

# Tissue Repair

*212- b group*

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# Tissue Repair

- may start early after tissue damage
- regeneration
  - by parenchymal cells of the same type
- reparation
  - replacement by connective tissue (fibrosis)
  - result - scar

# Regeneration and Reparation

- regeneration
  - restoration of normal structure and function
  - persistence of supportive „tissue skeleton“ necessary
    - BM of epithelia
    - reticulin frame in liver
- reparation
  - restoration of normal shape x function is impaired or lost
  - parenchyma replaced by fibrous tissue

# Tissue types

- **permanent**
  - nonproliferative in postnatal life
  - neurons (?), cardiomyocytes (?)
- **stable**
  - regeneration as response to injury
  - parenchyma – liver, pancreas, renal tubules
  - mesenchymal cells, endothelium
- **labile**
  - continuous regeneration from stem cells (self-renewal)
  - hematopoietic cells in bone marrow
  - surface epithelia – skin, oral cavity, vagina, cervix
  - duct epithelia – salivary glands, pancreas, biliary tract
  - mucosas – GIT, uterus, fallopian tubes, urinary bladder

# Cell-ECM interactions

- not only cells!
- EMC plays important role in healing
- interstitial matrix – by fibroblasts
- basement membrane – by fibroblast and epithelium
- components
  - collagen (18 types) – I, III, IV, V; tensile strength
  - elastin (+ fibrillin) – return to normal structure after stress
  - glycoproteins - adhesion, binding ECM to cells (fibronectin, laminin)
  - proteoglycans and hyalouronans – lubrication (gels)

# Cell-ECM interactions

- ECM function
  - mechanical support
  - determination of cell polarity
  - control of cell growth
  - maintenance of cell proliferation
  - establishment of tissue microenvironments
  - storage of regulatory molecules

# Replacement of necrotic tissue

- resorption by macrophages
- dissolution by enzymes
- replacement by granulation tissue
  - uniform mechanism irrespective of initial trigger
  - the same microscopic appearance
  
  - angiogenesis
  - migration and proliferation of fibroblasts
  - deposition of ECM
  - maturation and reorganization

# Granulation tissue

- new-formed connective tissue, apparent from 3rd day
- thin-walled capillary vessels
- fibroblasts
- loose extracellular matrix
- stimulation
  - PDGF, VEGF, FGF, TGF, TNF, EGF
- inhibition
  - INF $\alpha$ , prostaglandins, angiostatins
- control
  - cyclins, cyclin dependent kinases



# Granulation tissue

- pink soft granular appearance
  - richly vascularized
  - highly cellular
  - myxoid matrix
  - inflammatory cells
- 
- e.g. surface of wounds, bottom of ulcers

# Angiogenesis

- neovascularization
- x vasculogenesis (embryonic process only)
- highly complex phenomenon
- angiogenic factors (FGF, VEGF)
- antiangiogenic factors
- healing, collateral circulation, tumors

# Fibrosis and Remodeling

- scar formation
- fibroblasts
- myofibroblasts
  - spindle cells of both fibroblastic and smooth muscle phenotype
  - production of collagen fibres
  - wound contraction

# Fibrosis and Remodeling

- abundant collagen fibres bridging the defect
- devoid of inflammatory cells
- reepithelization of surface defect
  - from skin appendages and/or from periphery
- secondary changes
  - calcification (dystrophic)
  - ossification (metaplastic)
- remodeling
  - synthesis and degradation of ECM
  - metalloproteinases (MPs), tissue inhibitors of MPs

# Pathological aspects of healing

- proud flesh (*caro luxurians*)
  - excessive amount of GT
- keloid
  - excessive amount of collagen
- hyaline plaques
  - serous membranes (spleen, pleura)