotactic, phagocytic, and bactericidal activity of polymorpho-nuclear leucocytes
- ☐ Up to certain value, it stimulates the process of **antibody production**
- ☐ Slows down the **proliferation of microorganisms**.
- ☐ Increased body temperature causes a decrease in the amount of plasma **iron, zinc, and copper**.
  - ☐ This decrease is unfavorable for the growth of microbes
- ☐ The increased production of **interferon** also acts against viruses

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### HARMFUL EFFECTS OF FEVER

- ☐ Increased basal **metabolism**, minute **heart volume**, and **water and salt losses**
- ☐ Very high temperature **suppress immune mechanisms**.
- ☐ **Long lasting fever** causes dysfunctions of parenchymal organs.
- ☐ **Fast decrease of fever** may endanger the patient by fast lowering of the blood pressure.
- ☐ Changes in **mental condition** are present in very young and very old persons.
  - **TNF- $\alpha$**  and **IL-1** cause the release of  **$\beta$ -endorphins** in the brain may be responsible for changed mental condition.
- ☐ Fever is associated with subjective **discomfort** such as uncertain headache, arthralgia, pain in muscles and in the back.
- ☐ Disturbed function of the **digestive tract**
  - Lose of appetite is caused by direct activity of **TNF- $\alpha$**

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**MESSAGE**

**ALL HUMANS ARE EQUAL**  
**- AL QURAN**

**SPREAD HAPPINESS**  
**ELIMINATE ANGER**



**ONE WORLD**  
**ONE RACE**

*M. Tariq Javed*