Burns and Wound healing

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Molecular & Cellular Pathology
Be sure to keep hot liquids out of reach of small children
U.S. Burn Statistics

- Approximately **2.4 million burn injuries** are reported per year
- Medical professionals treat approximately 650,000 of the injuries;
- Between **8,000 and 12,000** of patients with burns die,
- Patients with major burns exceeding 60% of their total body surface area often do not survive
Hospital Costs

• Burns are one of the most expensive catastrophic injuries to treat.

• “The cost of waiting for your own skin to grow can be more painful than the burn itself!”
Occupational skin disease

- Physical
  – Heat, cold, radiation
Workers compensation

• Evaluation
  – Diagnosis
  – Causation
  – Impairment evaluation
  – Conclusions & recommendations
  – Physical examinations
Effective management requires an understanding of burns pathophysiology

- Different causes lead to different patterns of injury
- Knowing the cause will help predict the pathological response and therefore the treatment
Anatomy of skin

• **Epidermis**
  - Outer layer contains the stratum corneum
    • The rate limiting step in dermal or percutaneous absorption is diffusion through the epidermis

• **Dermis**
  - Much thicker than epidermis
  - True skin & is the main natural protection against trauma
  - Contains
    • Sweat glands
    • Sebaceous glands
    • Blood vessels
    • Hair
    • Nails

• **Subcutaneous Layer**
  - Contains the fatty tissues which cushion & insulate
Review of skin functions

• Functions of the skin
  • Protection
  • Heat regulation
  • Sensory perception
  • Excretion
  • Vitamin D production
Background Information

- Attempts to cover wounds and treat severe burns is cited as far back as 1500 B.C.

- Grafts from humans (allografts) or animals (xenografts)
• Burns
  – Types of burns include explosion, steam, hot-water, molten metal, hot-solid, flame, and electricity and radiant energy
  – Classified as:
    • First-degree
    • Second-degree
    • Third-degree
Classification of burns

• Partial thickness - characterized by varying depth from epidermis to the
  ➢ Superficial - includes only the epidermis
  ➢ Deep - involve entire epidermis and part of the dermis

• Full thickness - above + possible damage to the SC, muscle and bone
Mechanisms of burns injuries

- Electrical burns
- Inhalation burns
- Chemical burns
- Radiation burns
Electrical burns

- high intensity heat

- brain or heart damage or musculoskeletal injuries associated with the electrical injuries.

- safely remove the person from the source of the electricity. Do not become a victim.
Electrical Burns

Voltage → tissue damage

2 pathways of damage:

1. Electrical dysfunction of the cardiovascular conduction system and the nervous system

2. Conversion of electrical energy to heat energy when the current encounters the resistance of the tissues
Inhalation burns

• Occur in people trapped in burning buildings or vehicles

• Exposure to high temperature aerosolized flammable materials

• Damage to respiratory tract epithelium from the oral cavity to the alveoli
Chemical burns

- damage until it is completely removed
- Alkalis worse – penetrate deeper
- If cutaneous exposure remove clothes and wash area
- Usually seen in industrial setting or motor vehicle accident
CaOH
Radiation burns

• Treatment may result in burns

• Xray – medical imaging and radiotherapy
Radiation

• Ionizing radiation sources
  – Alpha radiation stopped by skin
    » Ingestion

  – Beta radiation can injure skin by contact
    » Localized at skin surface or outer layers of skin

  – Gamma radiation and x-rays are skin and systemic hazards
    » Skin cancer may develop
Burn ➔ Healing
Phases of Wound Healing

1. Vascular Response
2. Blood coagulation
3. Inflammation
4. Formation of new tissue
5. Epithelialisation
6. Contraction & Remodeling
Early wound healing events

- Hemostasis
  - Platelet aggregation
  - Intrinsic and extrinsic coagulation cascade
  - Thrombin, fibrin
  - Vasoconstriction
Early wound healing events

• **Inflammation**
  Vasodilatation
  Increase in vascular permeability
  Chemotaxis
  Cellular response
Early wound healing events

- Homeostasis
- Neutrophils
- 48-72h- macrophages
- 5-7 days- few inflammatory cells.
ROLE OF MACROPHAGES IN WOUND HEALING

- Phagocytosis, antimicrobial function
  - Oxygen radicals
  - $H_2O_2$, $O_2$, $OH$
  - Nitric oxide

- Wound debridement
  - Phagocytosis
  - Enzymes: collagenase, elastase

- Cell recruitment and activation
  - Growth factors: PDGF, TGF-$\beta$, EGF, IGF
  - Cytokines: TNF-$\alpha$, IL-1, IL-6
  - Fibronectin

- Angiogenesis
  - Growth factors: bFGF, VEGF
  - Cytokines: TNF-$\alpha$

- Matrix synthesis regulation
  - Growth factors: TGF-$\beta$, EGF, PDGF
  - Cytokines: TNF-$\alpha$, IL-1, IFN-$\gamma$
  - Enzymes: collagenase, arginase
  - Prostaglandins: PGE$_2$
Intermediate wound healing events

- Mesenchymal cell chemotaxis and proliferation
- Angiogenesis
- Epithelisation

- 2-4 days after injury
- Mediated by cytokines
Intermediate wound healing events

Mesenchymal cell chemotaxis and proliferation
- Fibroblasts - migration and proliferation
- Smooth muscle

Angiogenesis - reconstruction of vasculature
- Stimulate: High lactate, acidic Ph, low O2 tension
- Endothelial cell migration and proliferation
Intermediate wound healing events

Epithelisation

• Partial thickness- Cells derived from wound edges and epithelial appendages.

• Incisional wound: cellular migration over less then 1 mm. Wound sealed in 24-48h.

• Cellular detachment

• Migration
Late wound healing events

**Collagen synthesis**

- 3 helical polypeptide chains
- Lysine and proline hydroxylation

Required for cross-linking
Late wound healing events

Collagen synthesis

- 3-5 days post injury
- Primarily by fibroblasts
- Maximum synthesis rate 2-4 weeks
- Declines after 4 weeks
- Type 1 collagen most common (80-90% of skin collagen)
- Type 3- seen in early phases of wound healing
Wound contraction

- Centripetal movement of the wound edges toward the center. (0.6-0.7 mm/day)
- Begins at 4-5 days
- **Maximal contraction 12-15 days**
- Trivial component in closed incisional wounds, significant for closure of open wounds
- Rate - depends on tissue
- Circular wounds - slower closure but avoid stenosis
Wound contraction

- Mechanism: cell mediated processes, not requiring collagen synthesis
- Myofibroblasts: fibroblasts with myofilaments in cytoplasm
- Appear in wound day 3-21
- Located in periphery: pull wound edges together.
- Contractures: contraction across joint surface
Terminal wound healing events

- Remodeling- turnover of collagen. Type 3 replaced by type 1
- Day 21- net accumulation of wound collagen becomes stable
- Wound bursting strength- 15% of normal.
- Week 3-6- greatest rate of increase
- 6 weeks- 80-90% of eventual strength.
- 6 months maximum strength (90%). Process continues for 12 months
REMELING

Changes in physical properties of extracellular matrix

- Total collagen content
- Wound breaking strength

Days Postwounding:

- Total Collagen Content
- Wound Breaking Strength
Cytokines and growth factors

- Primary mediators in wound healing.
- Endo, para, auto, intracrine function
- EGF
- FGF
- PDGF
- TGF
Growth factors in wound healing

<table>
<thead>
<tr>
<th>Growth Factor</th>
<th>Cell Source</th>
<th>Function</th>
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<tbody>
<tr>
<td>PDGF</td>
<td>Macrophages</td>
<td>Stimulates fibroblast &amp; smooth muscle cell chemotaxis and proliferation,</td>
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<td></td>
<td>Platelets</td>
<td>collagen synthesis, collagenase activity, fibronectin synthesis</td>
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<td>Endothelial cells</td>
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<tr>
<td></td>
<td>Platelets</td>
<td>Stimulates fibroblast chemotaxis and proliferation, collagen synthesis,</td>
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<tr>
<td>TGF-β</td>
<td>Macrophages</td>
<td>proteoglycan synthesis, fibronectin synthesis, angiogenesis, wound</td>
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<td>Lymphocytes</td>
<td>contraction</td>
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<tr>
<td>EGF</td>
<td>Multiple</td>
<td>Stimulates epithelial cell chemotaxis and proliferation, fibroblast</td>
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<td></td>
<td></td>
<td>chemotaxis and proliferation, endothelial cell proliferation</td>
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<tr>
<td>FGF</td>
<td>Macrophages</td>
<td>Stimulates fibroblast proliferation, epithelial cell proliferation,</td>
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<tr>
<td></td>
<td>Endothelial cells</td>
<td>endothelial cell proliferation, collagen synthesis, proteoglycan</td>
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<tr>
<td></td>
<td></td>
<td>synthesis, fibronectin synthesis, angiogenesis, wound contraction</td>
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<tr>
<td>TGF-α</td>
<td>Macrophages</td>
<td>Same as EGF.</td>
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<td>Keratinocytes</td>
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<tr>
<td>IL-1</td>
<td>Macrophages</td>
<td>Stimulates inflammatory cell chemotaxis, epithelial cell chemotaxis,</td>
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<td></td>
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<td>fibroblast proliferation, collagen synthesis, collagenase activity</td>
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<tr>
<td>TNF</td>
<td>Macrophages</td>
<td>Stimulates fibroblast proliferation, collagen synthesis, collagenase</td>
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<td></td>
<td>Lymphocytes</td>
<td>activity, angiogenesis</td>
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<td>IGF</td>
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<tr>
<td></td>
<td>Liver cells</td>
<td>synthesis</td>
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Forensic pathology

- A large percentage of the work done by forensic pathologists involves burns.
- All types of burn injuries are seen.
- Commonly incineration cases occur especially in motor vehicle accidents.
Complications of burns

- process of healing
- immediate and delayed
- Skin – fluid retention
- Protection from infectious agents
- Fluid loss - haemoconcentration and poor vascular perfusion of the skin and viscera – shock and acute tubular necrosis
Delayed

- Poor perfusion – infections and sepsis
- Scar tissue – lack elastic properties – contractures
Are you one of those people that stays up to date on the latest sports scores and plays?
Wound care - grafting

Indications for grafting ➔
  full thickness
  priority areas
  wound bed pink, firm, free of exudate
  bacterial count < 100,000/gram of tissue