Pathophysiology

Module 1: Inflammation and Healing

Immune Defenses

Nonspecific (Innate) Immune system -
First line of defense

- Mechanical barrier
- Mucus membranes, skin
- Secretions - tears, sweat, gastric juices, etc

Second line of defense - Nonspecific immune system

Inflammation and Phagocytosis

Natural killer cells

Specific or Adaptive immunity

Production of specific antibodies

and cell-mediated immunity (B and T lymphocytes, etc)

Defense Mechanisms of the Immune System

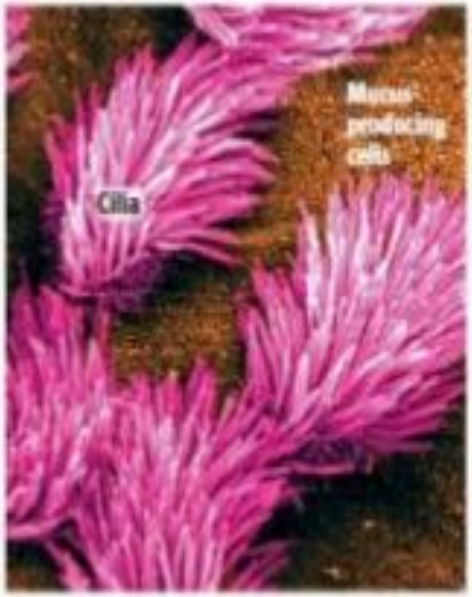
Figure 24.1 Overview of the body's defenses. Note that the lymphatic system is involved in both innate and adaptive defenses.

THE BODY'S DEFENSES

Innate Defenses
(always deployed)

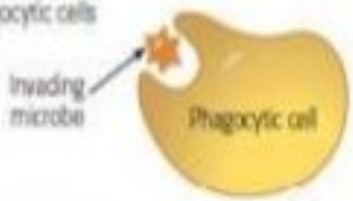
External innate defenses

- Skin
- Secretions
- Mucous membranes



Internal innate defenses

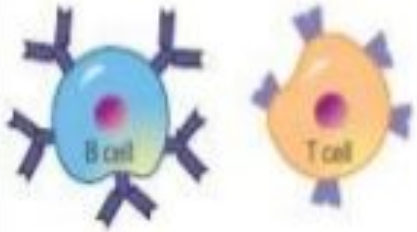
- Phagocytic cells



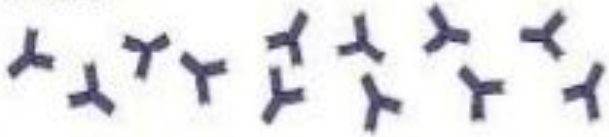
- Natural killer cells
- Defensive proteins
- Inflammatory response

Adaptive Defenses
(activated by exposure to specific pathogens)

- Lymphocytes



- Antibodies



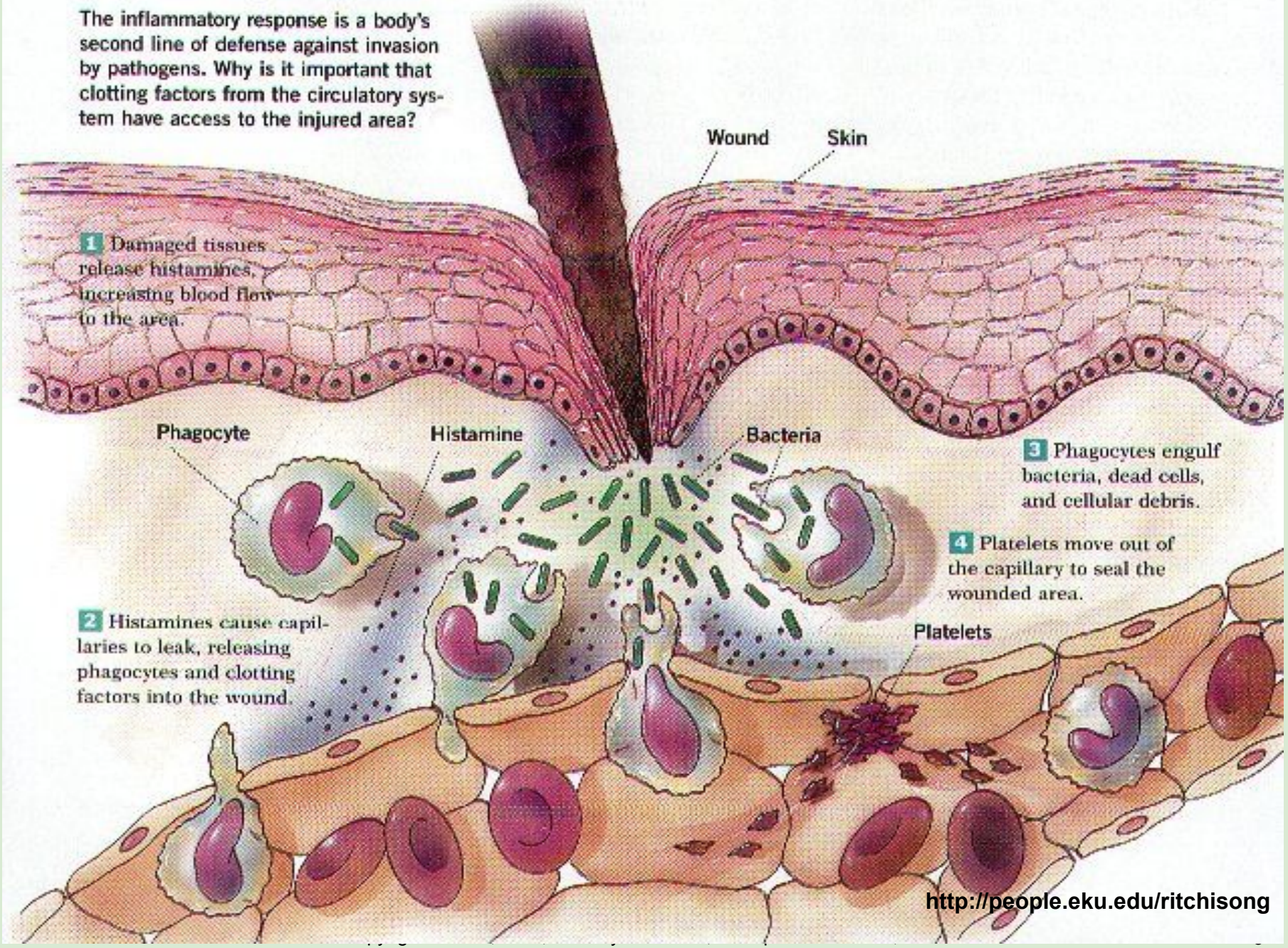
The Lymphatic System
(involved in internal innate defenses and adaptive defenses)

Physiology of Inflammation

- A protective mechanism and important basic concept in pathophysiology
- Disorders are named using the ending -*itis.*
- Inflammation is a normal defense mechanism.
- Signs and symptoms serve as warning for a problem:
  - Problem may be hidden within the body.
- It is not the same as infection.
  - Infection, however, is one cause of inflammation.

Inflammatory Response

The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?



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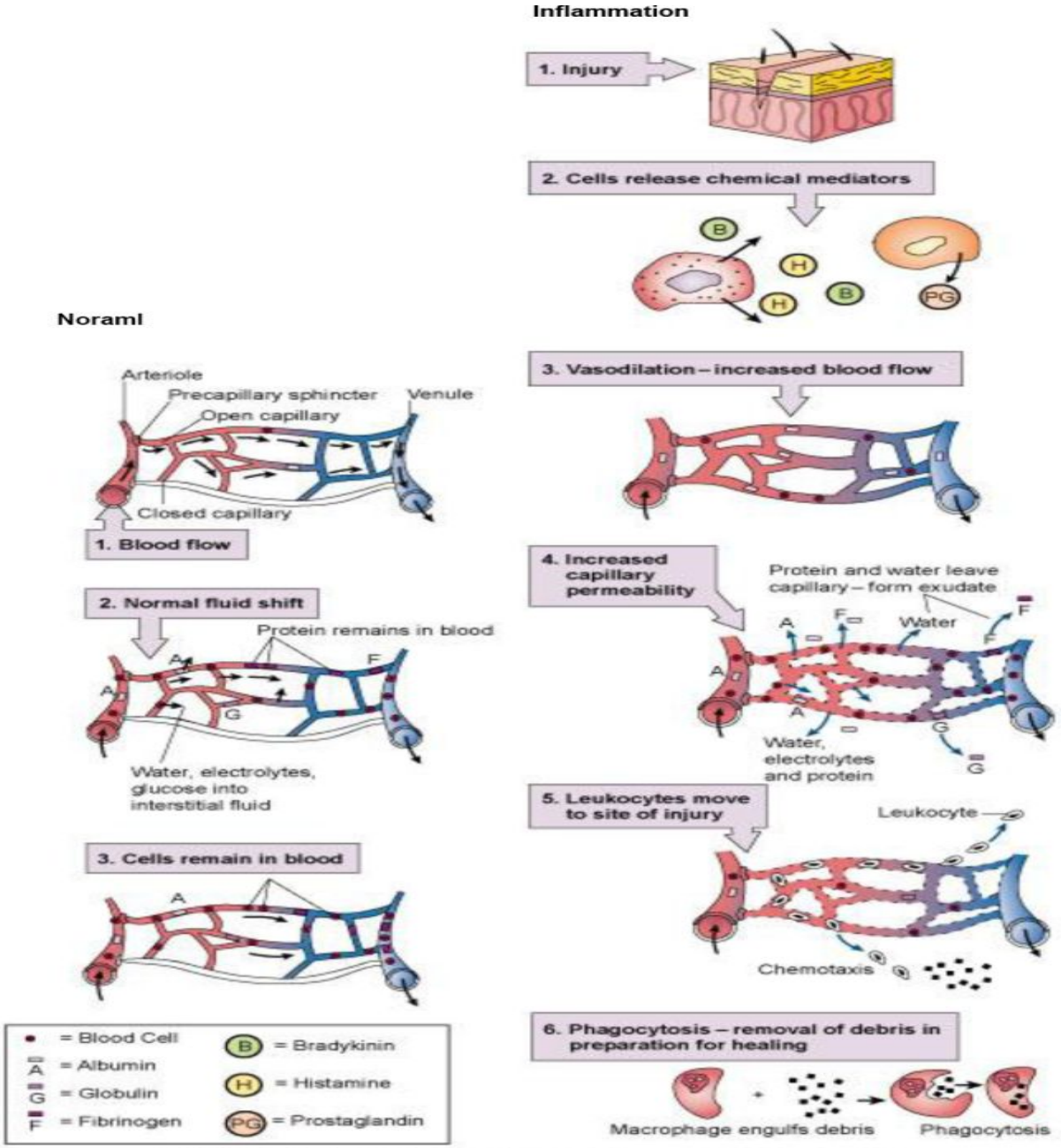
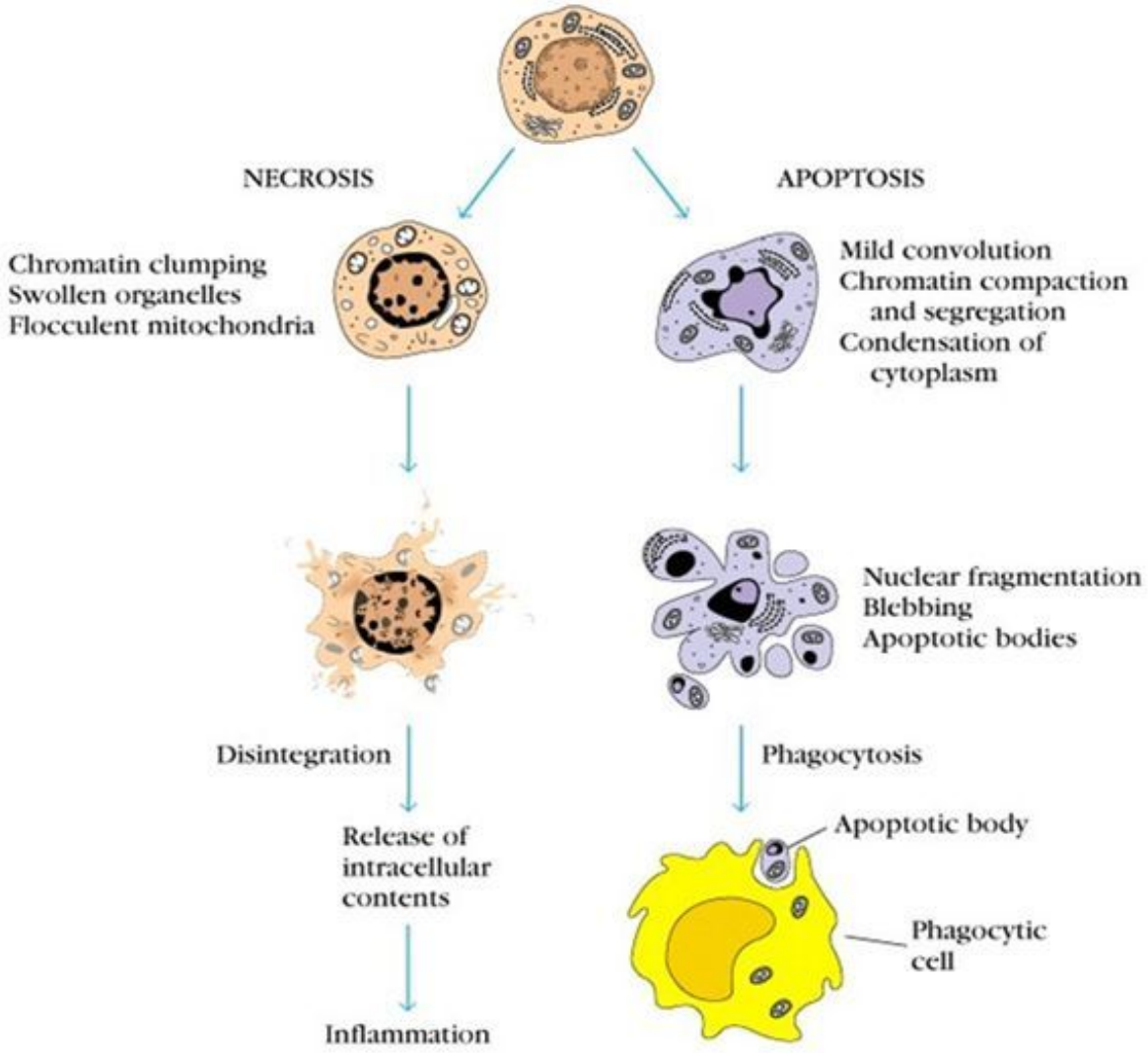
Normal Capillary Exchange

- Generally not all capillaries in a particular capillary bed are open.
  - Depend on the metabolic needs of the cells or need of removal of wastes
- Movement of fluid, electrolytes, oxygen, and nutrients on arterial end based on net hydrostatic pressure
- Venous end—osmotic pressure will facilitate movement of fluid, carbon dioxide, and other wastes.

Normal Capillary Exchange Versus Inflammatory Response



Necrosis vs. Apoptosis



- Apoptosis – programmed cell death
- Necrosis – un-programmed cell death

Causes of Inflammation

- Direct physical damage
  - Examples: cut, sprain
- Caustic chemicals
  - Examples: acid, drain cleaner
- Ischemia or infarction
- Allergic reactions
- Extremes of heat or cold
- Foreign bodies
  - Examples: splinter, glass
- Infection

Steps of Inflammation

- Release of bradykinin from injured cells
  Activation of pain receptors by bradykinin
- Mast cells and basophils release histamine.
- Capillary dilation (bradykinin and histamine)
  Increased blood flow and capillary permeability
- Bacteria may enter the tissue.
- Neutrophil and monocytes come to injury site.
  Neutrophils phagocytize bacteria.
- Macrophages leave bloodstream for phagocytosis of microbes.

Acute Inflammation

- Process of inflammation is the same, regardless of cause.
- Timing varies with specific cause.
- Chemical mediators affect blood vessels and nerves in the damaged area:
  - Vasodilation
  - Hyperemia
  - Increase in capillary permeability
  - Chemotaxis to attract cells of the immune system

Local Effects of Inflammation

Redness Warmth

- Both caused by increased blood flow to damaged area

Swelling (edema)

- Shift of protein and fluid into the interstitial space

Pain

- Increased pressure of fluid on nerves; release of chemical mediators (e.g., bradykinins)

Loss of function

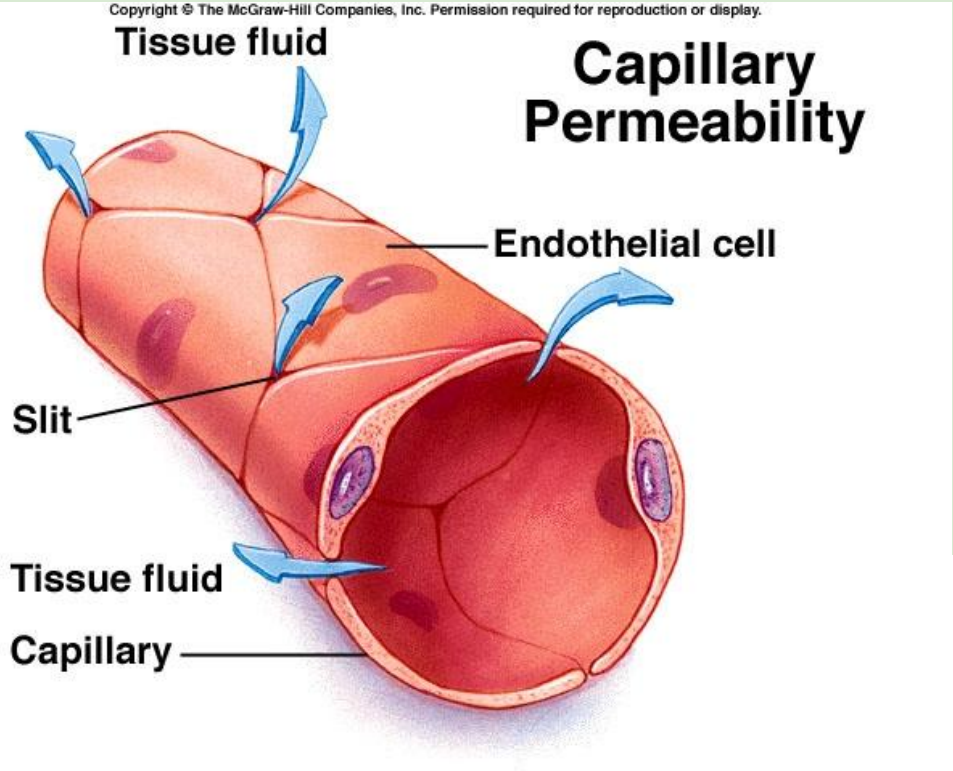
- May develop if cells lack nutrients; edema may interfere with movement

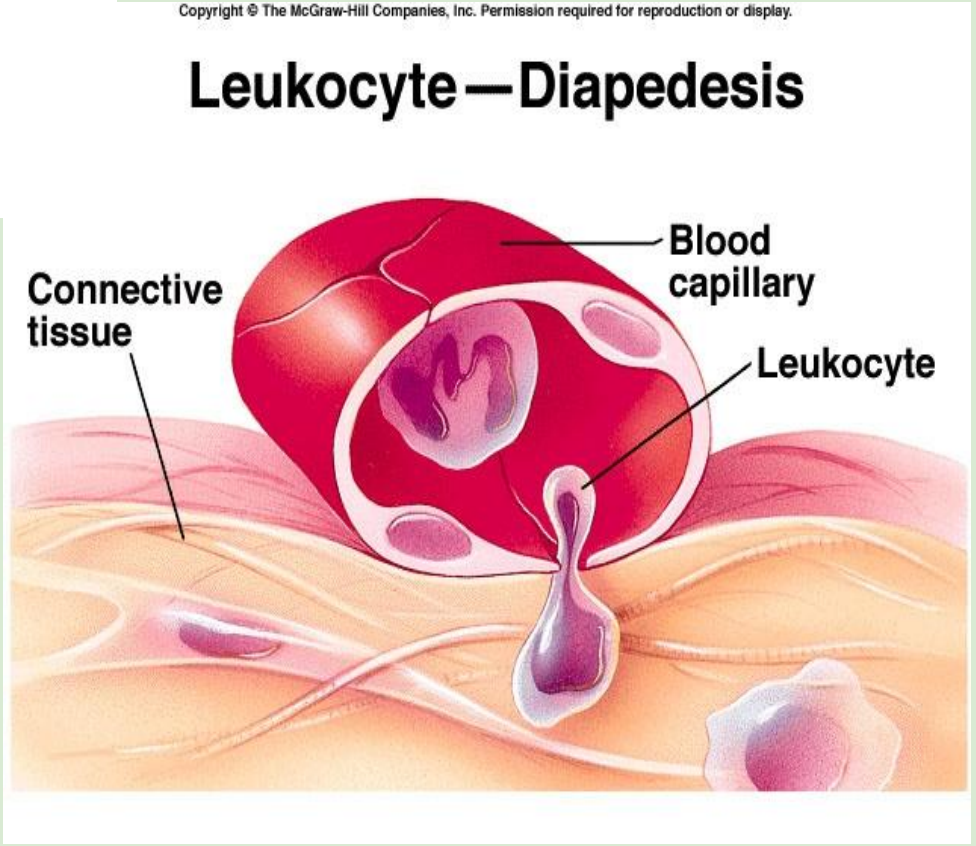
Systemic Effects of Inflammation

Mild fever (pyrexia) Common if inflammation is extensive release of pyrogens

Malaise - feeling unwell Fatigue

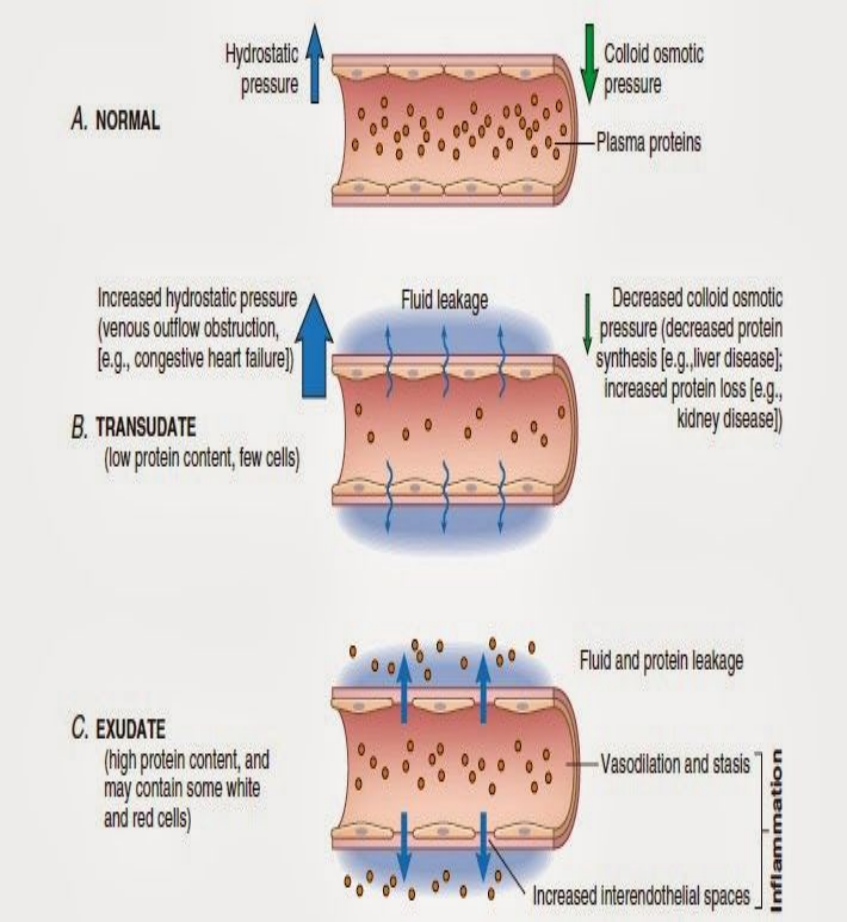
Headache Anorexia .





Exudate

- Serous
  - Watery, consists primarily of fluid, some proteins, and white blood cells
- Fibrinous
  - Thick, sticky, high cell and fibrin content
- Purulent
  - Thick, yellow-green, contains more leukocytes, cell debris, and microorganisms
  - Abscess
    - Localized pocket of purulent exudate in solid tissue
- Hemorrhagic exudate
  - Present when blood vessels are damaged



The Course of Fever

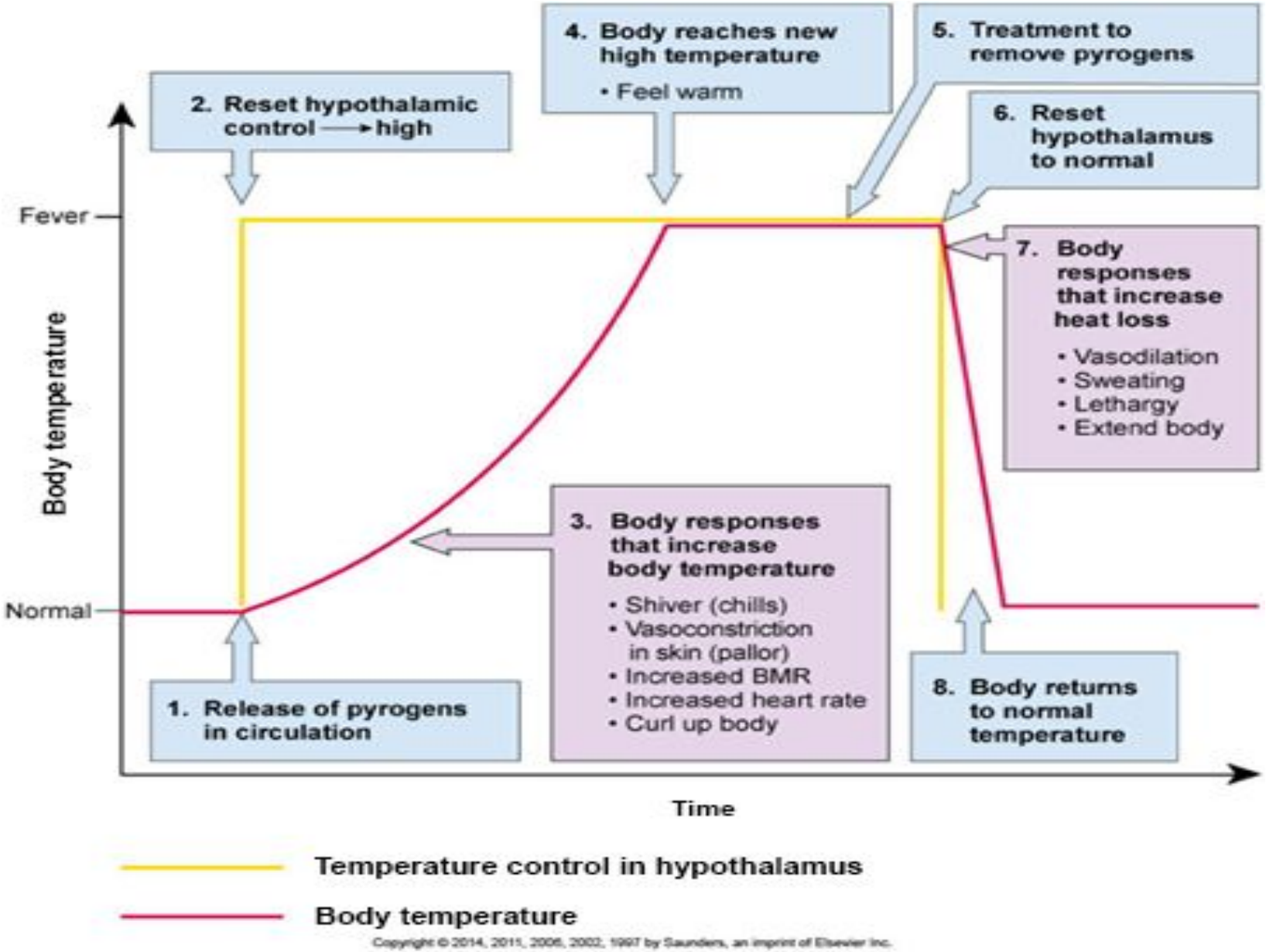
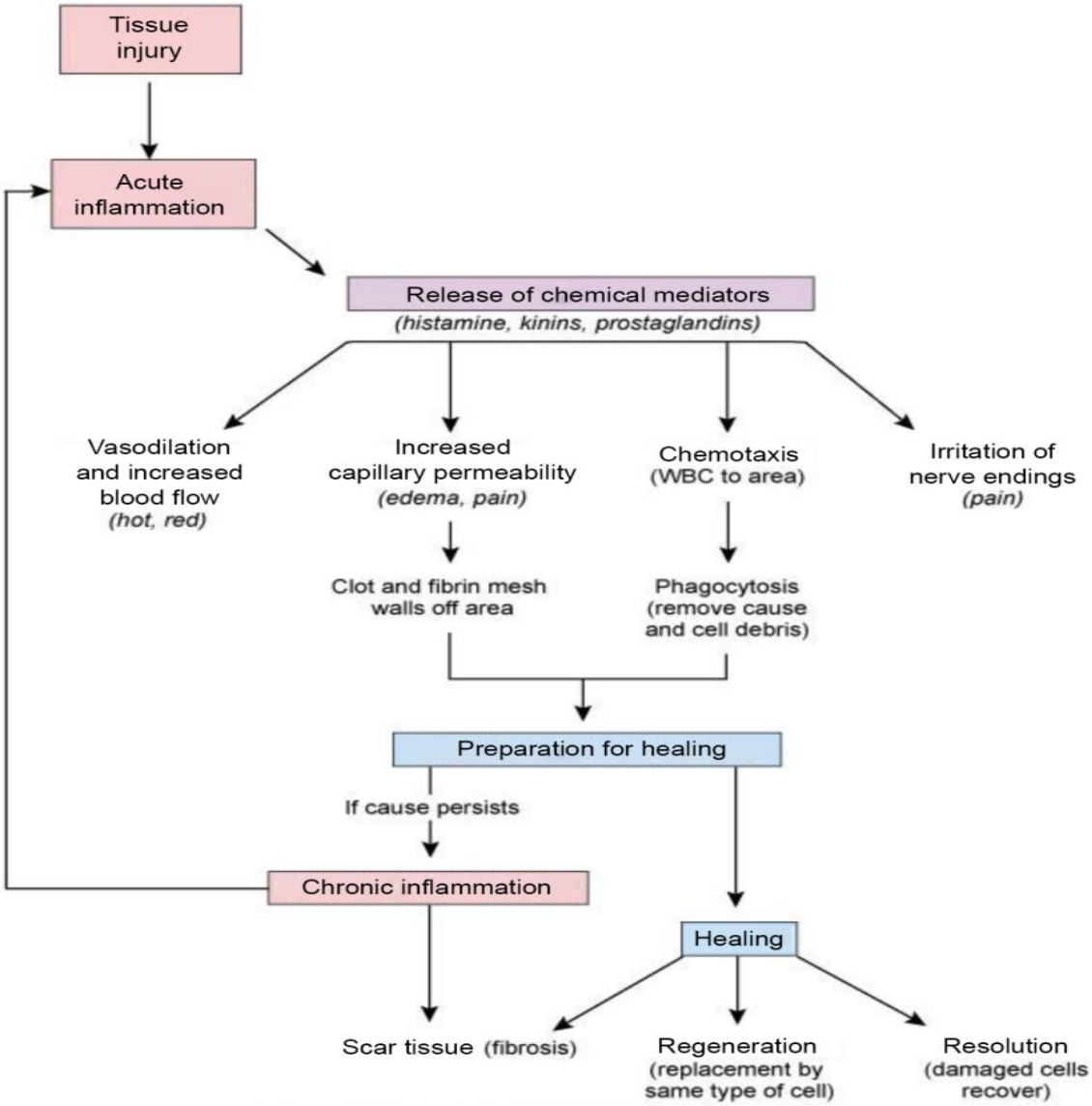


TABLE 5-3 Changes in the Blood with Inflammation

Leukocytosis	Increased numbers of white blood cells, especially neutrophils
Differential count	Proportion of each type of white blood cell altered, depending on the cause
Plasma proteins	Increased fibrinogen and prothrombin
C-reactive protein	A protein not normally in the blood, but appears with acute inflammation and necrosis within 24-48 hours
Increased ESR	Elevated plasma proteins increase the rate at which red blood cells settle in a sample
Cell enzymes	Released from necrotic cells and enter tissue fluids and blood: may indicate the site of inflammation

Course of Inflammation and Healing

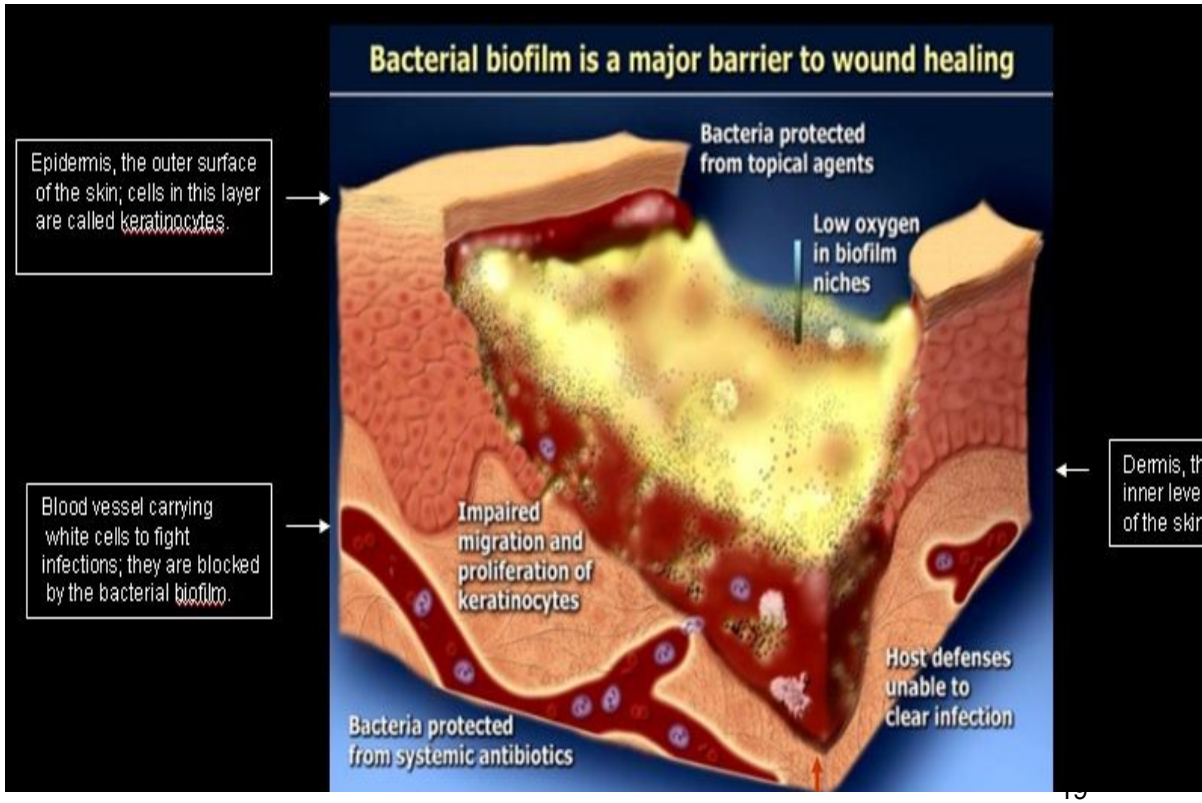


Diagnostic Tests

- Leukocytosis
  - Increased with blood cells in blood
- Erythrocyte sedimentation rate
  - Elevated
- Differential count
  - Helpful to distinguish between bacterial and viral infection
- Circulating plasma proteins
- Cell enzymes
  - Isoenzymes may be elevated.
- Necrosis

Potential Complications

- Infection
  - Microorganisms can more easily penetrate edematous tissues.
  - Some microbes resist phagocytosis. - Biofilms
  - The inflammatory exudate also provides an excellent medium for microorganisms.
- Skeletal muscle spasm
  - May be initiated by inflammation
  - Protective response to pain



Chronic Inflammation

- Follows acute episode of inflammation
- Less swelling and exudate
- Presence of more lymphocytes, macrophages, and fibroblasts
- Continued tissue destruction
- More fibrous scar tissue
- Granuloma may develop around foreign object

Potential Complications

Deep ulcers may result from severe or prolonged inflammation.

Caused by cell necrosis and lack of cell regeneration that causes erosion of the tissue

Can lead to complications such as perforation of viscera.

Extensive scar tissue formation .

“Treatment” of Inflammation

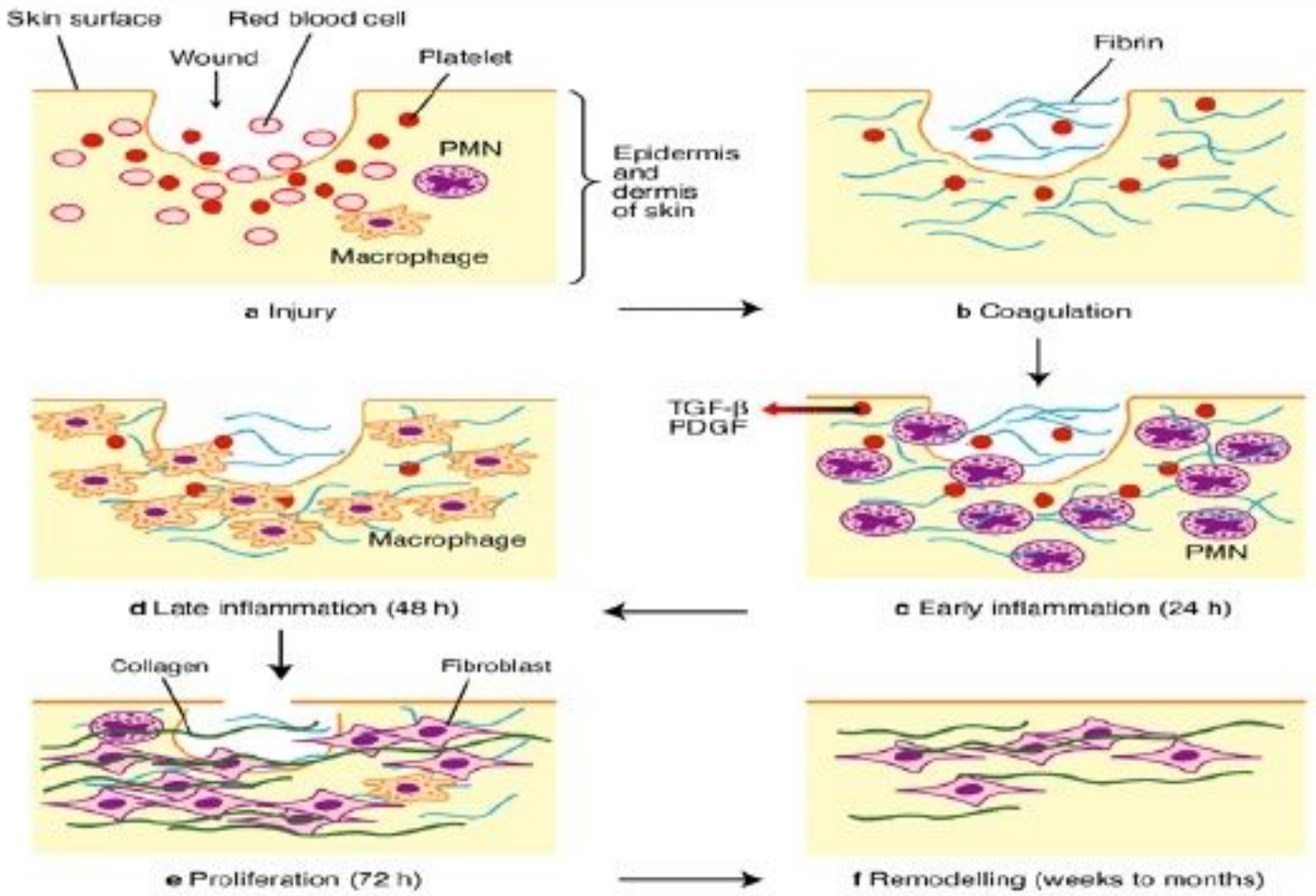
RICE” Therapy for Injuries

*R*est *I*ce *C*ompression *E*levation

Medications

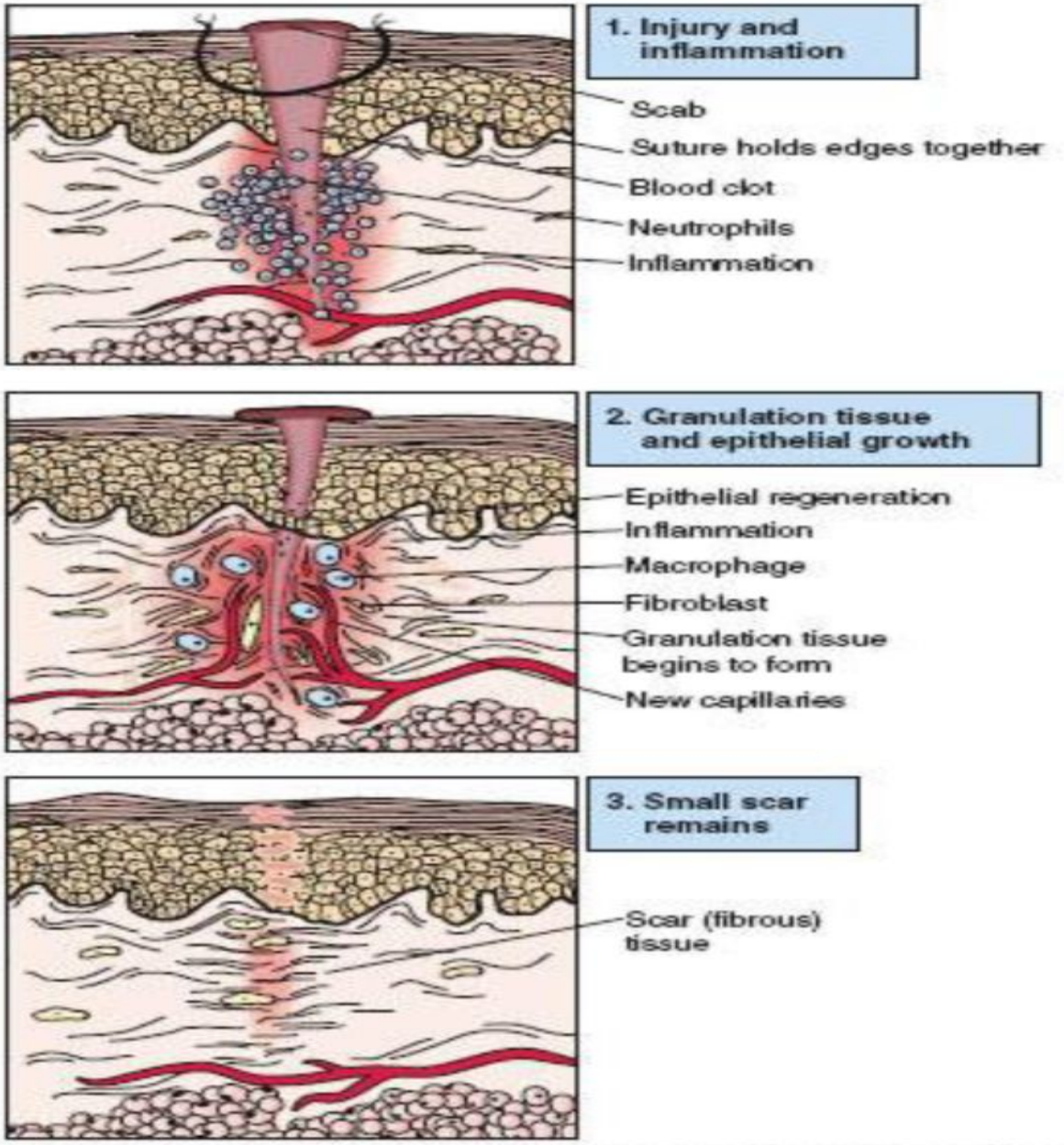
- Acetylsalicylic acid (ASA) (Aspirin)
- Acetaminophen (Tylenol)
- Other Nonsteroidal antiinflammatory drugs (NSAIDs)
- Glucocorticoids - Corticosteroids

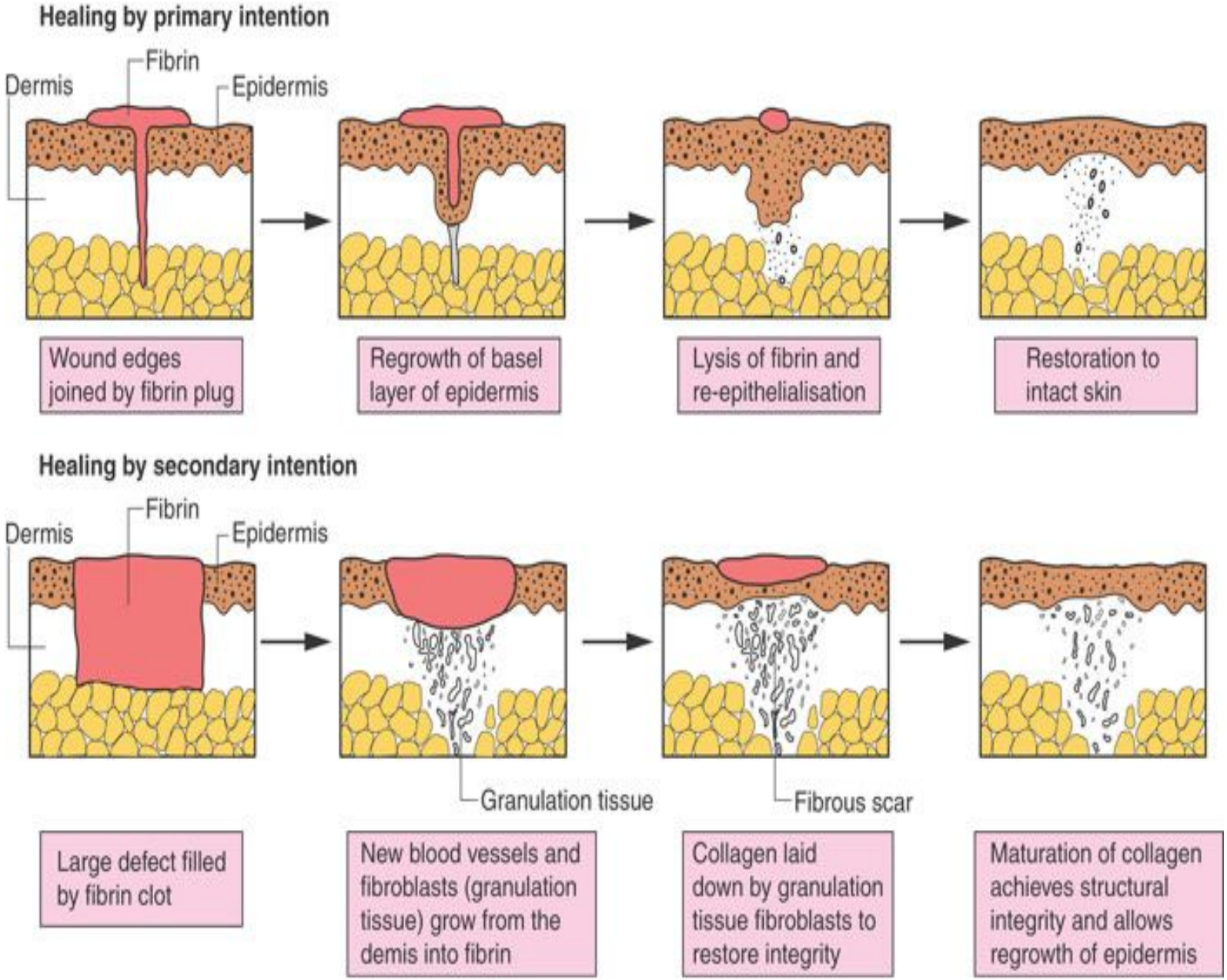
Stages of Wound Healing



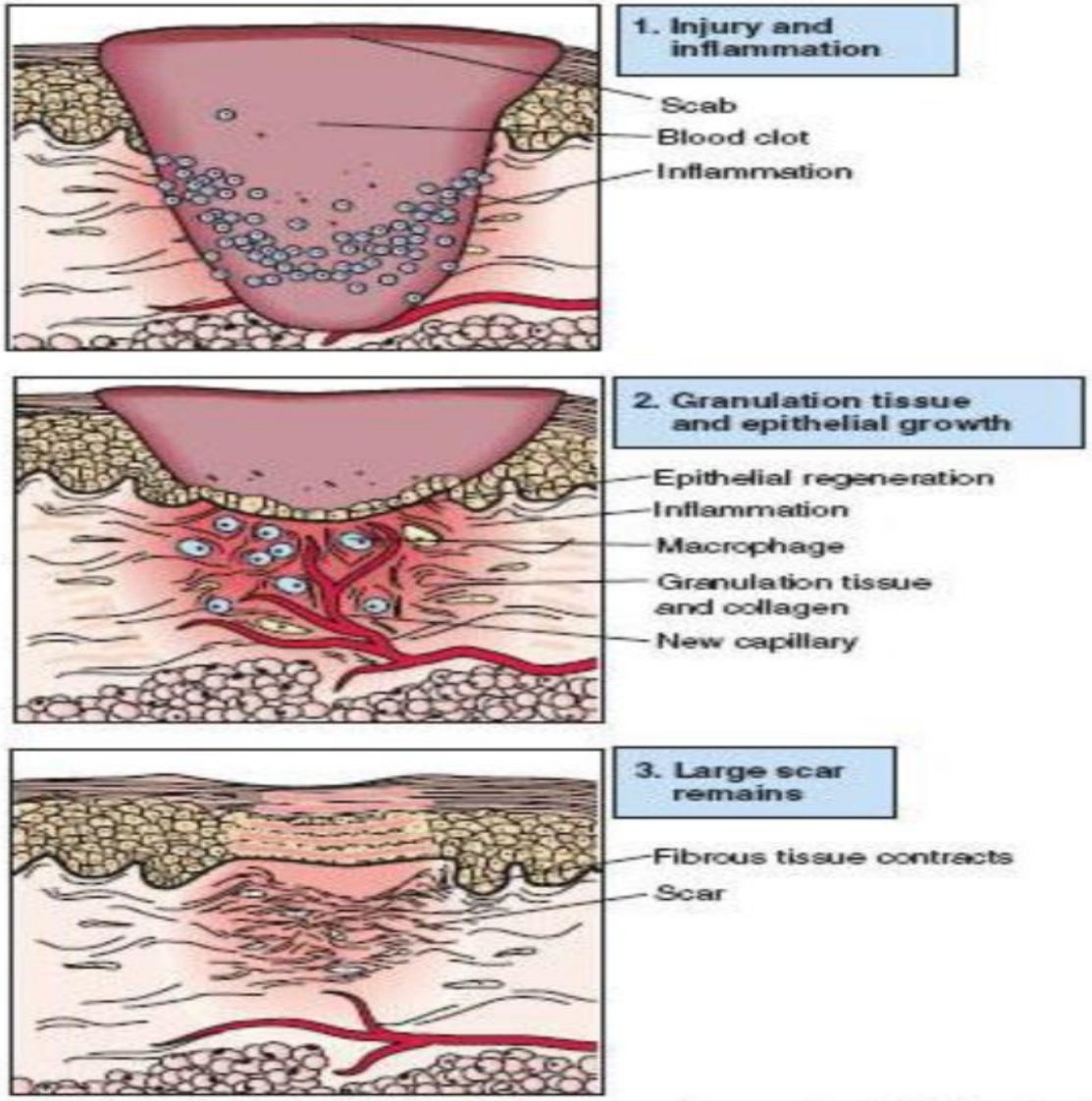
The phases of cutaneous wound healing

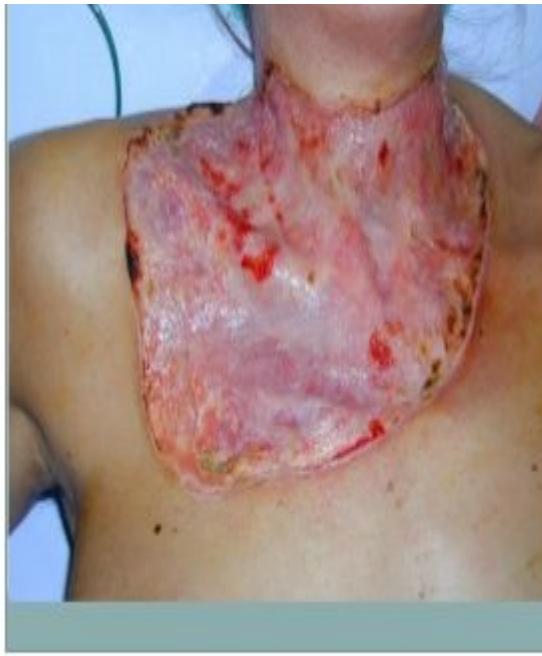
- Healing of incised wound by first intention





Healing by second intention





Scar Formation

- Loss of function
  - Result of loss of normal cells and specialized structures
    - Hair follicles
    - Nerves
    - Receptors
- Contractures and obstructions
  - Scar tissue is nonelastic.
  - Can restrict range of movement
- Adhesions
  - Bands of scar tissue joining two surfaces that are normally separated

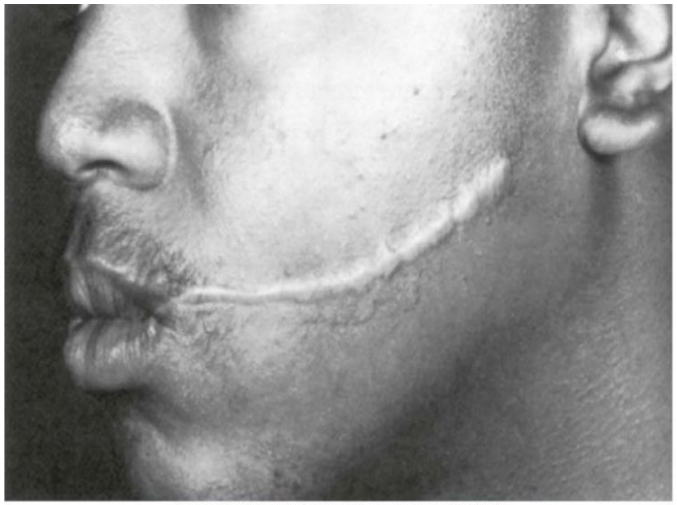
Hypertrophic scar tissue

Overgrowth of fibrous tissue leads to hard ridges of scar tissue or keloid formation

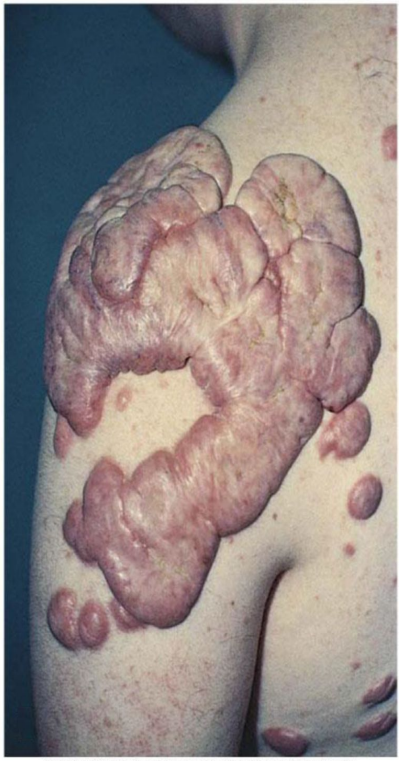
Ulceration Blood supply may be impaired around scar.

Results in further tissue breakdown and ulceration at future time

Complications of Scar Tissue



From Callen J, Greer K, Hood A, et al. Color Atlas of Dermatology. Philadelphia, WB Saunders, 1993



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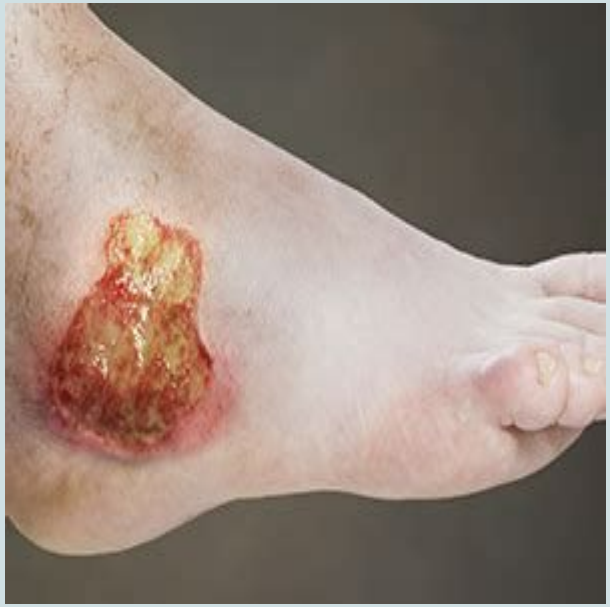
Factors affecting time of healing

Age
Size of wound
Location (epithelial?)
Nutrition
Immobility
Circulation
Virulence of wound infection
Presence of steroids



Glucocorticoids
Anti-inflammatory Effects

- Decreased capillary permeability
- Enhanced effectiveness of epinephrine and norepinephrine
- Reduced number of leukocytes and mast cells
- Reduces immune response

Adverse Effects of Glucocorticoids

- Atrophy of lymphoid tissue; reduced hemopoiesis
  - Increased risk of infection
- Catabolic effects
  - Increased tissue breakdown; decreased protein synthesis
- Delayed healing Delayed growth in children
- Retention of sodium and water
- Increased gluconeogenesis

Healing

Types

- Resolution
  - Minimal tissue damage
- Regeneration
  - Damaged tissue replaced with cells that are functional
- Replacement
  - Functional tissue replaced by scar tissue
  - Loss of function

Burns

Thermal—caused by flames or hot fluids

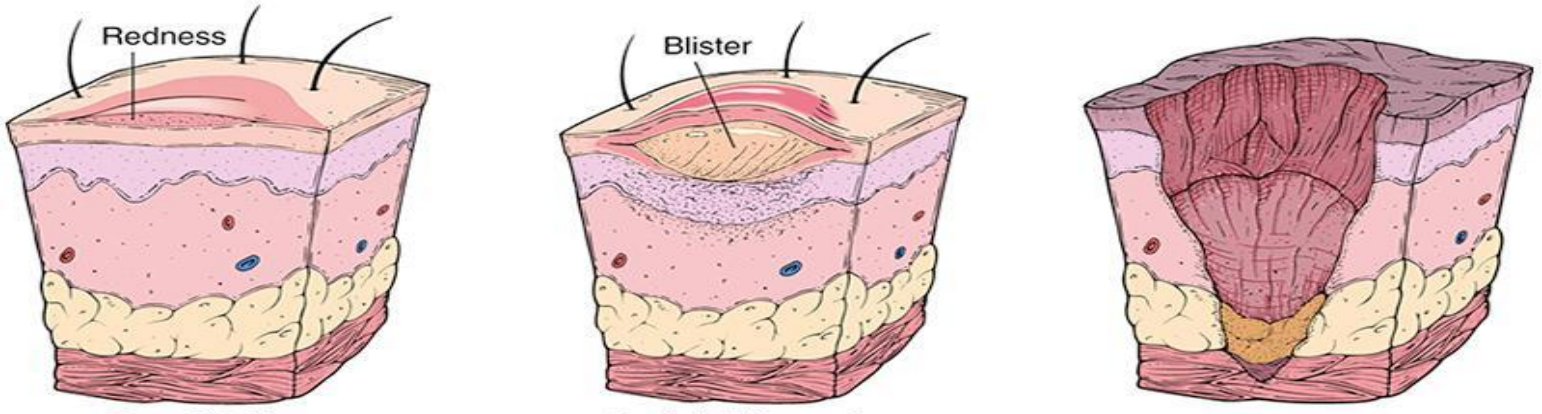
Chemical Radiation

Electricity Light Friction

Classification of Burns

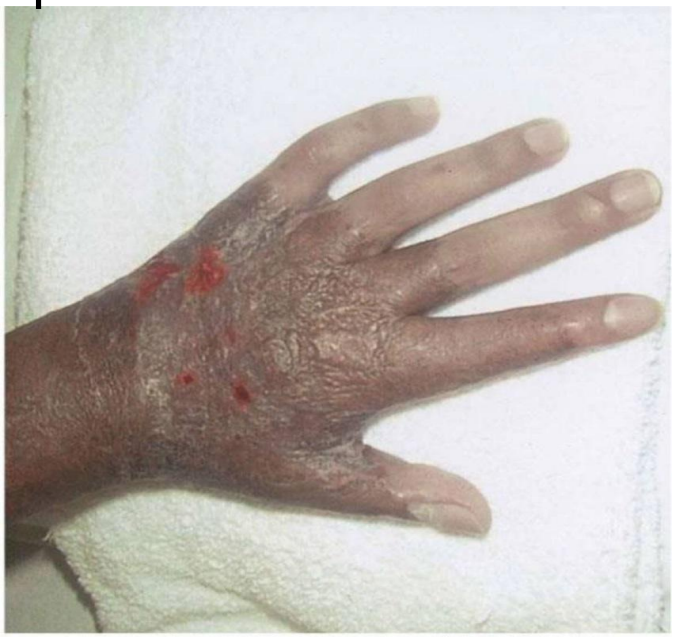
- Superficial partial-thickness (first-degree) burns
  - Involve epidermis and part of dermis
  - Little, if any, blister formation
- Deep partial-thickness (second-degree) burns
  - Epidermis and part of dermis
  - Blister formation
- Full-thickness (third- and fourth-degree) burns
  - Destruction of all skin layers and often underlying tissues

Classification of Burn Injury by Depth



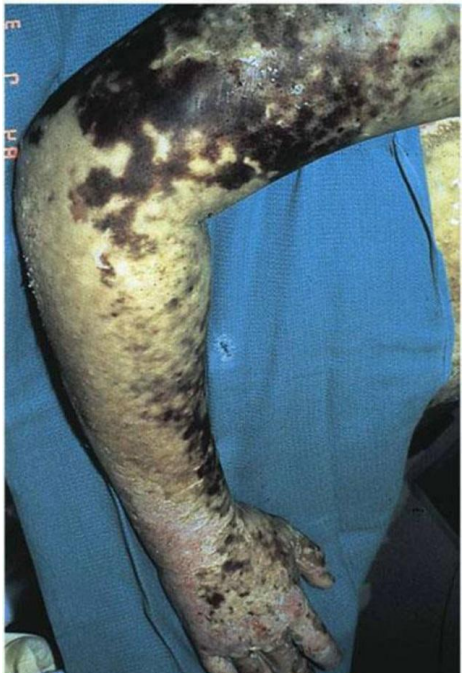
From Frazier M, Dzymkowski J: Essentials of Human Disease and Conditions, *ed 6, St. Louis, 2016, Elsevier.*

Deep Partial-thickness Burn



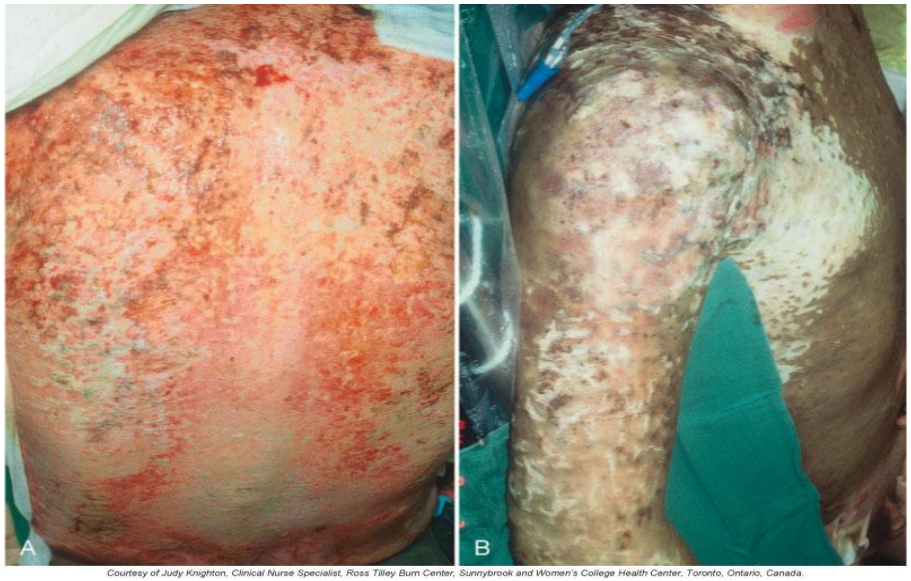
Courtesy of Judy Knighton, Clinical Nurse Specialist, Ross Tilley Burn Center, Sunnybrook and Women's College Health Center, Toronto, Ontario, Canada.

Full Thickness Burn



Effects of Burn Injury

- Both local and systemic
- Dehydration and edema
- Shock Infection
- Respiratory problems Pain
- Hypermetabolism during healing period after burn



Courtesy of Judy Knighton, Clinical Nurse Specialist, Ross Tilley Burn Center, Sunnybrook and Women's College Health Center, Toronto, Ontario, Canada.

Healing of Burns

- Hypermetabolism occurs during healing period.
- Immediate covering of a clean wound is needed to prevent infection.
- Healing is a prolonged process.
- Scar tissue develops, even with skin grafting.
- Physiotherapy and occupational therapy may be necessary.
- Surgery may be necessary to release restrictive scar tissue.

End of Lecture