Wound healing

• Healing of skin wounds- example of combination of regeneration and repair.
• Wound healing can be accomplished in one of the following two ways:
  – Healing by first intention (primary union)
  – Healing by second intention (secondary union)
Healing by First Intention (Primary Union)

• Healing of a wound which has the following characteristics:
  – clean and uninfected
  – surgically incised
  – without much loss of cells and tissue
  – edges of wound are approximated by surgical sutures
Sequence of events

• **Initial haemorrhage**- wound is filled with blood which clots, seals the wound against dehydration and infection.

• **Acute inflammatory response**- polymorphs, replaced by macrophages by 3rd day

• **Epithelial changes**- basal cells of epidermis start proliferating and migrating towards incisional space.
  - wound is covered by a layer of epithelium in 48 hours.
  - epidermal cells separate the underlying viable dermis from the overlying necrotic material, forming *scab*
  - By 5th day, a multilayered new epidermis is formed
Sequence of events

• Organisation-
  - By 3rd day, fibroblasts also invade the wound area.
  - By 5th day, new collagen fibrils start forming which dominate till healing is completed.
  - In 4 weeks, the scar tissue with scanty cellular and vascular elements is formed.
HEALING BY FIRST INTENTION

24 hours

Scab
Neutrophils
Clot

3 to 7 days

Mitoses
Granulation tissue
Macrophage
Fibroblast
New capillary

Weeks

Fibrous union
Healing by Second Intention (Secondary Union)

Healing of a wound having the following characteristics:

- open with a large tissue defect, at times infected
- having extensive loss of cells and tissues
- the wound is not approximated by surgical sutures but is left open
Sequence of events

• Similar to primary union
• Differs in having a larger tissue defect which has to be bridged.
• The healing by second intention is slow and results in a large, at times ugly, scar as compared to rapid healing and neat scar of primary union.
• Healing with more inflammation and granulation tissue formation, and more scarring
Sequence of events

- Initial haemorrhage
- Inflammatory phase
- Epithelial changes
- **Granulation tissue**
  - Main bulk of secondary healing is by granulation
  - With time, the scar on maturation becomes pale and white due to increase in collagen and decrease in vascularity.
  - Specialised structures of the skin like hair follicles and sweat glands are not replaced
Sequence of events

• Wound contraction
  - not seen in primary healing.
  - due to action of myofibroblasts, wound contracts to one-third to one-fourth of its original size.

• Presence of infection- Bacterial contamination delays the process of healing due to release of bacterial toxins that provoke necrosis, suppuration and thrombosis.
  - Surgical removal of dead and necrosed tissue, (debridement), helps
Wound Strength

Extracellular Matrix

• The wound is strengthened by proliferation of fibroblasts and myofibroblasts which get structural support from ECM
• In addition to providing structural support, ECM directs cell migration, attachment, differentiation and organisation.
• ECM has five main components: collagen, adhesive glycoproteins, basement membrane, elastic fibres, and proteoglycans.
HEALING BY SECOND INTENTION

Wound contraction
## Differences between primary and secondary union of wounds

<table>
<thead>
<tr>
<th>PRIMARY UNION</th>
<th>SECONDARY UNION</th>
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<tr>
<td>Clean</td>
<td>Unclean</td>
</tr>
<tr>
<td>Generally uninfected</td>
<td>May be infected</td>
</tr>
<tr>
<td>Margins surgical clean</td>
<td>Irregular</td>
</tr>
<tr>
<td>Sutures used</td>
<td>Not used</td>
</tr>
<tr>
<td>Scanty granulation tissue at the incised gap</td>
<td>Exuberant granulation tissue to fill the gap</td>
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<tr>
<td>Neat linear scar</td>
<td>Contracted irregular wound</td>
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<td>Complications Infrequent</td>
<td>Common</td>
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Complications of Wound Healing

- Infection of wound - delays the healing.
- Implantation (epidermal) cyst
- Pigmentation - rust-like colour due to haemosiderin
- Deficient scar formation - due to inadequate formation of granulation tissue.
- Incisional hernia - or wound dehiscence
- Hypertrophied scars and keloid -
  - the scar is excessive, ugly and painful
  - excessive formation of collagen may result in keloid formation, tumour-like projection of connective tissue.
- Excessive contraction - Dupuytren’s contracture
- Neoplasia - squamous cell carcinoma in Marjolin’s ulcer
Complications of Wound Healing
Factors Influencing Healing

Local factors
• Infection
• Poor blood supply
• Foreign bodies including sutures interfere with healing
• Movement delays wound healing.
• Exposure to ionising radiation delays
• Exposure to ultraviolet light facilitates healing.
• Type, size and location of injury
Factors Influencing Healing

Systemic factors:

• Age- wound healing rapid in young and slow in aged and debilitated people
• Nutrition- deficiency of protein, vitamin C, zinc delays the wound healing
• Systemic infection delays
• Administration of glucocorticoids
• Uncontrolled diabetics- more prone to develop infections and hence delay in healing.
• Haematologic abnormalities- defect of neutrophil functions, neutropenia and bleeding disorders slow the process of wound healing.
Healing in specialised tissues

Fracture Healing

Healing of fracture by callus formation depends on:
- Traumatic or pathological
- Complete or incomplete like green-stick fracture
- Simple, comminuted or compound
Fracture Healing

- Basic events resemble healing of skin wound
- **Primary union of fracture** - occurs when the ends of fracture are approximated as is done by application of compression clamps.
- **Secondary union** - more common process of fracture healing.
  - Procallus formation
  - Osseous callus formation
  - Remodelling
Secondary union- Procallus formation

- Haematoma - meshwork is formed by blood and fibrin clot which acts as framework for granulation tissue
- Local inflammatory response - macrophages clear away the fibrin, RBCs, inflammatory exudate and debris, fragments of necrosed bone
- Ingrowth of granulation tissue - neovascularisation and proliferation of mesenchymal cells from periosteum and endosteum.
- Callus composed of woven bone and cartilage- cells of inner layer of the periosteum lay down collagen as well as osteoid matrix in the granulation tissue, osteoid undergoes calcification and is called woven bone callus
Secondary union

- Osseous callus formation-
  - procallus acts as scaffolding on which osseous callus composed of lamellar bone is formed.
  - woven bone is cleared away by osteoclasts
  - newlyformed blood vessels and osteoblasts invade, laying down osteoid which is calcified and lamellar bone is formed by developing Haversian system concentrically around the blood vessels.

- Remodelling-
  osteoblastic laying and osteoclastic removal take place remodelling the united bone ends, which after sometime, is indistinguishable from normal bone.
Complications of fracture healing

• **Fibrous union**- results instead of osseous union if the immobilisation of fractured bone is not done.
  - a false joint may develop (pseudo-arhrosis)

• **Non-union**- if some soft tissue is interposed between the fractured ends.

• **Delayed union**- in infection, inadequate blood supply, poor nutrition, movement and old age.