Lecture 9 - Wound Healing

A wound is any disruption to tissue caused by injury
The injury is usually traumatic, i.e. physical, mechanical damage to tissue: Wound healing is a special case of acute inflammation and its sequelae with a combination of regeneration and repair occurring

Types of wounds

1. **Contusion** = haematoma or "bruise"
2. **Abrasion** = a "scrape" or a "graze"
3. **Avulsion** = large open wound
4. **Puncture** = small, deep, penetrating
5. **Laceration** = torn, mangled tissue
6. **Missile injury** = puncture due to high velocity missiles
7. **Surgical wound** = incisions, limited damage

Types of healing

Speed of healing and amount of scarring depend on type of wound
a) Incision wounds heal by **primary intention**
b) Avulsion wounds heal by **secondary intention**
Quantitative rather than qualitative difference

Wound healing by secondary intention

0 - 1 hours: Bleeding, exudation, **coagulum** forms
1 - 2 hours: Dehydration, **eschar** (scab) formation
2 - 36 hours : **Acute inflammation** atwound margins
≈ 36 hours : **Granulation tissue** begins to form
This is the repair tissue of the body and consists of:
Vascular sprouts (new vessel outgrowths)
Macrophages ("scavenger" cells)
Fibroblasts (for collagen deposition)
36 - 72 hours : Granulation tissue is fully developed. Collagen deposition is occurring as debris is being removed. Epithelium all around the wound begins to multiply and begins to migrate towards wounded area **Re-epithelialization**
3 - 7 days: Myofibroblasts form
Specialized fibroblasts that contain actin and myosin
Wound contraction: Very important in avulsion wounds
7 - 14 days : Re-epithelialization is complete, early scar formed
3 - 4 weeks: Blanching of scar i.e. vessels pinched off; Fully healed wound

New epithelium forms, i.e. regeneration, NB failure of specialized structures to regenerate

Wound healing by primary intention

These wounds have less tissue to be replaced
No wound contraction is needed
Not many myofibroblasts formed
Not much scar
Therefore large wounds are *simplified* so that they heal in less time and with less scar
Wounds are stitched together only if the risk of infection has been eliminated
Large, dirty, avulsion wound: Risk of infection, much scarring; Same wound after simplification Scarring minimized

Complications of healing

Cicatrization: Excessive scarring
Deformity, contracture; Bad cosmetic effects e.g. burns/scalds

Keloid: Genetic disorder; Masses of collagen scar even after trivial trauma
More common in the dark skinned races; Difficult to treat

Excessive granulation: = "Pyogenic granuloma" = "Proud flesh"
Too much granulation tissue forms; Interferes with wound closure; Must be surgically removed

Delaying factors in wound healing

Localized *versus* Generalized
Localized factors act only in the vicinity of the wound
Generalized factors affect the whole body and thus compromise wound healing also

Localized factors

1) Lack of adequate immobilization Wound movement delays healing as granulation tissue is damaged
2) Lack of O2 (blood supply); Healing is a very energy dependent process, much oxygen and many nutrients are needed
3) Infection
The commonest and most important factor

Generalized factors

1) Malnutrition
Wounds heal very slowly in malnourished people
2) Increasing age
A very complex set of factors in the elderly greatly delays wound healing
3) Hormonal effects
Corticoids, endogenous or exogenous
4) Low temperature
Wounds heal more slowly in cold climates
5) Other systemic disease
Diabetes mellitus, a systemic metabolic disorder

Healing in specialized tissues

BRAIN: Gliosis instead of fibrosis; **MUSCLE:** Scarring; **CARTILAGE:** Scarring**; SOLID ORGANS:** Mixtures of limited regeneration and scarring
e.g. LIVER - Cirrhosis

Recapitulation

Wound healing in soft tissues is a case of acute inflammation and its sequelae
Healing by primary intention is preferable as there is less scarring and no contraction
Healing by secondary intention occurs in large open wounds
A mixture of regeneration and scarring occurs
Granulation tissue formation is crucial for the healing response
Although there are many different types of wounds, the healing process is very similar in all of them
Some abnormalities of wound healing are: excessive scar formation; keloid and excessive granulation
Delays in wound healing may be due to localized or generalized factors
Of these, infection is by far the most important as it is so commonly seen clinically
Specialized tissues heal in essentially the same way as that considered for skin and subcutis, with minor variations

Lecture 10 - Fracture Healing

A fracture is any loss of continuity in the structure of a bone; Healthy bone is normally very strong; Much force to break it, therefore much soft tissue injury also occurs
Pathological fracture: Fracture in a diseased bone
e.g. Bone tumours (1˚ or 2˚); Osteoporosis; Osteomalacia

Types of fracture

Transverse; Oblique; Spiral
Avulsion fracture
Comminuted fracture
Complete fracture vs Incomplete fracture
Compound (open) fracture vs Simple fracture
Compression fracture (common in vertebrae)
Disclocation fracture
Double fracture
Greenstick fracture
Impacted fracture
Indirect fracture

Fracture Healing

Reduction of a fracture

Bone must be aligned correctly according to normal anatomy, **Otherwise the bone will not set in an anatomically correct position**
Immobilize through the use of Splinting, Pinning, Plaster casts; Traction
Treat soft tissue damage: Minimize risk of infection

Bone then regenerates

NB: Similarities and differences between fracture and soft tissue wound healing
Consider a complete, simple fracture as an example
0 - 24 hours: Haematoma formation equivalent to coagulum of soft tissue wounds
First attempt by body to re-unite broken bone ends
1 - 3 days: Traumatic inflammation Macrophages predominate
Not many neutrophils, unless there is infection present
2 - 7 days: Demolition by osteoclasts
Little necrotic fragments of bone are removed
The broken ends of the bone are decalcified
3 - 8 days: Granulation tissue formation
7 - 25 days: Provisional callus formation, **Osteoid** tissue is laid down
Very active osteoprogenitor cells differentiate into osteoblasts and chondroblasts
Alkaline phosphatase ↑; Bone spicules may be seen
Second and more successful attempt to reunite the broken bone
1 - 3 months: Definitive callus formation, **Orderly bone** tissue is laid down
Third and most successful reunification of broken bone
3 - 12 months: **Remodelling:** Bone is trimmed down and excess callus is removed; Remodelling of the bone can result in near perfect bone regeneration
This is the major difference between soft tissue wound healing and bone fracture healing

Aberrations of Fracture Healing

Fibrous union: Instead of bone, collagenous tissue is laid down, i.e. scar! This is repair of bone
Occurs with excessive movement or if soft tissues become interposed between the bony ends
Can result in a **pseudoarthrosis** - "false joint"
To **prevent malalignment** fractures can fixated
Inlay fixation - e.g. Kuntscher nail; Onlay fixation - plates

Delaying factors in fracture healing

Localized *versus* Generalized

Very similar to those considered in soft tissue healing
Although infection is not as common it is particularly troublesome when it occurs: **Osteomyelitis**

Local factors in fracture healing

1) Movement: Much more important in fractures
2) Infection: Osteomyelitis, gangrene, may need to amputate a limb

3) Lack of O2 (blood supply): Probably the most important factor
Avascular necrosis (e.g. hip joint) Arthroplasty, prosthesis
4) Localised bone disease:
Bone tumours, osteoporosis, osteomalacia can delay or even completely prevent fracture healing

General factors in fracture healing
1) Malnutrition: Calcium, protein, vitamin D
2) Generalized vascular disease: Atherosclerosis
3) Generalized bone disease: Paget's disease; hyperparathyroidism
4) Other systemic diseases: Diabetes mellitus
5) Increasing age: Very important

Recapitulation

Bone fracture healing resembles soft tissue healing with one important difference: Bone regenerates
A similar sequence of changes occurs with inflammation, granulation tissue formation and stimulation of synthetic activity
Osteoprogenitor cells differentiate into osteoblasts, bone is laid down
Although there are many different types of fractures, the healing process is very similar in all of them
Some abnormalities of fracture healing are: Fibrous union, pseudoarthrosis, deformity angulation and displacement
Factors that delay fracture healing are very similar to those considered in soft tissue healing

Familiarise yourself to the following: (important points in the topic)
Healing is replacement of dead and injured tissue by healthy tissue. This occurs by two process 1. Proliferation or Cell division and 2. Differentiation (functional maturity). During healing, dead tissue is removed by macrophages, and surrounding viable tissue divide to produce more cells which move into the area of wound and start dividing to replace dead tissue, these cells synthesise matrix and other non cellular elements of tissue. Newly formed Fibrous tissue in the process of healing is called scar tissue. It contains tough fibrous protein Collagen which gives the strength to the scar.

Healing of skin wounds: Two types 1. Primary Union - when clean cut wound healing within weeks. 2. Secondary Union - When large open wounds heal with large scars such as ulcers and burn wounds.
Stages of healing:

Immediate - Blood clot fills the wound

Within 24 hours - Inflammation, WBC move to site of injury.

3-7 days - Macrophage activity & granulation tissue, epithelial regeneration.

Weeks - Fibrous vascular union with intact epithelium, mild inflammation.

Months - No inflammation, Remodelling, avascular thin scar, minimal contraction.

In Secondary union the stages of healing are prolonged, with more scab and scar formation, more wound contraction.
Healing in special tissues:
Muscles: All striated muscles cannot regenerate, so healing by fibrosis.
Nerves: Axon only damage repairs by regrowth. Damage to nerve cells is healed by fibrosis, as

nerve cells cannot regenerate like striated muscle.
Bone Healing: Fracture heals by

Immediate - Blood clot

Hours - inflammation, neutrophils & macrophages.

Days - Granulation tissue with osteoblasts and matrix (soft callus)

Weeks - Deposition of Calcium (calcification) to form hard callus

Months - Remodelling - removal of excess irregular bone

Factors affecting healing:
Healing is a complex process and can be affected by several factors.

Systemic Factors which affect healing are 1. Age 2. Malnutrition, vitamin deficiency 3. Other diseases such as diabetes.

Local factors such as 1. Infection 2. presence of dead or foreign tissue 3. Blood supply 4.Mobility as in fractures.