Vesalius SCALpel™ : Wound healing

Inflammatory phase

transient (10min.) vasoconstriction (catecholamines)
then vasodilatation, cap permeability (prostaglandins and histamine)
endothelial cells release proteases, dissolve basement membrane, allow migration of cells
platelet aggregation, stick to exposed collagen -> fibrin plug
platelet-derived growth factors activate macrophages & fibroblasts
clotting cascade activated (thrombin catalyzes fibrinogen to fibrin)
complement system activated
complement C5a & pl factor attract WBCs & leukotriene B4
fibronectin cell attachment, cytokine binding
cellular infiltrate
    neutrophils first, oxidative burst, kill BT
    monocytes activated from circulation to macrophages, critical for healing
        phagocytosis
        secrete enzymes, cytokines, prostaglandins
        necessary for formation of granulation tissue

Proliferative phase

2-3d to 3-4w
angiogenesis and fibroplasia stimulated by cytokines, fibronectin, histamine
fibroblast growth factor (FGF) potent angiogenesis factor
    attracts fibroblasts and keratinocytes
produce granulation tissue and collagen
extracellular matrix deposition
    fibronectin and glycoseaminoglycans (GAGs) anchor proteins, allows cytokines to promote cell binding
collagen production and degradation stimulated by TGF beta, IGF, vit C
    inhibited by interferon, steroids
type III collagen, replaced by mature type I
matrix proteases digest necrotic tissue

Maturation/remodeling

epithelial cells detach, migrate, lose contact inhibition
    integrins for attachment, collagenase for degradation
laminin adhesive protein anchors epithelial cells
proliferate, differentiate
wound contraction 0.6-0.75mm/d, myofibroblasts
    inhibited by full thickness grafts, flaps

Factors

Oxygen
- tissue PO_2 >40mm adequate for collagen synthesis, epithelialization, angiogenesis
- adequate Hb > 50% normal necessary for O_2 transport; perfusion, vascularity
- hyperbaric O_2 does increase tissue oxygen if perfusion is adequate

steroids
- inhibit inflammatory phase, macrophages, angiogenesis, contraction

nutrition
- albumin < 2g inhibits
- vit C cofactor for collagen synthesis, fibroblast proliferation
- vit E: large doses inhibit collagen production
  - may be antioxidant in radiation wounds
- Zn deficiency impairs epithelial, fibroblast function

tissue adhesives
- fibrin sealant may increase tensile strength, epithelialization of skin graft interstices

smoking
- vasoconstriction, CO shifts O_2/Hb curve to L, decreases offloading of O_2 to tissues

free radicals
- bad for healing
- radiation injury, chemicals, ischemia-reperfusion, inflammation, aging
- break down extracellular matrix (ECM), collagen, cell membranes

age
- neonatal wounds heal without scar (role of TGFß?)
- old don't heal as well as young, but scar better
- decreased cell proliferation and function, prolonged phases
- intolerance to ischemia, recurrent disease

chemotherapy
- decreased fibroblast production and wound contraction
- adriamycin, actinomycin D, bleomycin, BCNU
- delay starting CT > 14d out of proliferative phase

radiation
- small vessel occlusion (endothelial damage)
- permanent injury to fibroblasts even years later
- impaired epithelialization
- hyperbaric induces angiogenesis, helps in radiated tissue; osteoradionecrosis
- single preop < 300Gy or post op in 5-7d no significant effect
- >1000 cGy within 3w retards early healing
- > 4500 significant retardation
- fluoro can cause significant ulcer, damage
- safe dose not known, may vary with tissue type

infection
- > 10 to the 5^{th} org/g tissue or any hemolytic strep prevents healing
- prolongs inflammatory phase
- collagenases release stimulated by bacterial endotoxin

growth factors

proteins that promote cell proliferation, migration and function by receptor binding
from platelets, macrophages, keratinocytes, fibroblasts, endothelial cells
clinical studies: PDGF (diabetic pressure), FGF (fibroblast growth factor)(pressure, donor sites)

Non-healing wound

arrest normal progress of phases
prolonged inflammatory phase
repeated trauma (pressure, FB, infection, ischemia, tissue hypoxia)
increase inflammatory cytokines, matrix metalloproteases (degrade proteins, cytokines, epithelium)

Dehiscence

risk factors
systemic: pulmonary disease (cough), malnutrition, obesity, diabetes, steroids, cytotoxic agents
local: emergency, contamination, technical, bowel distention, ascites, infection, hematoma, ischemia, radiation

Incisional hernia, recurrence rate 45%

non-absorbable, continuous suture best
COPD, low albumin, steroids

Hematoma

technical or coagulopathy
hypothermia, hypotension, epinephrine

Infection

I clean: 2-5%, atraumatic, no GU, GI, resp entry
II clean contaminated: 8-11%, minor tech break, entry " without spillage
III contaminated: 15%, trauma, gross spill, entry infected tissue, bone urine bile
IV dirty 35%, drain abscess, debride soft tissue infection
intraop risk factors: prep, shave, duration, prophylaxis, contamination, FB, hematoma, dead space, tissue trauma
clean/contaminated or contaminated
delay repair
autologous tissue: flap, free fascia lata (vascularizes), component separation
avoid synthetic mesh if possible
alloderm: human dermal matrix
oasis: porcine small intestine submucosa collagen matrix

New wound treatments

vac: decreases edema -> increases perfusion -> promotes granulation tissue
acticoat: release Ag ions, moist wound env, burns, chronic wounds

Bioengineered

apligraf: bilayered cultured skin: DM & venous ulcers
dermagraft: fibroblasts in absorbable mesh, DM
transcyte: fibroblasts in nylon mesh: partial thickness burns, temp cover after excision
interactive influx macrophages release cytokines: oasis, glucan

Hyperbaric oxygen

nec fasc, crush/compartment, radionecrosis, compromised flap or graft
also advanced diabetic foot ulcers
promotes angiogenesis,bacterial suppression, decreases edema

Scar

keloid: overgrows wound edges
hypertrophic scar: delay revision > 1y

Metabolic wound healing delay

osteogenesis imperfecta: defective type I collagen
Ehlers Danlos 10X
Marfans elastin defect, no delay wound healing