Inflammation and Healing

BIO 375
Pathophysiology

Review of Normal Defenses

Review of Normal Capillary Exchange
Inflammation

- Inflammation is a biochemical and cellular process that occurs in vascularized tissues.
- Most of the essential components of the inflammatory process are found in the circulation and most of the early mediators of inflammation affect the vascular bed so as to increase the movement of plasma and blood cells from the blood into the tissues surrounding the injury.

- These substances escaping from the circulation are called exudate and they defend the host against infection and facilitate tissue repair and healing.
- Inflammation and repair can be divided into several phases.
- The characteristics of the early inflammatory response differ from those of the later response.

- The different biochemical mediators and cells function together to:
  - Destroy injurious agents and remove them from the inflammatory site.
  - Wall off and confine these agents so as to limit their effects on the host.
  - Stimulate and enhance the immune response.
  - Promote healing.
Inflammation vs Immunity

- The immune system is **antigen specific** and has **memory**
- The inflammatory response is **nonspecific** because it takes place in approximately the same way regardless of the stimulus, and occurs in the same manner, even on second exposure to the same stimulus

Acute vs Chronic Inflammation

- Acute inflammation is self-limiting; that is, it continues only until the threat to the host is eliminated
- This usually takes 8-10 days from onset to healing
- Inflammation is considered chronic if it persists longer than two weeks

Inflammation

- Inflammation is the body’s response to tissue injury
- -itis is ending used to denote disorders involving inflammation
- **Causes include** direct damage (cuts, sprains), chemicals like acids, ischemia and cell necrosis or infarction, allergic reactions, physical agents (thermal injuries, burns, radiation), foreign bodies (splinters or dirt) and infection
Acute Inflammation

Key Words:
- chemical mediators
- vasodilation
- hyperemia
- capillary permeability
- chemotaxis
- neutrophils
- diapedesis or emigration
- lysosomal enzymes

In the area of injury, endothelial cells produce cell-adhesion molecules (CAMs) that make their membranes sticky and they snag leukocytes. The leukocytes slow down and accumulate on the linings of capillaries and post capillary venules and then enter the damaged tissue by diapedesis. Chemicals released by basophils, mast cells, blood plasma and damaged tissue cells stimulate chemotaxis and phagocytosis.

Inflammation-Local Effects

- Redness
- Warmth
- Swelling or edema
- Pain
- Loss of function due to:
  - Lack of nutrition, e.g. liver cells
  - Swelling, e.g. joint movement
Local Effects

- Exudate refers to the interstitial fluid formed in the affected area.

Characteristics of exudate vary with cause of trauma:

- Serous
- Fibrinous
- Purulent
- Abscess
- Bloody
- Granuloma

Inflammation-Systemic Effects

- General manifestations:
  - Malaise
  - Fatigue
  - Headache
  - Anorexia
  - Fever
Course of the Inflammatory Response

- If the cause of the inflammatory response is brief (touching hot object), the response often subsides in about 48 hours.

- If the cause of the inflammatory response persists, the inflammatory response continues until the causative agent is removed.

- The amount of tissue destruction (necrosis) depends on the specific cause of the trauma and contributing factors.

- Potential complications include:
  - Ulcers with possible perforation
  - Skeletal muscle spasms
  - Chronic inflammation may develop following an acute episode when the cause is not completely eradicated, or may develop insidiously due to chronic irritation, specific bacteria or long term immune responses.
**Chronic Inflammation**

- Characteristics include:
  - Less swelling but more lymphocytes, macrophages and fibrocytes than acute inflammation
  - More collagen is produced in the area resulting in more scar tissue.
  - Granulomas may develop as an area is walled off by fibrous tissue as in tuberculosis
  - Frequently, more tissue destruction occurs in chronic inflammation

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**Course of Inflammation and Healing**

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**Drugs used to treat Inflammation**

<table>
<thead>
<tr>
<th>ASA</th>
<th>Acetaminophen</th>
<th>NSAIDs</th>
<th>Prednisone (oral corticosteroids)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actions</td>
<td>Anti-inflammatory</td>
<td>Analgesic (pain)</td>
<td>Analgesic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anti-inflammatory</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Decreased immune response</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Increased risk of infection</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Increased blood pressure and edema</td>
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<td></td>
<td></td>
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<td>Osteoporosis and skeletal muscle wasting</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Delays blood clotting</th>
<th>Delays blood clotting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nausea, stomach ulcers, and bleeding</td>
<td>Some nausea, stomach ulceration, and bleeding</td>
</tr>
</tbody>
</table>
Types of Healing

- **Resolution** occurs when there is minimal damage, e.g. mild sunburn
- Resolution is the restoration of original structure and physiological function
- **Regeneration** is the healing process that occurs in damaged tissue when cells are replaced through mitosis by nearby cells.
- **Replacement** by connective tissue occurs when there is extensive damage or the cells (e.g. brain or muscle) are incapable of mitosis (this is referred to as repair rather than resolution or regeneration)

Healing by Regeneration: First and Second Intention

The Healing Process

- Blood clot forms and seals the area
- Inflammation develops in the surrounding area
- After 3-4 days, foreign material and cell debris have been removed by phagocytes, monocytes and macrophages
- Granulation tissue grows into the gap from surrounding connective tissue
Granulation Tissue

- This is a highly vascular tissue that appears moist and pink or red in color
- It is a very fragile tissue and can be broken down by bacteria or physical stress on the tissue
- Simultaneously, epithelial cells undergo mitosis, extending across the wound from the outer edges inward (epithelialization)

- Fibroblasts invade the area and produce collagen, the protein that is the basic component of a scar
- Eventually, the capillaries decrease and the scar turns from pink to white
- Scar tissue is NOT normal tissue, it just fills in the gap in the tissue.
  - A small gap results in complete healing within a short time and with little scarring
  - A large or deep area of tissue damage requires a prolonged healing time and results in a larger scar

Factors Affecting Healing

<table>
<thead>
<tr>
<th>FACTORS PROMOTING HEALING</th>
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</thead>
<tbody>
<tr>
<td>Youth</td>
</tr>
<tr>
<td>Good nutrition: protein, vitamins A and C</td>
</tr>
<tr>
<td>Adequate hemoglobin</td>
</tr>
<tr>
<td>Effective circulation</td>
</tr>
<tr>
<td>Clean, undisturbed wound</td>
</tr>
<tr>
<td>No complications</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FACTORS DELAYING HEALING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced age, reduced mitosis</td>
</tr>
<tr>
<td>Poor nutrition, dehydration</td>
</tr>
<tr>
<td>Anemia (low hemoglobin)</td>
</tr>
<tr>
<td>Circulatory problems</td>
</tr>
<tr>
<td>Irritation, bleeding, or excessive mobility</td>
</tr>
<tr>
<td>Infection, foreign material, exposure to radiation, insulin deficit</td>
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</table>
Complications of Healing by Scar Formation

- Loss of function which results from loss of normal cells and lack of specialized structures of normal tissue, e.g. skin
- Contracture is due to the fact that scar tissue is nonelastic and tends to shrink over time. This can restrict the movement of a joint and may eventually lead to fixation and deformity of the joint
- Shortening of the scar tissue may also cause shortening or narrowing of structures, particularly tubes and ducts, e.g. hiatal hernia and difficulty in swallowing due to stenosis
- Adhesions are bands of scar tissue joining two surfaces that are normally separate, e.g. intestinal or pleural adhesion
Hypertrophic scar tissue is an excess of fibrous tissue which can shrink and distort and also includes keloid formation.

Ulceration may occur due to impaired blood supply around the scar. This causes additional tissue breakdown and formation of ulcers, e.g. after stomach surgery.

Burns

Burns are classified by the percentage of the body surface damaged and the depth of the skin damage.

- Partial thickness involves the epidermis and part of the underlying dermis
- Full thickness burns destroy all skin layers and require skin grafts for healing
- Following severe burns, shock frequently occurs due to fluid and protein loss
Partial thickness Burn                Full thickness burn

BODY SURFACE AREA (BSA)

<table>
<thead>
<tr>
<th>Body Part</th>
<th>% BSA</th>
</tr>
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<tbody>
<tr>
<td>Total head</td>
<td>9%</td>
</tr>
<tr>
<td>Two arms</td>
<td>18%</td>
</tr>
<tr>
<td>Trunk</td>
<td>30%</td>
</tr>
<tr>
<td>Pelvis</td>
<td>1%</td>
</tr>
<tr>
<td>Two legs</td>
<td>30%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
</tr>
</tbody>
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Anterior body surface

Posterior body surface

(Images and diagrams courtesy of W.B. Saunders Company)
- Infection is a threat due to loss of protection
- Inhalation of toxic or irritating fumes may cause respiratory impairment
- Healing of burns is a prolonged process and may require multiple skin grafts