Wound Healing

BASIC CONCEPT
Tissue Damage

• Wound: tissue integrity compromised
• What are the 2 main types of tissue damage?

Example:
- Trauma
- Infection
- Gouty tophi
- Varicose ulcer

Is tissue damage always accidental?
Response of body to tissue damage

Mechanisms of healing:

- **regeneration** or replication of lost or damaged tissue with similar material
- **replacement** or repair of damaged tissue with connective (scar) tissue

Think of a construction site:
- Clearing of damaged cells and other unwanted elements
- Protection of viable tissue
- Reconstitution of the area
Types of wound healing

• **Primary intention**—wound edges approximated
  - Primary healing involves re-epithelialization, in which the skin's outer layer grows closed. Cells grow in from the margins of the wound and out from epithelial cells lining the hair follicles and sweat glands.

What types of wound can you think of that are healed by primary intention?
Healing by primary intention

- Wounds that heal through primary intention are, most commonly, superficial wounds that involve only the epidermis and don't involve the loss of tissue, for example, a first-degree burn.
- A wound that has well-approximated edges (edges that can be pulled together to meet neatly), such as surgical incision, also heals through primary intention.
- Because there is no loss of tissue and little risk of infection, the healing process is predictable. These wounds usually heal in 4 to 14 days and result in minimal scarring.

(Slachta, 2003)
Types of wound healing

- **Secondary intention**
- A wound that involves some degree of tissue loss heals by secondary intention. The edges of these wounds can't be easily approximated, and the wound itself is described as partial thickness or full thickness, depending on its depth: (Johnstone, Farley, & Hendry, 2005)

- Partial-thickness wounds extends through the epidermis and into, but not through, the dermis.
- Full-thickness wounds extend through the epidermis and dermis and may involve subcutaneous tissue, muscle, and, possibly bone.

*Can you think of any example?*
Healing by secondary intention

• During healing, wounds fill with granulation tissue, a scar forms, and reepithelialization occurs, primarily from the wound edges.

• Pressure ulcers, burns, dehisced surgical wounds, and traumatic injuries are examples of this type of wound. These wounds also take longer to heal, result in scarring, and have a higher rate of complications than wounds that heal by primary intention.

(Slachta, 2003)
Types of wound healing

Tertiary intention:

• Considered appropriate to delay the closure of a wound
• Might be to permit further observation or manipulation of the underlying structures or to permit the drainage of infected material
• Scaring in these tertiary intention wounds will depend on the extent of tissue damage
• Length of delay between injury and repair.

So what are examples of this type?
• When a wound is intentionally kept open to allow edema or infection to resolve or to permit removal of exudate, the wound heals by tertiary intention, or delayed primary intention. These wounds result in more scarring than wounds that heal by primary intention but less than wounds that heal by secondary intention.

(Johnstone, Farley, & Hendry, 2005)
Wound Healing Cascade

1. injury
2. bleeding
3. Platelets exposed to collagen and become sticky
4. Plug formed at site of vessel injury
5. Enzymes released to limit blood loss through vasoconstriction

Towards healing:

- Scar Maturation
- Collagen Fibril Crosslinking
- Remodelling
- Endothelial cells
- Epithelial cells
- Collagen
- Fibroblasts
- Proliferation
- Lymphocytes
- Macrophages
- Neutrophils
- Inflammation
- Proteoglycans
- Fibrin
- Platelets
- Haemostasis

Time from injury
Phases of wound healing

1 - Inflammatory phase:
• The inflammatory phase begins with the injury itself:

Immediate to 2-5 days
  
  *Bleeding, Vasoconstriction*

Hemostasis
  
  *Platelet aggregation and Thromboplastin–clot formation*

Inflammation
  
  *Vasodilation: Chemical substances release that begin the healing process*
  
  *Phagocytosis: Specialized cells clear the wound of debris*
Phases of wound healing

2 -Proliferative Phase
• 2 days to 3 weeks
• Matrix or latticework of cells forms - new skin cells and blood vessels will form on this matrix

Granulation
  – *Fibroblasts lay bed of collagen*
  – *Fills defect and produces new capillaries*
  – *These new blood vessels will supply the rebuilding cells with oxygen and nutrients to sustain the growth of the new cells and support the production of proteins (primarily collagen).*

Contraction
  – *Wound edges pull together to reduce defect*

Epithelialization
Phases of wound healing

3 - Remodeling Phase

- 3 weeks to 2 years
  Phase begins when the wound has been closed by connective tissue and epithelialization and continues for a further year or more
- New collagen forms which increases tensile strength to wounds
- Scar tissue is only 80 percent as strong as original tissue
Wound Healing Cascade

- Bleeding
- Platelets exposed to collagen and become sticky
- Plugs formed at site of vessel injury
- Enzymes released to limit blood loss through vasoconstriction

Towards healing:
- Haemostasis
- Fibrin
- Platelets
- Inflammation
- Proteoglycans
- Neutrophils
- Macrophages
- Lymphocytes
- Fibroblasts
- Collagen
- Remodelling
- Scar maturation

Time from injury
The Healing Sequence

HAEMOSTASIS
Platelet aggregation and factor release

EARLY INFLAMMATION
Neutrophil accumulation

LATE INFLAMMATION
Monocyte and lymphocyte accumulation

GRANULATION TISSUE FORMATION
Fibroblast and endothelial cell proliferation (vessel formation)

EXTRACELLULAR MATRIX FORMATION
Synthesis primarily by fibroblasts

REMODELLING
Proteolytic ECM degradation and restructuring

SCAR FORMATION

Towards healing

Time from injury

Scar Maturation
Collagen Fibril Crosslinking
Remodelling

Endothelial cells
Epithelial cells
Collagen

Fibroblasts
Proliferation

Lymphocytes
Macrophages

Neutrophils
Inflammation
Proteoglycans

Fibrin
Platelets

Haemostasis
Wound healing principle

• Factors affecting wound healing

Extrinsic Factors

Intrinsic Factors
Extrinsic Factors

**Mechanical stress**
- Pressure, (the application of forces perpendicular to tissues)
- Friction, (lateral forces)
- Shear (rotational and lateral disruption)

- All affect vascular and lymphatic supply
- Interrupts oxygenation at cellular level
- Lateral forces can lead to the traumatic de-epithelialization of the various stratum
  - NB – overzealous packing of a wound exerts pressure and mechanical stress to a wound
Debris

- Naturally occurring (necrotic tissue, slough)
  - Promotes inflammatory stage of healing
  - May lead to formation of chronic wound
- Introduced:
  - During time of injury (e.g. debris, grit, grass)
  - Intentionally left in situ by clinician (e.g. drain, sutures)
Desiccation

Who is Dr. George D. Winter (1927-1981)?

Formation of the scab and the rate of epithelisation of superficial wounds in the skin of the young domestic pig (Nature 193:293 1962)

THE FATHER OF MOIST WOUND HEALING

Read more about moist wound healing – if you do not understand this concept you do not understand wound management
Epidermal cells migrate only over viable tissues as they require a blood and nutritional supply that is adequate to meet their energy needs. Because the migration tongue of epithelium must burrow between eschar, crust, or a scab and the underlying living tissue.
Maceration

- Excess moisture in the stratum corneum leads to reduction in the barrier function of the skin and provides an environment for microbial ingress and proliferation.

How can you avoid maceration?
Extrinsic Factors

Chemical stress

Presence of toxic chemicals in the wound (iatrogenic factor!)

Think – What chemicals do you use to cleanse wounds – are you a 100% sure they are safe.

If not – WHY DO YOU USE THEM?
Extrinsic Factors

Smoking
Nicotine, carbon monoxide, and hydrogen cyanide undermine wound repair

- Vasoconstriction leading to lack of oxygen and nutrients
- Increases in platelet adhesiveness, raising the risk of thrombotic microvascular occlusion and tissue ischemia
- Proliferation of red blood cells, fibroblasts, and macrophages is reduced
- Diminished metabolism
Radiotherapy

• Has a significant negative effect on wound healing.
• During acute exposure to radiation, wound healing does not occur.
• Tissue, if damaged exhibits delayed or non-healing characteristics due to its ischemic nature.
Health factors

• General health of the individual has a bearing on their ability to heal.

Try and find out a list of diseases that affect wound healing and what is the mechanism of each one that would delay wound healing.
Intrinsic Factors

**Stress**
- Stress affects the immune system and therefore has a detrimental effect on wound healing

**Temperature**
- Optimum temperature for secretory action of inflammatory cells and cell reproduction is 37°C.
- If wound temperature drops below 28°C then leukocyte activity can stop
**Intrinsic Factors**

- Aging

<table>
<thead>
<tr>
<th>Effect of Aging on Skin</th>
<th>Effect of Aging on Healing</th>
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<tbody>
<tr>
<td>Decreased keratinocyte maturation</td>
<td>Decreased skin repair</td>
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<tr>
<td>Decreased melanocytes</td>
<td>Decreased wound contraction</td>
</tr>
<tr>
<td>Decreased Merkel cell production</td>
<td>Decreased reaction time to sun exposure</td>
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<tr>
<td>Flattening of dermal/epidermal junction</td>
<td>Reduced sensation</td>
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<td>Increased risk of junction rupture (skin tear)</td>
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<td></td>
<td>Reduced delivery of nutrients to epidermis</td>
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<td></td>
<td>Increased risk for shearing and blistering</td>
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<tr>
<td></td>
<td>Decreased microcirculation</td>
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<tr>
<td>Decreased Langerhans cells</td>
<td>Decreased immune response</td>
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<tr>
<td>Decreased sebaceous and sweat gland activity</td>
<td>Decreased skin hydration</td>
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<td>Increased skin pH</td>
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<td></td>
<td>Decreased ability to maintain normal acid mantle</td>
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<td>Abnormal scaling, fissuring, cracking and itching</td>
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<tr>
<td>Loss of normal barrier properties</td>
<td>Increased susceptibility to irritants and contact allergens</td>
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<td>Decreased transdermal permeability of lipids</td>
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<td></td>
<td>Increased transdermal permeability of water</td>
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<tr>
<td>Decreased sensory perception</td>
<td>Decrease in ability to differentiate between</td>
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<tr>
<td>Dermal atrophy</td>
<td>Decrease in protective “padding”</td>
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<tr>
<td></td>
<td>Increased risk of damage to underlying structures</td>
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<tr>
<td>Decreased vascularity</td>
<td>Decreased ability to regulate temperature</td>
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<tr>
<td></td>
<td>Decreased new capillary growth</td>
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<tr>
<td></td>
<td>Decreased granulation tissue formation</td>
</tr>
<tr>
<td></td>
<td>Decreased nutrient delivery to skin</td>
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</table>
Intrinsic Factors

Extremes of body build:

• **Emaciated** individuals lack in the essential energy reserves to fuel adequate cell regeneration and may be lacking in basic vitamin and essential minerals.

• Contributing factors associated with wound breakdown in **obesity** can be classified as:
  – mechanical, (due to the weight of pendulous layers of fat causing dead spaces into which hematoma can form)
  – tissue oxygenation, (the reduction of oxygen tension in adipose tissue capillary network)
  – infection.
## Nutritional elements

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<tr>
<th>Nutritional Element</th>
<th>Description</th>
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| **Protein**         | • Required as part of the inflammatory process, in the immune response and in the development of granulation tissue  
• Main protein synthesised during the healing process is collagen, and the strength of the collagen determines wound strength. |
| **Carbohydrate**    | • As part of the healing process the body enters a hypermetabolic phase, where there is an increase in demand for carbohydrate  
• In the case of insufficient carbohydrate, the body breaks down protein to provide glucose for cellular activity |
| **Fats**            | • Certain fatty acids are essential, as they cannot be synthesised in sufficient amounts, so must be provided by diet  
• Involved in the synthesis of new cells |
## Nutritional Element

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| **Vitamins**| • B-Complex vitamins are co-factors or co-enzymes in a number of metabolic functions involved in wound healing, particularly in the energy release from carbohydrates  
  • Vitamin C has an important role in collagen synthesis, in the formation of bonds between strands of collagen fibre, helping to provide extra strength and stability  
  • Vitamin K is involved in the formation of thrombin, and deficiency in the presence of wounds could lead to a haematoma.  
  • Vitamin A is also involved in the cross-linking of collagen and the proliferation of epithelial cells                                                                 |
| **Minerals**| • Zinc - required for protein synthesis, a co-factor in enzymatic reactions, inhibitory effect on bacterial growth, and is involved in the immune response  
  • Iron and copper are co-factors in collagen synthesis |
Complications

• **Infection**
  Drainage of purulent material and inflamed wound edges that, if uncontrolled, can lead to osteomyelitis, bacteremia, and sepsis.

• **Hemorrhage**
  Internal hematoma or external bleeding.

• **Dehiscence**
  Separation of skin and tissue layers that commonly occurs 3 to 11 days after injury.

• **Evisceration**
  Protrusion of visceral organs through a wound opening.

• **Fistula**
  Abnormal passage between two organs or between an organ and the surface of the body.
Post-op Wound Infection

- Surgical wounds are classified according to the likelihood of contamination and wound infection
  - **Clean Wound**
    - E.g. Knee arthroscopy. Wound infection rate <1%
  - **Clean-contaminated wound**
    - E.g. gastrectomy. Wound infection rate <5%
  - **Contaminated wound**
    - E.g. open fracture. Wound infection rate >5%