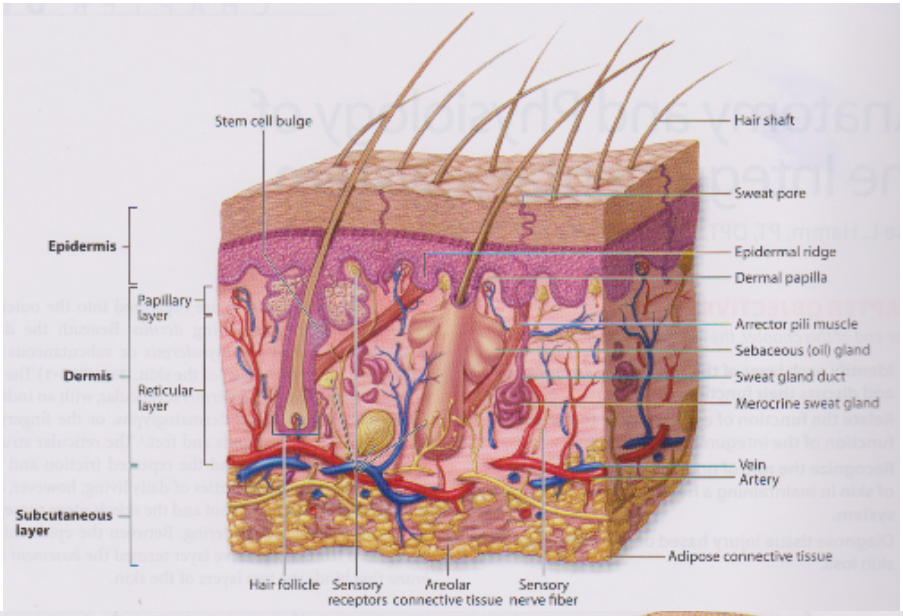
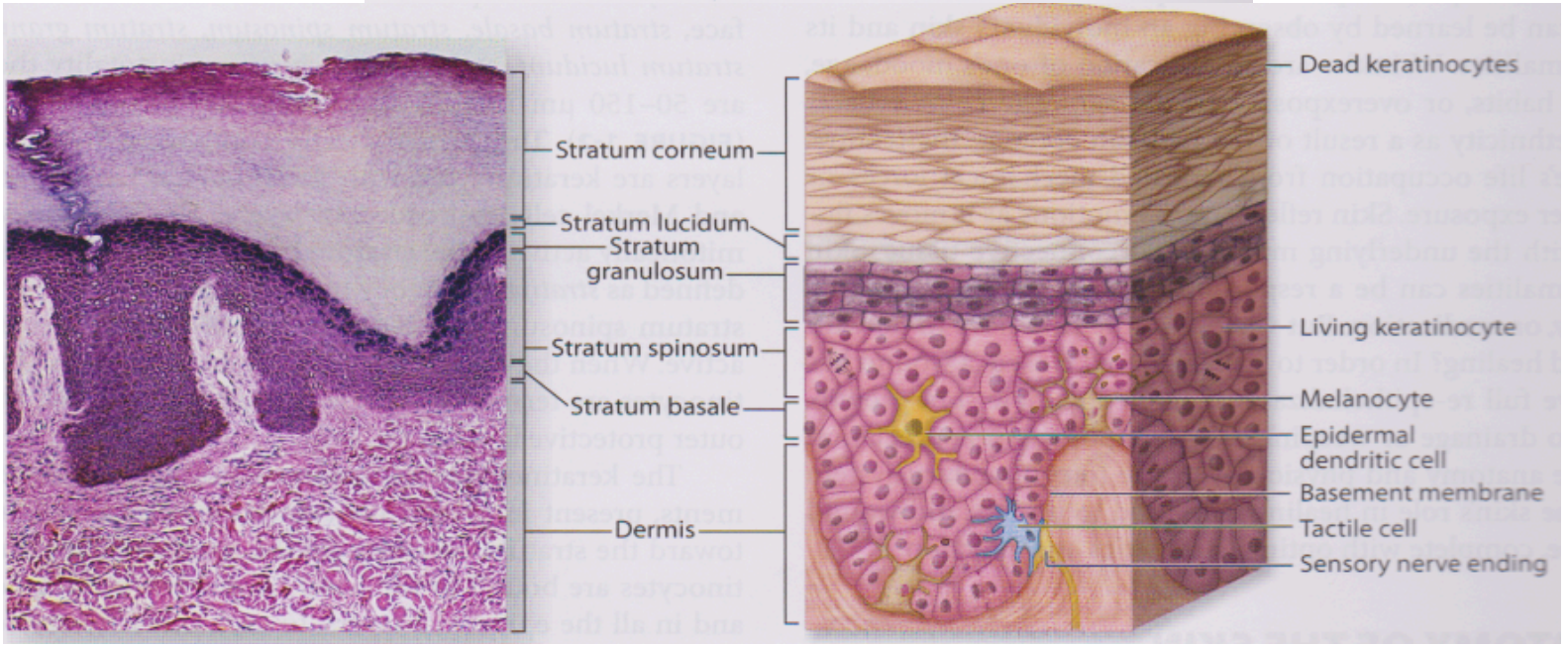
Wound healing process

Anatomy of the skin





Physiology & Function of the skin

Physiology

- vascular supply
- nerve suply
- skin nutrition
- skin renewal

Function

- protection from enviroment
- sensation
- prevention of fluid loss
- immunity
- thermoregulation
- protection from ultraviolet rays
- synthesis & storage of vitamin D
- Esthetic & communication

Skin: Constitution and Function

① Protection against cold, heat, radiation

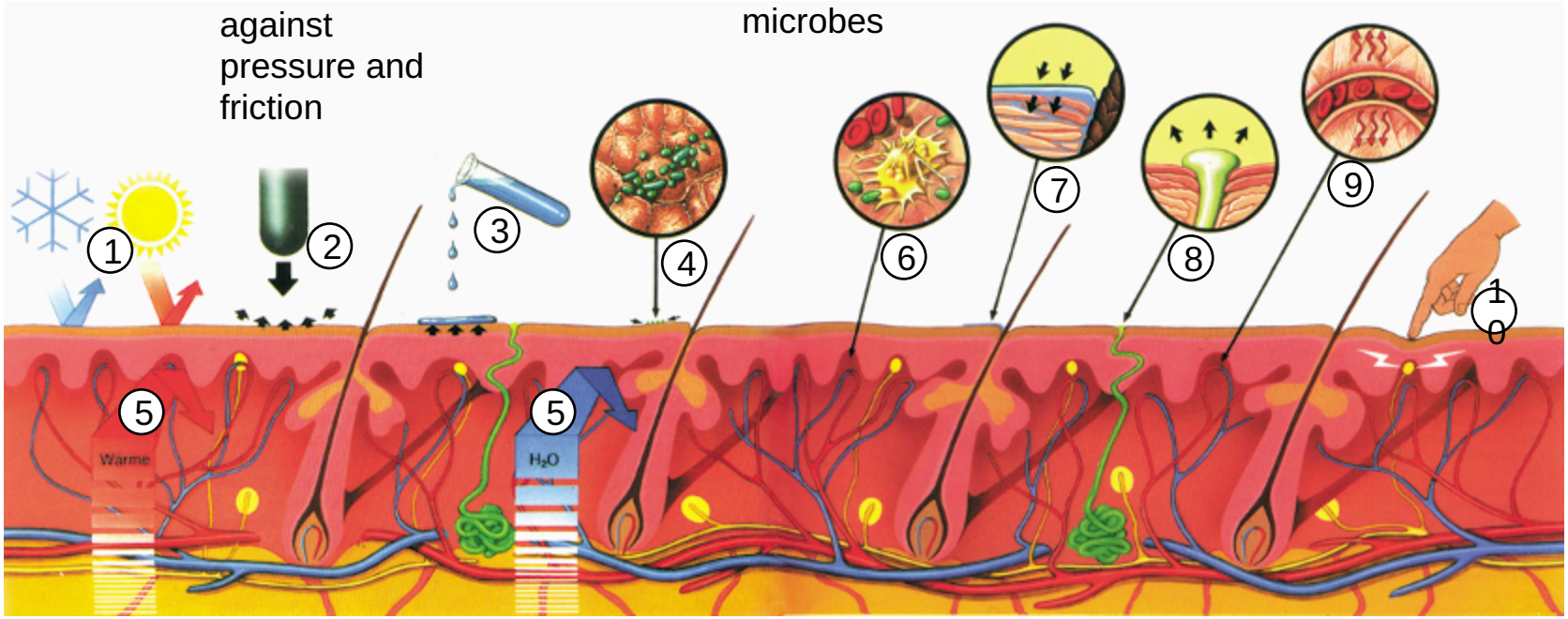
② Protection against pressure and friction

③ Protection against chemicals

④⑥ Protection against microbes

⑦ Absorption of active agents

⑧⑨ Regulation of circulation and temperature



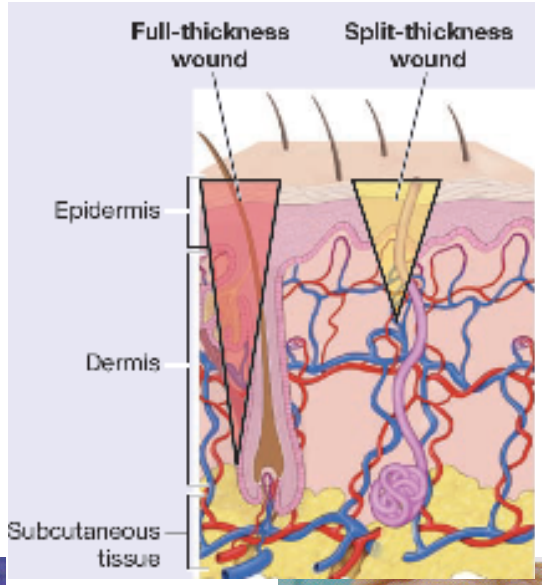
⑤ Protection against loss of temperature and water

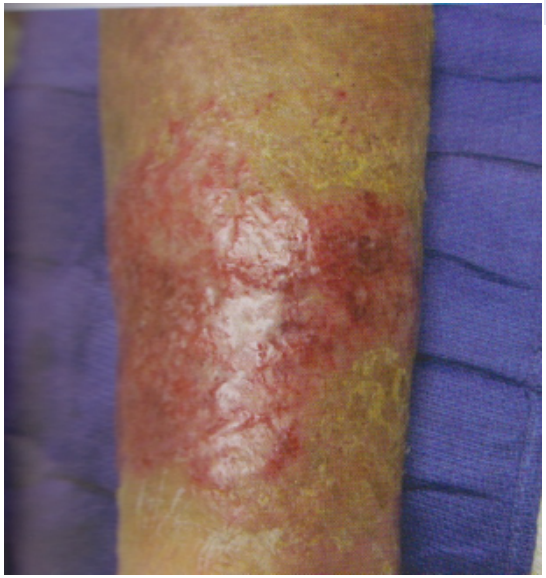
⑩ Sense of pressure, touch, pain and temperature

What’s is wound

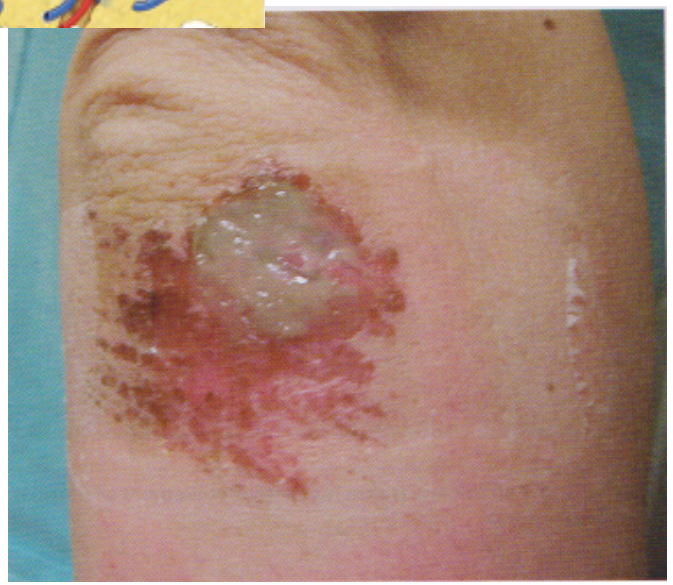
- Defines Wound (Dorland medical dictionary) a diruption in normal contuinity of a body structure
- The term “Wound “
  - Usually related to an acute injury or an acute mechanicel trauma such as gunshot wound or a stab wound
  - Chronic wound related to any wound that fails to heal within a reasonable periode

Definition of skin loss



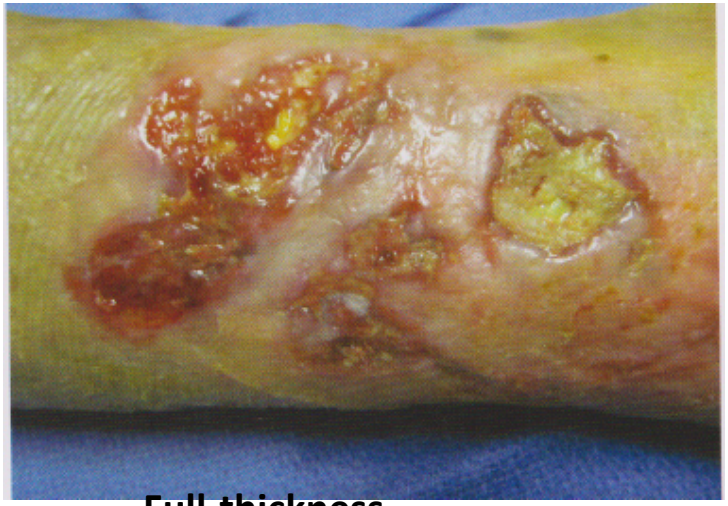


Erosion loss of superficial epidermis, dermis no involvment

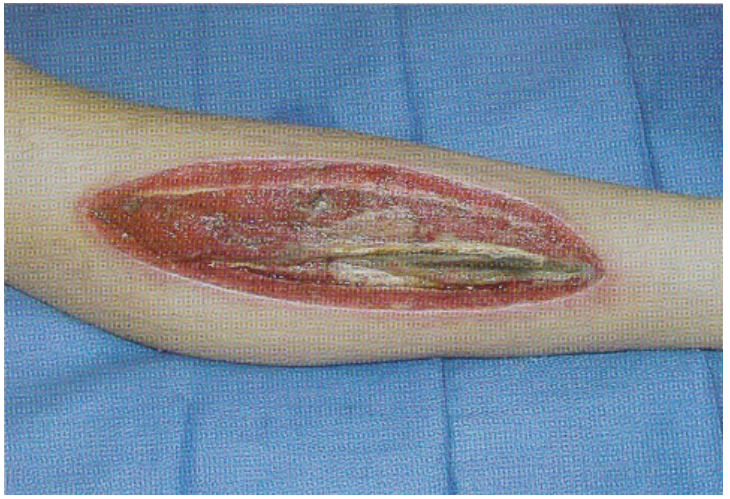


Partial thickness skin loss loss of epidermis & part of dermis

Definition of skin loss…



Full-thickness loss



Full-thickness loss with envolvement of muscle, bone and tendon

Loss of the epidermis & dermis extending into subcutaneous tissue, in some cases involving bone tendon or muscle

Wound Healing

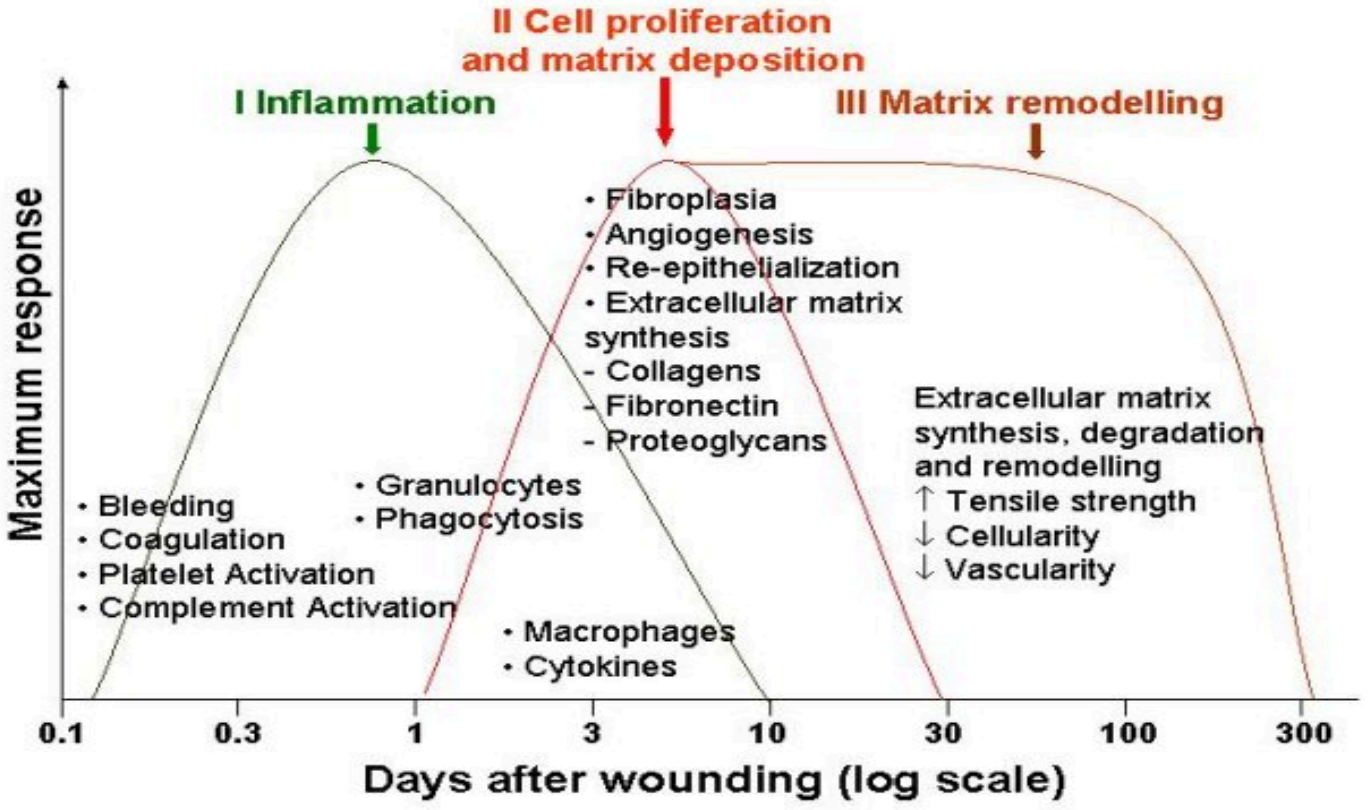
Why is it important to understand how wounds heal?

- An understanding of normal wound healing enables recognition of abnormal healing (Dealey 1994).

- Recognition of the phases of wound healing will assist with planning implementation and evaluation of wound management, including the selection of appropriate dressings.

Wound healing stages

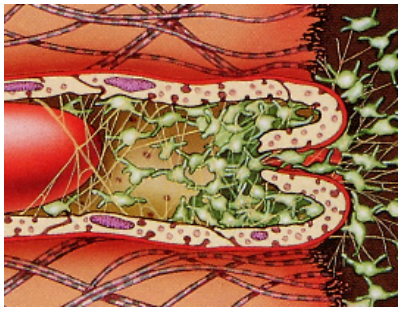
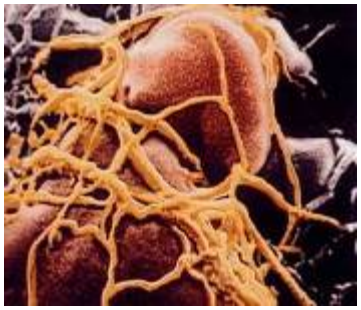
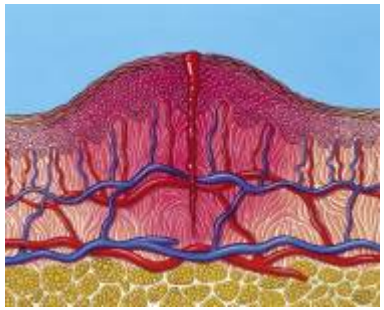
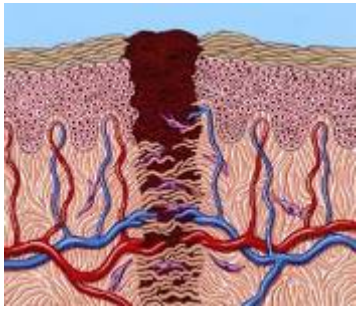
I. Inflammatory phase
II. Proliferative phase
III. Remodelling phase



Physiology of Wound Healing

Wound Healing Phases

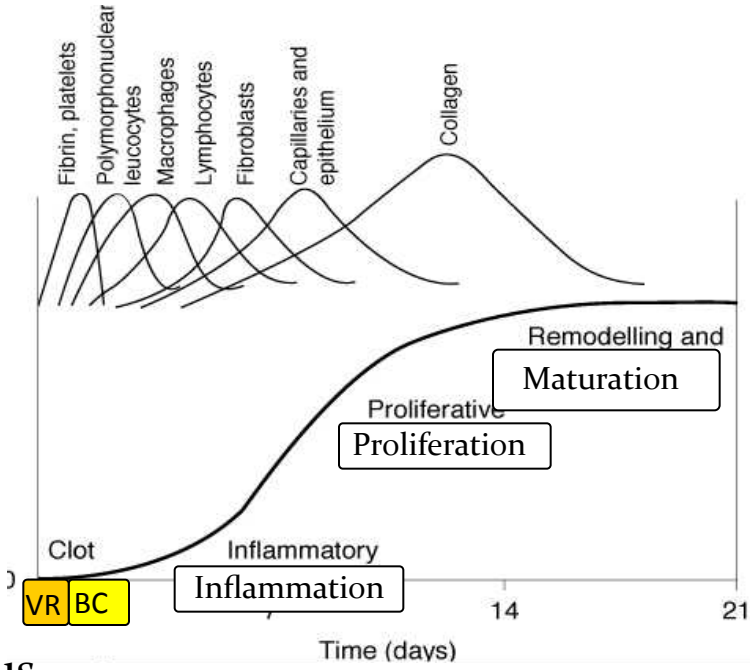
Vascular Response	Blood Coagulation	Inflammation	Formation of New Tissue
By the release of tissue factors vasoconstriction followed by vasodilatation	Plasma factors	Activation of the immune system	Vascularisation Rebuilding of the connective tissue Granulation Epithelisation Remodelling

Wound Healing Phases

Vascular Response (VR)

- by the release of tissue factors
- vasoconstriction followed by vasodilation



Blood Coagulation (BC)

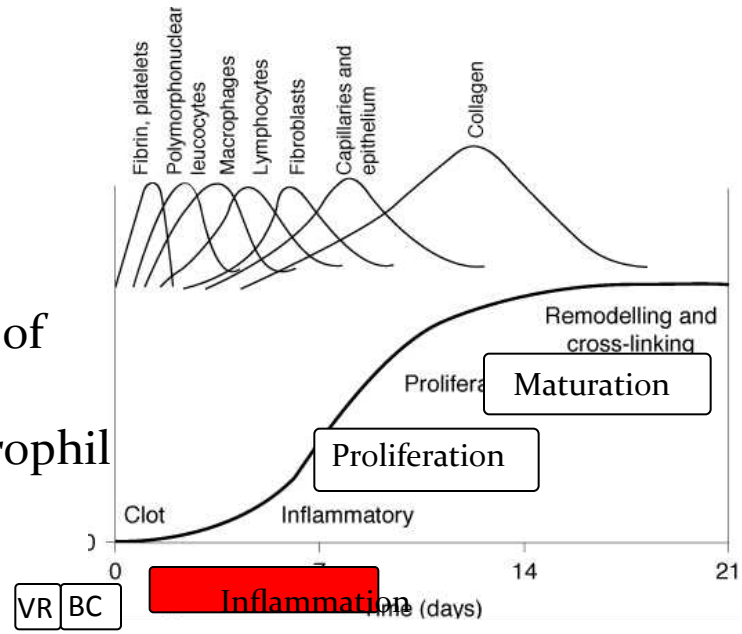
- Platelets adhere to the exposed vessel wall and change their form.
- Afterwards they release substances attracting further platelets.
- Than they clump together to form a thrombus leading to the release of platelet factors and fibrin synthesis.
- This induces the blood coagulation process, which is a chain reaction involving 13 coagulation factors.

Wound Healing Phases

Inflammation

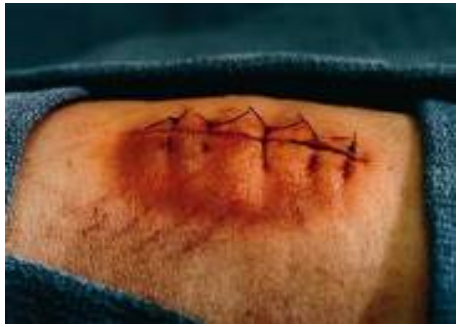
- Catabolic processes by which the wound is cleansed
- Activation of the immune system consisting of the non-specific defence system: Complement factors, phagocytic cells, neutrophil granulocytes, monocytes, macrophages

  and the specific defence system: B-lymphocytes, T-lymphocytes



Main symptoms of inflammation:

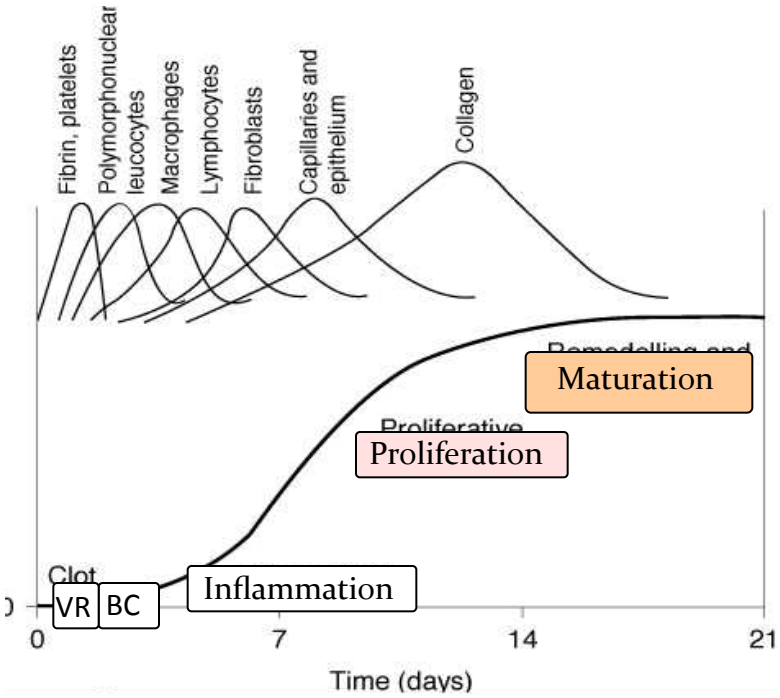
- Redness of the skin
- Increased temperature of the skin
- Swollen skin
- Pain
- Functional disorder



Wound Healing Phases

Formation of New Tissue (Proliferation)

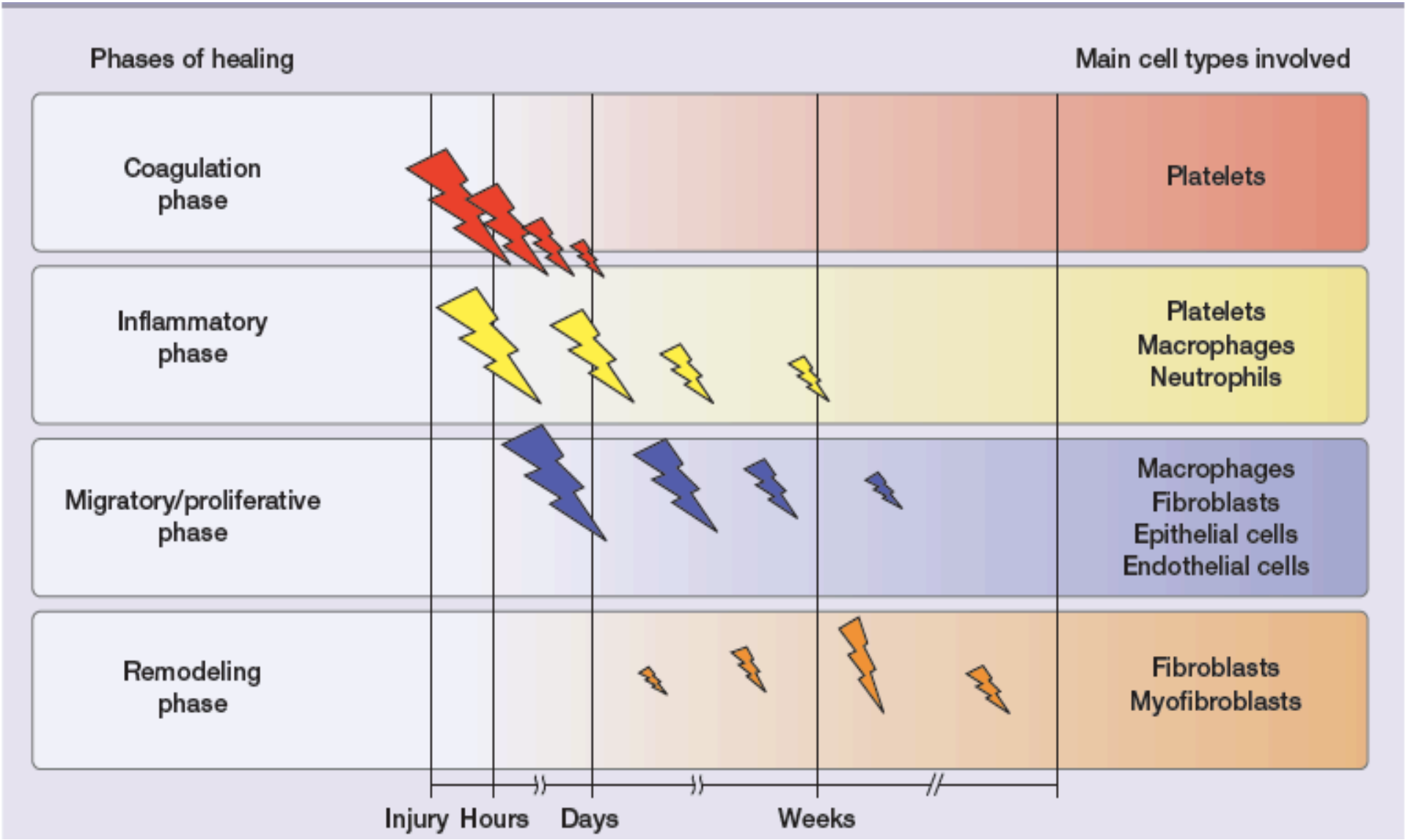
- Granulation formation / growth of blood vessels and connective tissue
- Endothelial cells form capillary network growing into the wound.
- Fibroblasts produce collagen network.
- Fibroblasts divide and make up the dermis.
- Wound contraction
- Special fibroblasts start the process of wound contraction
- allowing edges to come together.
- Epithelialisation
- Resurfacing of the wound by new epithelial cells.



Maturation / Remodelling

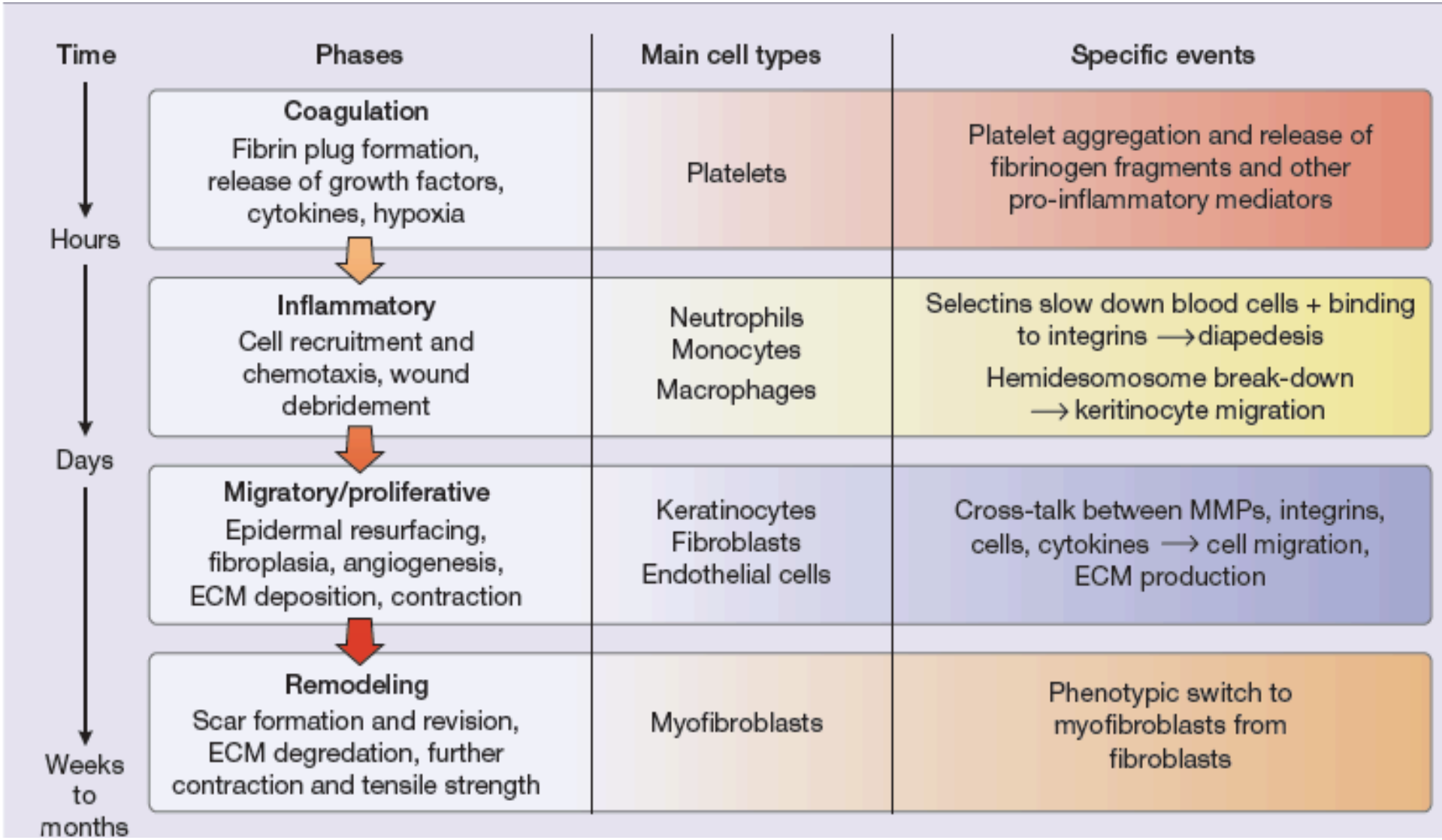
- For a long time after the injury, the scar tissue is reorganised by restructuring of the collagen. collagen fibres are broken down again by collagenases and are newly cross-linked.

The phase of wound healing & key cell & events involved



Fitzpatrick's, 2012

The phase of wound healing & key cell & events involved



Fitzpatrick's, 2012

Growth factors &cytokine, the roles in some function & matrix production

Responses	EGF	FGF	GMCSF	IL-1	PDGF	TGF-β1	VEGF	CTGF	IGF
Fibroblast proliferation	+	+		+	++	+		+	+
Keratinocyte proliferation	+	+		+		−			+
Angiogenesis	+	+	+	+	+	+	++		
Matrix formation		+			++	++		++	+
Inflammatory cell migration/ chemotaxis			++	+		+			

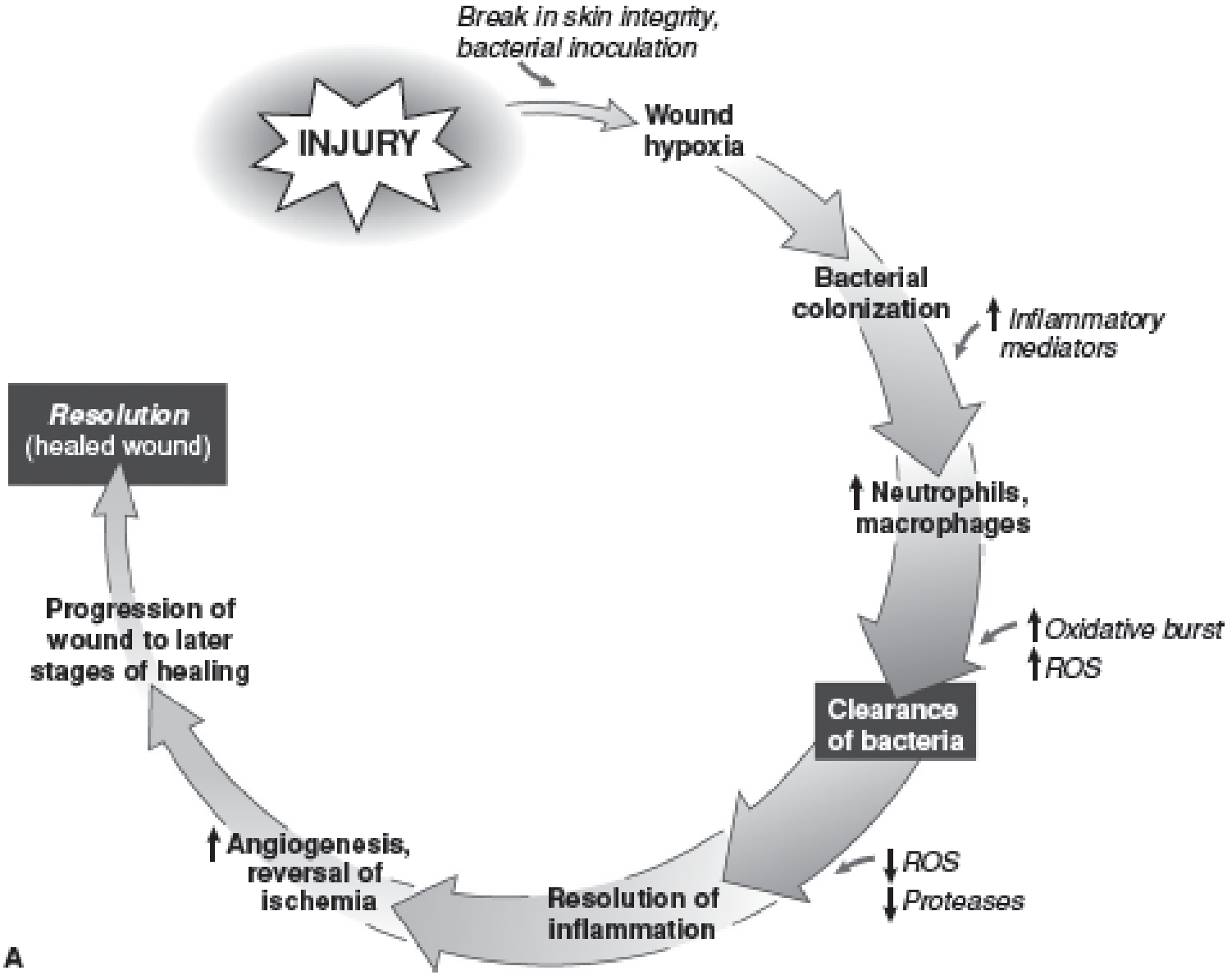
EGF = epidermal growth factor; FGF = fibroblast growth factor; GMCSF = granulocyte-macrophage colony-stimulating factor; HGF = hepatocyte growth Factor; IL-1 = interleukin-1; IGF-1 = insulin growth factor-1; PDGF = platelet-derived growth factor; TGF-β1 = transforming growth factor-β1, VEGF = vascular endothelial growth factor, CTGF = connective tissue growth factor.
Blank cell: no definite response
+ = definite but mild response
++ = definite and marked response

Matrixmetallo protein (MMP) functional effects on wound healing

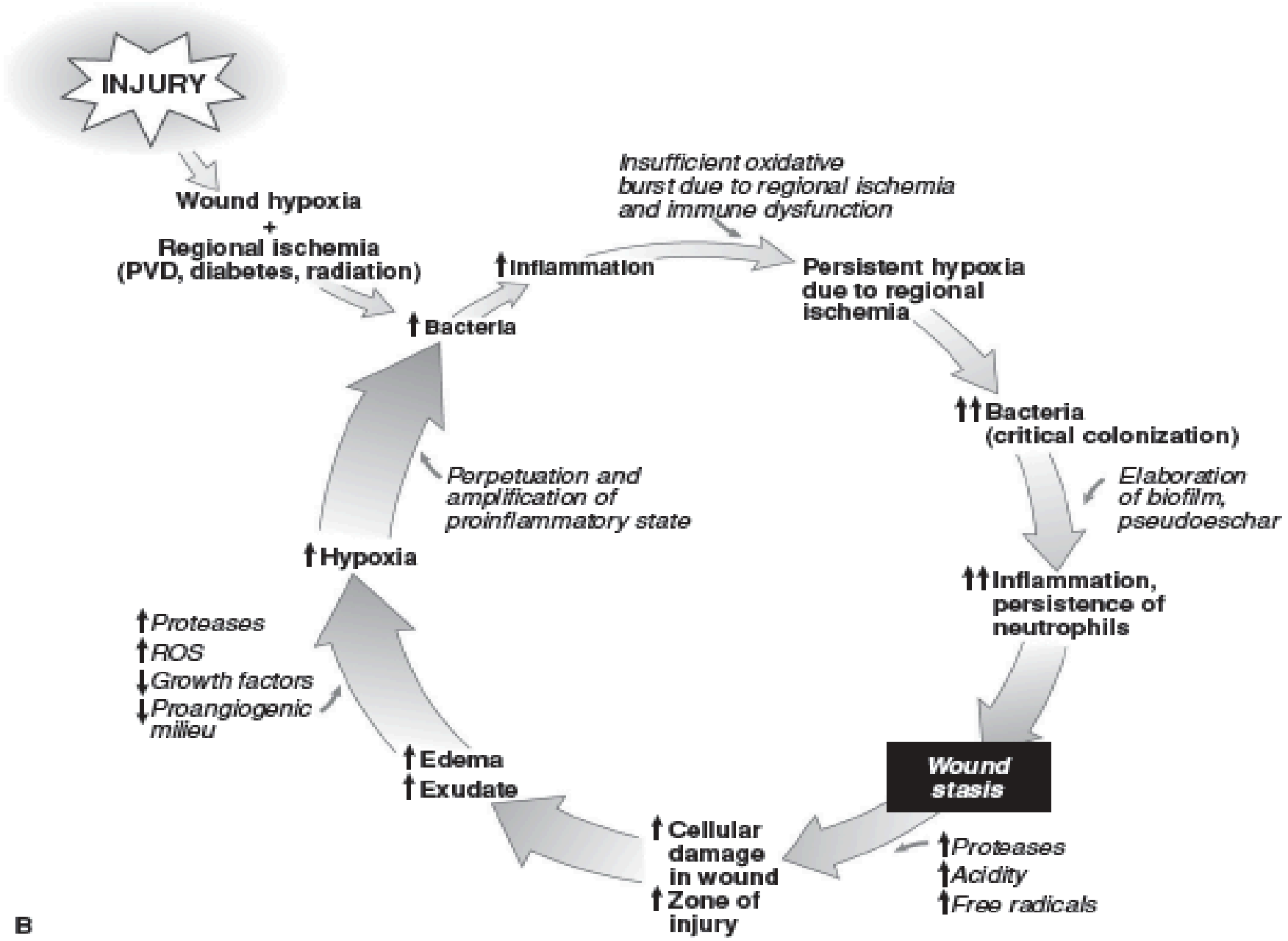
Effect	Common Names	Corresponding MMP Designation	Some Specific Effects
Keratinocyte Proliferation and Migration	Collagenase 1 Gelatinase A Stromolysin 2 Matrilysin-1 Epilysin	MMP-1 MMP-2 MMP-10 MMP-7 MMP-28	Increased migration
Endothelial cell (EC) migration	Collagenase 3 Gelatinase A MT1-MMP	MMP-13 MMP-2 MMP-14	Increases (EC) migration Needed for angiogenesis Needed for angiogenesis
Cell migration	Stromolysin 1 Stromolysin 2 Matrilysin-2	MMP-3 MMP-10 MMP-26	Required for excisional wounds
Inflammation	Collagenase 2 Gelatinase A Gelatinase B Matrilysin-1	MMP-8 MMP-2 MMP-9 MMP-7	Anti-inflammatory Anti-inflammatory Promotes inflammation
Neutrophil Migration	Gelatinase B MT6-MMP	MMP-9 MMP-25	Increases neutrophil migration
Apoptosis	Collagenase 2 MT1-MMP MT2-MMP MT6-MMP	MMP-8 MMP-14 MMP-15 MMP-25	Prevents apoptosis Antiapoptotic

MMP = matrix metalloprotease; MT = membrane type.

Fitzpatrick's, 2012



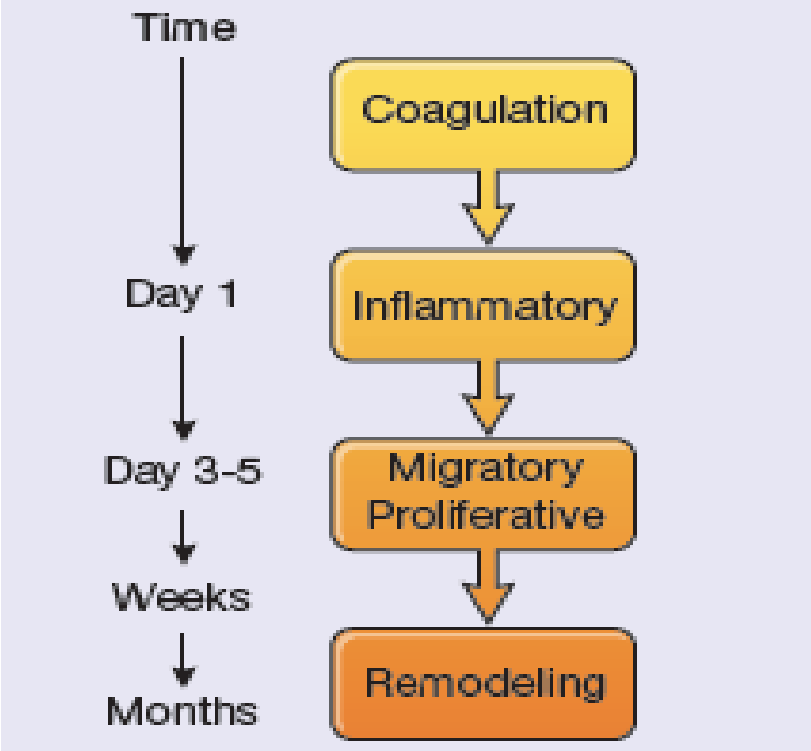
Grabb and Smith's Plastic Surgery, 6ed, 2007



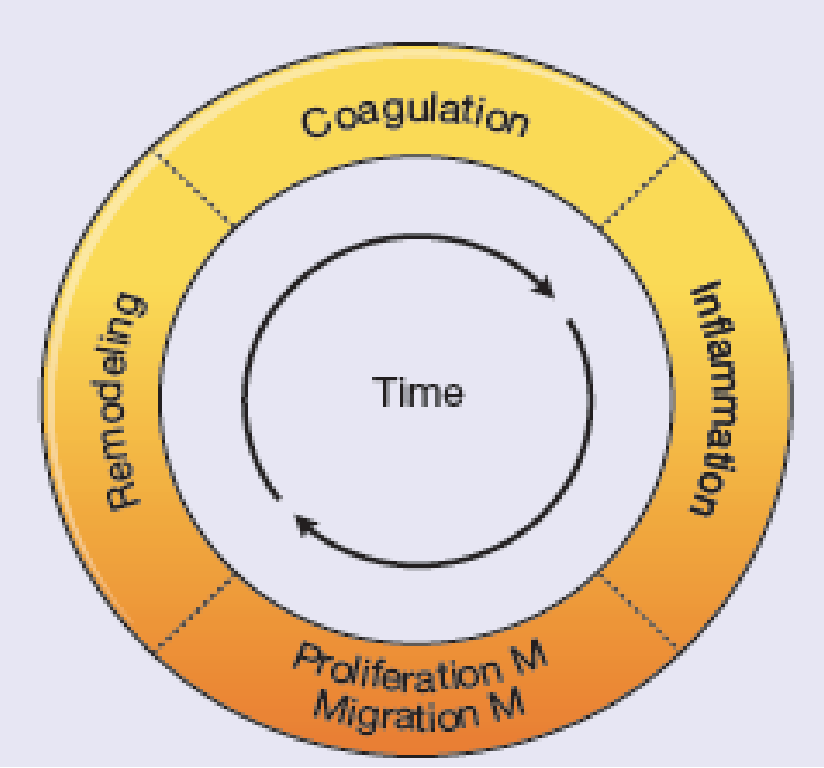
Grabb and Smith's Plastic Surgery, 6ed, 2007

Phases of Wound repair

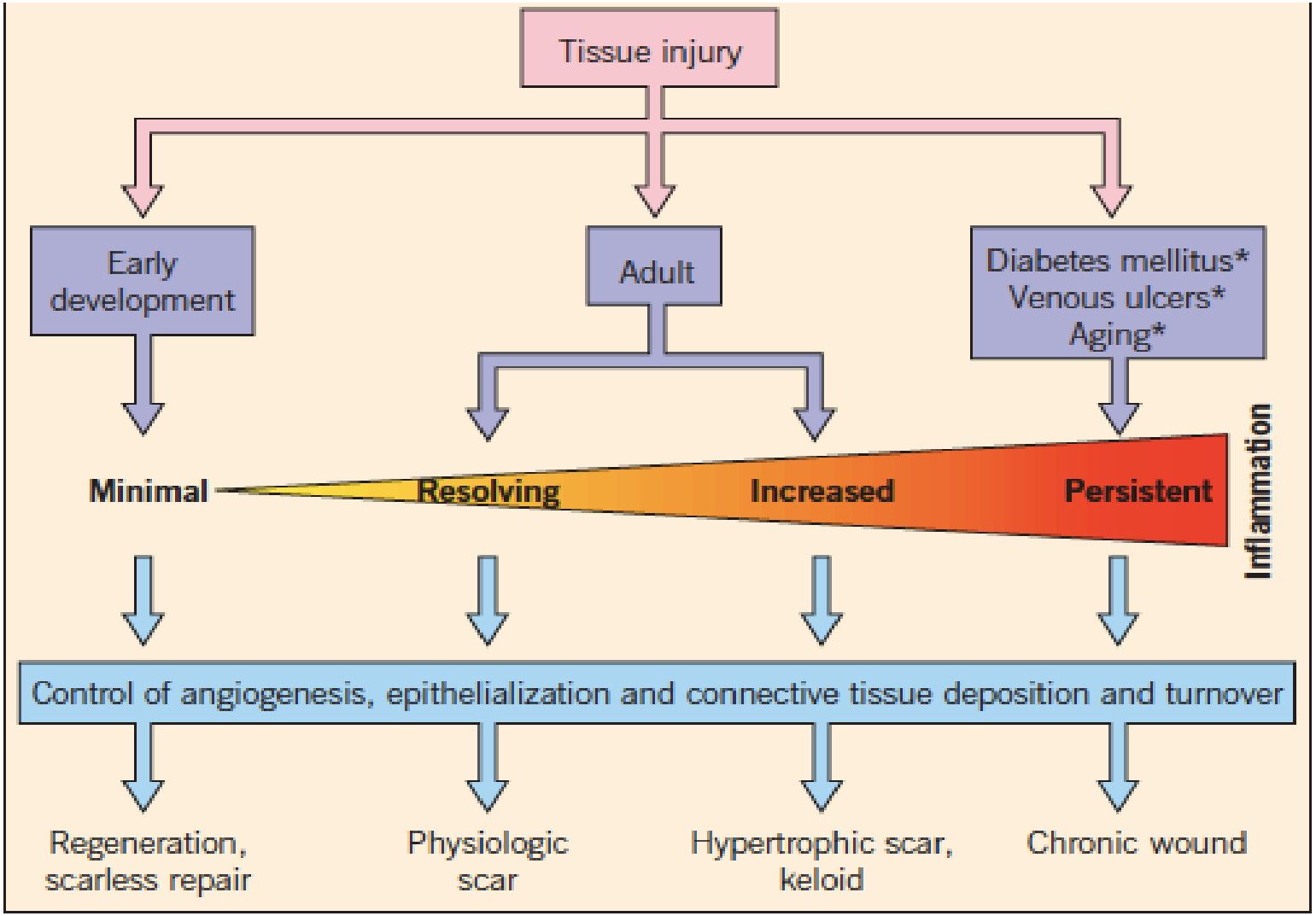
Acut wound



Chronic wound



Inflammation influences the quality of the repair response



Interference with wound healing

Technical Factors

Inadequate wound preparation
Excessive suture tension
Reactive suture materials
Local anesthetics

Anatomic Factors

Static skin tension
Dynamic skin tension
Pigmented skin
Oily skin
Body region

Associated Conditions and Diseases

Advanced age
Severe alcoholism
Acute uremia
Diabetes
Ehlers-Danlos syndrome
Hypoxia
Severe anemia
Peripheral vascular disease
Malnutrition

Drugs

Corticosteroids
Nonsteroidal antiinflammatory drugs
Penicillamine
Colchicine
Anticoagulants
Antineoplastic agents

Acute vs Chonic Wounds

	Acute wounds	Chronic wounds
Healing Process	Regulated	Haphazard
Pathology	None	Underlying
Time to healing	Rapid	Slow
Inflammatory response	Short	Prolonged
Exudate	Reduced after 48 hours Promotes cellular proliferation	Prolonged Inhibits cellular proliferation
Bacterial Load	Low	High
Fibroblast proliferation	Active	Inactive
Excoriation/maceration	Infrequent	Frequent
Extracellular matrix	Normal remodelling	Defective remodelling
Vascular network	Good	Poor
Complications	Infrequent	Frequent
Progress	Heal	Fail to heal / recur

Acute vs Chonic Wounds

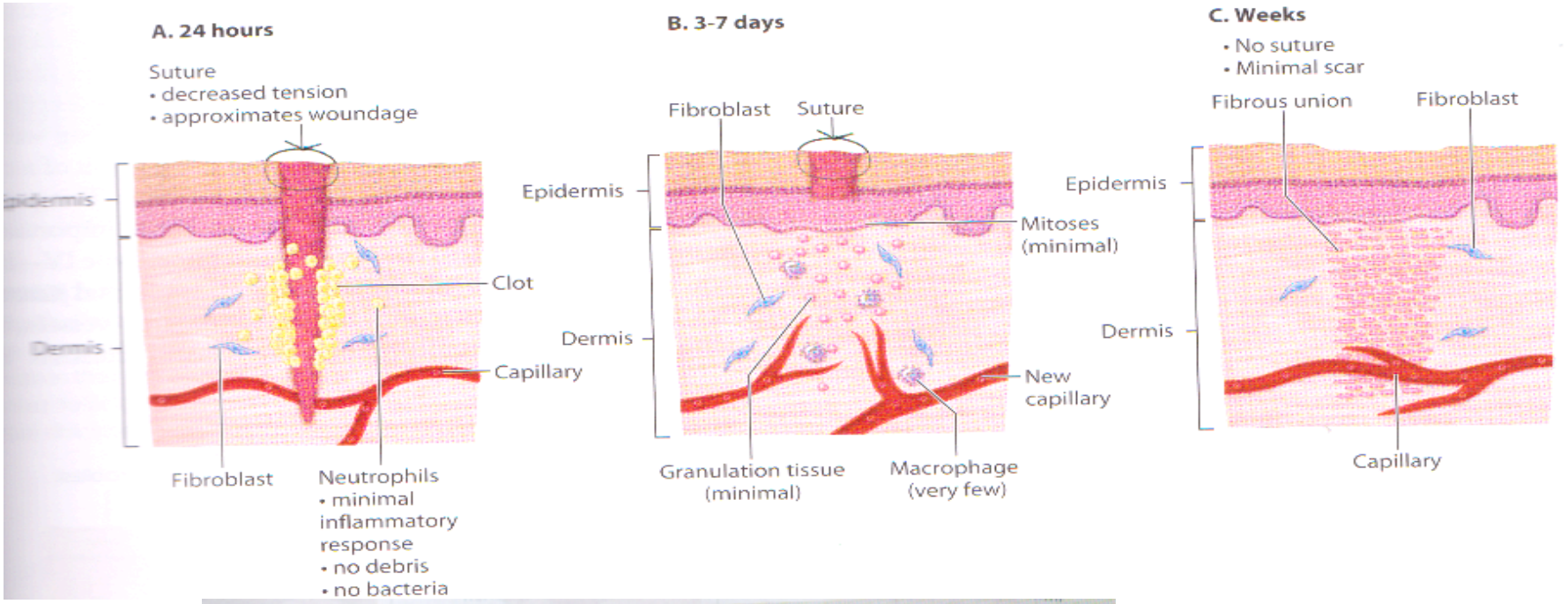
	Acute wounds	Chronic wounds
Time bound	Of short duration	Do not heal within 4 weeks (Cullum et al 1997)
Recurrence	Unlikely to recur	Characterised by episodes of recurrence
Pathophysiology	No underlying disease process	Multiple underlying pathologies
Healing process	Orderly healing	Disordered healing, wound may improve and then deteriorate in a cyclical fashion
Inflammatory response	Progresses through inflammation to proliferative phase	Appears to be ‘stuck ‘ in late inflammatory phase (Hart 2002)
Exudate	Thought to be beneficial, exerts antimicrobial effect and contains growth factors	May be detrimental due to imbalance in production of MMPs and suppression of TIMPS
Quantity of exudate	Reduces as healing progresses	May remain high due to persistent inflammation
Aetiology	Surgical wounds, traumatic wounds, burns	Pressure ulcers, leg ulcers, diabetic foot ulcers, fungating wounds

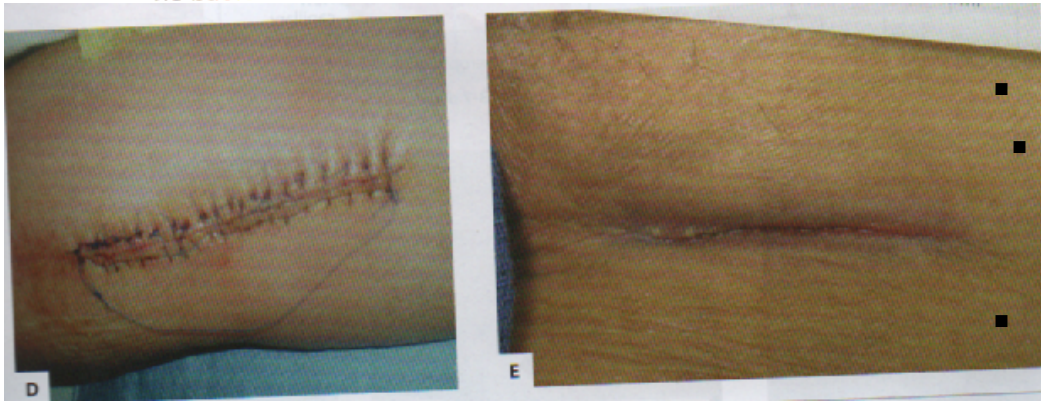
Abnormalities chronic dermal ulcers

Category	Defect	Ref.
Provisional matrix	Rapidly degrading provisional matrix	4, 5
Extracellular matrix	Increased neutrophil elastase	4
Wound fluid	Increased gelatinolytic activity and superactive gelatinases	23, 24, 180
	Decreased α-1antitrypsin activity	5, 207
	Decreased levels of TIMPs	28, 86, 200
	Unbalanced MMPs (MMP-2, 8, and 9)	184–186, 189, 220
Bacterial colonization	Prolonged inflammation	31
Bio-burden	Increased levels of inflammatory cytokines (TNFα, IL-1, IL-6)	30
Cellular senescence	Decreased growth capacity of repairing cells	33, 179, 202
	Increased levels of beta-Gal	32
	Decreased response to growth factor stimuli	179, 202
	Upregulation of elastase/matrix degradation	211
Keratinocytes	Impaired keratinocyte activation cycle	170, 172
	Increased expression of collagenases	14, 188, 191, 192
	Expression of stromelysin 1 and 2	20, 194

Type of healing response

Primary intention

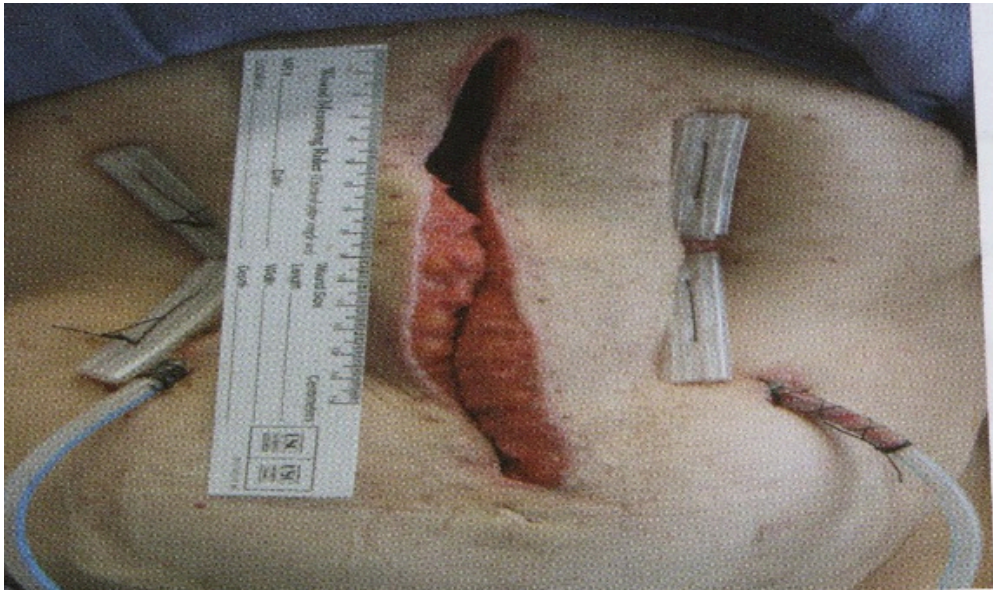




- Clean Incision surgical
- No contamination from bacteria, yeast, forein bodies
- mInimal tissue loss

Classifications of healing response

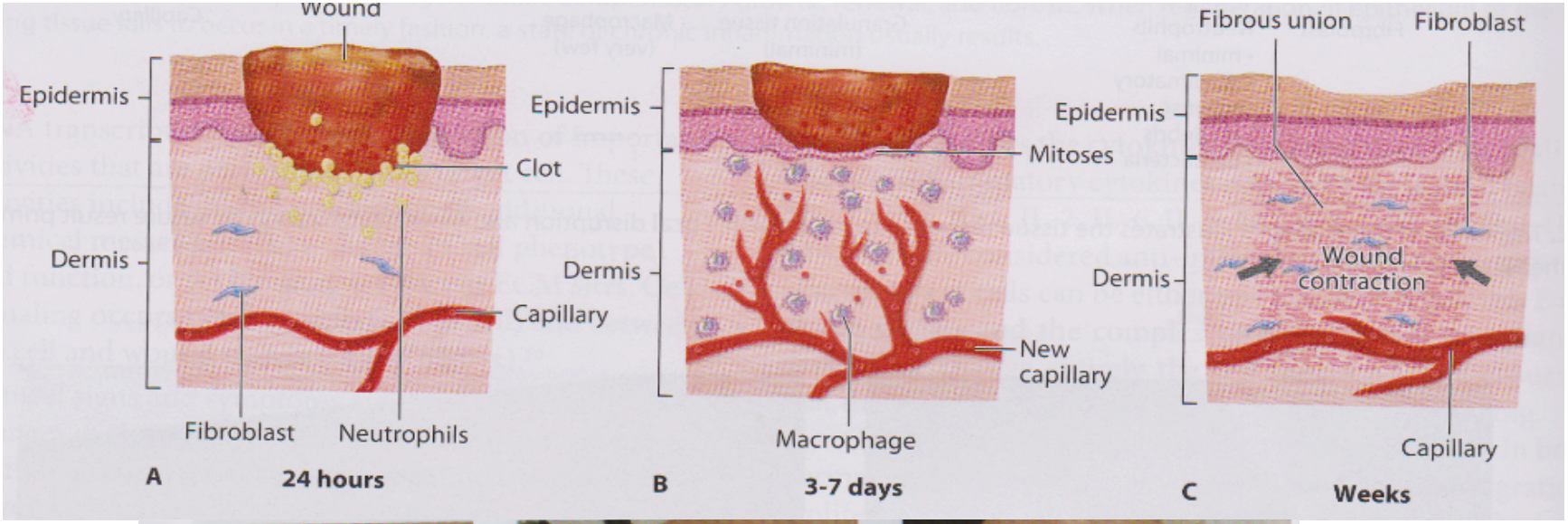
Delayed primary intention

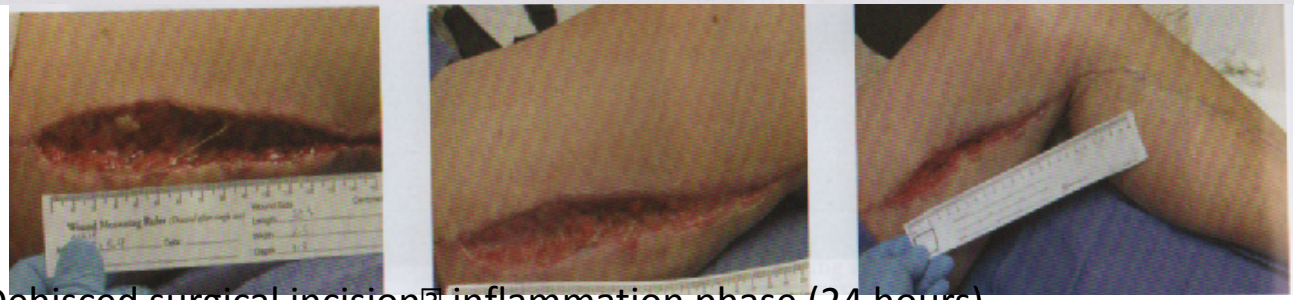


- Wound edges are not approximated the precence pathogen or debris, abcess or extensive tissue loss
- Delayed surgical closure after surgical removal granuloma, abcess, debris

Classifications of healing response

Healing by secondary intentions

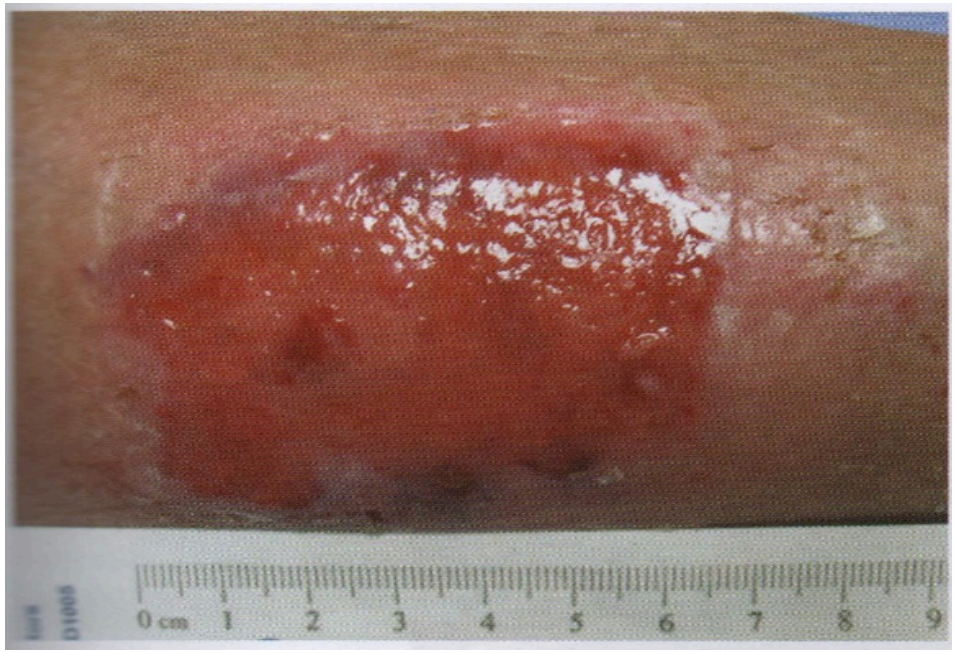




A. Dehisced surgical incision inflammation phase (24 hours)
B. Phase proliferatif with granulation visible through the wound bed (2 weeks)
C. Remodelling phase (2 weeks later) completed closure by secondary intention without surgical intervention

Classifications of healing response

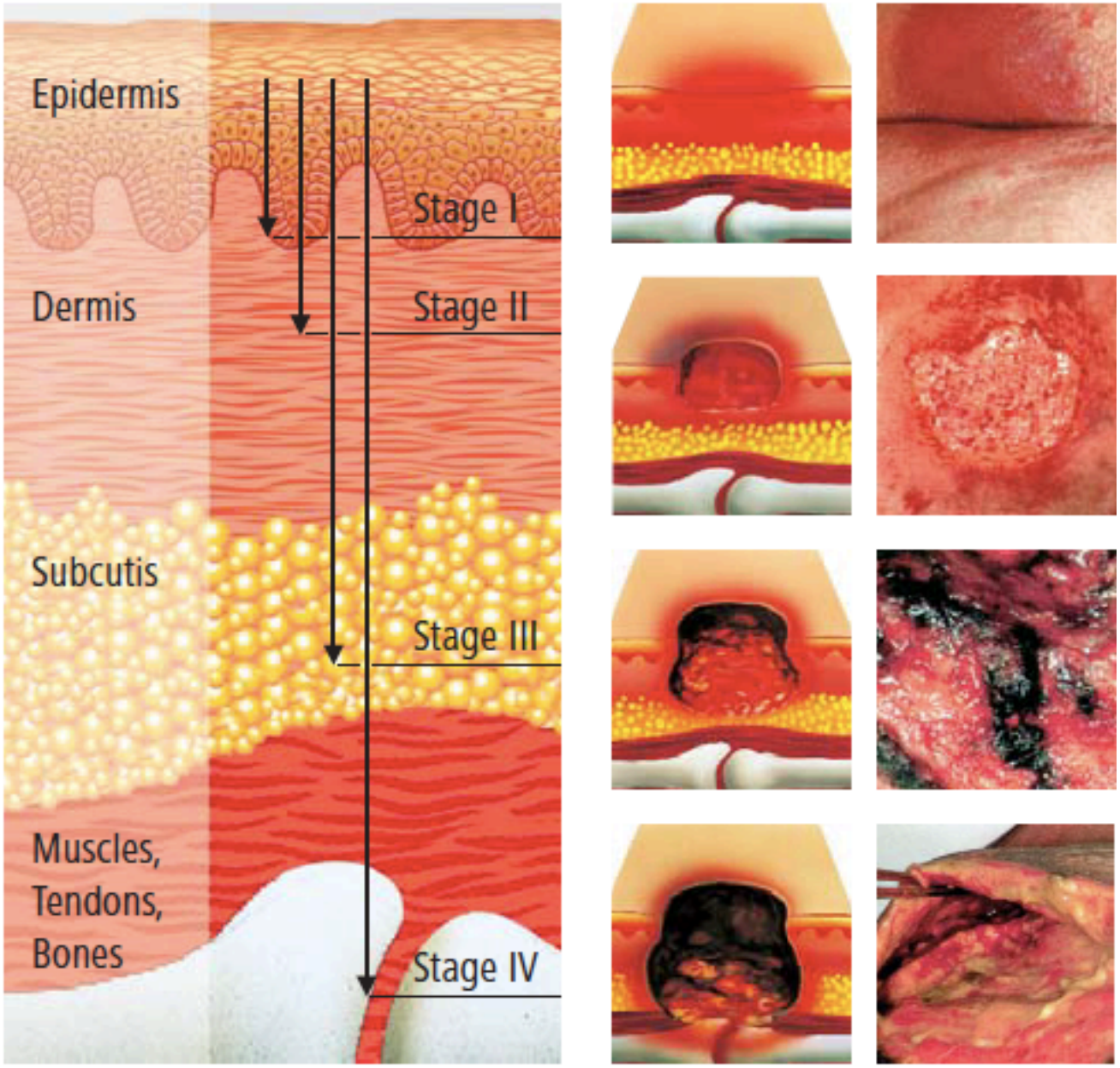
Partial thickness wounding



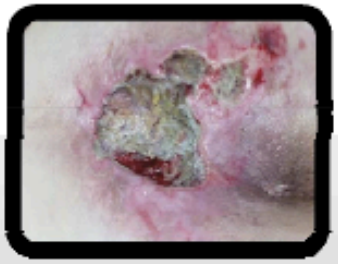
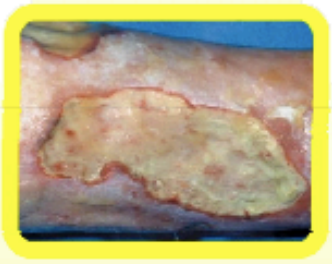
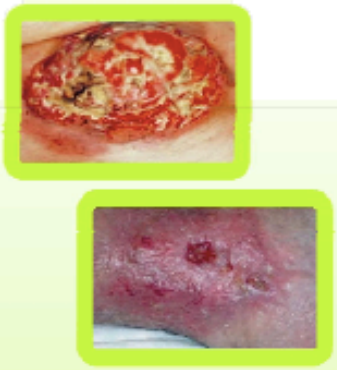
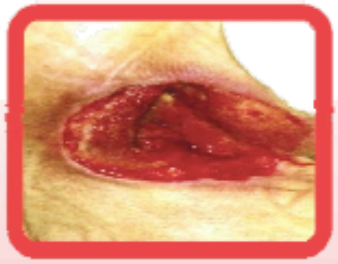
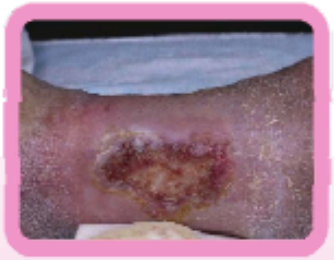
Loss or partial loss of epidermis or epidermis & superficial dermis the basement membrane is intact & hypodermis is not exposed

Pressure Ulcer Classification system (International NPUAP/EPUAP)

- St 1: Non-blanchable erythema
  - Intact skin, painful, firm, soft, warmer or cooler.
- St 2: Partial thickness skin loss
  - Partial-thickness loss of dermis, red pink wound bed, wo slough.
- St 3: Full thickness skin loss
  - Subcutaneous fat may be visible, but bone, tendon/ muscle are not exposed.
- St4: Full thickness tissue loss
  - Full-thickness tissue loss where exposed bone, muscle, tendon., slough/eschar.
- Unstageable: depth unknown
  - Base of the ulcer is covered by slough and/or eschar in the wound bed.


Epidermis
Dermis
Subcutis
Muscles,
Tendons,
Bones
Stage I
Stage II
Stage III
Stage IV

CLASSIFICATION AND MANAGEMENT OF WOUNDS

Necrotic	Sloughy	Malodorous/ Infected	Granulating	Epithelialisation
				
AIMS OF TREATMENT				
Debride Remove eschar Protect wound	Remove slough Absorb Exudate Provide clean base for granulation tissue Protect wound	Absorb Exudate Treat infection Manage Smell Protect wound	Maintain moisture Promote granulation Provide healthy base for Epithelialisation Protect wound	Maintain Moisture and protect
TREATMENT CHOICES				
Hydrogels Hydrocolloids Films Desloughing Agents* Enzymes Surgical Debridements	**Low Exudate** Hydrogels Hydrocolloids Low absorbent foams Desloughing Agents **High Exudate** Hydrofibre Alginates Foams Dextranomer agents	**Low Exudate** Antimicrobial Creams Low absorbent foams Silver impregnated dressings **High Exudate** Hydrofibres Alginates Bordered foam dressings	**Low Exudate** Hydrogels Hydrocolloids Low absorbent foams Non adherent foams **High Exudate** Hydrofibres Alginates Bordered foam dressings	Hydrogels Films Low absorbent foams Non adherent foams

Conclusion

- Skin complex multilayer organ that function to protective organ & maintain homeostasis
- Injury process can stimulate that cell to accomplish repair& regeneration
- Acute wound healing phases hemostasis, inflammation, proliferation & remodeling
- Inflammation phases subdivided 3 overlapping phases
- Acute & chronic wound are different but overlap
- Chronic wound in one way relationship between different phase is lost
- Chronic wound complex result of ischemic, pressure, infection healing dependent of this factor
- Classification of wound management