DEFINITION OF A WOUND

Loss of continuity of epithelial lining
Classification of wounds

- Incised
- Laceration
- Abrasion/contusion
- Partial or full thickness
- Acute or chronic
Practical clinical classification of wounds

- Clean
- Clean contaminated
- Dirty contaminated
- Infected
- Sloughy
- Necrotic
STAGES OF WOUND HEALING

• A complex array of sequential and overlapping interactive molecular and cellular processes
• Haemostasis and clot formation
• Inflammatory Response
  – Phagocytic Cellular Invasion
  – Humoral Factors
• Cell migration Re-epithelialization
• Cell proliferation and Granulation Tissue Formation
• Organization / Remodeling
• Wound Contraction
• DR between cells and ECM. Cells synthesize ECM components and also degrade and remodel CM, the latter events occurring through the production and regulation of matrix metalloproteases and other enzymes. The ECM regulates cellular tension and polarity.
HAEMOSTASIS/ CLOT FORMATION

Vasoconstriction $\rightarrow$ decrease blood flow

Platelets plug $\rightarrow$ GFs and cytokines

Fibrin clot $\rightarrow$ temporary matrix (removed by plasminogen dissolving fibrin lot)

NB: clotting factors
INJURY
Key events in inflammation

- Vasoactivity, mainly vasodilatation (vascular endothelium secretes nitric oxide)
- Chemo-attraction
- Complement activation (classical pathway: C1/C2; alternative pathway: factor B)(activated C3a: fibrocytic pathway, activation of factor B and C4; and C3b)
- Coagulation activation
- Collagen and other matrix digestion
- Inflammatory cell accumulation and multiplication
Humoral response

- Complement cascade
- Coagulation cascade
- Acute phase proteins (all increased, apart from albumin)
Phagocyte cell invasion

- Chemo attractants:
  - Complement derived C5a, C5b
  - Platelet derived (platelet derived growth factor)
  - Leucocyte derived (chemo attractants)
  - Other eg FDP (act as chemo attractants)
- Neutrophils (rapid response)
- Macrophages (slow response)
Biology of wound healing

• Role of neutrophils:
  – Phagocytosis
  – Oxidative and enzymatic killing of microbes
  – Secretion of proteases

• Role of macrophages:
  – Phagocytosis
  – Scavenging of debris
  – Orchestration of inflammatory/immune response
Macrophages, matrix metalloproteinases and their tissue inhibitors

- Breakdown of matrix to allow for early cellular ingress ion
RE-EPITHELIALISATION

- Epithelial and fibroblast migration
- Proteases
- Matrix metalloprotease
- Leucocyte derived proteases
- tPA an uPA
- Other
Proliferation & GRANULATION TISSUE

• Fibroblasts: derived from normal tissue surrounding wound, attracted by chemo attractants into wound, proliferate by stimulation of growth factors (PDGF). Purpose: lay collagen

• The matrix - collagen
  - glycans
  - other

• Angiogenesis
Role of adhesion molecules

- Matrix
  - Fibronectin
  - Vitronectin
  - Thrombospondin
  - Collagen
  - Others

- Cellular
  - Selectins
  - Integrin, fibronectin, vitronectin receptors

Interaction: part of dynamic reciprocity
Macrophage stimulation increase collagen biosynthesis

- Murine model of full thickness incision and colon anastomosis
- Pre and post-op Rx with glycan phosphate
- Increased collagen synthesis measured by hydroxyproline
- Increased tensile strength of both skin and colon repair
<table>
<thead>
<tr>
<th>Factor</th>
<th>PDGF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Platelet, Macroph, Fibrobl, Endoth, Sm Muscle</td>
</tr>
<tr>
<td>Target</td>
<td>Neutrophils, Macroph, Fibrobl, Sm Muscle</td>
</tr>
<tr>
<td>Function</td>
<td>Chemotaxis, Proliferation, Collagen breakdown (chemo attractant to phagocytes)</td>
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<tr>
<td>Factor (factor)</td>
<td>TGF alpha (tissue derived growth factor)</td>
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<tr>
<td>----------------</td>
<td>-----------------------------------------</td>
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<tr>
<td>Source</td>
<td>Platelet, Keratino, Macroph</td>
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<tr>
<td>Target</td>
<td>Epith, Fibroblast, Endoth</td>
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<tr>
<td>Function</td>
<td>Proliferation</td>
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</table>
SELECTED GROWTH FACTORS IN WOUND HEALING - III

Factor - IL-1 (endogenous pyrogen) (causes Pyrexia)

Source - Macrophage

Target - Fibrobl, Neutrophils

Function - Proliferation, Collagen breakdown, Chemotaxis
### SELECTED GROWTH FACTORS IN WOUND HEALING - IV

<table>
<thead>
<tr>
<th>Factor</th>
<th>TGF-β</th>
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<tbody>
<tr>
<td>Source</td>
<td>Ubiquitous</td>
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<tr>
<td>Target</td>
<td>Ubiquitous</td>
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<tr>
<td>Function</td>
<td>Fibrosis, Proliferation</td>
</tr>
</tbody>
</table>
SELECTED GROWTH FACTORS IN WOUND HEALING - V

Factor: IGF-I / Isomatomedian C
Source: Fibrobl
Target: Fibrobl, Endoth
Function: Cell replication, Collagen synth
WOUND CONTRACTION

Organization

Remodeling
Reference

Wound rep reg (p137)
• Hemostasis: platelets
• Inflammatory: monocytes
• Proliferative: fibroblasts, endothelial cells
• Remodeling: fibroblasts (collagen), myofibroblasts
Wound healing in embryo and fetus

- Regeneration
- Non scarring healing
- Role of neutrophils
Disordered wound healing

- Poor wound healing
- Hypertrophic scar and keloid (accelerated process of healing)
LOCAL FACTORS THAT AFFECT WOUND HEALING

- Ischaemia - reduced arterial perfusion
  - venous stasis
  - smoking
  - radiation
  - oedema (↑ compartment P°)
  - constant compression pressure
- Infection
  - bacterial
  - fungal
  - parasitic
- Foreign Body
- Topical Steroids
SYSTEMIC FACTORS THAT AFFECT WOUND HEALING

General Malnutrition
Specific

- Micro Nutrient Deficiencies
- Vit A & C
- Minerals, eg Cu, Se

Immunosuppression

Diabetes Mellitus

Collagen Disorders

- Marfans
- Collagen vascular disorders

Systemic Infection