

Healing & Repair

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Healing and Repair

Healing and Repair

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- Regeneration
 - Control of Regeneration
 - Cell cycle
- Repair
 - Biosynthesis of proteoglycans
 - Biosynthesis of collagen
 - Types of collagen
 - Induction of Repair
 - 1. Organization
 - 2. Progressive fibrosis
 - Cell-Matrix Interactions

Healing and Repair – Continue ...

- Wound Healing
 - Stages in wound healing
 - Healing by First Intention:
 - Healing by second Intention:
 - Factors influencing wound healing
 - Factors accelerating wound healing
 - Complications of wound healing
 - Healing of Fractures
 - Healing of tooth socket
 - Complications of fracture healing
 - Pathological Fractures

Definitions

Healing is the replacement of destroyed or lost tissue by viable tissue. Healing is achieved in two ways:

- **Regeneration:** Is the replacement of the damaged tissue by the same tissue type as was originally there.
- **Repair:** The proliferation and migration of connective tissue cells leading to fibrosis and scar formation.

Most organs heal using a mixture of both mechanisms.

Major Causes of Tissue Destruction

1. Loss of blood supply- ischemic necrosis
 2. Inflammatory agents
 1. By direct physical or toxic effects
 2. Indirectly as a result of the host response
 3. Traumatic excision
 1. Accidental
 2. Surgical
 4. Radiotherapy
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Regeneration

1. Control of Regeneration
 2. Cell cycle
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Regeneration

- Labile cells (**intermitotic**) continue to proliferate throughout life, e.g. epidermis, endothelium, haemopoietic tissue, endothelial cells
 - Stable cells (**reversibly postmitotic**) which retain the capacity to regenerate and occasionally exhibit mitoses by virtue of normal cell-turnover, e.g. , liver, renal tubular epithelium, smooth muscle
 - Permanent cells (**irreversibly postmitotic**) which cannot reproduce themselves after attaining maturity, e.g. neurones of the C.N.S., sensory organs, renal glomeruli, striated muscle
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Regeneration

- Labile tissues heal by **regeneration** with little or no repair.
 - Permanent tissues are incapable of regeneration and heal entirely by **repair**.
 - Most organs show evidence of both processes.
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Control of Regeneration

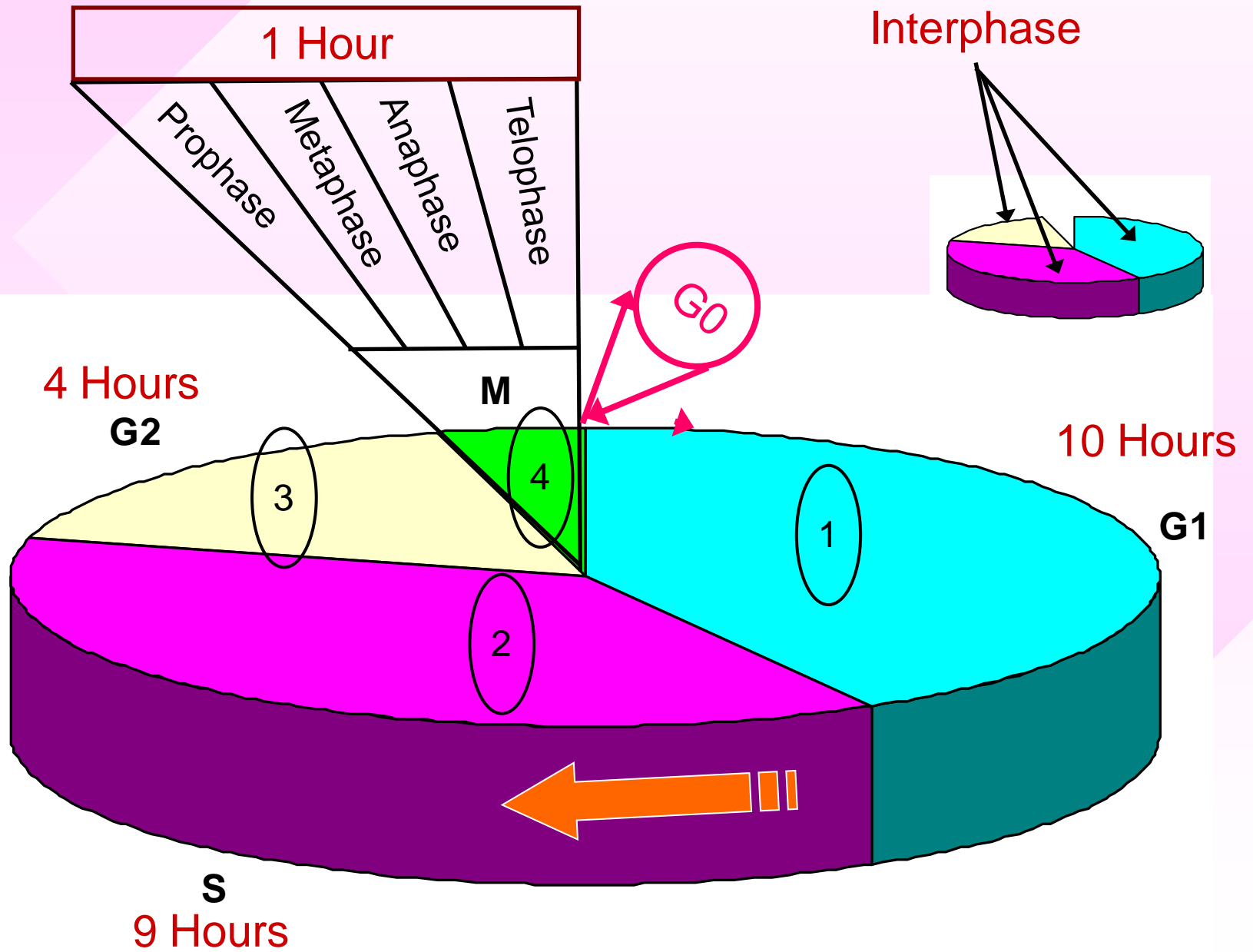
Regeneration controlled by stimulatory and inhibitory factors. Stimulation is a two-stage process:

- **Initiation:** Cells in growth arrested phase (G0) are primed for progression to cell division. Initiation is brought about by tissue--specific growth factors such as Epidermal Growth Factor (EGF) and Platelet Derived Growth Factor (PDGF).
 - **Potentialiation:** Non-specific growth factors such as insulin, hydrocortisone, and growth-hormone. These potentiators stimulate cells which have already been primed by the appropriate initiator to enter S phase.
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Cell cycle

- **G₀**: Resting phase of stable parenchymal cells
 - **G₁**: Synthesis of RNA, protein, organelles, and cyclin D
 - **S** (synthesis) phase: Synthesis of DNA, RNA, protein
 - **G₂**: Synthesis of tubulin, which is necessary for formation of the mitotic spindle
 - **M** (mitotic) phase: Two daughter cells are produced.
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Cell Cycle



Cell Cycle

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Repair - Outline

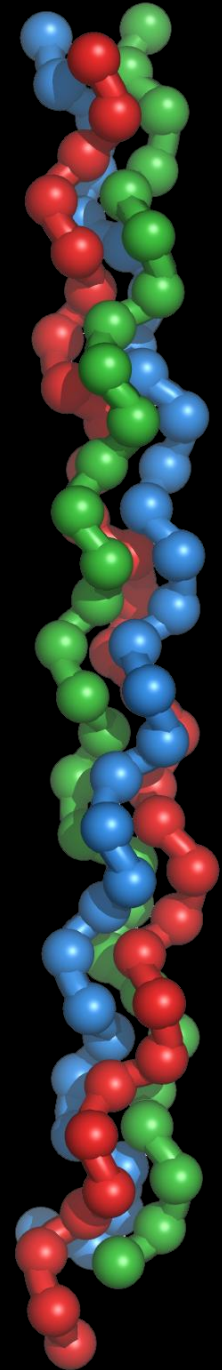
- Biosynthesis of proteoglycans
 - Biosynthesis of collagen
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-

Biosynthesis of proteoglycans

- The proteoglycans or “ground substance” of connective tissues are divided into 2 types:
 - Sulphated:
 - Heparan sulphate, Keratan sulphate, Chondroitin sulphates A, B, and C
 - Non-sulphated:
 - Hyaluronic acid
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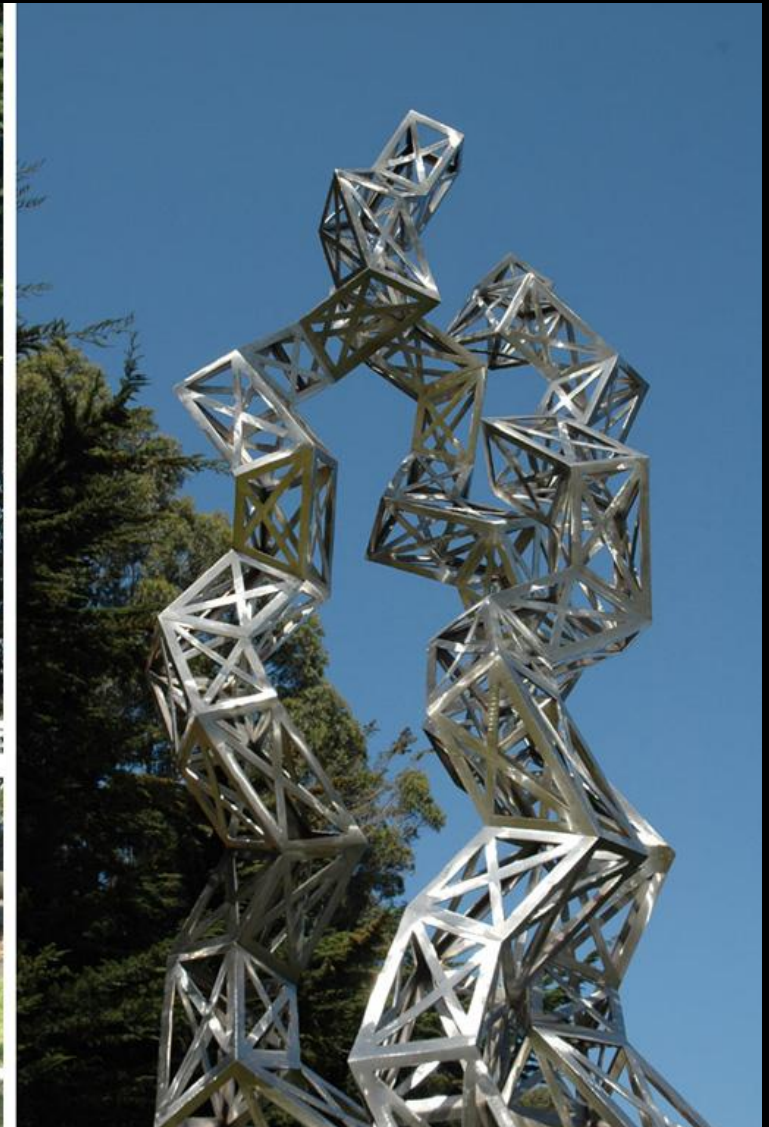
Biosynthesis of collagen

- Collagen is the most abundant protein in the body and forms the major structural component of many organs.
 - Collagen molecules consist of three polypeptide chains arranged in a **triple helix**, known as **alpha chains**.
 - The molecule undergoes a complex series of post-translational modifications.
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Art Based on collagen Structure

- Artist: Julian Voss-Andreae
- Sculpture shown: "Unraveling Collagen", 2005, stainless steel, height:(3.40 m.
- Location: Orange Memorial Park Sculpture Garden, City of South San Francisco.



Types of collagen

- Type 1 : bone, tendon, skin, fascia, cornea
 - Type 2 : cartilage, vitreous body
 - Type 3 : (reticulin) : skin, blood vessel, uterus, granulation tissue
 - Type 4 : basement membrane or basal lamina
 - Type 5: cells surfaces, hair and placenta
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Types of collagen

- **Mnemonic:** Collagen "types" go from hard to soft.
 - Type I = bone
 - type II = cartilage
 - type III (in addition to type I) = skin
 - type IV = basement membrane.
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Induction of Repair

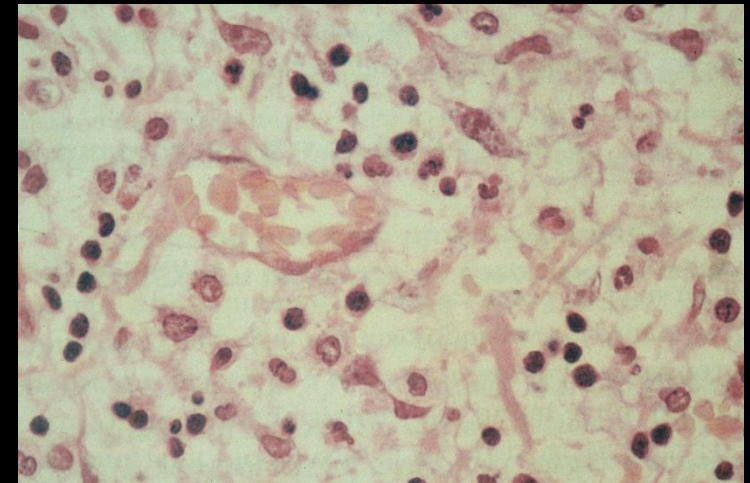
1. Organization
 2. Progressive fibrosis
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1. Organization

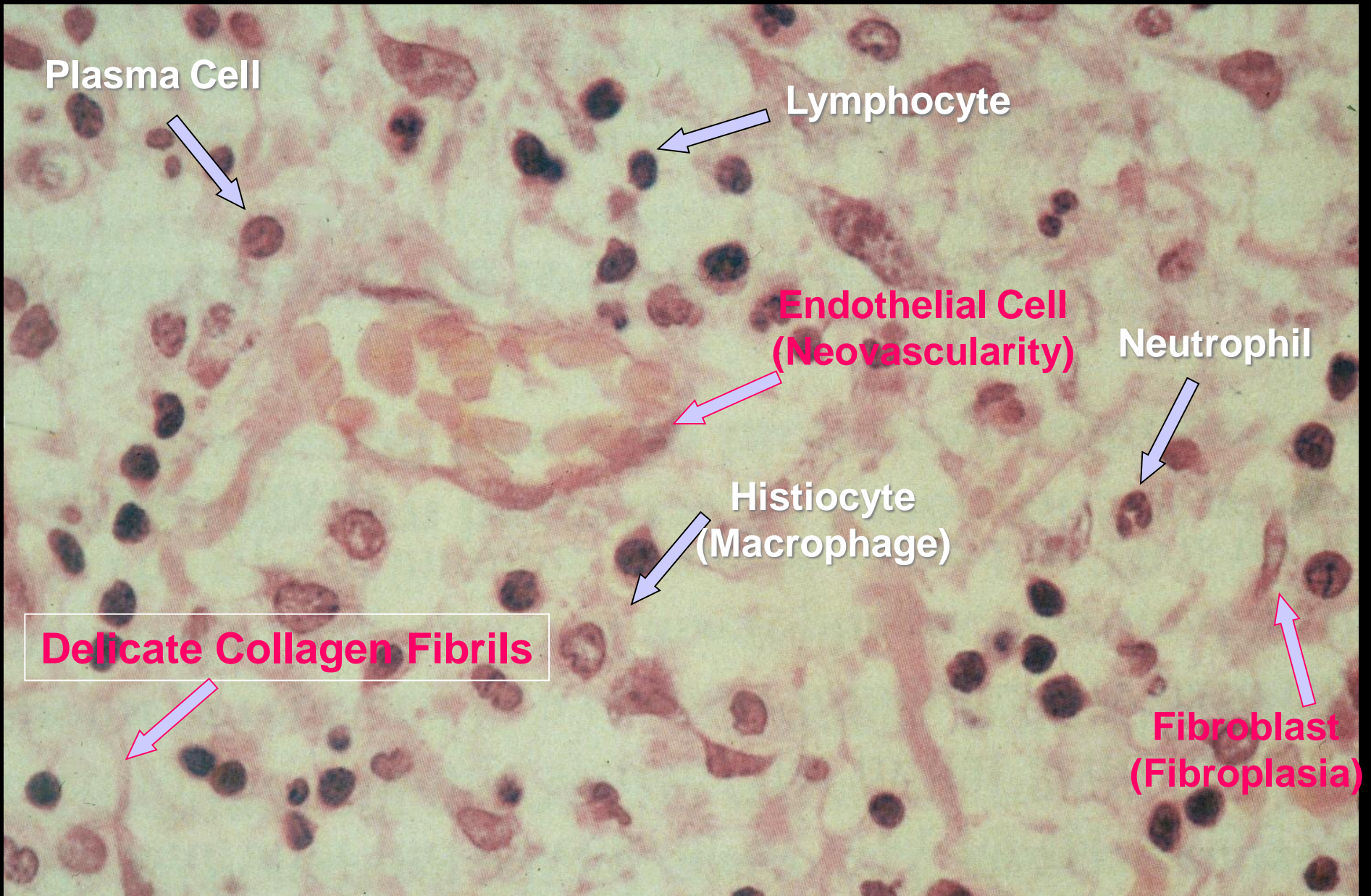
- Is the replacement of dead tissue or hematoma by granulation tissue.
 - Organization is seen in:
 - Hematomas in wound and fracture healing
 - Thrombi
 - Infarcts
 - Fibrinous exudates
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Granulation Tissue

- Is the young immature connective tissue
- It can mature into fibrous tissue (scar formation)
- It forms during the process of chronic inflammation, wound healing or obscure conditions such as sarcoidosis



Granulation Tissue



Granulation Tissue

- Histologically consists of:
 - Proliferating capillaries
 - Proliferating fibroblasts
 - Delicate collagen fibrils.
 - Chronic inflammatory cell infiltration.
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Granulation Tissue – Mechanism of Formation

1. Demolition: Removal of foreign and dead tissues by macrophages
 - Fibroblast activity
 - Ingrowth of capillaries
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2. Progressive fibrosis

- Continued accumulation of intercellular collagen and diminution of vascularity and cellularity
 - Collagen re-orientation along lines of stress - remodeling
 - Diminished cellularity
 - Formation of an avascular, hypocellular scar
 - Further changes in scars:
 - Cicatrization -a late diminution in size resulting in deformity
 - Calcification
 - Ossification
-

Cell-Matrix Interactions

- **Fibronectin** attaches fibroblasts to collagen
 - **Chondronectin** binds chondrocytes to Type II collagen, the matrix of cartilage
 - **Laminin** binds epithelial cells to the Type IV collagen of basement membranes
 - **Osteonectin** binds hydroxy-apatite and calcium ions to Type I collagen (bone matrix) and initiates mineralization
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Wound Healing

- Stages in wound healing
- Healing by First Intention:
- Healing by second Intention:
- Factors influencing wound healing
- Factors accelerating wound healing
- Complications of wound healing
- Healing of Fractures
- Healing of tooth socket
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- Pathological Fractures

Wound Healing - Types

- A clean wound with closely apposed margins - an incised wound (healing by first intention)
 - An open or excised wound (healing by second intention).
 - There are no fundamental differences between these two types, they merely differ in the degree to which the various stages apply.
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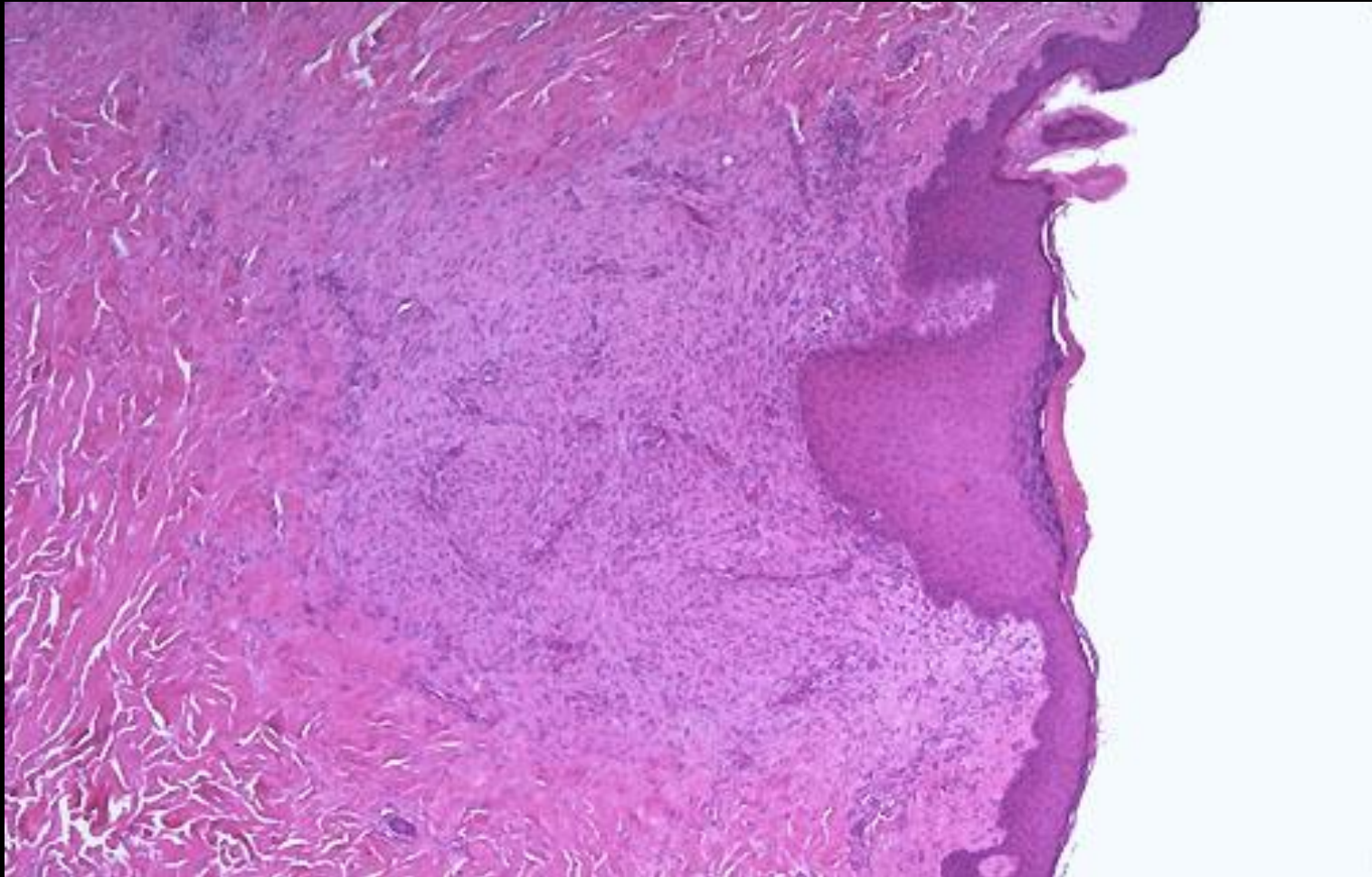
Stages in wound healing

- Escape of blood and exudate
 - Acute inflammatory response at the margins
 - Hardening of the surface forming a scab
 - Demolition by macrophages
 - Organization
 - Epidermal proliferation
 - Contraction of the wound
 - Progressive increase in collagen fibers
 - Loss of vascularity and shrinkage of the scar
-

Healing by First Intention:

- Occurs in small wounds that close easily
 - Epithelial regeneration predominates over fibrosis
 - Healing is fast, with minimal scarring/infection
 - Examples:
 - Paper cuts
 - Well-approximated surgical incisions
 - Replaced periodontal flaps
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Granulation Tissue - Healing



Healing by second Intention:

- Greater tissue loss
 - More inflammatory exudate and necrotic tissue to remove
 - Wound contraction is necessary
 - More granulation tissue is required, a bigger scar is formed and this may result in deformity
 - Slower process
 - Increased liability to infection
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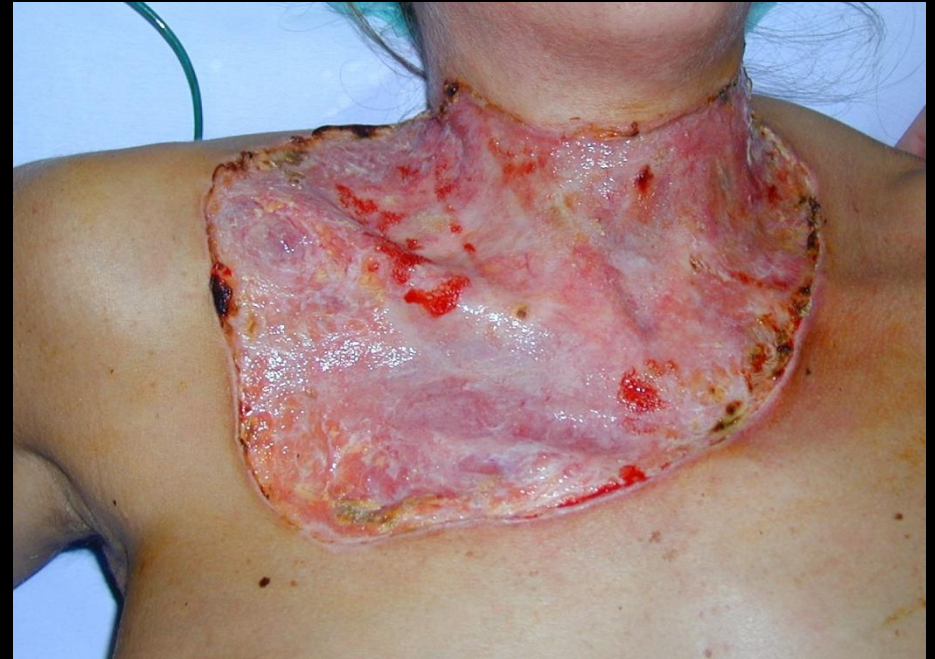
Healing by Second Intention **Key Facts:**

- Occurs in larger wounds that have gaps between wound margins
 - **Fibrosis** predominates over epithelial regeneration
 - Healing is slower, with more inflammation and granulation tissue formation, and more scarring
 - Examples: large burns and ulcers, extraction sockets, external-bevel gingivectomies
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First Intention Versus Second



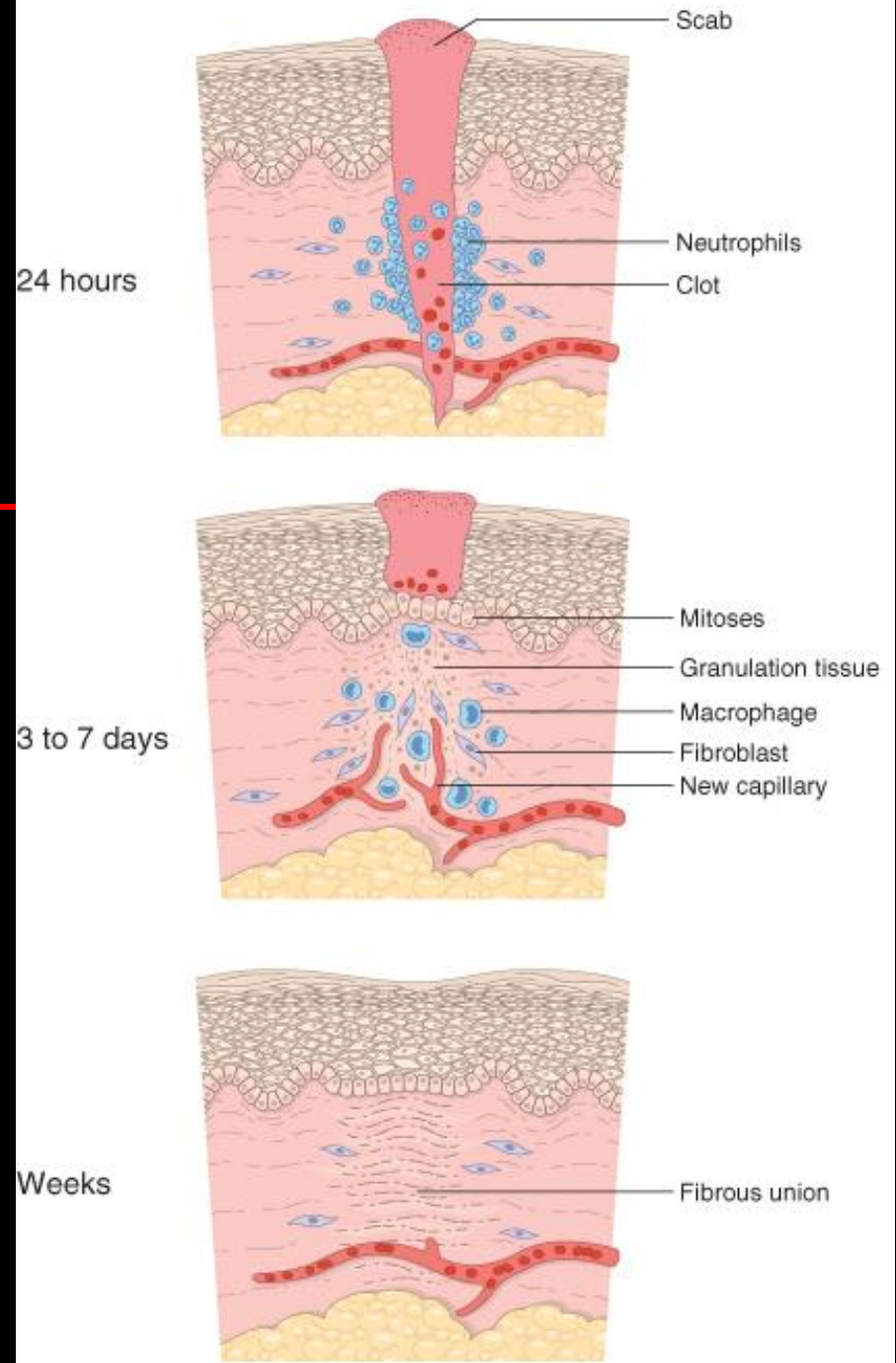
first intention healing



second intention healing

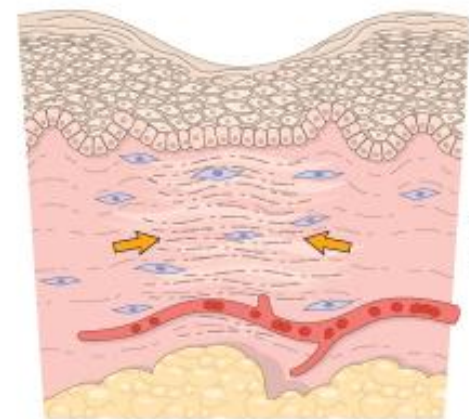
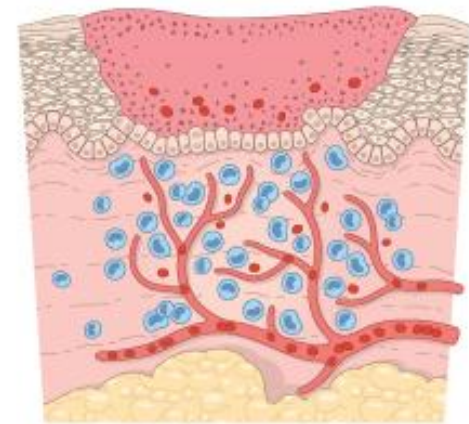
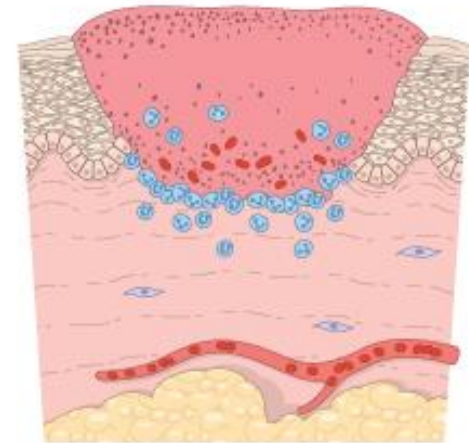
Healing by First Intention

HEALING BY FIRST INTENTION



Healing by Secondary Intention

HEALING BY SECOND INTENTION

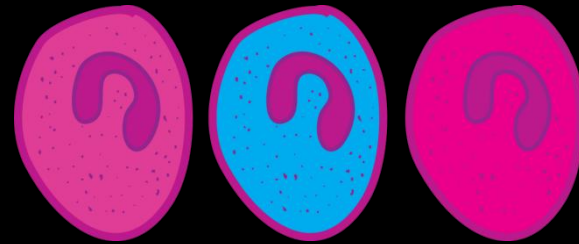


Wound contraction

Inflammatory Cells

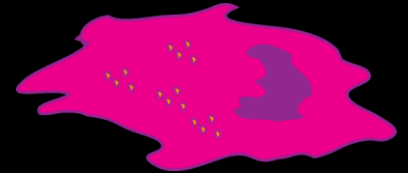
Acute Inflammatory Cells

- PNL – Microphages

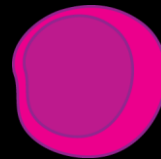


Chronic Inflammatory Cells

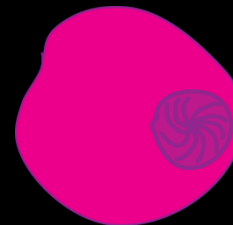
- Macrophages – Histiocytes – Monocytes



- Lymphocytes



- Plasma cells



Factors influencing wound healing

1. Local factors adversely affecting healing
 2. General factors adversely affecting healing
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Local factors adversely affecting healing

- Type of wounding agent; blunt, crushing, tearing etc.
 - Infection
 - Foreign bodies in wound
 - Poor blood supply
 - Excessive movement
 - Poor apposition of margins, e.g. large hematoma formation
 - Poor wound contraction
 - Infiltration by tumor
 - Previous irradiation
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General factors adversely affecting healing

- **Poor nutrition**
 - Deficiency of protein
 - Lack of ascorbic acid (vitamin C)
 - Zinc deficiency
 - **Excessive glucocorticosteroid production or administration**
 - **Fall in temperature**
 - **Jaundice**
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Factors accelerating wound healing

- Ultraviolet light
 - Administration of anabolic steroids, deoxycorticosterone acetate, and growth hormone
 - Rise in temperature
 - Hyperbaric oxygen
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Complications of wound healing

- Wound rupture
 - Infection
 - Implantation of epidermal cells giving rise to keratin-filled epidermoid cyst
 - Weak scars
 - Cicatrization and deformity
 - Keloid formation
 - Proud flesh: The swollen flesh that surrounds a healing wound, caused by excessive granulation tissue.
 - Malignant change
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Keloid scar

Excessive fibrosis and Cicatrization



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Proud flesh

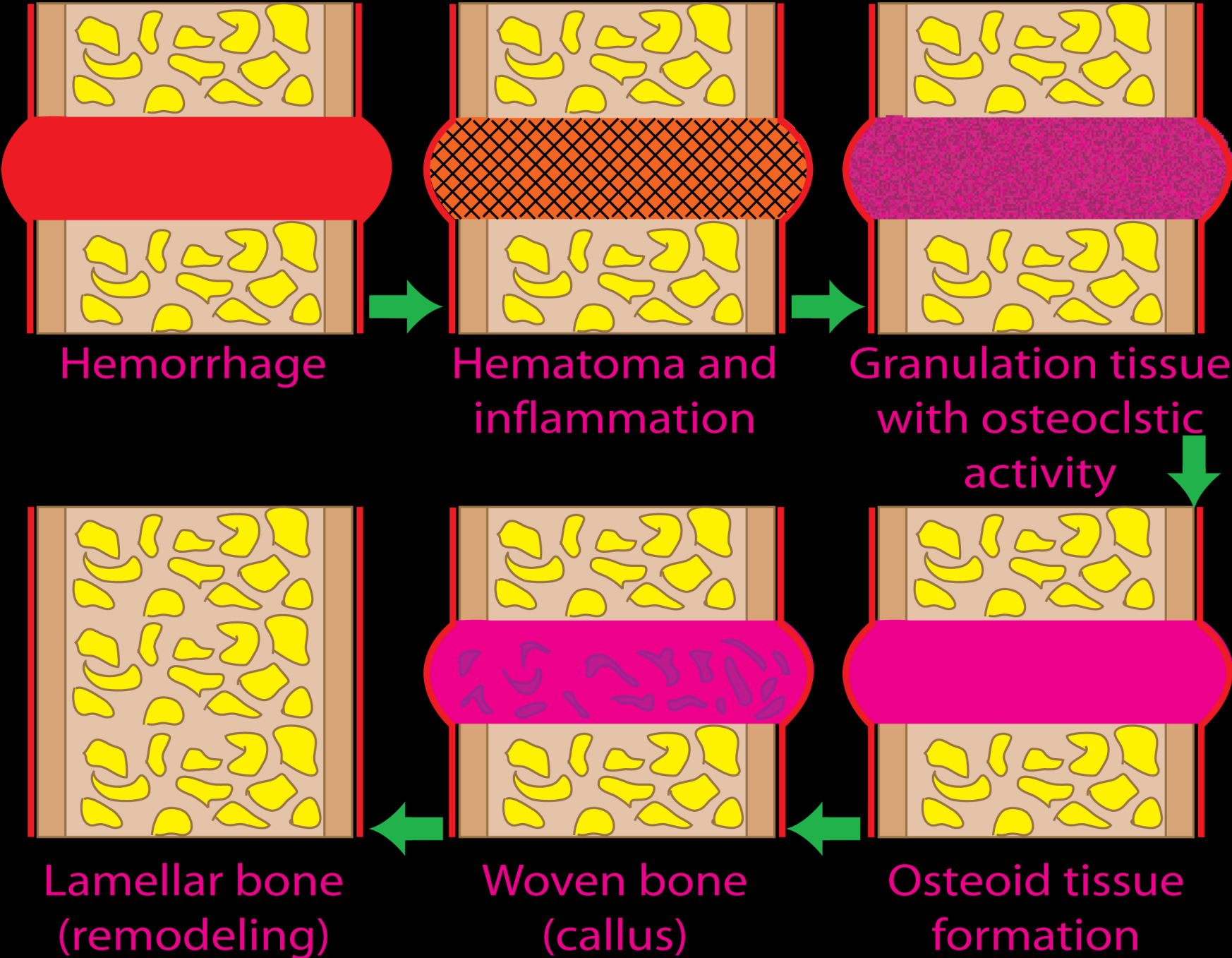
The swollen flesh that surrounds a healing wound, caused by excessive granulation tissue.

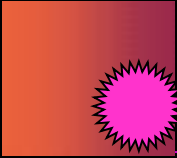


Healing of Fractures

- Hemorrhage: This is due to torn blood vessels.
- Hematoma formation
- Transient inflammatory reaction
- Demolition
- Organization of the clot
- Osteoclastic activity
- Osteoid tissue formation
- Calcification of osteoid
- Remodeling

Uncomplicated bone repair





Healing of tooth socket

- Extravasated blood which then coagulates
 - The blood clot is organized to form granulation tissue
 - Transient inflammatory reaction
 - Osteoclastic resorption of the crestal bone and small sequestra of bone
 - Gingival epithelial proliferation and migration occurs across the defect (10-14 days)
 - Osteoblasts appear and the GT is replaced by woven bone
 - After approximately 6 weeks, the outline of the socket can be discerned both histologically and radiographically
 - Formation of cortical and cancellous bone and disappearance of the lamina dura.
 - Radiographically, the socket is generally obliterated between 20 and 30 weeks after extraction (around 6 months)
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Complications of fracture healing

- Delayed union
 - Mal-union e.g. Angulation, Shortening,
 - Fibrous union resulting from: Excessive movement, Infection, Ischemia.
 - Non-union if soft-tissues such as muscle or fat are interposed between the severed ends
-

Pathological Fractures

- Osteoporosis, especially steroid induced
 - Metastatic tumors
 - Primary tumors (benign and malignant)
 - Paget's disease
 - Bone lesions of hyperparathyroidism
 - Osteogenesis imperfecta
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