WOUND HEALING

Anatomy of Skin

• **Epidermis:**

– composed of several thin layers:
stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, stratum corneum

– the several thin layers of the epidermis contain the following:

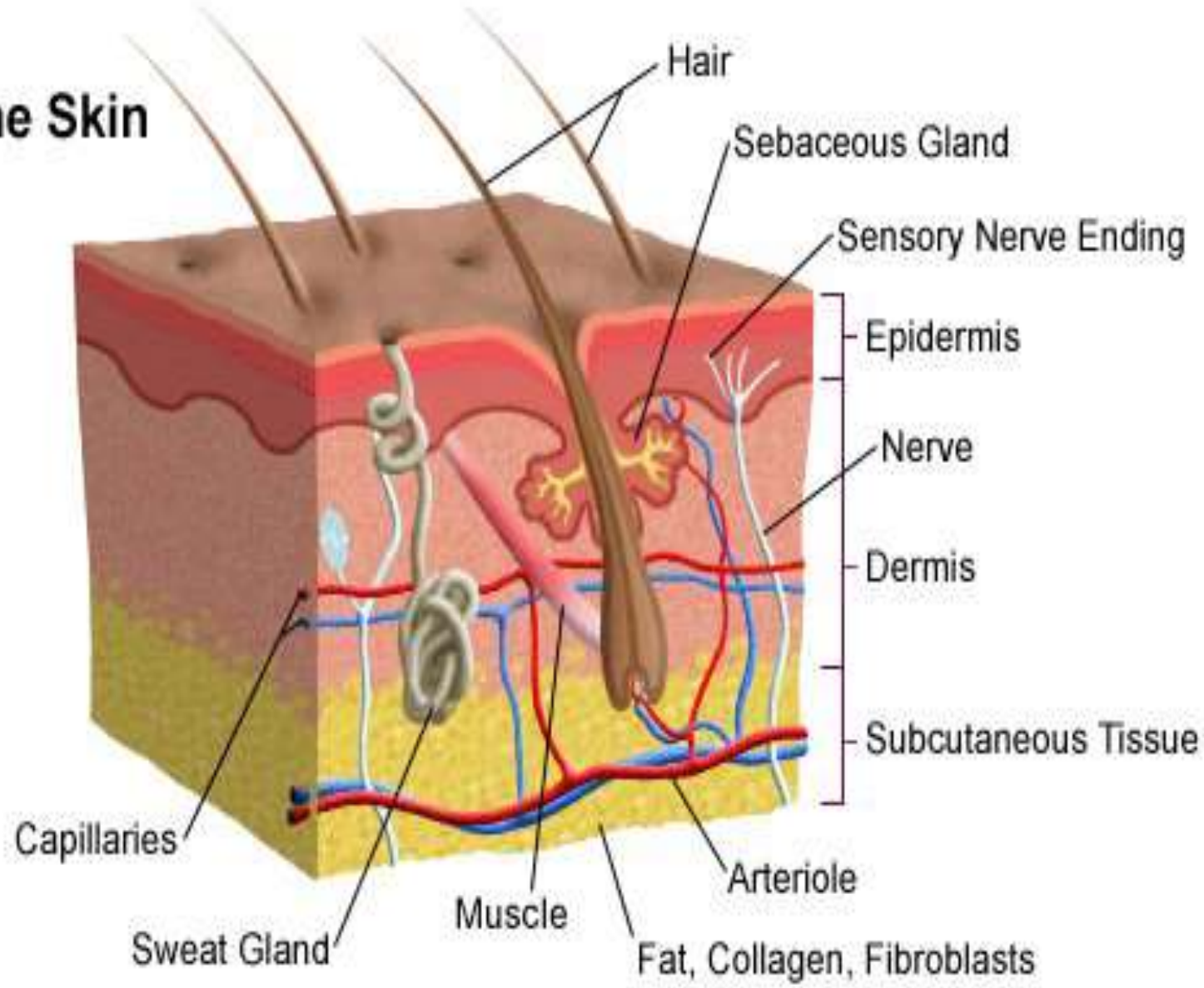
a) melanocytes, which produce melanin, a pigment that
gives skin its color and protects it from the damaging effects of ultraviolet radiation.

b) keratinocytes, which produce keratin, a water Repellent protein that gives the epidermis its tough, Protective quality.

Dermis:
– composed of a thick layer of skin that contains collagen
and elastic fibers, nerve fibers, blood vessels, sweat and sebaceous glands, and hair follicles.

Subcutaneous Tissue:
– composed of a fatty layer of skin that contains blood vessels, nerves, lymph, and loose connective tissue filled with fat cells

The Skin


Hair
Sebaceous Gland
Sensory Nerve Ending
Epidermis
Nerve
Dermis
Subcutaneous Tissue
Capillaries
Sweat Gland
Muscle
Arteriole
Fat, Collagen, Fibroblasts

Function of Integument

- **Protection:**

– intact skin prevents invasion of the body by bacteria

- **Thermoregulation:**

• intact skin facilitates heat loss and cools the

body when necessary through the following

processes:

– production of perspiration which assists in cooling the body through evaporation

– production of vasodilatation which assists in facilitating heat loss from the body through radiation and conduction

– production of vasoconstriction which assists in preventing heat loss from the body through radiation and conduction

Fluid and Electrolyte Balance:

– intact skin prevents the escape of water and electrolytes from the body

- **Vitamin D Synthesis**
- **Sensation**
- **Psychosocial**

‘God heals, and the doctor takes the fees ”

Benjamin Franklin(American Statesman, scientist, Philosopher)

wound

- A wound is a break in the integrity of the skin or tissues often which may be associated with disruption of the structure and function. (SRB 4th edition) – A cut or break in the continuity of any tissue, caused by injury or operation

Classification of Wounds

- • 1) **Clean Wound:**
- – Operative incisional wounds that follow nonpenetrating
- (blunt) trauma.
- • 2) **Clean/Contaminated Wound:**
- – uninfected wounds in which no inflammation is
- encountered but the respiratory, gastrointestinal,
- genital, and/or urinary tract have been entered.
- • 3) **Contaminated Wound:**
- – open, traumatic wounds or surgical wounds involving a
- major break in sterile technique that show evidence of
- inflammation.
- • 4) **Infected Wound:**
- – old, traumatic wounds containing dead tissue and
- wounds with evidence of a clinical infection (e.g.,
- purulent drainage).

Wound healing

- Healing is the body's response to injury in an attempt to restore normal structure and function. • The process of healing involves 2 distinct processes:

- A. REGENERATION
- B. REPAIR

•REGENERATION – Regeneration: Is when healing takes place by proliferation of parenchymal cells and usually results in complete restoration of the original tissues. – The goal of all surgical procedures is regeneration which returns the tissues to their normal microstructure and function.

• REPAIR – Repair: It is a healing outcome in which tissues do not return to their normal architecture and function. – Repair typically results in the formation of scar tissue.

Classification of Wounds Closure

- **Healing by Primary Intention:**
- – All Layers are closed. The incision that heals by first
- intention does so in a minimum amount of time, with no
- separation of the wound edges, and with minimal scar
- formation.
- • **Healing by Secondary Intention:**
- – Deep layers are closed but superficial layers are left to
- heal from the inside out. Healing by second is
- appropriate in cases of infection, excessive trauma,
- tissue loss, or imprecise approximation of tissue.
- • **Healing by Tertiary Intention:**
- – Also referred to as delayed primary closure.

HEALING OF WOUNDS BY PRIMARY INTENTION

- Healing of wound with following characteristics: Clean and uninfected Surgically incised Without much loss of cells and tissue Edges of wound are approximated by surgical sutures. Wounds with opposed edges Primary union
- HEALING OF WOUNDS BY PRIMARY INTENTION – The incision causes death of a limited number of epithelial cells and connective tissue cells disruption of epithelial basal membrane continuity – The narrow incisional space immediately fills with clotted blood containing fibrin and blood cells; dehydration of the surface clot forms the well known scab that covers the wound.

HEALING BY PRIMARY INTENTION

•WITHIN 24 HOURS – Neutrophils appear at margins of incision, moving toward fibrin clot – Epidermis at its cut edges thickens as a result of mitotic activity of basal cells – Within 24 to 48 hours, spurs of epithelial cells from the both edges migrate and grow along the cut margins of the dermis, depositing BM components as they move. They fuse in the midline beneath the surface scab, thus producing a continuous but thin epithelial layer.

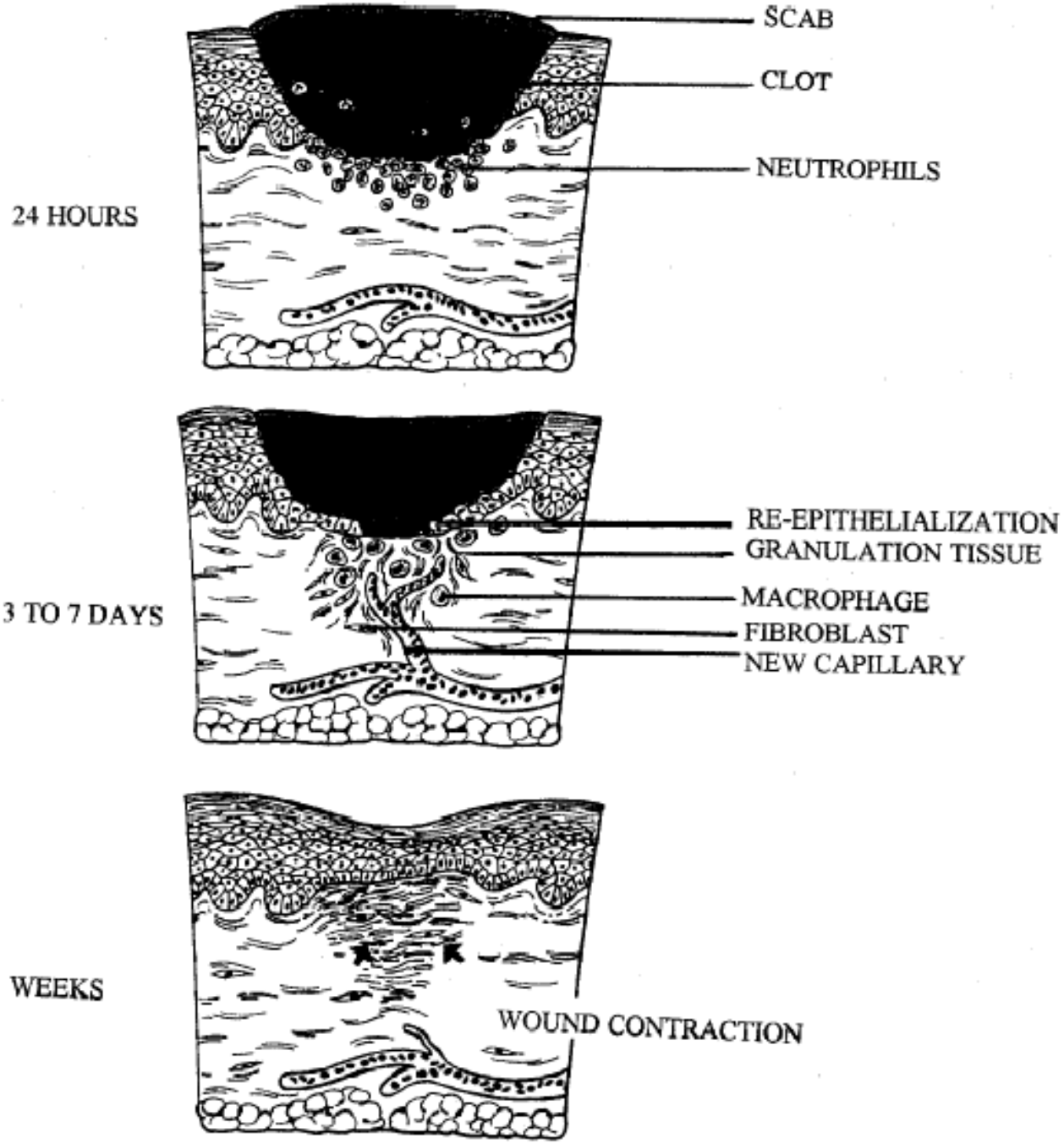
- BY DAY 3 – Neutrophils replaced by macrophages – Granulation tissue progressively invades incision space – Collagen fibers are now present in the margins of the incision, but at first these are vertically oriented. – Epithelial cell proliferation continues, thickening epidermal covering layer
- BY DAY 5– Incisional space is filled with granulation tissue – Neovascularisation is maximal – Collagen fibrils become more abundant and begin to bridge incision – The epidermis recovers its normal thickness, and differentiation of surface cells yields a mature epidermal architecture with surface keratinizatio

•DURING THE SECOND WEEK – Continued accumulation of collagen and proliferation of fibroblasts – Leukocytic infiltrate, edema, and increased vascularity have largely disappeared.

BY THE END OF THE FIRST MONTH – Scar comprises a cellular connective tissue devoid of inflammatory infiltrate, covered now by intact epidermis. – Dermal appendages that have been destroyed in the line of the incision are permanently lost. – Tensile strength of the wound increases thereafter, but it may take months for the wounded area to obtain its maximal strength.

HEALING BY SECONDARY INTENTION

Wounds with separated edges – Secondary union – When there is more extensive loss of cells and tissue – Regeneration of parenchymal cells cannot completely reconstitute the original architecture. – Abundant granulation tissue grows in from the margin to complete the repair.


SCAB
CLOT
NEUTROPHILS
24 HOURS
RE-EPITHELIALIZATION
GRANULATION TISSUE
MACROPHAGE
FIBROBLAST
NEW CAPILLARY
3 TO 7 DAYS
WEEKS
WOUND CONTRACTION

DIFFERNCES BETWEEN HEALING BY PRIMARY AND SEONDARY INTENTION

- DIFFERNCES BETWEEN HEALING BY PRIMARY AND SEONDARY INTENTION Secondary healing differs from primary healing in several respects: Inflammatory reaction is more intense Much larger amounts of granulation tissue are formed Wound contraction occurs in large surface wounds Substantial scar formation and thinning of the epidermis occurs

PHASES OF WOUND HEALING

- PHASES OF WOUND HEALING – Normal wound healing follows a predictable pattern that can be divided into overlapping phases: –

- Hemostasis and inflammation –
- Proliferation –
- Maturation and remodeling

PHASES OF WOUND HEALING

•HEMOSTASIS AND INFLAMMATION – Hemostasis precedes and initiates inflammation, with the ensuing release of chemotactic factors from the wound site. – Wounding > disrupts tissue integrity > division of blood vessels and direct exposure of extracellular matrix to platelets >platelet aggregation, degranulation, and activation of the coagulation cascade

PHASES OF WOUND HEALING

HEMOSTASIS AND INFLAMMATION – Platelet -granules release a number of wound-active substances, such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF), platelet-activating factor, fibronectin, and serotonin. – In addition to achieving hemostasis, the fibrin clot serves as scaffolding for the migration into the wound of inflammatory cells such as polymorphonuclear leukocytes (PMNs, neutrophils) and monocytes

HEMOSTASIS AND INFLAMMATION

•PMN: POLYMORPHONEUCLEAR LEUKOCYTES – The first infiltrating cells to enter the wound site, peaking at 24 to 48 hours – Stimulated by: – Increased vascular permeability – local prostaglandin release – The presence of chemotactic substances(co,IL- 1,TNF,TGF beta, PF 4,bacterial product)

PMN: POLYMORPHONEUCLEAR LEUKOCYTES – Primary role: – Phagocytosis of bacteria and tissue debris – Major source of cytokines early during inflammation, especially TNF- alpha – Release proteases such as collagenases, which participate in matrix and ground substance degradation in the early phase of wound healing. – No role in collagen deposition or acquisition of mechanical wound strength.

- MACROPHAGE – The second population of inflammatory cells that invades the wound. – Derived from circulating monocytes, macrophages achieve significant numbers in the wound by 48 to 96 hours postinjury. – Present until wound healing is complete

- LYMPHOCYTE – Less numerous than macrophages – T-lymphocyte numbers peak at about 1 week postinjury – It bridge the transition from the inflammatory to the proliferative phase of healing. – The role in wound healing is not fully defined – Believed to play an active role in the modulation of the wound environmen

PROLIFERATION

- PROLIFERATION – Is the second phase of wound healing and roughly spans days 4 through 12 – It is during this phase that tissue continuity is re- established. – Fibroblasts and endothelial cells are the last cell populations to infiltrate the healing wound. – The strongest chemotactic factor for fibroblasts is PDGF

PROLIFERATION

- FIBROBLASTS – Upon entering the wound environment, recruited fibroblasts first need to proliferate – Then become activated by the cytokines and growth factors released from wound macrophages. – Primary function is matrix synthesis remodeling – Fibroblasts isolated from wounds synthesize more collagen than non wound fibroblasts – They proliferate less, and they actively carry out matrix contraction. – Cytokine-rich wound environment and lactate plays a significant role in this phenotypic alteration and activation.

- ENDOTHELIAL CELLS – Endothelial cells migrate from intact venules close to the wound. – Proliferate extensively during this phase of healing. – These cells participate in the formation of new capillaries (angiogenesis) – Their migration, replication, and new capillary tubule formation are under the influence of such cytokines and growth factors as TNF-, TGF, and VEGF

- MATRIX SYNTHESIS Collagen biochemistry – Its deposition, maturation, and subsequent remodeling are essential to the functional integrity of the wound. – Type I collagen is the major component of extracellular matrix in skin. – Type III, which is also normally present in skin, becomes more prominent and important during the repair process.

- MATRIX SYNTHESIS – Collagen synthesis is highly dependent on systemic factors such as : – adequate oxygen supply, – the presence of sufficient nutrients (amino acids and carbohydrates) – cofactors (vitamins and trace metals), and – the local wound environment (vascular supply and lack of infection

PROLIFERATION

- PROTEOGLYCAN SYNTHESIS – Glycosaminoglycans comprise a large portion of the "ground substance" that makes up granulation tissue. – The major glycosaminoglycans present in wounds are dermatan and chondroitin sulfate. – It is thought that the assembly of collagen subunits into fibrils and fibers is dependent on the lattice provided by the sulfated proteoglycans. – As scar collagen is deposited, the proteoglycans are incorporated into the collagen scaffolding. – With scar maturation and collagen remodeling, the content of proteoglycans gradually diminishes.

PROLIFERATION

- MATURATION AND REMODELING – Begins during the fibroplastic phase, and is characterized by a reorganization of previously synthesized collagen. – The net wound collagen content is the result of a balance between collagenolysis and collagen synthesis. – Collagenolysis is the result of collagenase activity, a class of matrix metalloproteinases that require activation

MATURATION AND REMODELING

- MATURATION AND REMODELING – Fibril formation and fibril cross-linking result in decreased collagen solubility, increased strength, and increased resistance to enzymatic degradation of the collagen matrix – Scar remodeling continues for many (6 to 12) months postinjury, gradually resulting in a mature, avascular, and acellular scar. – The mechanical strength of the scar never achieves that of the uninjured tissue.

•**EPITHELIALIZATION** – Is a process restoring external barrier characterized primarily by proliferation and migration of epithelial cells adjacent to the wound. – Begins within 1 day of injury and is seen as thickening of the epidermis at the wound edge. – Marginal basal cells at the edge of the wound lose their firm attachment to the underlying dermis, enlarge, and begin to migrate across the surface of the provisional matrix.

EPITHELIALIZATION – Re-epithelialization is complete in less than 48 hours in the case of approximated incised wounds. – Take substantially longer in the case of larger wounds, in which there is a significant epidermal/dermal defect. – If only the epithelium and superficial dermis are damaged, then repair consists primarily of re-epithelialization with minimal or no fibroplasia and granulation tissue formation

CLINICAL CONSIDERATIONS EXCESSIVE HEALING

- EXCESSIVE SCAR FORMATION – Excessive healing results in a raised, thickened scar, with both functional and cosmetic complications. – If it stays within margins of wound it is hypertrophic. Keloids extend beyond the confines of the original injury. – Dark skinned, ages of 2-40. Wound in the parasternal or deltoid area, wounds that cross langerhans lines.

- KELOIDS AND HYPERTROPHIC SCARS
- . KELOIDS AND HYPERTROPHIC SCARS
- KELOID HYPERTROPHIC SCAR

Factors affecting Wound Healing

- Infection
- Nutrition (↓proteins, vit.C, vit.A, Zn, Fe)
- Steroids / Adriamycin
- Mechanical factors

  (a) Increased pressure/torsion)

  (b)Ischemia
- Malnutrition
- Advanced age
- Ionising Radiation
- Diabetes Mellitus

Growth Factors affecting Wound Healing at Different Stages

Epithelial Proliferation: EGF TGFa KGF HGF

Monocyte chemotaxis: PDGF FGF TGFb

Fibroblast Migration: PDGF FGF TGFb

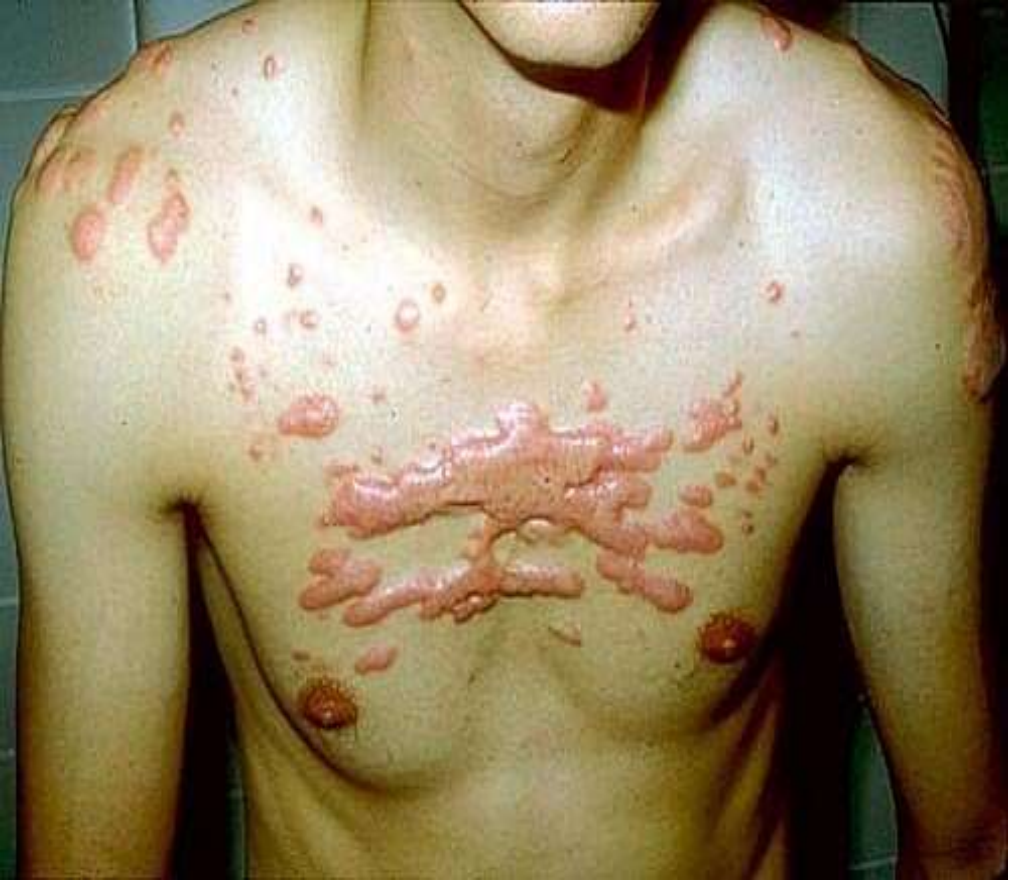
Fibroblast Proliferation: PDGF FGF EGF TNF

Angiogenesis: Collagen VEGF Ang FGF

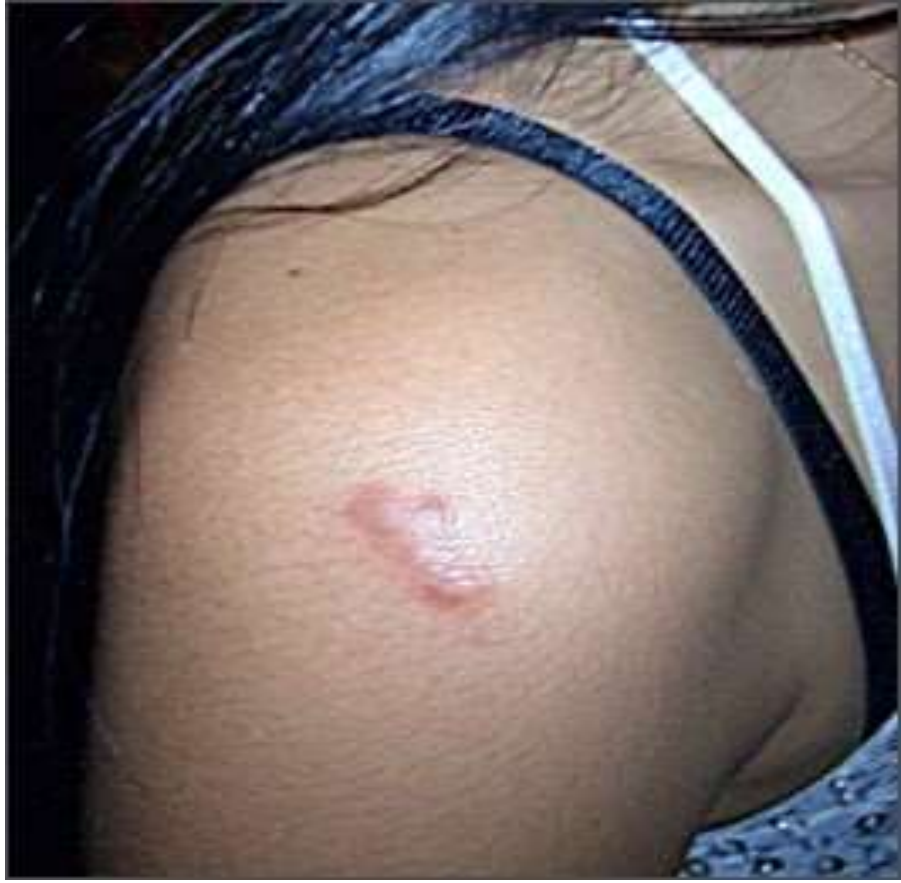
Synthesis: TGFb PDGF

Collagen secretion: PDGF FGF EGF TNF

TGFb inhibits



Keloid



Hypertrophic scar