BURNS

- **Local effects of burns:**
  - Vasodilatation and increased vascular permeability leading to edema.
  - Inflammation with its cardinal signs:
    - *Dolor (pain)*: due to compression of the swelling on nerves.
    - *Calor (heat)*: due to increased blood flow to the affected area.
    - *Rubor (redness)*: due to increased blood flow to the affected area.
    - *Tumor (swelling)*: due to increased vascular permeability leading to edema.
    - *Function laesa (loss of function)*.
  - There are 3 degrees of burn:
    - *First degree*: skin erythema (redness) and local heat.
    - *Second degree*: epidermal necrosis and formation of blisters (a small bubble on the skin filled with serum).
    - *Third degree*: epidermal and dermal damage with loss of sensation.
  - Repair and healing is achieved by:
    - *Scar formation (fibrous tissue)*.
    - *Deformities*.
    - *Keloid*: an area of irregular fibrous tissue formed at the site of a scar or injury.
    - *Cicatric* (ندبة): the scar of a healed wound.
  - Local secondary infection: due to the exposure of tissue under the skin (there is no presence of the physical barrier).

- **Systemic effects of burns:**
  - Increased vascular permeability and denuded (naked) skin surface will lead to plasma + fluid loss (hypovolemic shock: poor vascular perfusion of tissue). In 3rd degree of burn, 1ml of body water is lost for every 3cm$^2$ of burned area/day. This condition can lead to ischemic acute tubular necrosis.
  - Myoglobinuric acute renal failure.
  - Systemic sepsis.
  - Fat embolism.
  - Inhalation injury (ARDS: Acute Respiratory Distress Syndrome).
  - VF in electrical burns.

---

CELLS AND TISSUE RENEWAL

- **There are 4 types of cells:**
  - **Stable cells**: they divide at slow rate but retain the capacity to divide if necessary. Examples include: hepatocytes (liver cells) and renal tubules.
  - **Labile cells**: these cells have good capacity to regenerate. Examples include: hematopoietic cells in the bone marrow and surface epithelial cells.
  - **Permanent cells**: they have no ability of effective regeneration. Examples include: nerve cells and striated muscle fibers.
  - **Stem cells**:
    - They are present in many stable and labile cell populations (ex. Skin, bone marrow and intestine).
    - *Mitotic division of stem cells produce two daughter cells*:
      - One which will progress along differentiation.
      - Other which will retain stem cell characteristics.
    - *They are vulnerable to radiation and this will result in*:
      - Cell death and cell loss.
      - Mutations transmitted to daughter cells and subsequently leading to malignancy.
- **Important terms:**
  - **Regeneration:** replacing dead or injured tissue by functionally identical cells/tissues.
  - **Repair:** healing with replacement of the lost tissue but not by similar tissue or identical cells.
  - **Organization** (a common consequence of pneumonia and infarction): specialized tissues (lungs, pilosebaceous units, abscess… etc) are repaired by mature fibrovascular tissue through the formation of granulation tissue. Granulation tissue contracts and accumulates collagen to form scar.

---

**WOUNDS**

- **Classification of wounds:**
  - **Legal classification:**
    - Simple.
    - Dangerous.
    - Fatal.
  - **Medicolegal classification:**
    - Abrasions (الخدوش).
    - Bruises/contusions (الكدمات): a region of injured tissue in which blood capillaries have been ruptured.
    - Incised (cut).
    - Stab (النحافة): it is penetrating.
    - Laceration (التمزق): deep cut or tear in skin or flesh.
    - Firearm and blast injuries (الجرح الناتجة عن الأسلحة النارية أو الانفجار).
    - Thermal injuries.
    - Fractures (compound fractures in which the bone is penetrating the skin).

- **Wound healing:**
  - **First intention:** healing of surgical (clean) wound.
    - Healing is achieved by resolution/repair.
  - **Second intention:** healing of infected wound, ulcer or abscess.
    - Healing is achieved by organization.
  - **Control mechanisms (3 levels):**
    - Paracrine: relating to a hormone that has effect only in the vicinity of the gland secreting it.
    - Endocrine: relating to glands that secrete hormones or other products directly into the blood.
    - Autocrine: in which a cell secretes a hormone that binds to autocrine receptors on that same cell, leading to changes in the cell.

- **Principles of healing:**
  - Hemorrhage, platelets aggregates and thrombus plug defect.
  - Hemorrhage controlled by hemostatic mechanism.
  - Interaction between coagulation and complement initiates chemotaxis to inflammatory cells.
  - **Angiogenesis:** the development of new blood vessels.

- **Granulation tissue and repair:**
  - Angiogenesis.
  - Phagocytosis of debris and blood clot element.
  - Absorption of exudates into vascular system.
  - The fibrin meshwork.
  - Regeneration and migration of specialized cells.
  - Myofibroblasts secrete collagen and other matrix components.
  - Repair and replacement by fibrous tissue.
  - Repair is regulated by low-molecular weight proteins known as growth factors.
**VERY IMPORTANT**

![Diagram of wound healing](image)

**Fig. 5.11 Factors mediating wound healing.** A wound is shown penetrating the skin and entering a blood vessel. (1) Blood coagulation and platelet degranulation, releasing platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-β). (2) PDGF and TGF-β are chemotactic for macrophages, which migrate into the wound to phagocytose bacteria and necrotic debris (3). *In the epidermis:* (4) the released PDGF activates epidermal basal epithelial cells, which are also under autocrine and paracrine stimulation by epidermal growth factor (EGF) and insulin-like growth factors (IGF) (5), some derived from dermal myofibroblasts (6). Nutrients and oxygen (7) and circulating hormones and growth factors diffusing from blood vessels (including insulin, thyroxine, IGF-1 and IGF-2), and EGF (8) from saliva (if the wound is licked) all contribute to epidermal growth. *In the dermis:* (9) PDGF and TGF-β stimulate cell division in myofibroblasts, and (10) TGF-β stimulates these cells to produce collagen and fibronectin. Fibronectin stimulates migration of dermal myofibroblasts (11) and epidermal epithelial cells (12). Angiogenic growth factors (not shown) stimulate the proliferation and migration of new blood vessels into the area of the wound (13).

<table>
<thead>
<tr>
<th>Growth factor</th>
<th>Abbreviation</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermal growth factor</td>
<td>EGF</td>
<td>Regeneration of epithelial cells</td>
</tr>
<tr>
<td>Transforming growth factor α</td>
<td>TGFα</td>
<td>Regeneration of epithelial cells</td>
</tr>
<tr>
<td>Transforming growth factor β</td>
<td>TGFβ</td>
<td>Stimulates fibroblast proliferation and collagen synthesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Controls epithelial regeneration</td>
</tr>
<tr>
<td>Platelet-derived growth factor</td>
<td>PDGF</td>
<td>Mitogenic and chemotactic for fibroblasts and smooth muscle cells</td>
</tr>
<tr>
<td>Fibroblast growth factor</td>
<td>FGF</td>
<td>Stimulates fibroblast proliferation, angiogenesis and epithelial cell</td>
</tr>
<tr>
<td></td>
<td></td>
<td>regeneration</td>
</tr>
<tr>
<td>Insulin-like growth factor-1</td>
<td>IGF-1</td>
<td>Synergistic effect with other growth factors</td>
</tr>
<tr>
<td>Tumour necrosis factor</td>
<td>TNF</td>
<td>Stimulates angiogenesis</td>
</tr>
</tbody>
</table>
- **Paracrine:**
  - Platelets Derived Growth Factor (PDGF) and Transforming Growth Factor-β (TGF-β) are produced by platelet degranulation and they are chemotactic to inflammatory cells (including macrophages) which are required to clear necrotic debris and blood clot.
  - PDGF also activates epidermal basal cells.
  - Insulin-like Growth Factor (IGF) which is produced from dermal fibroblasts also acts on epidermal basal cells.
  - PDGF and TGF-β stimulate the dermal myofibroblasts to secrete collagen and fibronectin. Fibronectin will aid in the migration of epidermal epithelial cells and dermal myofibroblasts.

- **Autocrine:**
  - Represented by Epidermal Growth Factor (EGF) which aids in regeneration of epithelial cells.

- **Endocrine-represented by:**
  - Insulin-Like Growth Factor-1 (IGF-1) and Insulin-Like Growth Factor-2 (IGF-2).
  - Thyroxine, insulin, glucose, nutrients, oxygen… etc.
  - Saliva EGF.
  - Angiogenic Growth Factor.

- **Outcome of wound healing:**
  - Organization of granulation tissue → repair by fibrous tissue.
  - Scar formation if small.
  - Contractures and limitation of movement.
  - Adhesions.
  - Keloid formation.

- **Factors affecting cell renewal/tissue repair:**
  - Age of patient.
  - Vascularity of the tissue.
  - Impairment of lymph drainage.
  - Early movement of affected part.
  - Fixation to underlying tissue.
  - Presence of foreign body or irritant substances.
  - Infection.
  - State of immunity.
  - Denervation.
  - Constitutional factors including: diabetes, anemia, hypoproteinemia, vitamin/mineral deficiencies, deficiency of sulpha-containing amino acids and excessive adrenal glucocorticoid hormone.