NEW YORK INSTITUTE OF TECHNOLOGY

College of Osteopathic Medicine

HEALING AND REPAIR

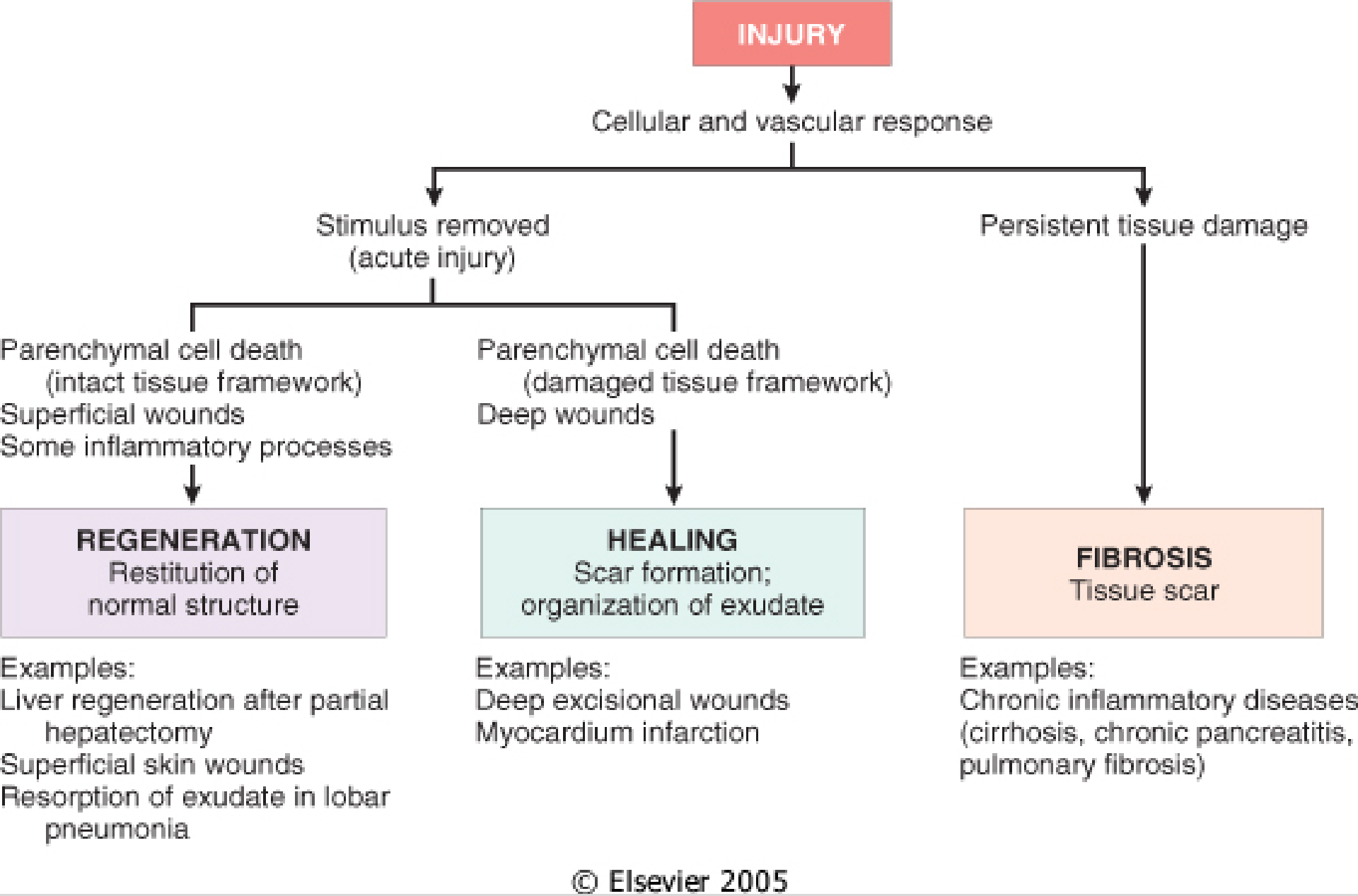
FOUNDATIONS OF OSTEOPATHIC MEDICINE

Maria M. Plummer, M.D.
Associate Professor
Department of Clinical Specialties
Rockefeller Room #306
mplummer@nyit.edu

Do.
Make.
Heal.
Innovate.
Reinvent the Future.

Session Objectives

- 1. Discuss and explain the basic principles of **healing, repair, and regeneration in regards to different types of tissues (labile, stable, permanent), and differentiate some important growth factors (e.g., PDGF, VEGF, TGF-beta, FGF-2) which mediate the healing/repair process.**
- 2. Describe **granulation tissue** and discuss the role of **angiogenesis** and the **importance of connective tissue elements, which include collagen**, in healing and repair.
- 3. Discuss and compare **healing by first and second intention.**
- 4. Discuss/describe **wound contraction and connective tissue remodeling.**
- 5. Give examples of tissue and organs in the process of healing/repair and **describe factors which deter that process**.



HEALING/REPAIR

- Tissue repair – restoration of tissue architecture and function after injury
- Proliferation of remnants of injured tissue, vascular endothelial cells, fibroblasts
- Repair of damaged tissue
  - Regeneration – restores normal cells
  - Laying down scar formation (collagen deposition)
- Healing with **scar formation when the extracellular matrix framework is damaged**
- Pure repair with scar formation mostly occurs in tissues which do not have regenerative abilities (permanent tissue)

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020,Ch. 3

REGENERATION

- Replacement of damaged or dead cells/tissue by cells of the same type
- May occur by proliferation of differentiated cells that survive injury and retain capacity to proliferate (e.g., hepatocytes)
- May occur when tissue stem cells and their progenitors contribute to restoration of damaged tissue (e.g. skin, GI mucosa)
- Tissues with high proliferative capacity
- **Intact basement membrane…and intact immature cells**
- **Must have intact connective tissue scaffold**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Cell types based on proliferation potential

- **Labile cells:** renewing cellular populations…(continuously dividing):
  - Examples: epithelial cells, lymphoid, hematopoietic, GI mucosa
- **Stable Cells:** low rate of proliferation or no proliferation… have the ability to re-enter the cell cycle under specific stimuli (quiescent):
  - Examples: parenchymal cells, liver, kidney, smooth muscle cells, osteoblasts, chondroblasts, endothelial cells, smooth muscle, fibroblasts
- **Permanent Cells:** terminally differentiated, (nondividing):
  - Examples: neurons, cardiac muscle, skeletal muscle

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

GROWTH FACTORS

- Proteins which regulate cell proliferation
- Macrophages important sources - may also come from epithelial and stromal cells
- Function as ligands that bind to specific receptors which deliver signals to target cells
- Signals stimulate transcription of genes that may be silent in resting cells, including genes that control cell cycle entry and progression

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

IMPORTANT GROWTH FACTORS

- PDGF causes migration and proliferation of fibroblasts, smooth muscle cells, monocytes to inflammatory areas and healing skin wounds
- VEGF important in **new blood vessel formation (angiogenesis),** promotes angiogenesis in chronic inflammation, wound healing, and tumors
- FGF-2 contributes to re-epithelization of skin wounds, induces new blood vessel formation, etc.
- **TGF-beta is potent fibrogenic agent** - stimulates fibroblast chemotaxis, enhances production of collagen, fibronectin, and proteoglycans; inhibits collagen degradation, anti-inflammatory

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Growth Factor	Sources	Functions
Epidermal growth factor (EGF)	Activated macrophages, salivary glands, keratinocytes, many other cells	Mitogenic for many cell types; stimulates epithelial cell migration; stimulates formation of granulation tissue
Transforming growth factor-α (TGF-α)	Activated macrophages, keratinocytes, many other cells	Stimulates proliferation of hepatocytes and many other epithelial cells
Hepatocyte growth factor (HGF) (scatter factor)	Fibroblasts, stromal cells in the liver, endothelial cells	Enhances proliferation of hepatocytes and other epithelial cells; increases cell motility
Vascular endothelial growth factor (VEGF)	Mesenchymal cells	**Stimulates proliferation of endothelial cells; increases vascular permeability**
Platelet-derived growth factor (PDGF)	Platelets, macrophages, endothelial cells, smooth muscle cells, keratinocytes	**Chemotactic for neutrophils, macrophages, fibroblasts, and smooth muscle cells; activates and stimulates proliferation of fibroblasts, endothelial cells, and other cells; stimulates ECM protein synthesis**
Fibroblast growth factors (FGFs) including acidic (FGF-1) and basic (FGF-2)	Macrophages, mast cells, endothelial cells, many other cell types	**Chemotactic and mitogenic for fibroblasts; stimulates angiogenesis and ECM protein synthesis**
Transforming growth factor-β (TGF-β)	Platelets, T lymphocytes, macrophages, endothelial cells, epithelial cells, smooth muscle cells, fibroblasts	**Chemotactic for leukocytes and fibroblasts; stimulates ECM protein synthesis; suppresses acute inflammation**
Keratinocyte growth factor (KGF) (i.e., FGF-7)	Fibroblasts	Stimulates keratinocyte migration, proliferation, and differentiation

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Table 1.1

THREE PHASES IN WOUND HEALING

- **Inflammatory phase** – previously discussed- injury…extrinsic coagulation cascade….reflex vasoconstriction…aggregation of platelets...release of PDGF…chemotaxis…vasodilatation…mediated by prostaglandins….acute and chronic response
- **Proliferation phase**
  - granulation tissue formation
  - proliferation and migration of connective tissue cells
  - re-epithelization of wound surface
- **Maturation phase**
  - scar tissue (decreased cells, decreased vessels, increased collagen): ECM deposition, tissue remodeling, wound contraction

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

REPAIR BY CONNECTIVE TISSUE DEPOSITION (SCAR)

- Inflammation
- Angiogenesis
- Migration and proliferation of fibroblasts
- Scar formation
- Connective tissue remodeling
- Prototype – skin
- **Most healing is combination of regeneration and repair; depends on ability of tissue cells to proliferate, integrity of ECM, resolution or chronicity of injury or inflammation**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

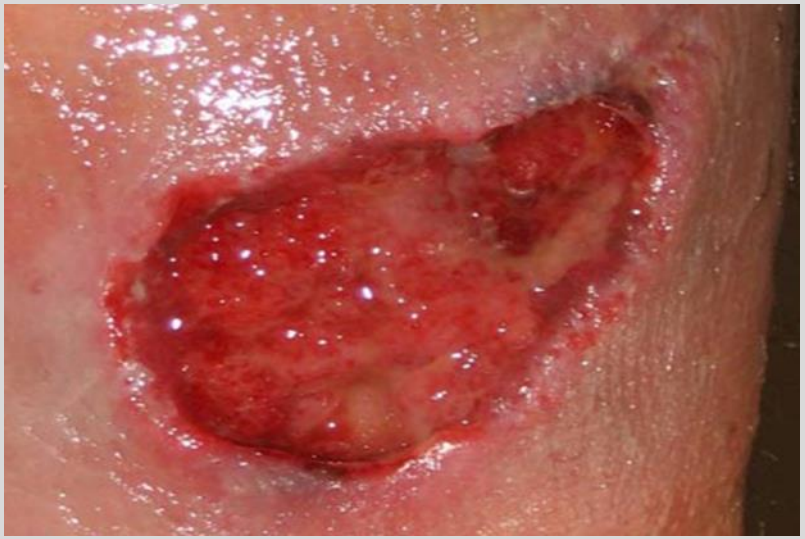
GRANULATION TISSUE

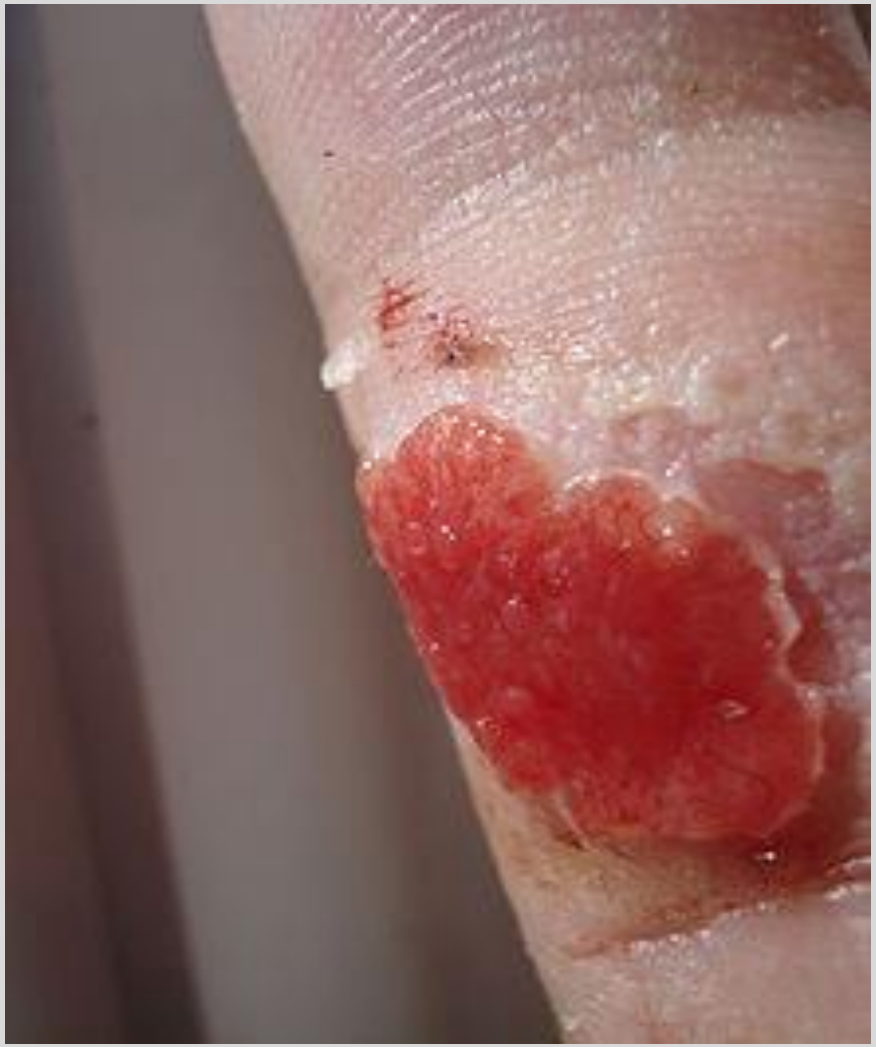
- Migration, **proliferation of fibroblasts and deposition of loose connective tissue along with new vessels and leukocytes (mostly macrophages)**
- New vessel formation - angiogenesis
- Type III collagen (immature) synthesis
- Cellular-cellular interactions via (growth) factors
- Sit in ECM: glycoproteins and proteoglycans
- Glycoproteins- for cross linking of collagen fibers to make stronger
- Proteoglycans – for hydrated gel formation (increased tissue turgor)

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Granulation Tissue: angiogenesis

- Endothelial cells grow extensions (pseudopodia) toward wound site
- The cells divide, and the new cells create a new lumen
- Main control: VEGF-A





http://www2.nau.edu/~bio372-c/class/cancer/angiogen.htmRobbins and Cotran, Pathologic Basis of Disease, 9th edition, 2014, Ch. 3, pgs. 100-110

http://vet.uga.edu/ivcvm/courses/VPAT5200/03_inflammation/09_repair/rep01a.htm

ANGIOGENESIS

- **VEGF** – most important growth factor, especially in chronic inflammation, wound healing, and tumors; promotes vasodilation by stimulating production of NO; also increases vessel permeability

- **VEGF-A -** most important in angiogenesis; stimulates survival, proliferation and motility of endothelial cells, initiating sprouting of new capillaries, promotes vasodilation and contributes to vessel lumen formation

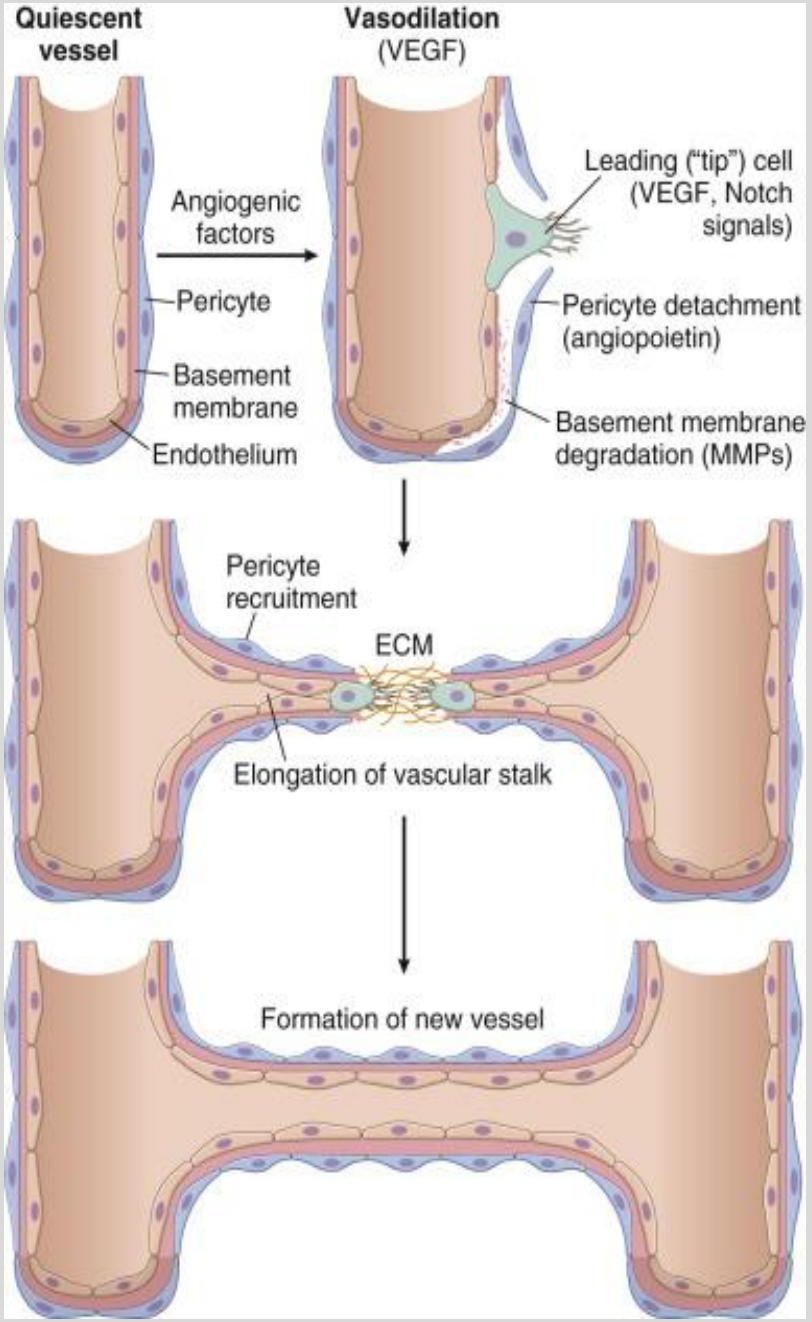
- **FGF-2** stimulates proliferation of endothelial cells and promotes migration of macrophages and fibroblasts to damaged area

- **Newly formed vessels fragile,** stabilization requires recruitment of pericytes and smooth muscle cells and deposition of ECM proteins; angiopoeitins 1 and 2, PDGF, and TGF-beta participate in stabilization and these processes

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Angiogenesis: new blood vessel development from existing vessels

- Pericytes from abluminal surface separate, breakdown basement membrane, form vessel sprout
- Endothelial cells migrate towards angiogenic stimulus (area of tissue injury)
- Endothelial cells proliferate and mature
- Periendothelial cells (pericytes and vascular smooth muscle cells) recruited to form mature vessel



Angiogenesis:
In tissue repair, angiogenesis occurs mainly by sprouting of new vessels.
The newly formed vessel joins up with other vessels (not shown) to form the new vascular bed.
ECM, Extracellular matrix; MMPs, matrix metalloproteinases; VEGF, vascular endothelial growth factor.

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3, Fig. 3.28

CONNECTIVE TISSUE DEPOSITION

- Migration and proliferation **of fibroblasts** into injury site
- **Deposition of ECM proteins produced by these cells**
- Orchestrated by cytokines and GFs which include PDGF, FGF-2, and TFG-beta. Major sources are inflammatory cells, especially M2 macrophages

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, ch. 3

CONNECTIVE TISSUE: FIBROBLASTS

- 48-96 hrs- macrophages are dominant cell
- Controlling fibroblasts: Macrophages
  - Migration by chemokines (TNF, PDGF, TGF-B, FGF),
  - Proliferation by growth factors (PDGF, EGF, TGF-B, FGF, IL-1, TNF)
  - **Fibrinogenesis: TGF-B**
- Fibroblast actions:
  - Create matrix of type III collagen and fibronectin (tensile strength ≈ 10%)
  - **Replaced eventually (3 months) by type I collagen (tensile strength ≈ 70 - 80%)**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

EXTRACELLULAR MATRIX

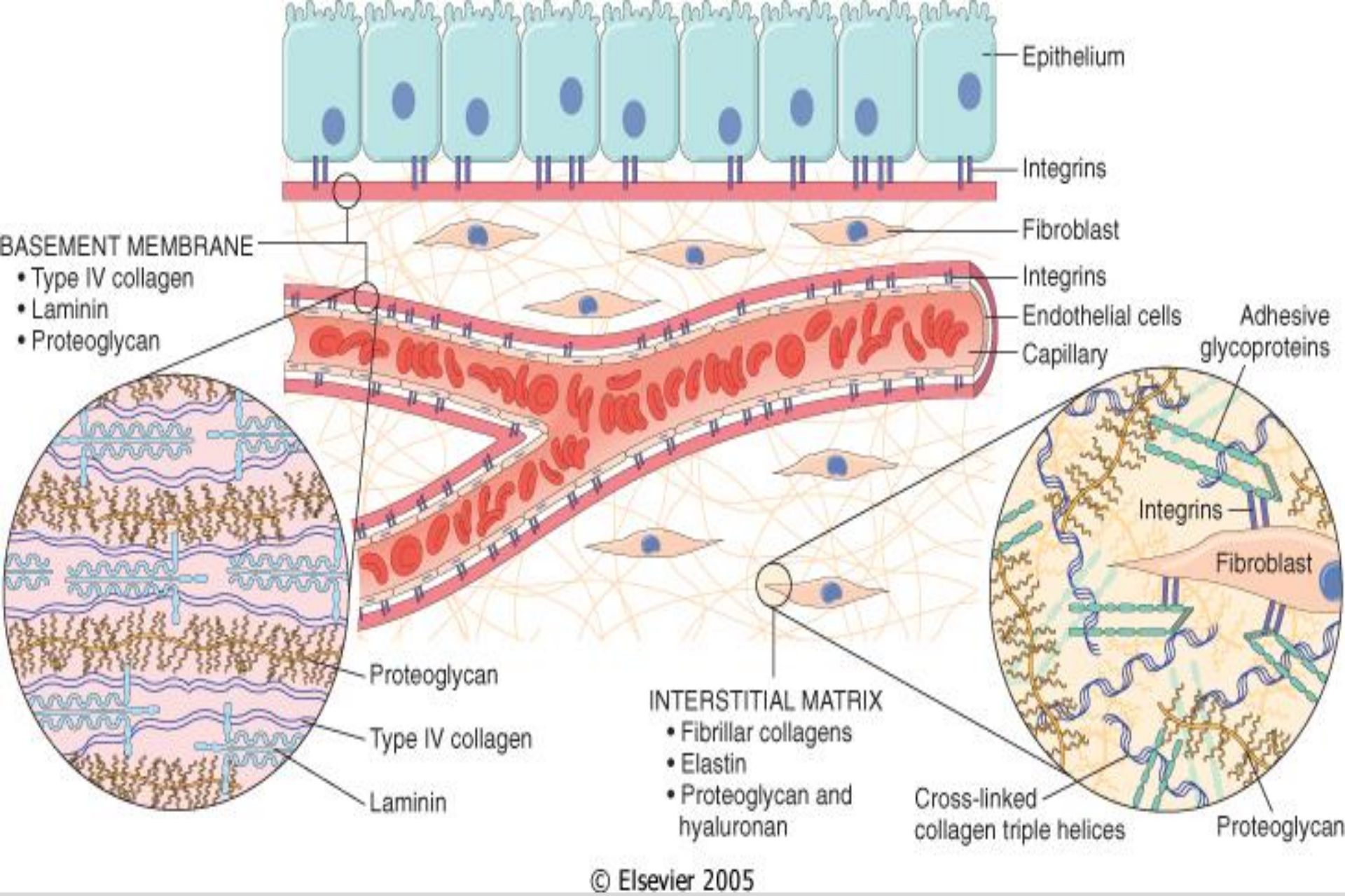
- Provides mechanical support for cells (anchorage and migration)
- Control of cell growth – regulation of cell proliferation via signaling by receptors of the integrin family
- **Scaffold for tissue renewal (must not be destroyed)**
- Establishment of tissue microenvironment – basement membrane is boundary between epithelium and underlying connective tissue

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

TWO FORMS OF ECM

- (1) interstitial matrix - found in spaces between epithelial, endothelial, and smooth muscle cells - made up mostly of collagen, elastin, fibronectin, proteoglycans, and hyaluronan
- (2) basement membrane – closely associated with cell surfaces, made up of mostly type IV collagen (nonfibrillar), laminin, heparin sulfate, and proteoglycans

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3



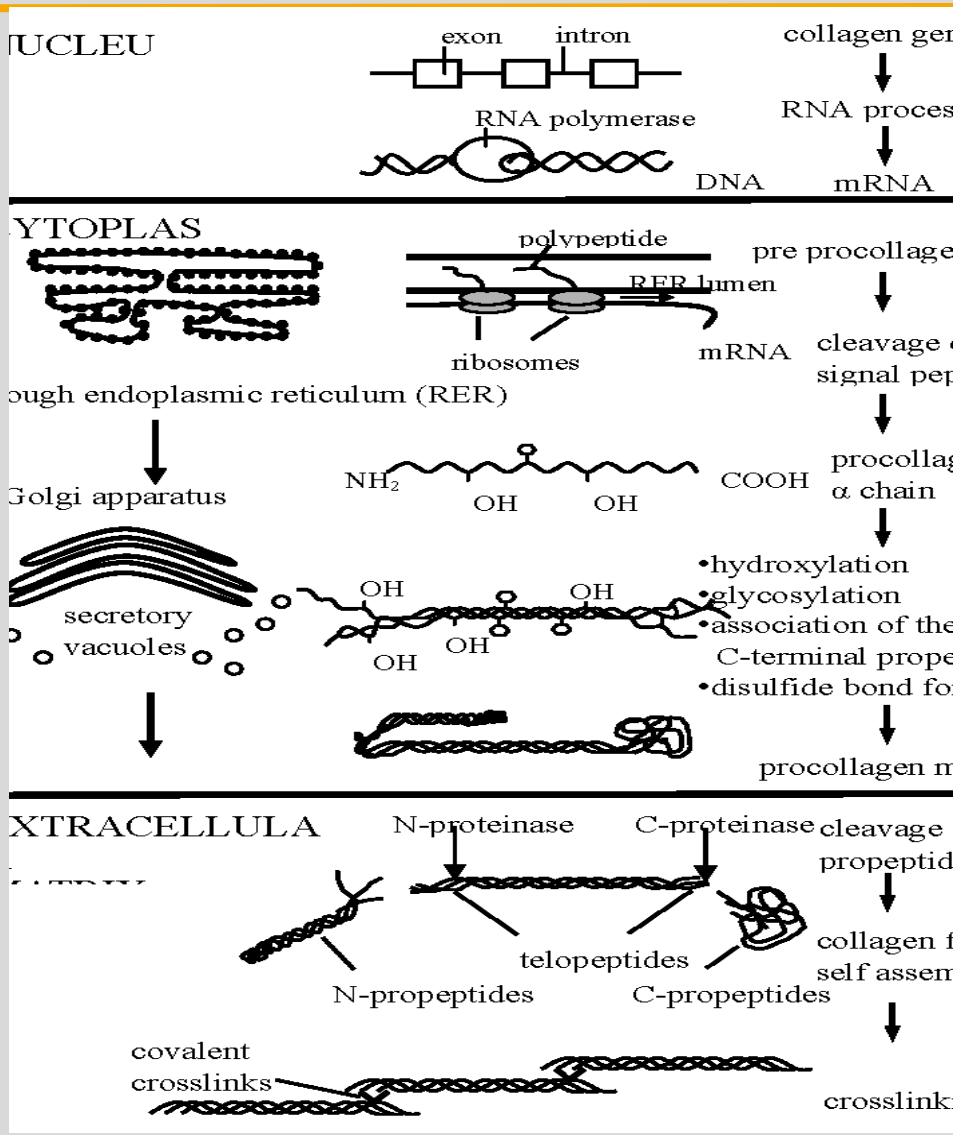
ECM

- **Collagens and elastic fibers** (fibrous structural proteins) – provide tensile strength and recoil
- **Adhesive glycoproteins** – connect matrix elements to one another and to cells
- **Proteoglycans** – provide resilience and lubrication

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

COLLAGEN

- Laid down by fibroblasts in proliferative phase, modified in maturation phase
- Made up of 3 polypeptide chains (alpha chains) forming triple helix
- Preprocollagen to procollagen to collagen
- Extensive posttranslational modification
- Requires Vitamin C (Scurvy)



Robbins and Cotran, Pathologic Basis of Disease, 10th ed. , 2020,Ch. 3

- **COLLAGENS**

- **Type I** - high tensile strength (tendons, bone skin, scars (MATURE)
- **Type II** - cartilage, nucleous pulposus, vitreous humor
- **Type III** - embryonic tissues, pliable organs such as wall of blood vessels, uterus, GI tract. **1st collagen deposited in wound healing**
- **Type IV** - associated with laminin, found in all basement membranes

Collagen Type	Tissue Distribution	Genetic Disorders
FIBRILLAR COLLAGENS		
I	Ubiquitous in hard and soft tissues	Osteogenesis imperfecta; Ehlers-Danlos syndrome—arthrochalasias type I
II	Cartilage, intervertebral disk, vitreous	Achondrogenesis type II, spondyloepiphysea dysplasia syndrome
III	Hollow organs, soft tissues	Vascular Ehlers-Danlos syndrome
V	Soft tissues, blood vessels	Classical Ehlers-Danlos syndrome
IX	Cartilage, vitreous	Stickler syndrome
BASEMENT MEMBRANE COLLAGENS		
IV	Basement membranes	Alport syndrome
OTHER COLLAGENS		
VI	Ubiquitous in microfibrils	Bethlem myopathy
VII	Anchoring fibrils at dermal-epidermal junctions	Dystrophic epidermolysis bullosa
IX	Cartilage, intervertebral disks	Multiple epiphyseal dysplasias
XVII	Transmembrane collagen in epidermal cells	Benign atrophic generalized epidermolysis bullosa
XV and XVIII	Endostatin-forming collagens, endothelial cells	Knobloch syndrome (type XVIII collagen)

Robbins and Cotran, Pathologic Basis of Disease, 9th edition, 2014, Ch. 3, pgs. 100-110

ECM

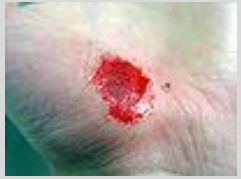
Structural Glycoproteins- responsible for overall structure of scar

- **Fibronectin** – CROSS LINKING
- **Osteonectin** - contributes to tissue remodeling in response to injury
- **Tenacin**…chondrogenesis and osteogenesis; involved in cell adhesion
- **Laminin** - basement membrane, can mediate attachment of cells to connective tissue substrates
- **Cadherins and integrins**…link cell surface with cytoskeleton by binding to actin and intermediate filaments

Proteoglycans and Glycosaminoglycans (GAGS)

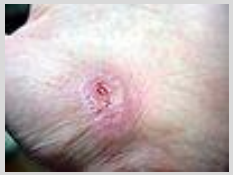
- **GAGS** - long repeating polymers of specific disaccharides; most linked to core protein, forming proteoglycans
  - Regulate connective tissue structure and permeability
  - Four families - heparan sulfate, chondroitin/dermatan sulfate, keratan sulfate, and hyaluronan
  - HA in ECM of different tissues - – binds a lot of water and forms viscous hydrated gel giving cell turgor

Robbins and Cotran, Pathologic Basis of Disease, 9th edition, 2014, Ch. 3, pgs. 100-110

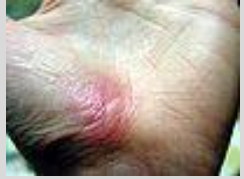


Day 0

Day 2



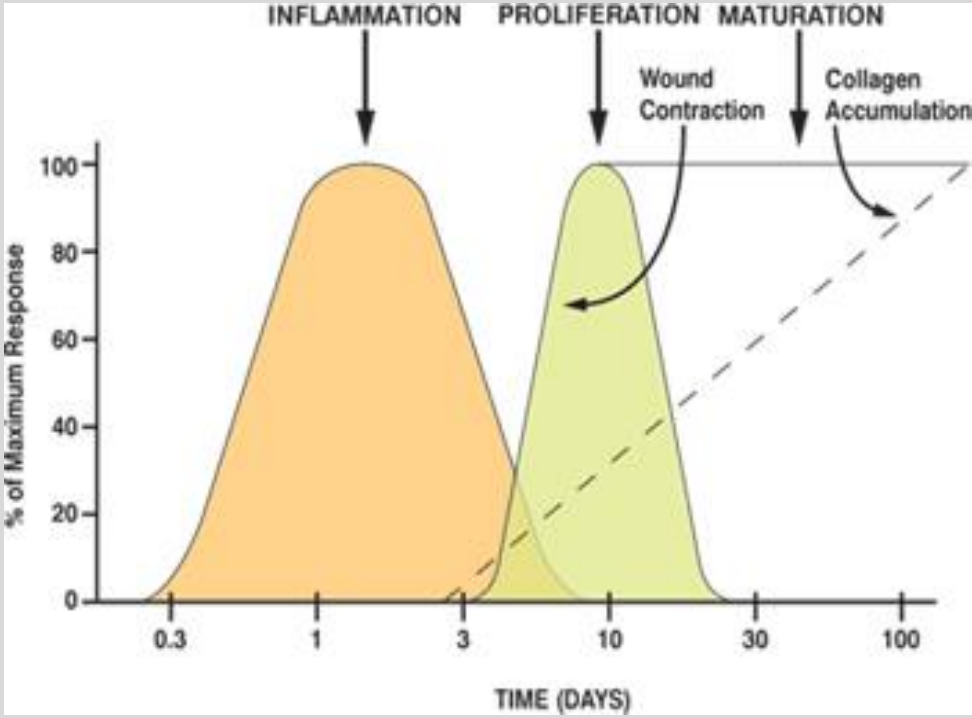
Day 17



Day 30

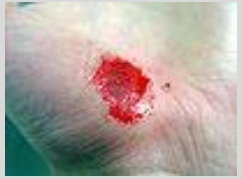
A cutaneous injury

- Three phases of cutaneous wound healing:
  - Phase 1- Inflammation
  - Phase 2- Proliferation
  - Phase 3- Maturation



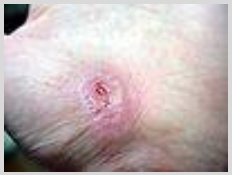
These phases are artificial constructs to help understand what is a dynamic, overlapping process

http://emergencypedia.com/2013/06/10/suturing-knots-and-wound-care/

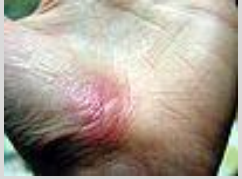


Day 0

Day 2

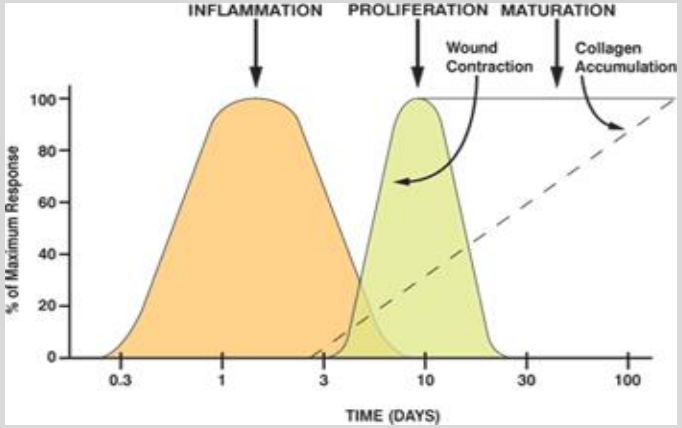


Day 17

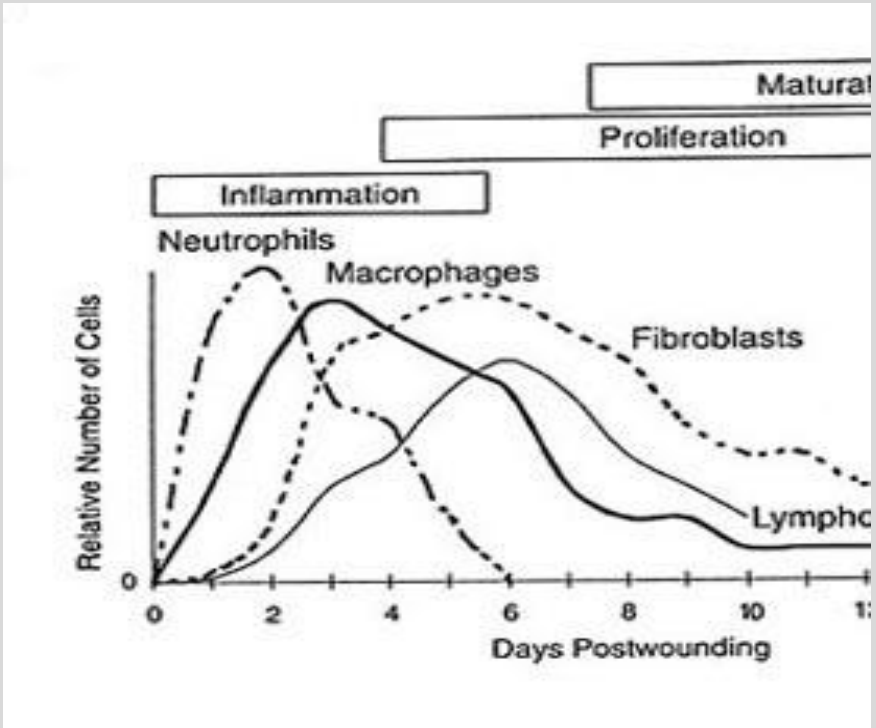


Day 30

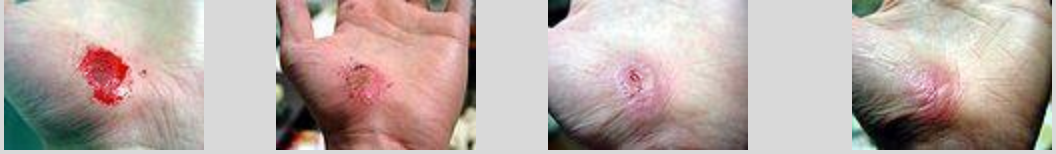
PHASE 1 - INFLAMMATION



- Immediate→ 2-5 days
- Bleeding stops- constriction of vessels, **formation of clot**
- Triggers for acute inflammation:
  - Cell damage, bacteria, and **clotting cascade**
- Acute inflammation- vasodilation, phagocytosis
- Cells- neutrophils then macrophages

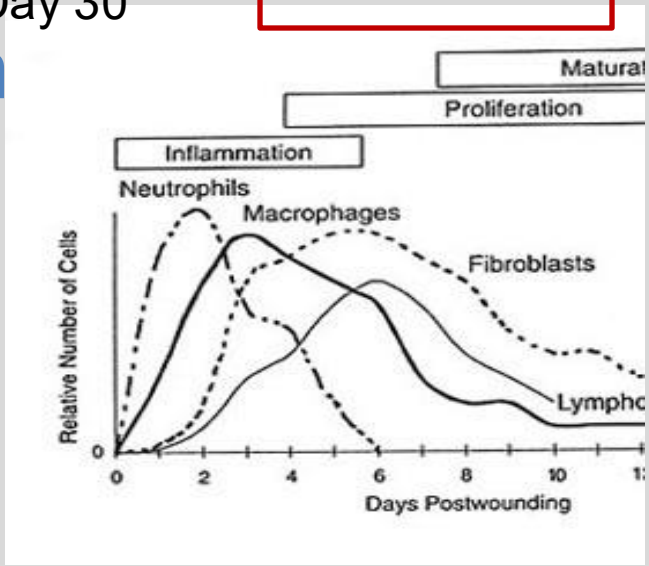


http://emergencypedia.com/2013/06/10/suturing-knots-and-wound-care/

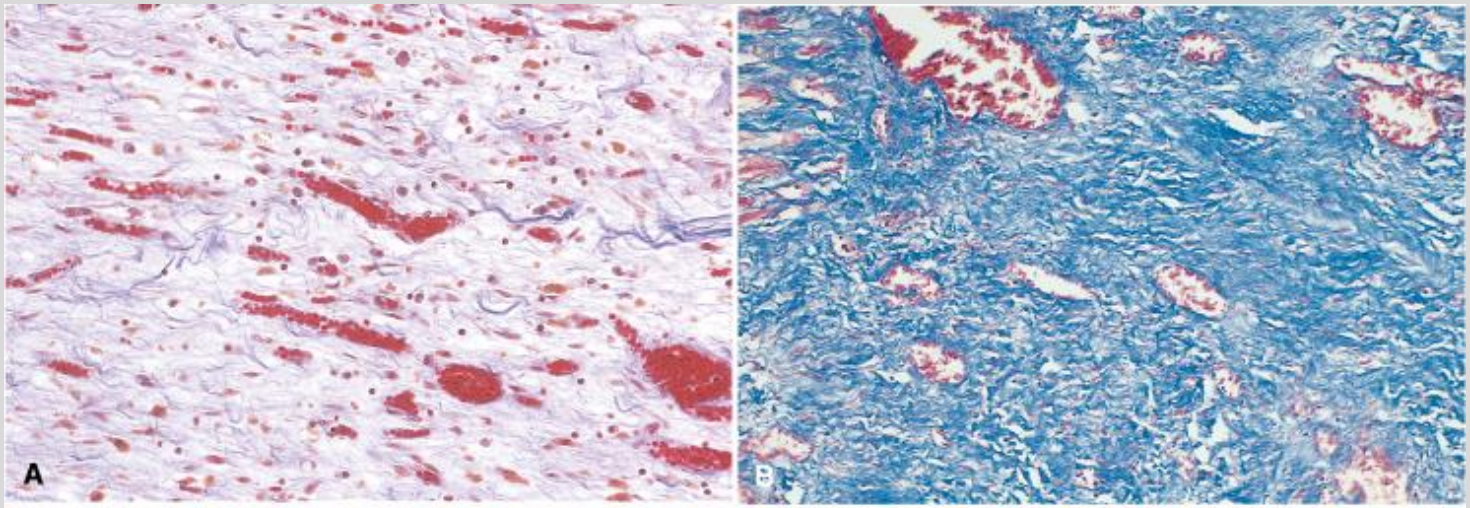


Day 0 Day 2 Day 17 Day 30

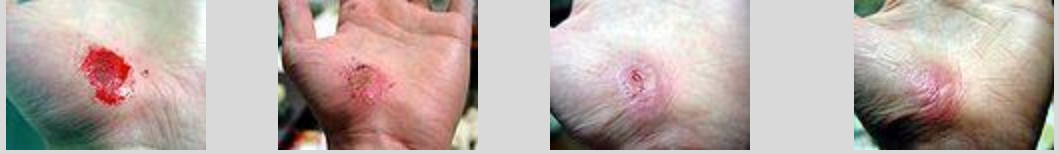
Phase 2- proliferation



- 2 days to 3 weeks
- Granulation tissue-
  - 1- fibroblasts: to lay down collagen
  - 2- angiogenesis : to supply the repair/regeneration process

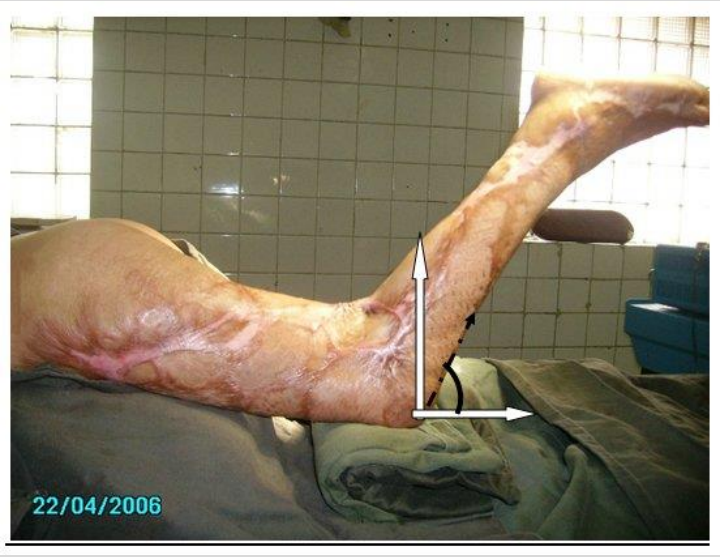


http://jdc.jefferson.edu/cgi/viewcontent.cgi?article=1026&context=otograndroundshttp://es.slideshare.net/victoriamedicina/reparacion-patologia-profesor



Phase III: Maturation

- **Type III collagen is replace by type I**
  - Acquires final tensile strength
- **Remodeling: scar tissue becomes avascular and acellular**



- Wound contraction- wound edges pull together to close the defect
  - **Myofibroblasts-** fibroblasts with muscle filaments
    - Display feature of fibroblasts and smooth muscle cells

http://www.slideshare.net/csbrprasad/inflammation-1

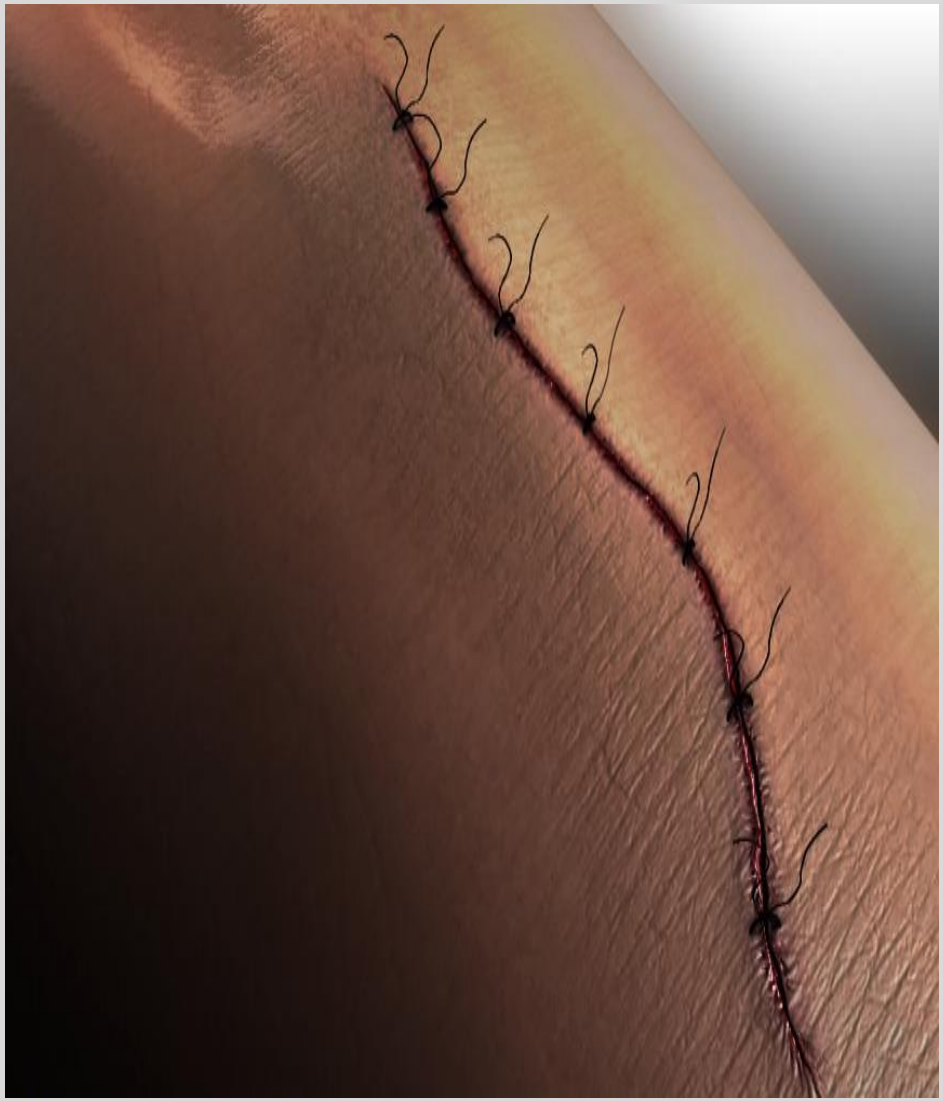
Healing by combinations of regeneration and repair

- Best example - skin wound
- Healing by **first intention or primary union** (epithelial regeneration):
  - When injury **only involves epithelial layer**
  - Clean skin wounds **(e.g., surgical excision)** – death of limited number of epithelial and connective tissue cells
- Healing by **second intention**
  - Edges of skin cannot be brought together
  - **tissue loss greater**
  - epidermal cells need longer time to cover surface
  - **more intense inflammatory reaction**
  - **abundant granulation tissue, extensive collagen deposition forming substantial scar**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Healing by Primary (First) Intention – Epithelial Regeneration

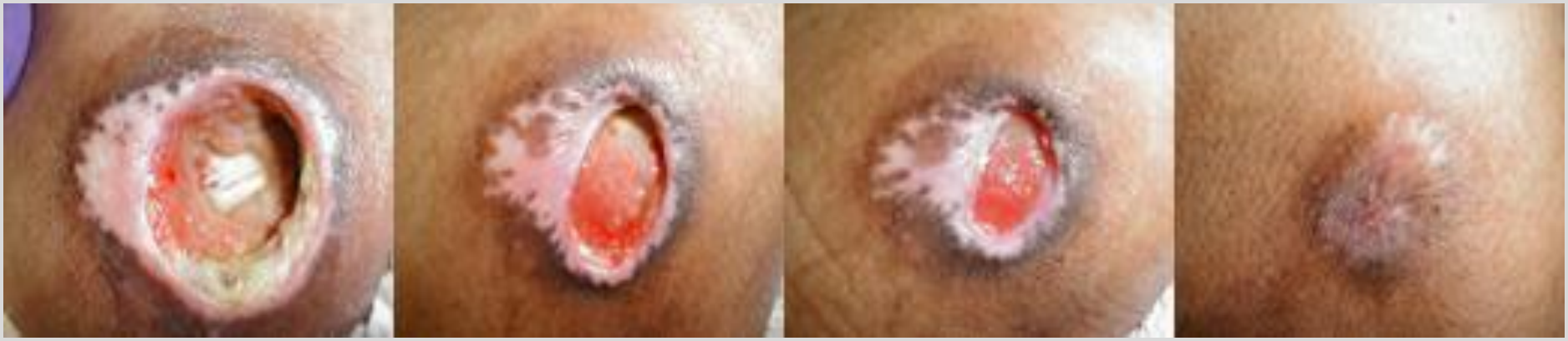
- Inflammation, proliferation of cells, maturation of connective tissue
- Wounds with opposed edges; involves only epithelial layer
- Ex; healing of a clean, uninfected surgical incision approximated by surgical sutures



Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Healing by Secondary Intention

- Wounds with unopposed/separated edges
- More extensive loss of cells and tissue
- Regeneration of parenchymal cells cannot completely restore the original architecture; granulation tissue grows in from the margin to complete the repair



Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020,Ch. 3

HEALING BY FIRST INTENTION

HEALING BY SECOND INTENTION

24 hours

3 to 7 days

Weeks

Scab

Neutrophils

Clot

Mitoses

Granulation tissue

Macrophage

Fibroblast

New capillary

Fibrous union

Wound contraction

© Elsevier 2005

WOUND CONTRACTION

- Occurs in large surface wounds (secondary intention)
- Helps close wound by decreasing gap between dermal edges and by reducing wound surface area
- Formation at edge of wound of network of **myofibroblasts** - have characteristics of smooth muscle cells, contract in wound tissue
- Myofibroblasts made from tissue fibroblasts via PDGF, TGF-beta, and FGF-2 released by macrophages at wound site

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020,Ch. 3

Remodeling of Connective tissue

- Granulation tissue replacement by scar involves changes in ECM composition
- **Balance between synthesis and degradation of ECM proteins**
- **Degradation accomplished by matrix metalloproteinases (MMPs)**
- MMPs produced by fibroblasts, macrophages, neutrophils, synovial cells, and some epithelial cells
- MMP synthesis and secretion regulated by growth factors, cytokines, and other agents
- MMPs include:
  - interstitial collagenases (cleave fibrillary collagen)
  - gelatinases (degrade amorphous collagen and fibronectin)
  - stromelysins (degrade variety of ECM components including proteoglycans, laminins, fibronectin, and amorphous collagen)
- **Activity shut down by tissue inhibitors of metalloproteinases (TIMPs)**

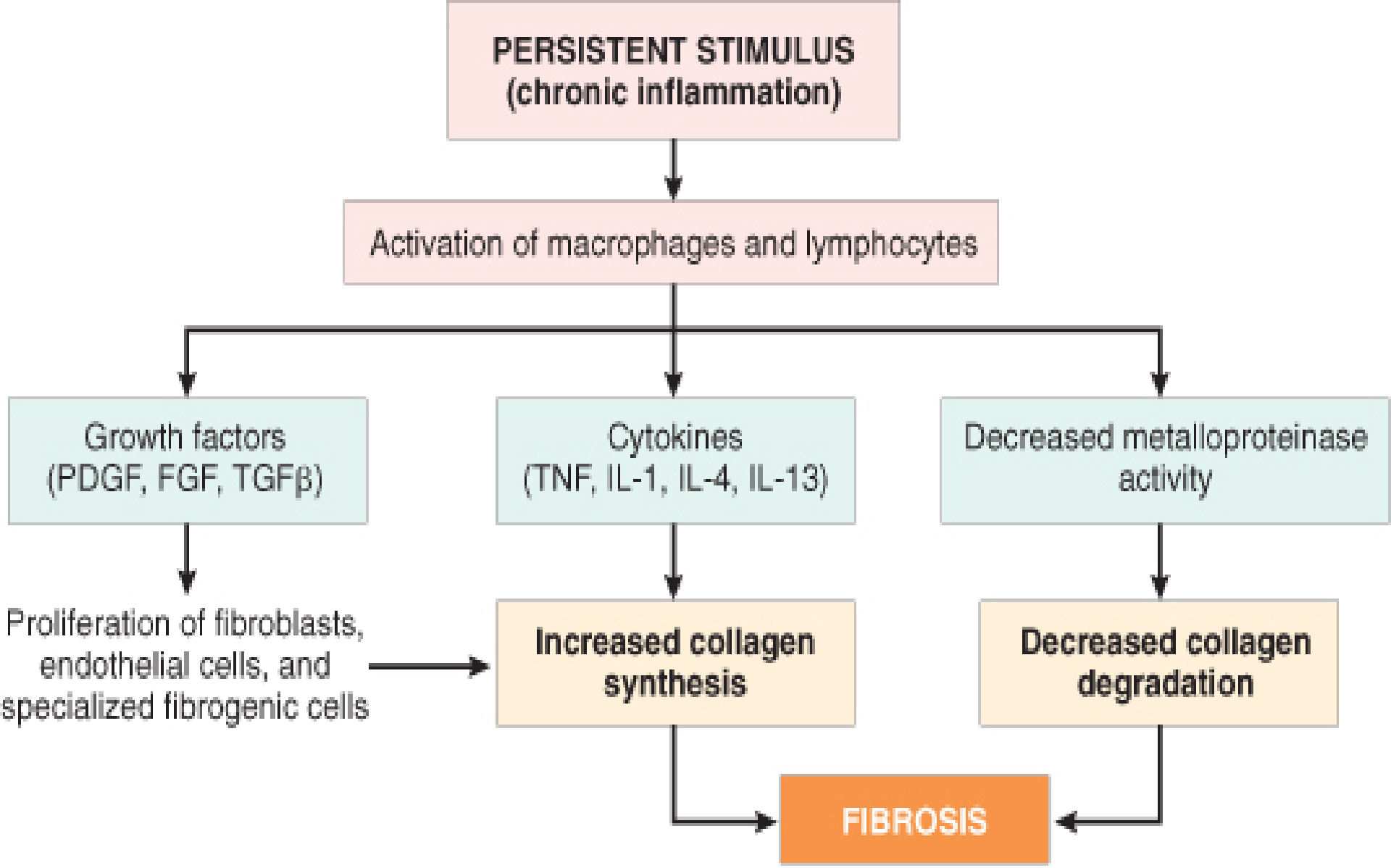
Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Tensile Strength of Wound

- Amount of collagen in wound depends on increased collagen synthesis AND decreased degradation

- End of first week, wound strength- about 10% of unwounded skin; **after a few months plateaus at about 70 to 80% (approximately 3 months)**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3



REGENERATION OF THE LIVER

Partial hepatectomy of 60% of the liver → doubling of the size of the liver remnant within 1 month

- Mechanism= proliferation of remaining hepatocytes and repopulation from progenitor cells
- Situation where proliferative capacity of hepatocytes is impaired (e.g chronic liver injury)
- NOT regrowth of the lobes that were resected
- **Primary phase** – hepatocytes primed by cytokines made by Kupffer cells (macrophages) to receive and respond to GF signals
- **Growth factor phase** – hepatocytes are stimulated into metabolism
- **Termination phase** – hepatocytes return to quiescence

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Deterrents to wound healing

- **Local infection**….pro-inflammatory cytokines and tissue proteases degrade granulation tissue; persistent tissue injury and inflammation
- **Hypoxia**….deters collagen fibril crosslinking (hydroxylation of proline and lysine), e.g, arteriosclerosis, inadequate circulation
- **Trauma**
- **Foreign bodies**
- **Diabetes**….glycosylation (bonding of glucose to RBC and protein) impairs neutrophil and macrophage phagocytosis
- **Malnutrition**….decrease in proliferation phase, Vit C needed for hydroxylation
- **Immunodeficiency**
- **Medications**..corticosteroids blunt inflammatory process; NSAIDS inhibit platelet function

Hormones – glucocorticoids (anti-inflammatory and inhibit collagen synthesis)

Mechanics – early motion of wound can separate edges

Size, location, type of wound – e.g. face (more vascular) heals faster than foot

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

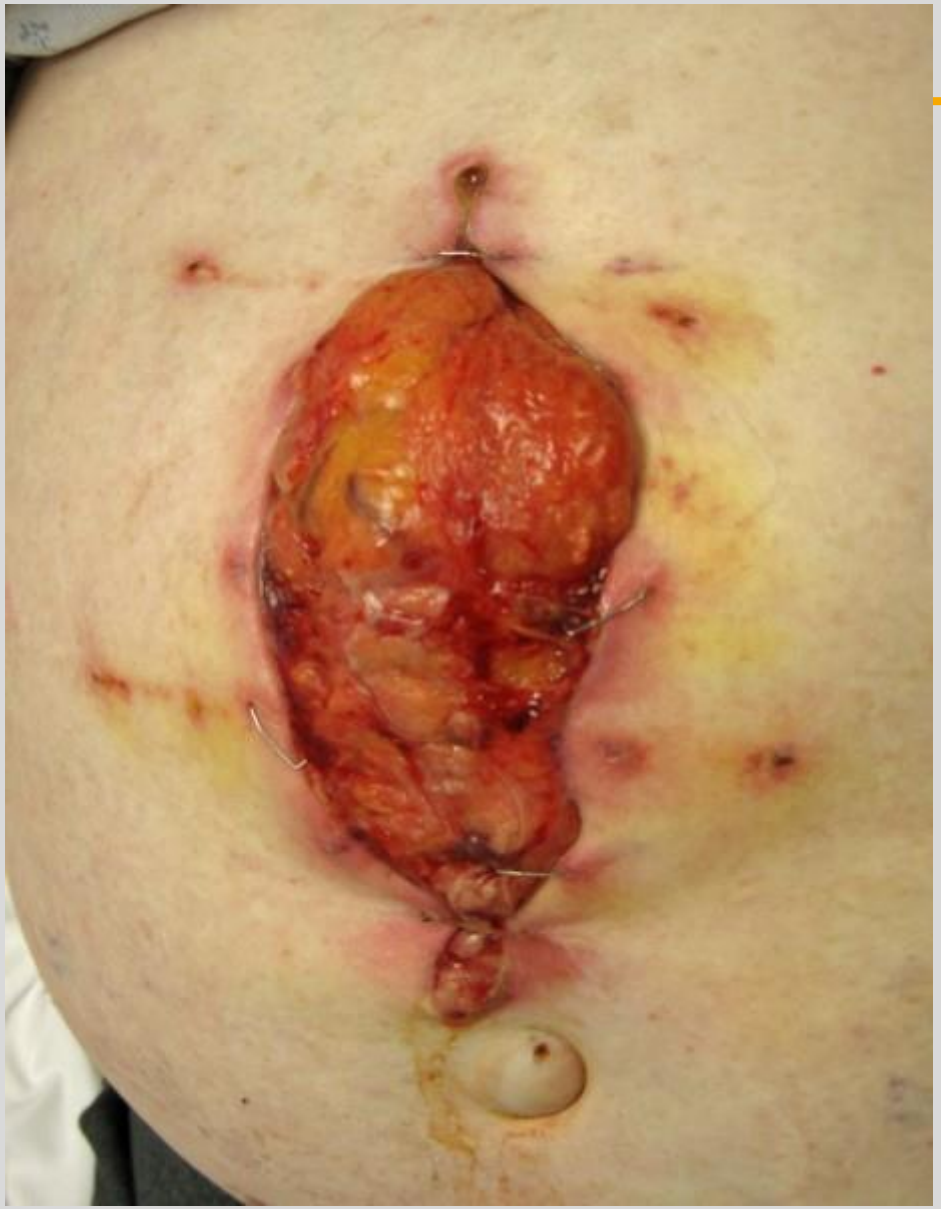
COMPLICATIONS

- Deficient scar formation – **wound dehiscence** and ulceration
- Excessive scar formation **– keloid (scar tissue extends beyond boundary of original wound)**

(versus Hypertrophic scar – excessive amounts of collagen resulting in raised scar)

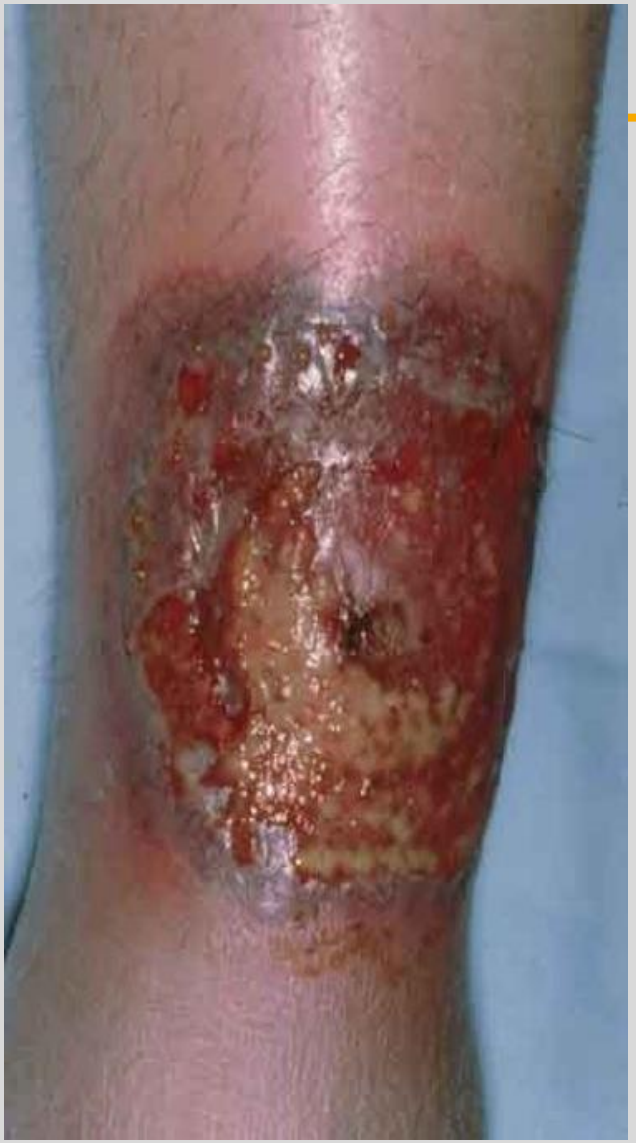
- **Contractures** – especially in palms, soles, anterior thorax commonly after serious burns; exageration of contraction

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020,Ch. 3



Dehiscence:
Most commonly after abdominal surgery secondary to increased abdominal pressure:
obesity, vomiting, coughing, etc.

http://usmlepathslides.tumblr.com/post/34870481649/wound-dehiscence-with-evisceration-abdomen-wound



Ulceration –
e.g., lower extemity, poor circulation in diabetes, PVD

http://missinglink.ucsf.edu/lm/DermatologyGlossary/ulceration.html

Keloid following ear piercing

Keloid v. Hypertrophic scar

Disorganized collagen formation	Parallel collagen formation
Extends beyond borders of original wound wound	Confined to borders of original
Frequently recur after resection	Infrequently recur after resection

http://medicalpictures.net/keloid-pictures/

HEALING - REVIEW

- Injury activates coagulation pathway and blood clot forms on wound surface
- VEGF increases vessel permeability and edema
- Neutrophils appear within 24 hours, clean out debris and bacteria
- Neutrophils replaced by macrophages by 48 - 96 hours which clear debris, fibrin, foreign material and promote angiogenesis, ECM deposition
- Fibroblast migration to injury site mediated by cytokines, TNF, PDGF, TGF-beta, and FGF
- Fibroblast proliferation triggered by growth factors – macrophages main source

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch.3

HEALING – REVIEW (continued)

- 24 to 48 hours - epithelial cells move from wound edge along cut margins of dermis, deposit basement membrane components; produce thin, continuous epithelial layer
- Increase in collagen fibrils to bridge incision
- Fibroblasts, vascular endothelial cells proliferate to form **granulation tissue** by **5 to 7 days**, fills wound, neovascularization maximal
- Wbc infiltrate, edema, increased vascularity disappear by second week
- **TGF-beta is most important fibrogenic agent: causes fibroblast migration and proliferation, increased synthesis of collagen and fibronectin, and decreased ECM degradation by MMPs**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

HEALING REVIEW (continued)

- Increased collagen accumulation and regression of vascular channels – original granulation tissue scaffold converted to **pale, avascular scar made up of fibroblasts, dense collagen, elastic tissue, other ECM components**

- By end of first/second month – scar is composed of **acellular connective tissue without inflammation, covered by intact epithelium**

Robbins and Cotran, Pathologic Basis of Disease, 10th ed., 2020, Ch. 3

Case Question

- An experiment is being conducted on the effects of certain drugs on wound healing. After the administration of drug A, a cut is made in the thigh of a laboratory rat and **one week later**, a biopsy is taken of the area. At high magnification, the tissue has capillaries, fibroblasts, and a variable amount of inflammatory cells (mostly mononuclear such as macrophages, but with occasional neutrophils still present). What type of tissue does this best represent?
- A. scar tissue
- B. granulation tissue
- C. purulent tissue
- D. permanent tissue

Case Question

- A 70 year old woman presents with acute chest pain and shortness of breath. She undergoes a cardiac catherization which shows an occlusion of the left anterior descending coronary artery. Lab studies and EKG are consistent with an acute myocardial infarction. Which of the following is the most likely pathological finding in the affected heart muscle 6 weeks later?

- A. Capillary-rich granulation tissue
- B. Granulomatous inflammation
- C. Neutrophils and necrotic debris
- D. Collagen-rich scar tissue
- E. Vascular congestion and edema

Case Question

A 10 year old boy receives a deep laceration over his right eyebrow playing ice hockey. The wound is cleaned and sutured. Which of the following describes the principal function of macrophages that are present in the wound approximately 48 hours after injury?

A. Antibody production

B. Collagen deposition

C. Histamine release

D. Phagocytosis

E. Wound contraction

Case question

- In the previous question, which of the following collagens is deposited first during wound healing?
- A. Type I
- B. Type II
- C. Type III
- D. Type IV
- E. Type V

Summary Slide

- Definitions of healing, repair, regeneration
- Labile, stable, permanent cells – see slide 6
- Three phases of wound healing
- Repair by scar – granulation tissue, angiogenesis, connective tissue deposition (collagen and ECM)
- Example of skin injury – healing by primary and secondary intention
- Wound contraction, connective tissue remodeling, tensile strength
- Liver regeneration, examples of repair and healing
- Deterrents to wound healing – see slide 38
- Complications of wound healing – slides 39 - 42

Lecture Feedback Form:

https://comresearchdata.nyit.edu/redcap/surveys/?s=HRCY448FWYXREL4R