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SKIN WOUNDS: GENERAL ASPECTS AND HEALING STAGES

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ABSTRACT

Few diseases affect so many people, regardless of age, country, religious belief, economic class or any other personal characteristic, such as skin wounds. As for the potential for contamination, skin wounds are classified as clean, potentially contaminated, contaminated and infected. Depending on the depth, they are types I (affects only the epidermis), II (epidermis and dermis), III (all layers of the skin) or IV (compromises the deeper tissues). The healing that has the phases of inflammation, proliferation and maturation can occur for the first, second or third intention. As for the duration of the wounds, these are said to be acute when they are less than 6 weeks and chronic when they are ≥ 6 weeks. Each of the 3 healing stages has its own characteristics. Skin wounds can have different origins and depending on specific characteristics. In this review, we covered general aspects of the wounds as well as their healing phases.

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INTRODUCTION

Few diseases affect so many people, regardless of age, country, religious belief, economic class or any other personal characteristic, such as skin wounds (Agale, 2013). In all stages of life, the human being is subject to an accident or trauma that causes everything from a small cut to the most complex surgeries (Sem, 2009). The loss of skin integrity, in addition to causing major bleeding, can also lead to infection, motor and aesthetic sequelae or even death (Phillips, 1994). Old texts already showed the concern with this subject and indicated treatments with substances such as plants, honey, clay, bile, egg white, meat. Not much has changed for more than two thousand years, until, from the 19th century, some surgeons began to observe that cleaning and debridement improved the evolution of wounds (Forrest, 1982; Broughton , 2006). However, it was only in the last half century (mainly in the last 30 years) that there was a greater understanding of the healing process, as well as greater investment by the industries in the development of specific substances and materials that could interfere with healing (Broghton, 2006). Skin wounds can be caused by trauma (mechanical, chemical, physical, pressure ulcers), surgery (incision, excision, puncture) and by localized or systemic diseases (chronic venous insufficiency, peripheral arterial disease, diabetic foot, vasculitis, neoplasia, metabolic and hematological disorders, mainly), being classified into four main aspects (Phillips, 1994; Forrest, 1982; Broghton, 2006).

Degrees of Contamination

Clean: they are lesions that usually occur in a surgical environment, maintaining all asepsis and antisepsis techniques. There is no opening of the hollow viscera (respiratory, digestive, genito-urinary tract) and there are no signs of infection.

Potentially contaminated: injuries that occur after accidents with less than 6 hours of evolution or in cases of scheduled surgeries and without complications that involve the opening of hollow viscera (respiratory, digestive, genito-urinary tract), except the colon / rectum.

Contaminated: Lesions with more than 6 hours of evolution without assistance or when there was a gross break in the surgical technique, without inflammatory signs. Surgeries involving the colon, rectum and anus are also considered contaminated.

Infected: When inflammatory signs (pain, redness, heat and edema) occur associated with the presence of purulent

secretion and a foul odor (Favas, 2012; Nelzen,1991: Mesquita, 2013).

Healing

First intention: When the wound has the edges approached directly by a professional, for exemples stitch, grafts or flaps Second intention: In this case, the wound remains open, being healed by natural contraction of the edges. This process is usually chosen when the wound is contaminated / infected or when there has been a lot of tissue lost. Third intention: Initially the wound is open to treat mainly infection, then the edges are approached directly by suture, grafts or flaps (Leong M, 2015).

Depth

I: It affects only the epidermis.
II: It affects the epidermis and dermis.
III: It affects all layers of the skin (epidermis, dermis and subcutaneous cellular tissue).
IV: Compromises the deepest tissues (muscle fascia, muscles, tendons and bones) (Mesquita, 2013).

Classification according to duration of the wound: The wounds are classified as chronic (more than 6 weeks) and acute (less than 6 weeks) (Nelzen, 1991: Mesquita, 2013). Chronic wounds are more frequent in the elderly population, due to the appearance of comorbidities, especially peripheral vascular diseases. These lesions generally affect the most superficial layers of the skin (epidermis and dermis) and involve the lower limbs more (Kahle, 2011). They affect 3% of the population over 60 years, reaching up to 5% in patients over 80 years of age (Kahle, 2011; Mekkes, 2003). They cause a decrease in quality of life (pain, changes in the sleep-wake cycle, social embarrassment), as well as being away from work, with an important economic impact (Agale, 2013; Mekkes, 2003). The main causes of chronic skin injuries in the lower limbs are related to diseases of the circulatory system such as chronic venous insufficiency, diabetic foot, obstructive arteriopathies and pressure ulcers, the latter being more common in patients who remain bedridden for long periods. Periods (Soares, 2012; Nicks, 2010). Ulcers of venous origin (Figure 1) are the most frequent, affecting 1-3% of the adult population, which corresponds to 70% of the lesions diagnosed in the lower limbs (Agale, 2013; Nelzén, 1991; Aguiar, 2005). These wounds occur due to reflux or obstruction of the venous system (deep, superficial or perforating), which leads to increased pressure at the level of capillaries, resulting in the leakage of fibrin and plasma components in the interstitial space. In addition to having an intense inflammatory response, the presence of fibrin outside the capillaries causes a decrease in collagen synthesis and inhibits cell growth factors (Mekkes, 2003; Demidova-Rice, 2012). Clinically, the disease can manifest itself with edema, hyperpigmentation (consequence of the deposit of hemosiderin / hemoferritin in the skin), lipodermatosclerosis (fibrosis of the subcutaneous cell tissue and dermis due to the continuous inflammatory process) and, in the most severe cases, the occurrence of ulcers that they are characterized by their red color and predominant location at the level of the medial malleolus (Aguiar ; Agus, 2005). It is estimated that 15% of patients with diabetes end up developing ulcers in the plantar region at some point in life, with this condition being responsible for about 50% of lower limb amputations (Reiber, 2002).

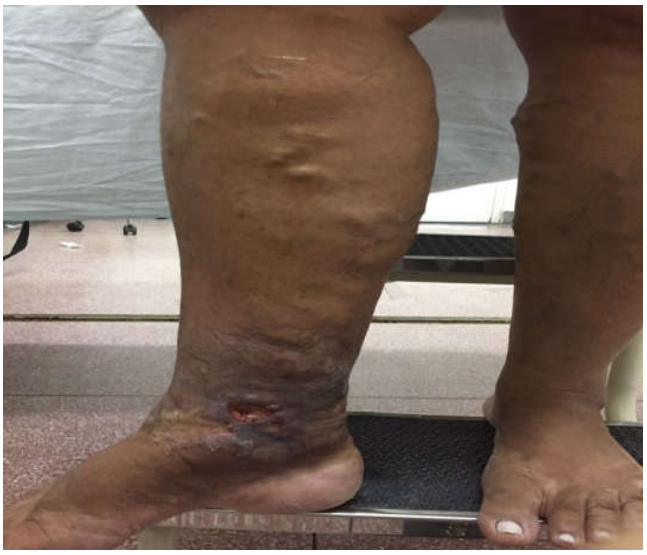

Figure 1. Ulcers of venous origin - location at the level of the medial malleolus, with a red background, accompanied by hyperchromia and dermatosclerosis

Studies show that there is an increased risk of developing ulcers that are difficult to heal, due to the thickening of the basement membrane of the microcirculation with consequent poor oxygenation of the tissues, leading to the emergence of sensory and motor neuropathy (Figure 2) in the lower limbs (Adler, 1999; Apfel, 1999). Neurotrophic injuries, therefore, not only increase the chance of the patient being subjected to surgical debridement or amputation, but also greatly increase the costs of hospital admissions (Holzer,1981). In our contry, the number of diabetic patients has practically doubled in 30 years, from 7.6% of the population in 1980 to 15% in 2010. Thus, there are almost 12 million Brazilians with this chronic disease, of which a significant part has already presents or will develop trophic lesions, with the most diverse sequelae, overloading the health system (Milech, 2016).

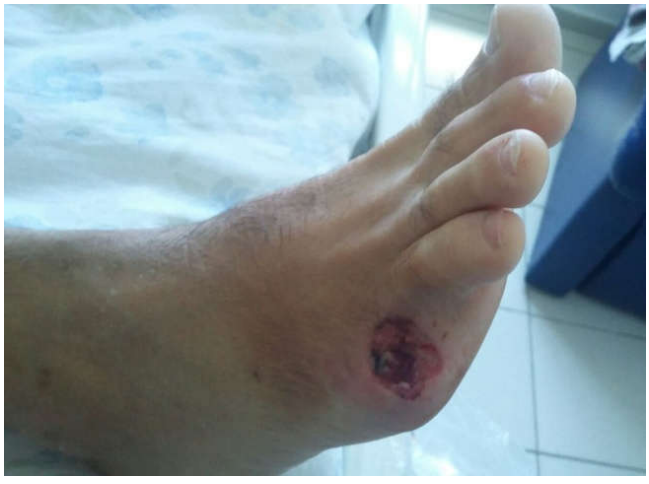

Figure 2. Amputation stump in a diabetic patient with neuropathy

Obstructive arterial diseases mainly represented by atherosclerosis and vasculitis are also responsible for the appearance of ulcers in the lower limbs (Figure 3) and upper limbs. This is a more serious situation, considering that limb amputation or revascularization surgery is often necessary due to necrosis or even pain (Johnston, 2007; Olin, 2000). Acute wounds occur more often in young trauma victims (Figure 4)

or in patients undergoing a surgical procedure. They generate millions of injuries annually in Brazil, mainly due to the high number of accidents (including work) and interpersonal aggressions. Violence causes physical, emotional and economic damages that are difficult to calculate, especially due to the great underreporting.Direct spending is estimated at 3.3% of the Brazilian GDP, reaching up to 10.5% of indirect spending (rehabilitation, reduction of the productive force and with social security) (Reichnheim, 2011; Ministerio da Saúde, 2005). Some of these patients occupy hospital beds to treat skin lesions that can also develop into a chronic condition.Annually, in the United States alone, more than 50 million surgical procedures are performed, in addition to 11 million acute injuries, with expenditures in the order of billions of dollars (Sem, 2009; Franz, 2007; Singer, 2008).

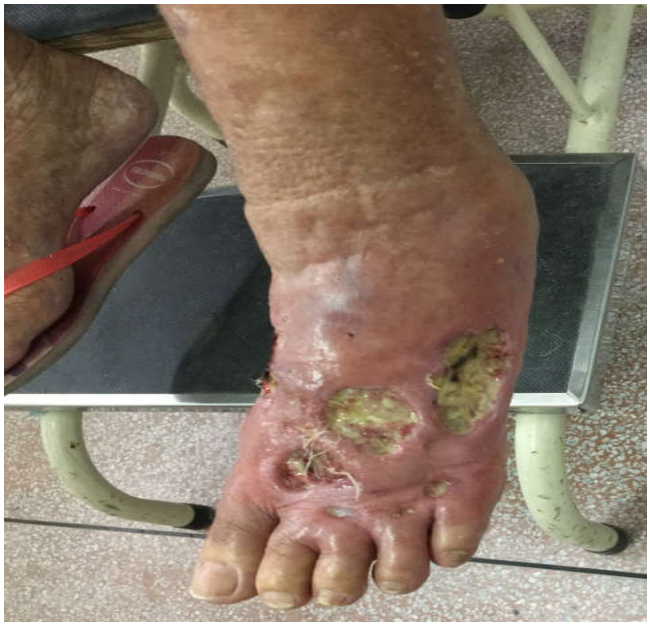

Figure 3. Ulcer of arterial origin - located at the level of the dorsum of the foot, with a pale bottom, absent wrists and very painful

Figure 4. Severe traumatic injury with bone and soft tissue loss in a young patient victim of a motorcycle accident

Healing and its Phases: The moment an aggression occurs, a complex reaction occurs immediately in order to try to preserve or restore the morphology and physiology of the tissues, regardless of the region of the body or the cause (Leong, 2015 ;Singer, 1999). Healing, however, is influenced by several factors, such as age, presence of foreign body, devitalized tissue, infection, tissue hypoxia, anemia, use of immunosuppressive drugs (Leong, 2015). Understanding this process is of fundamental importance for health professionals, considering that the conducts to be taken, including with the use of medications, depend on the correct interpretation of the clinical aspects of the wound (Sem, 2009; Leong, 2015). For a better understanding, the healing process can be divided into three phases (inflammation, proliferation and maturation), although they happen simultaneously and are related to each other (Leong, 2015).

Inflammation: The trauma caused in a tissue injures the blood vessels in the region, with consequent exposure of the endothelium. This, in turn, releases an important protein in the regulation of the coagulation cascade (thrombomodulin) that acts on reflex vasoconstriction (decreases hemorrhagic loss and brings the elements closer to the injury site). Immediately below the endothelium, there is a connective tissue rich in collagen types I and III, which, when exposed, initiates the phenomenon of platelet adhesion (Mandelbaum, 2013). This initial response, in addition to playing a key role in controlling bleeding, stimulates platelets to release various mediators and chemotactic factors (platelet-derived growth factor, transforming growth factor beta, epidermal growth factor, alpha growth factor and growth of endothelial cells) that attract other fundamental cells to the wound bed in the healing process, such as neutrophils, monocytes, macrophages, lymphocytes and fibroblasts (Leong, 2015; Agha, 2011). Polymorphonuclear cells (PMNs) are neutrophils that are characterized by presenting the nucleus in a multilobulated form. They are found circulating in the bloodstream, reaching the sites quickly due to the chemotaxis of inflammatory mediators. They are, therefore, the first cells recruited to the wound where they initially adhere to the endothelial surface and then cross the vessel wall in the space between the endothelial cells. This movement is facilitated by vasodilation caused by histamine and heparin released by mast cells (Smith, 2000). The main function of these cells is to fight infectious agents and foreign bodies, exercised, above all, by the ability to perform phagocytosis (Leong, 2015; Franz, 2007; Brinkmann, 2004).

Similar to PMNs, monocytes are defense cells with phagocytic capacity that are present in the peripheral blood and are soon attracted to the inflammatory site. They also act by releasing inflammatory mediators such as interleukin 1 and the tumor necrosis factor that contribute to the inflammatory process, but their main function is to become a macrophage in the tissues. Thus, after 48-72 hours, macrophages become the predominant defense cells (Smith, 2000; Neves, 2015). This new agent is characterized by presenting the kidney-shaped or irregular nucleus, with a large cytoplasm rich in lysosomes, which helps in the great capacity to perform phagocytosis (as the number of macrophages in the wound increases, there is a decrease in PMNs). Macrophages undergo morphological and functional transformations and then assume the role of coordinating the rest of the inflammatory phase. The intense release of mediators by these cells (platelet-derived growth factor, transforming growth factor beta, epidermal growth factor,

alpha growth factor, endothelial cell growth factor, fibroblast growth factor, insulin growth factor- simile, interleukins, tumor necrosis factor, gamma interferon and nitric oxide) shows its importance in tissue repair (Leong, 2015; Singer, 1999; Smith 2000). Lymphocytes, in addition to acting in the immune response to antigens, participate by stimulating fibroblasts (essential cells in the proliferative phase), through interleukin II and the fibroblast activating factor. They become more present in the wound around the fifth and sixth days (Leong, 2015; Boyce, 2000).

These cells have spherical nucleus with some irregularity and intense staining, in addition to thin cytoplasm with little or no visible organelle. There are three types of lymphocytes (T, B and natural Killer), however it is not possible to differentiate them in blood smears or histological sections, requiring the use of immunohistochemical techniques for this Purpose (Smith, 2000). Tissue damage also causes mast cells to release histamine and serotonin, causing vasodilation, increased blood flow and vascular permeability. These changes have local inflammatory consequences (heat, flushing, edema and pain) and, depending on the intensity of the response, they can also cause systemic repercussions (fever, asthenia) (Leong, 2015).

Proliferation: The proliferation phase starts around the third day and lasts until two or three weeks after the trauma. It represents the moment when the wound prepares the bed to be repaired, being possible to identify three distinct stages: angiogenesis, fibroplasia and epithelialization (Leong, 2015; Singer, 1999). Angiogenesis is the formation of new vessels, where endothelial cells migrate to the site from pre-existing vessels, stimulated by activating factors released by macrophages, platelets, fibroblasts and keratinocytes (fibroblast growth factor - FCF, vascular permeability factor - FPV and vascular endothelial cell growth factor - FCCEV). Activated endothelial cells release enzymes that degrade the capillary basement membrane and facilitate the migration of these cells to the surrounding tissue (Leong, 2015; Singer 1999). The decrease in oxygen tension in the wound bed, resulting in the formation of nitric oxide and vasodilation in the remaining capillaries, also seems to favor the appearance of new vessels (Akhavani, 2008, Arnold, 1991). This step is essential because it is from these new vessels that oxygen and nutrients will reach the injured area (Leong, 2015; Singer, 1999). The endothelial cells are elongated and shown to be flattened in a single layer, with the nuclei facing the lumen, and may undergo a differentiation process for arterioles or venules (Leong, 2015; Smith, 2000). Fibroblasts are mesenchymal cells that are in a quiescent phase, located in the connective tissue, being attracted by the mediators of the inflammatory phase. They arrive at the wound site from the third day, through movements of diapedesis, where they differ, stimulated mainly by factors released by macrophages and platelets. They are elongated and, because they are responsible for fibroplasia, with the production of the components of the extracellular matrix and collagen, they have developed endoplasmic reticulum and Golgi complex. However, due to the usual staining techniques with hematoxylin and eosin, only the nucleus, also of elongated shape, is visualized (Leong, 2015; Singer, 1999; Singer, 2000; Junqueira, 2013).

In normal epidermis, it is possible to distinguish four main cell layers (basal stratum, spinous stratum, granular stratum and lucid stratum). Keratinocytes are formed in the deepest layer (basal layer) and, from there, progress to the most superficial segments. During this movement, they lose organelles, dehydrate and accumulate keratin, thus forming the stratum lucid or horny (thicker skins), which allows the body to be isolated from the external environment. Therefore, they can appear with a columnar, polyhedral or pavement aspect, according to the layer in which they are found. Wounds that do not reach the basal layer, that is, that do not interfere with the germinative portion of the epidermis, present faster healing (Smith, 2000; Junqueira, 2013). Epithelialization occurs from the first 24 hours, through migration, (release of basal layer bonds, retraction of intracellular tonofilaments, dissolution of desmosomes, formation of peripheral cytoplasmic actin) and proliferation of keratinocytes located on the lesion and follicle margins nearest hairy hairs (Santoro, 2015). These cells participate in covering the lesion, forming a crust and also assist in the contraction of the wound (Leong, 2015; Smith, 1999).

Maturation

In addition to promoting a favorable environment for healing from the production of collagen and the extracellular matrix, fibroblasts participate in the contraction of the wound edges with actin and myosin fibrils, functioning as contractile muscle cells (myofibroblasts). This structural change can be seen from the sixth day onwards, disappearing after four weeks (Leong, 2015; Agha, 2011). From the third week on, there is a significant decrease in the granulation tissue formed in the proliferative phase, as well as in fibroblasts and the wound starts to show greater tensile strength, due to the cross-links between the collagen fibers.

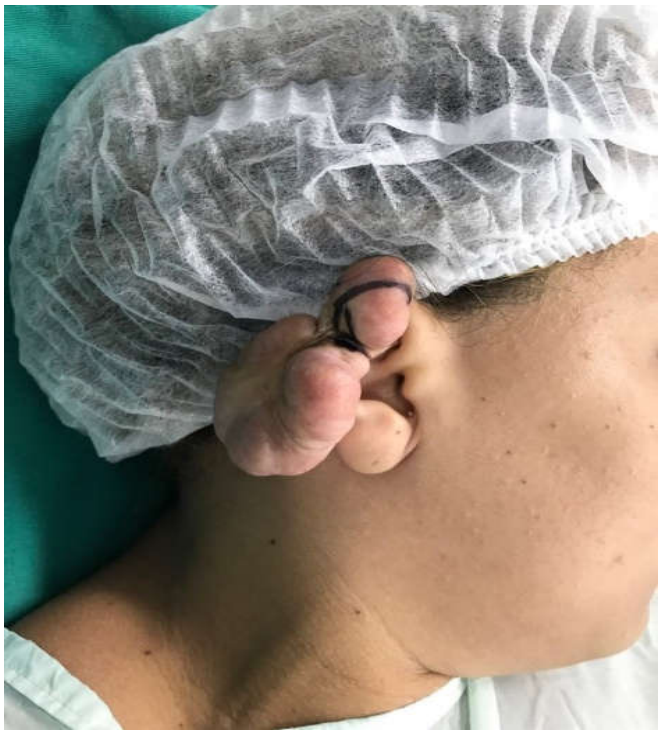

Figure 5. Keloid scar causing great deformity in the auricular region, with important aesthetic repercussions

This, in turn, is the most important protein in the entire healing process, being responsible for maintaining the support of the wound, preventing its rupture during the repair. It is initially produced in ribosomes, passing as pro-alpha chains to the endoplasmic reticulum of fibroblasts. In this organelle, the proline and lysine moieties receive a hydroxyl group and are

excreted as a pro-collagen molecule. After undergoing cleavage of some pro-peptides by proteases of the extracellular matrix, they become monomers which, when joined, then form collagen fibers. These fibers can be stained with eosin, and visualized in the optical microscope as wavy structures of variable width and length (Leong, 2015; Smith, 2000; Junqueira, 2013; Boggio, 2014). At this stage of maturation, the wound rapidly decreases in size and undergoes a remodeling process; however, if there is an imbalance between collagen synthesis and degradation, scars can have extremely undesirable effects from an aesthetic and functional point of view, as in situations hypertrophic scars (proliferation within the wound margins that may regress over time) and keloids (proliferation beyond the wound margins that normally do not regress over time) (Leong, 2015; Smith, 1999) (Figure 5).

Conclusions

Skin wounds are common, associated with high direct and indirect costs and sometimes with harmful consequences for patients. The knowledge of the classifications of these wounds and of the healing phases allows a more adequate approach and management with minimizing thechances of permanent damage to patients.

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