Healing 2

* First intention (primary union) → epithelial regeneration with minimal scaring as ① Healing of skin + ② Surgical incision

* second intention (secondary union) → combination of regeneration and scaring as (larger

* Mechanism of tissue regeneration *

① Restoration of normal tissue can occur only if the residual tissue structurally intact as partial surgical resection of liver

② If the entire tissue is damaged by infection or inflammation → regeneration is incomplete and is accompained by scarring as → liver abscess.

* Liver regeneration

* Two major mechanisms

→ prolifration of remaining hepatocytes + progenitor cell → depending on nature of the injury

→ prolifration of hepatocyte following partial hepatctomy by (IL-6) + growth factor (HGF)

* Steps of scar formation

① hemostatic plug comprised of pletelets is formed → stop bleeding
② inflammation
③ cell prolifration
④ Activation of fibroblasts and deposition of CT
⑤ remodeling of CT.

* Inflammation * (6 - 48h)

- recruit neutrophils and monocytes

* The macrophage ~~clear~~ are the central cellular players in the repair process: → ① clear microbes and necrotic tissue ② produce growth factor that stimulate proliferation

* As injorious agents and necrotic cell are cleared → inflammation resolves.

* Cell proliferation (to days)

→ Functions of cells:-

① Epithelial cell respond to produce growth factor (+) migrate over the wound to cover it.

② Endothelial cell + vascular cell proliferate to form new blood vessel (Angiogenesis)

③ Fibroblasts → proliferate and migrate into the site of injury + lay down collagen fibers that form scar.

The Family of (MMPs)

① Interstitial collagenases (MMP-1, 2, 3) → cleave collagen
② Gelatinases (MMP-2 and 9) → degrade collagen and fibronectin
③ stromelysins (MMP-3, 10, 11) → degrade ECM consituents

* Neutrophil elastase, cathepsin G, plasmin and serine proteinase → degrade ECM.

* Angiogenesis → process of new B.V development from existing vessels

GF ⊕ VEGF-A → stimulates both migration and proliferation of Endothelial cell. and thus initiating process of capillary sprouting

VEGF-A → promotes vasodilation by production of Nitric oxide ⊕ Contributes to Formation of vascular lumen.

FGFs → ① promote migration of macrophages and Fibroblasts to damaged area ② Stimulate epithelial to cover epidermal wounds

* Stabilization of new formed vessel is done by:
① recruitment of pericytes and smooth muscle cell
② deposition of C.T ③ PDGF → recruits S.M.C
④ TGF-β → suppresses endothelial proliferation and migration + production of ECM proteins.

Matrix metalloproteinases → degrade the ECM to permit remodeling and extension of vascular tube.

PRENKO

* cell proliferation *

* Granulation tissue → combination of proliferating fibroblasts, loose CT, new B.V, scattered chronic infl. cells in healing wounds, it has pink, soft granular,

* Activation of fibroblasts and deposition of C.T

→ These processes orchestrated by ① cytokines ② growth factors (PDGF, FGF-2, TGF-β)

→ Fibroblasts may differentiate into myofibroblast

• Collagen → The major component of fully developed scar.

TGF-β

① The most important cytokines for synthesis and deposition of C.T protein ② produced by Activated macrophages ③ Stimulates fibroblast migration and proliferation ④ increase the synthesis of collagen and fibronectin ⑤ decrease degradation of ECM ⑥ has anti-inflammatory effect.

* Remodeling * (2-3 weeks)

→ Wound strength increases because ① cross-linking of collagen + ② increased size of collagen fiber

→ * Shift of the type of collagen deposition from III to I

Healing 3

* Factors affecting wound healing

(*) Local Factors

① Type, size and location

Rapid wound
① clean
② small
③ ↑ vascularized area (face)

slow wound
① produced by blunt trauma
② large
③ ↓ vascularized area (foot)

② Diminished Blood supply (poor B.s) → slowly heal
① Ischemia → bedsores
② ischemia → atherosclerosis and arterial obstruction

③ Infection (delays healing) →
① prolongs inflammation
② increase tissue injury
③ ↑ granulation. T + ↑ scar

④ Foreign bodies such as steel, glass Fractured bone

⑤ Mechanical injury
↑ local pressure

⑥ Movement → ↑ exercise → ↑ circulating corticosteroids which inhibit repair

⑦ Exposure to ionizing radiation + UV light

- block cell proliferation
- retards granulation tissue formation
- interferes with blood supply

* Accelerates of healing (sterilization and kill bacteria)

PRENKO

* Systemic factors *

① Cardiovascular circulation
Impaired circulation in old age → cause poor healing.

② Systemic infections
delay healing

③ Haematological disease
neutropenia

④ Metabolic status
delay healing occur in
① protein calorie malnutrition
② vit. C deficiency
③ Zinc deficiency

⑤ Diabetes mellitus
① Affecting the nerve
② Lead to poor blood circulation
③ Lead to 2nd infection ④ effects on immune system function
⑥ Hormones (corticosteroids)
① inhibition of collagen synthesis
② Anti-inflamatory effect.

* Defects in Healing

~~Chronic~~ Wounds

① venous leg ulcers:
- Most in elderly people
- As a result of chronic venous hypertension
- caused by severe varicose veins or congestive heart failure

② Deposits of irons pigments (Hemosiderin)
- resulting from red cell breakdown
- accompanying chronic inflammation

③ Arterial ulcers
- Most in atherosclerosis and diabetes

PRENKO

④ Ischemia
- result in atrophy and necrosis of skin and underlying tissue.

⑤ pressure sores → skin ulceration caused by:
- bedridden
- immobile
+ elderly individuals with numerous morbidities

→ caused by: ① pressure ② local Ischemia

⑥ Diabetic ulcer
- in lower extremities (feet)
- Ischemia - Tissue necrosis
- neuropathy - systemic metabolisic abnormalities
- secondary infection.
- it characterized by
① epithelial ulceration ② extensive granulation tissue

→ Excessive scarring → give rise to:
① Hypertrophic scars
- develop after thermal or traumatic injury
② Keloid → accumulation of large amounts of collagen at wound site. - give rise to prominent scar
- due to disturbances of cell growth
- Genetic - Most common in blacks

PRENKO

* Excessive granulation is called (proud flesh) and must be removed by cautery or surgical excision.

* Exaggeration of wound contraction give rise to (contracture)

↳ - develop in palms, soles and anterior aspect of the thorax - commonly seen after serious burns

→ Fibrosis in parenchymal organs

* The main source of collagen in (lung, kidney) is
→ myofibroblasts

* The major collagen producers in liver cirrhosis is → stellate cells

Healing Bone Fracture

(*) Hematoma (rupture of B.V)
↳ organization by Granulation tissue and phagocytosis End with (Fibro-vascular granulation T.)

PDGF, TGF-β, FGF → activate osteoprogenitor cells which surrounding soft tissue and stimulate osteoclastic and osteoblastic activity

(*) Soft callus or procallus (mass of uncalcified tissue) is transformed into bony callus

(*) Endochondral ossification
- activated osteoprogenitor cell deposit woven bone

The fractured ends are bridged

(*) Remodeling
→ reduces the size of callus until the shape and out line of fractured bone are established as lamellar bone

→ The healing complete with restoration of medullary cavity