

## 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 glycosaminoglycans (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  $PO_2 > 40\text{mm}$  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  $< 2\text{g}$  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  $O_2/\text{Hb}$  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  $TGF\beta$ ?)  
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  $> 14\text{d}$  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  $< 300\text{Gy}$  or post op in 5-7d no significant effect  
 $> 1000\text{ cGy}$  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  $5^{\text{th}}$  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/compartament, 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