To manage wounds
Fundamentals of wound healing
WH – series of events that involves:
- migration
- accumulation
- interaction of cells
\[\downarrow\]
SYNTHESIZE NEW EXTRACELLULAR MATRIX

The golden period
- 6-hour after trauma
  Anatomic area
  Distal limbs
  Face, neck
  Presence of infection
  Pregnancy – 2nd half

Stages of wound healing
- Inflammatory stage
- Debridement stage
- Proliferative stage
- Maturation stage

Inflammatory stage
- Bleeding – Pain
  Immediately
- Vasoconstriction - 5-10 minutes
  - mediated by:
    sympathomimetic amines
    thromboxane

- Vasodilatation
- Increased capillary permeability
  mediated by:
  Histamine
  Bradykinin
  Prostaglandines (E1, E2)\[\leftrightarrow\] pain
  Leukotriene B4

Cellular and noncellular blood components can enter into the wound by diapedesis
Blood components will form
Fibrinogen -- Fibrin – Fibronectin accumulation

- Organic glue
- Barrier to protect the subcutaneously tissues

PMNs die – release enzymes -- pus

Fibrocellular clot dehydrates
Scab – natural bandage

Accumulation of an inflammatory exsudate

The 4 clinical signs of inflammation
Heat
Pain
Swelling
Redness

Duration – 6-12 hours

Cellular components in the wound in this stage

Neutrophils – lysis – protease
break down tissue debris
kill microorganisms

Monocytes, Lymphocytes, complements, Ig

Remove damaged tissues
Combat infection
Provide the building blocks needed for subsequent Wound repair

The role of neutrophiles

Phagocytosis: detect resorbable agents – incorporation them – development of phagolyosoma (phagosome + lysosoma) – degradation.

Lysosoma: lysosomal enzyme, neutral protease (elastase, collagenase, catepsin), acid hydrolase, myelopeperoxidase, lizozyme, other chemotactic mediator (mastocyte degranulation – more neutrophils).

Degranulation, secretio (exocytosis) into the EC matrix.
Debridement stage

Commences 6 hours after injury
Removal of damaged and necrotic tissues
Elimination of any infection

Duration depends on
quantity of necrotic tissue
contamination of the wound

Polimorphonuclear leukocytes
Aid breakdown of injured tissues

Immunoglobulins and Complement serve
Opsonins – removal of bacteria

Monocytes and Macrophages
Phagocytize cellular, EC, debris, fibrin
Also regulate fibroblast functions and attract fibroblasts to the wound

Type of wound

Uninfected – macrophages
Contaminated – lavage, dissection, bandages

Veterinarian influence

Fibroblast influx means end of this stage

Proliferative stage

- presence of fibroblasts
- epithelialization
- formation of granulation tissue
- wound contraction

Begins when blood clots, necrotic tissue, debris, infection have been removed

12 h, epithelialization (0,09-0,2 mm/day)
Fibroplasia (migration of fibroblasts, collagen formation 3-5 days)
Granulation tissue (vascular loops)
Wound contraction (myofibroblasts 0,2-1 mm/day)

Undifferentiated mesenchymal cells --
-- Fibroblasts - Endothelial buds from capillaries

Determines the connective tissue repair

Synthesize immature collagen (tropocollagen) in the 4-5th days

Tropocollagen fibrils bind together to form mature collagen fibers tensile strength of the wound

Major gain in wound strength 5-15 days after injury
Connective tissue

Collagen fibers and ECM production
IC tropocollagen – EC fibrils - ECM binder – reticulin -argyrophil fibers

First fibroblasts in the 2-3 days
First collagen fibers 5-7 days
First elastic fibers 4 weeks

The rate of gain of the wound strength is the same in the first 21 days of healing, regardless of the tissue involved.

Epithelialization – appears concomitantly with wound debridement and collagen formation.

Epithelial cells in the wound edge – mitosis – migrate to the area of cell deficits.

Granulation tissue

- Hallmark of this stage
- Composed of:
  Capillaries
  Fibroblasts
  Macrophages
  Mast cells

Also in sutured wounds
Basically to encourage wound contraction and
Epithelialization, resistant to infection (vascularity)

Wound contraction

- Myofibroblast – contractile properties of smooth muscle
- Contractile – centripetal movement
- Areas with minimal excess skin

Wound contraction can cease before closure of the wound - tension of surrounding skin equilibrates with the pulling forces of wound contraction.
Maturation stage

- Maturation of the collagen scar
- Decrease in vascularity
- Decrease number of fibroblasts and macrophages
- Wound gains tensile strength by collagen cross linking reorientation along lines of tension more contract bundles

- The stronger the original tissue the longer it takes to regain near-normal tissue strength
- Scar tissue covered by epithelium 20% weaker than surrounding tissue and never regains the normal appearance of uninjured tissue – reparative process not regenerative

The bone tissue

Healing of bone fractures

Fractura: Dislocation

Periostal rupture – callus formation
1. Haematom
2. After few days acute inflammation (neutrophiles, monocytes, histiocytes)

3. From the periostum, endostum
   granulation tissue formation
   (fibroblast and blood vessel proliferation)
   temporary callus – fibroblasts differentiation = osteoblasts

4. Temporary osteoid, cartilage callus;
5. Temporary bone callus (irregular structure)
6. Regular lamellar bone callus
The lamellar bone callus

1. Intermediate callus
   Lamellar bone in the line of the cortex of fractured bone edges
2. Endocallus
   Forms in the previously bone marrow area
3. Ectocallus
   Extra bone formation around the fractured area

The callus formation

Ectocallus -- deorganisation
Intermediate – Havers ducts, compact substance
Endocallus – bone marrow

Clinical signs of wound healing

1. Primary wound healing
   (sanatio per primam intentionem)
2. Second-intention healing
Steps of primary wound healing

1. The incised space fills up immediately with blood (blood cells, fibrin) and clot.
2. At the border of the wound neutrophil accumulation in 24 hours.
3. Mitotic activation of the basal cells – activated epithel cell migration in 24-48 hours.
4. Macrophags dominant on the 3rd day – granulation tissue proliferation – collagen fibers – epithel expansion

Steps of primary wound healing II

5. Angiogenesis maximum on the 5th day. Increased collagen mass wich overbridge the incision.
6. Collagen and fibroblast proliferation on the 2nd week, decreased edem, less leukocyte and vascularity.
7. No sign of inflammation after 1 month, avascularated scab.
In the case of primary wound healing, the wound is closed, thus the steps of the healing process are not visible. The signs of the second intention wound healing are well visible.

Differentation:
- Regular
- Irregular
- With complication

Second intention wound healing

Second intention
(sanatio per secundum intentionem):
- Loss of materia
- Granulation tissue
- Open, lacerated edged
- Closed, but infected
Disorders in primary wound healing
Hematoma
Seroma
Resorption fever
Local and general septic signs
Suture failure
Wound disjunction

Steps of the regular second intention
1. Clean up the wound – regressive process
2. Granulation tissue formation, fill up the wound
3. Constriction of the granulation tissue, scar tissues
4. Epithelization

Complications can occur in every stage of the healing period
Disorders in second intention wound healing

1. Increased duration of the regressive processes
   - general reason
   - vascularity ↓
   - large area injured
   - necrosis
2. Quantitative problems in granulation tissue formation
   not enough
   too much
   irregular
3. Quality problems
   Break up
   Keloid

4. Complication in the constriction phase

   No constriction
   The disadvantageous result of the constriction
4. Complications during epithelialization

---"tired" wound -- torpid wound

By large, lacerated wounds
Imperfect epithelialization, epithel detachment
Usually by irregular granulation tissue

• By some cases there are no wound healing complication
  • -Sarcoid
  • -Tumor
  • -Foreign body
### Factors affecting wound healing

- Age and condition
- Anaemia, loss of blood
- Uraemia
- Protein deficit
- Zink, copper, mineralia deficit
- Vitamins
- NSAID’s
- SAID’s
- Trauma
- Infection

### Factors affecting wound healing II

- Efficiency of local clean-up
- Local anaesthetics
- Suture materials and technic
- Hematoma and seroma
- Movement of the wound edges
- Local insulin
- Bandages
- Magnetic field therapy
- Dehydration and edem
- Vascularity and saturation
- Temperature and pH

### Age and condition

- Young-old
- General disease

### Anaemia and loss of blood

- Local hypoxia inhibits the first phases of wound healing
  - Fibroblast function
  - Replication
  - Migration

### Uraemia

- Complications till the 5th day
- Infusion

### Loss of protein

- TPP is under 6 mg/dl – the wound healing stops
- Under 5.5 mg/dl – disjunction (70%)
- Under 2 mg/dl – edem – disjunction (100%)
Zn deficit
- Delayed wound healing, epithelialization, elasticity
- Zn – enzyme functions
- With Zn overdosage – will not be earlier wound healing

Cu deficit
- Cu is in the ceruloplasmin – collagen synthesis – collagen fiber junction – collagen maturation

Other mineralies are also important in collage synthesis, but the deficit of them does not cause problem (Ca, Fe, Mn)

Vitamins
- Vitamin-A
  - epithelialization, elasticity, collagen synthesis
- Vitamin-K
  - hemorrhage
- Vitamin-C
  - epithelialization, angiogenesis, collagen synthesis
- Vitamin-E
  - Membrane stabilisation, overdosage decreases

NSAID’s
Decreases inflammation and granulation tissue formation

Painkiller effect
Increases blood flow

SAID’s
- Stops the wound healing (5th day)
- Decreases collagen synthesis, angiogenesis, granulation tissue formation
- Decreases constrictions, and epithelializations

Trauma
- Sensitivity for infections
- Dull trauma causes severe problems
- Decrease contractility
**Infections**

- The granulation tissue is a good border against infection agents – elongates the wound healing period

**Wound toilette**

- Povidon-jodid (0.1 - 0.2 %)
- Chlorhexidin (0.05%)
- Hydrogen-peroxid (3%)

**Wound excision**

**Local anaesthetics**

- Less leukocyte can adhere to the endothelium
- Decreases blood vessel lumens

**Suture technic and materials**

- Suture method
- Suture materials
  - absorbent
  - Non absorbent
  - natural
  - synthetic
  - monofil, polifil, pseudomonofil

**Hematoma, seroma**

- Blood and serum can delay wound healing
**Movement**

- Angiogenesis
- Good choice of suture technic can help

**Local insulin**

- Protein synthesis, constriction, phagocytosis and cell division will be better
- Decreases edem

**Bandages**

- Infection
- Wounds under pressure
- Immobilisation

**Magnetic field therapy**

- Better circulation
- Antiinflammatoric effect
- Better collagen synthesis
- Inhibit to form keloids

**Dehydration and edem**

- Dry out wounds — complication in wound healing
- Decreasing perfusion

**Temperature and pH**

- Increased wound healing on higher temperature (30 °C) and lower pH.
- Cold situation – decreased elasticity of the wound
- Use of bandages – higher T