OPEN ACCESS TEXTBOOK OF GENERAL SURGERY

WOUND HEALING **G Chinnery**

INTRODUCTION

Wound healing is a complex interplay of a multitude of sequenced events in response to injury. It involves the activation of basic cellular processes of inflammation, cell proliferation and growth, as well as regulation of these processes once repair is complete.

HISTORY OF WOUND HEALING

Galen of Pergamum (120 — 201 A.D.), appointed as the doctor to the Roman gladiators, dealt with all the wounds following gladiatorial combats. He was convinced of the importance of maintaining a moist wound environment to ensure adequate healing. Approximately 19 centuries later this fact was to be proven scientifically, when it was shown that the epithelialization rate of wounds inflicted on pigs increases by 50% in a moist environment. Discovering antiseptics was the next major advance in the reduction of wound infections. Ignaz Philipp Semmelweis (1818 — 1865), a Hungarian obstetrician, noticed the decrease in occurrence of puerperal sepsis if medical students first washed their hands with soap and hypochlorite after cadaver dissections, before they attended to pregnant women in the labour wards. Louis Pasteur (1822 — 1895) proved that wounds develop infection by the introduction of bacteria from the surrounding environment. On a visit to Glasgow, Scotland, Joseph Lister noted that some areas of the city's sewer system were clearer and cleaner than others. He discovered that this was due to the dumping of waste containing carbolic acid. From 1865 he began to soaking his instruments in carbolic acid, as well as spraying the operating rooms. The mortality dropped dramatically from 50% to 15%. After an initial suspension by sceptics, confirmation of his results paved the way for his triumphant return to Edinburgh. In 1876, Robert Wood Johnson began 10 years of research that would ultimately result in the production of an antiseptic dressing in the form of cotton gauze impregnated with iodine. He was inspired after attending a lecture given by Joseph Lister. A multitude of other materials and antiseptics have subsequently been tested and developed to aid in optimal wound healing.

ANATOMY OF SKIN

The skin consists of three layers, the epidermis, dermis and_ subcutaneous fat layer. Each layer has its own specific function. Skin is thicker on the dorsal and extensor surfaces with one of its main functions being as a protective barrier.

Epidermis

The epidermis is the outer layer of the skin and consists of stratified squamous epithelium. The epidermis is of varying thickness; only 0.05mm on the eyelids and up to 1.5mm on the palms and soles. The innermost layer consists of the basal cells, which is a single row of columnar cells. These further divide to form keratinocytes, which comprise the spinous layer. Intercellular bridges connect the individual cells of the spinous layer. Keratinocytes synthesize an insoluble protein which becomes a major strengthening component of the outer layer. These cells continue to flatten and their cytoplasm becomes more and more granular. As they reach the surface, the cells die and form the stratum corneum.

Three types of branched cells are present in the epidermis.

- Melanocytes — which synthesize melanin
- Langerhans cells — involved in skin immunity
- Merkel cells — as yet undetermined function

Dermis

The dermis too varies in thickness from 0.3mm on the eyelid to 3mm on the back. lt is composed of three types of connective tissue.

- Collagen
- Elastic tissue
- Reticular fibers

The dermis is composed of a thin upper layer of randomly arranged collagen fibers, and a second thicker lower reticular layer, which extends from the base of the papillary layer to the subcutaneous tissue. The reticular layer is composed of thick collagen fibers arranged parallel to the skin surface. The haemosiderin, melanin and by-products of inflammation are cleared by histiocytes (wandering macrophages). Mast cells congregating mainly around blood vessels are responsible for the release of histamine and heparin. Touch and pressure are perceived by Meissner's and Vater-Pacini corpuscles. Pain, itch and temperature sensations are received by unmyelinated nerve endings in the papillary dermis. The motor innervation of the skin is supplied by the autonomic system. Adrenergic fibers innervate the blood vessels causing vasoconstriction, the hair erector muscles and the apocrine glands. Autonomic fibers to eccrine sweat glands are cholinergic. Sebaceous glands are regulated by the endocrine glands.

Subcutaneous layer

This is the deepest and thickest of the three layers and it consists of a network of collagen and adipose cells. The subcutaneous layer helps to conserve body heat and protects underlying tissues from injury.

WOUND HEALING

Wound healing is a complex, involved response to tissue injury. The injury may be acute or chronic and involve multiple different tissues. Primary wound healing will occur within hours of repairing a full- thickness surgical incision. However, if the wound edges are not approximated immediately, delayed primary wound healing occurs. Secondary wound healing occurs when the wound edges of a full- thickness wound are not approximated. The wound is instead allowed to close and heal by mainly granulation tissue which is deposited into the wound following an intense local inflammatory reaction. This secondary wound healing will result in a pronounced contraction of the wound.

Partial thickness wounds, which involve only the epidermis and superficial dermis, will heal by epithelialization. This involves replication and migration of epithelial cells across the wound. Contractions are generally not a problem.

Although a simplification with much overlap in time, it is still helpful to consider wound healing in four separate phases.

- Haemostasis (occurring in seconds to minutes)
- Thromboxane and prostaglandin release will cause immediate vasoconstriction. Platelets then adhere to any exposed collagen and release the contents of their granules. Tissue factor further activates both platelets and the coagulation cascade. The resulting fibrin- matrix is able to control bleeding, allows concentration of growth factor and serves as a scaffolding for wound healing.

- Inflammation (3 — 5 days). Prostaglandins, histamine, serotonine, kinins and bacterial products cause vasodilatation and capillary permeability and result in localized oedema. A wide variety of factors and cytokines released attract granulocytes to the wound environment. Neutrophils appear in the wound shortly after injury and begin clearing debris and bacteria by phagocytosis. Proteases

secreted by neutrophils digest debris and injured tissue; oxygen-dependent killing mechanisms are used to control bacterial contamination. Within 24-48 hours monocytes have migrated to the wound and transformed themselves into macrophages. These too have a phagocytotic role, but also produce various growth factors necessary for wound healing. Although inflammation is vital in both controlling contamination and inducing the proliferative phase of wound healing, prolonged or intense inflammation can damage viable tissues. In addition to local effects, inflammatory mediators may result in a systemic inflammatory response. Failure of progression to the proliferative phase results in a chronic wound.

- Proliferation (4 — 14 days)
  Re-epithelialization begins soon after injury and relies on the lateral emigration of epithelial cells from the wound edges or from any remaining adnexal structures in the dermis, for example hair follicles. Epithelial migration and proliferation continue until an intact epithelial barrier is re-established covering the whole wound surface. The low oxygen tension and high lactate levels characteristic of a poorly perfused wound stimulate the production of angiogenic factors which encourage new capillary growth into the wound area. Within 2 — 3 days, activated fibroblasts will have migrated into the wound. The original wound matrix, composed primarily of fibrin and fibronectin, is supplemented and strengthened by glycosaminoglycans,
  proteoglycans and other proteins produced by the fibroblasts. Fibroblasts begin by secreting mainly immature type lll collagen into this provisional matrix. Some fibroblasts are stimulated into transforming into myofibroblasts, which will later be responsible for wound contraction.

- Remodeling (day 8 to 1 year)
- Fibroblasts will continue to produce collagen even as various
- proteases are released to digest it. This continues for approximately
- 4 — 5 weeks, but increased collagen turnover usually continues for up
- to a year after the initial injury. With time, type lll collagen is
- gradually replaced by type l collagen and collagen fibrils which is
- stronger and more organized. After one week the wound has only
- 3% of its pre-injury strength; increasing to 30% at 3 weeks and
- approximately 80% by 3 months.

SURGICAL SITE INFECTION

Surgical site infection (SSI) is the second most common nosocomial infection in hospitalized patients. It is an infection that occurs somewhere within the operative field within 30 days of a surgical intervention. lncisional SSI may be superficial if limited to the skin or subcutaneous tissues, or deep if it extends down to the fascial or muscle layers. Organ or cavity SSI may occur anywhere within the operative field other than where the body wall tissues were incised, for example an intra-abdominal abscess following a laparotomy.

Clinical Criteria for diagnosing a SSI

- Purulent drainage from the surgical incision
- Organisms isolated from an aseptically obtained culture of fluid or
- tissue from the surgical site
- At least one of the following signs or symptoms: pain or
- tenderness, localized swelling, redness, heat
- Systemic findings such as pyrexia, raised white cell count,

- tachycardia, raised inflammatory markers *
- An abscess or other evidence of an infection involving the deep layers of the surgical incision or within the operated organ or cavity, discovered either by direct examination, during re- operation or by histopathological or radiological examination.

SURGICAL WOUND CLASSIFICATION

The likely hood of developing a SSI depends largely on the cleanliness of the operative environment.

- Class One: Clean
  - Operative wound clean.
  - Non-traumatic with no inflammation encountered
  - No break in surgical technique
  - Respiratory, gastrointestinal and genito-urinary tracts not entered

- Class Two: Clean-contaminated
  - Operative wound clean-contaminated
  - Respiratory, gastrointestinal and genitourinary tracts entered under controlled conditions without unusual contamination
  - Operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered
- Class Three: Contaminated
  - Operative wound contaminated
  - Open, fresh, accidental wounds from a clean source
  - Operations with major breaks in sterile technique (for example open cardiac massage), or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered
- Class Four: Dirty-infected
  - Operative wound dirty
  - Traumatic wound from a dirty source or with delayed treatment
  - Faecal contamination
  - Presence of a foreign body
  - Retained devitalized tissue
  - Operative wound with pre~existing infection, or perforated viscus

- Class Five: Unclassified
  - Unable to accurately classify an operative wound

Acute wounds

In healthy individuals with no underlying factors, an acute wound should heal within three weeks with remodeling continuing for the next year.

Chronic wounds

A chronic wound persists beyond three months. A chronic wound fails to proceed through an orderly and timely process to produce anatomic and functional integrity. Alternatively, it may proceed through the repair process but without resulting in a sustained anatomic or functional outcome. A chronic wound should encourage a search for unresolved underlying causes for delayed healing. The factors affecting chronic wound closure are usually multi-factorial.

Systemic factors affecting wound healing

- Poor nutritional status
- Ageing
- initial or repetitive trauma
- Animal bites, insect stings
- Continuous pressure
- Vascular compromise (arterial, venous or a combination thereof)
- Immunodeficiency
- Malignancy
- Connective tissue disorders
- Metabolic diseases including Diabetes Mellitus
- Smoking

- Radiation
- Psychosocialdisorders
- Adverse effects of chronic medication including steroids
- Scalds and burns, flame or chemical

WOUND DRESSING

A multitude of synthetic and natural wound dressings are available, with new products constantly being developed. The ideal dressing should:

- Remove exudates and toxins
- Maintain a high humidity at the dressing-wound interface
- Debride necrotic tissue
- Allow for gaseous exchange
- Be antibacterial
- Hypoallergenic
- Be free from particulate matter and toxic components
- No trauma to wound on removal of the dressing
- Reasonably priced and easily available

SPECIFIC CHRONIC WOUNDS

Pressure sores

In Europe the incidence of pressure sores is estimated at 9.2% among institutionalized patients. A pressure sore is a wound that develops in the upper layers of the skin, usually over a boney prominence, due to prolonged externally applied pressure. Sustained pressure results in tissue ischaemia by occlusion of the microcirculation, this occurs once the tissue pressure exceeds the capillary filling pressure. The time before pressure causes tissue ischaemia varies greatly between individuals and may lie between 30 and 240 minutes. Often a relatively small skin ulceration is found overlying a much larger area of subcutaneous necrosis. This is because the skin is more resistant to pressure than are the underlying subcutaneous fat and muscle. Once the skin is open the local inflammatory reaction may be complicated by bacterial colonization which can lead to systemic sepsis. If bone is visualized in the ulcer base an accompanying osteomyelitis is likely. Risk factors for the development of pressure sores include:

- Immobilization
- Peripheral vascular disease
- Congestive cardiac failure
- Advance age
- Malnutrition
- Cachexia
- Obesity

Local wounds should be treated with hydroactive atraumatic dressings, however on occasion surgical debridement may be required, followed by plastic surgical closure of the remaining defect. A pressure sore develops within a few days but can take weeks to months before it heals, therefore prevention remains the key.

Leg ulcers

Chronic wounds of the lower extremities affect a substantial proportion of the population. The most common types of wounds include those associated with venous disease, arterial insufficiency or diabetes with insensate neuropathy possibly in combination with arterial insufficiency. The prevalence lies at around 2% of the adult population. Venous ulcers contribute to 40 — 70% of lower limb wounds. 40 —50% of venous ulcers are due to superficial venous insufficiency and or perforating vein incompetence alone with a normal deep system. 95% will present in the gaiter area of the leg, characteristically around the malleoli with irregular, gently sloping edges and a champagne glass-shape to the lower leg. The mainstay of treatment is graded compression dressings with physical activity, as activation of the calf muscle pump reduces venous hypertension. The type of dressing applied beneath the compression bandage should depend on local cost and physician preference as it has not been shown to affect ulcer healing. 30 — 60% will heal after 24 weeks. The

reported annual recurrence rate of venous ulcers is 20% and largely dependent on patient compliance. Surgical management of venous ulcers will be discussed elsewhere. Arterial ulceration is due to a reduced arterial in-flow to the lower limb. The most common cause is atherosclerosis. Other conditions such as diabetes, thromboangiitis, vasculitis, pyoderma granulosum, thalassaemia, sickle cell disease may predispose to atheroma formation. Concurrent hypertension will further damage the arterial intima. A decreased arterial blood flow results in tissue hypoxia and damage. Thrombotic and athero-embolic episodes may –further contribute to tissue damage and ulcer formation. Typically these ulcers occur over the toes, heel and boney prominences and have a ”punched-out” appearance. The management involves improving the arterial inflow by arterial reconstructive surgery, controlling all co-morbidities, stopping smoking, continuing with exercise and careful foot care to avoid any injuries or infection of open wounds.

Diabetic foot ulcers are caused by pressure over boney prominences in the setting of neuropathy and often complicated by secondary infection. 15% of diabetes will develop a foot ulcer. in 20% this is mainly due to associated arterial insufficiency, in 50% due to diabetic neuropathy, with the remainder due to a combination thereof. Standard treatment is wound debridement, infection control, moist wound dressings and off-loading of pressure from the affected lower limb. Cure rates of 20 — 47% in clinical trials are improved to 80% after 20 weeks if off-loading of weight is included in the management.