Introduction

Wounds can be defined as injuries to the body that result in disruption of the continuity of the body structure. They are encountered frequently in veterinary practice and therefore a veterinarian should be familiar with all processes involved in wound healing and the options for wound management. Although there are differences in the types of wounds, which include incisions, abrasions, burns, avulsions, ruptures, punctures, contusions, lacerations and bite and shot wounds, the main principles of wound healing are the same for all types.

Wounds can be classified in several ways. One of the most important distinctions to make is between open and covered, or closed, wounds. In closed wounds the superficial layer is still intact and protects the wound against contamination; in open wounds there is a disruption of the skin or mucous membrane. Further classification of open wounds can be based on the degree of contamination, which partly depends on the duration of the injury.2,4

- Category 1. Clean wounds: nontraumatic wounds not involving the respiratory, oropharyngeal, gastrointestinal or urogenital organs with no visible contamination; within 0–6 hours after surgery.
- Category 2. Clean-contaminated wounds: non-traumatic wounds where respiratory, oropharyngeal, gastrointestinal or urogenital organs are open without spillage of contents; clean wounds in which a drain is placed; in cases of small breaches in aseptic technique; within 0–6 hours after surgery.
- Category 3. Contaminated wounds: traumatic wounds less than 4–6 hours old; inflammatory processes without purulent exudate; procedures that are contaminated or infected urine; serious breaches in aseptic technique; cases of small breaches in aseptic technique; within 0–6 hours after surgery.
- Category 4. Infected or dirty wounds: traumatic wounds more than 4–6 hours old or with obvious contamination or signs of infection; inflammatory processes with purulent exudate or necrotic tissue; perforation of the gastrointestinal organs or infected urogenital organs and serious faecal contamination. An infected wound contains more than 10^5 bacteria per gram of tissue.

Wounds can also be classified by the length of time they have been present (acute or chronic wounds) and by the thickness of the skin surface that is lost (full-thickness or partial-thickness). In chronic wounds, underlying factors preventing wound healing can usually be identified and need to be addressed for standard treatment to be successful. With full-thickness skin loss the complete dermis and epidermis are lost, but with partial-thickness skin loss the dermis is still partly intact. Adnexal structures in the partly intact dermis can serve as a source for epithelial cells, which are needed for wound healing.1

Wound healing

As stated above, all wounds heal in a similar fashion, divided into four distinctive phases. However, depending on the type of wound and its classification, one or several phases of wound healing can be accelerated, delayed or complicated by several factors. In addition, several phases of wound healing can be found at the same time in all wounds. Although the phases of wound healing are the same in dogs and cats, there are some important differences in wound healing between these two species and the clinician must take these into consideration.5,6 Every wound will follow the general wound healing pathway of four consecutive phases: the acute inflammatory phase; the breakdown or debridement phase; the repair or proliferation phase; and the remodeling or maturation phase.2,4 To aid and wound healing process to direct and stimulate the healing process and to make the right decisions in wound management, a clinician has to be familiar with these processes of wound healing.

Inflammatory phase

Directly after wounding, the wound fills with blood and lymph from damaged vessels. This is followed by an immediate vasoconstriction of the damaged vessels, mediated by catecholamines, serotonin, bradykinin, prostaglandins and histamine, which lasts 3–10 minutes and helps minimize blood loss.7 Subsequent vasodilation dilutes toxic substances, provides nutrients and results in blood clot formation induced by activated platelets. The blood clot protects the wound, dries to form a scab and enables wound healing to proceed underneath it. Vasodilation also allows fluid containing cells, such as polymorphonuclear neutrophils (PMNs) and macrophages, and chemoattractant factors, such as cytokines and growth factors, to reach the injured area.1,3,4,5 The activated platelets are also needed for initiation of wound healing through the release of cytokines and essential growth factors. Within 24–48 hours, local monocytes migrate into the wound and become macrophages, which also produce a wide array of essential growth factors. Wound macrophages, endothelial cells and fibroblasts mediate the healing process from this point on.1,3,4,5,7 The migration of PMNs, lymphocytes and macrophages is stimulated by chemotactic factors such as complement, growth factors and cytokines.1,3,4,5,7 Research has shown that PMNs, which dominate the wound in the early stages, are not essential in uncomplicated wound healing, but macrophages, more dominant from day 5 on, are needed.3,12

The mediators that initiate inflammation in healing wounds are soluble factors released by resident cells of the wound bed and by platelets and leukocytes delivered by the circulation after the disruption of intact skin. These factors initiate a series of events that attempt to stabilize the wound, remove invading organisms and return the wound to its pre-injury architecture. This depends on the production, regulation and control of several factors (IMs).1,3 IMs are cytokines that are found in two groups of wound healing soluble factors: cytokines and growth factors. Cytokines are extremely potent and usually act within a short distance of their release as intracrine, autocrine or paracrine signals. They can be subcategorized as chemokines, lymphokines, monokines, interleukins (ILs) and interferons (IFNs).13,14 The growth factors that play a key role in wound healing, such as platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF), but also connective tissue growth factors given their function locally and rarely systemic effects.13,14

The IMs currently known to be crucial to the wound healing process are IL-1, IL-2, IL-4, IL-6, IL-8, granulocyte–macrophage colony-stimulating factor (GM-CSF), G-CSF, M-CSF, macrophage inflammatory protein (MIP)-1, monocyte chemotractant protein (MCP)-1, neutrophil-activating peptide (NAP)-2, IFN-inducible protein (IP)-10, IFNs, transforming growth factor (TGF)-β, tumour necrosis factor alpha (TNF-α), platelet factor 4 (PF4) and PDGF.8–11

More specifically, in the inflammatory stage, platelets release PDGF, TGF-β, FGF and EGF, which stimulate the early chemotaxis and activation of cells involved in wound healing. After clot formation, epithelial cells begin to migrate from the wound periphery onto the exposed tissue in response to TGF-β, GM-CSF and FGFs. These induce the epithelial cells to migrate and cover the wound. Fibroblast proliferation is stimulated by TGF-β and IL-1, angiogenesis is activated by EGF and PDGF, and neutrophil wound infiltration is triggered by TNF-α and NAP-2.2,8–12

The inflammatory phase is characterized by the five classic signs of inflammation (i.e. redness, pain, heat, swelling and loss of function; also known as rubor, dolor, calor, tumor and functio laesa, respectively).

Debridement phase

Necrotic or dead tissue impedes wound healing and therefore its removal is an essential phase in the healing process.1,4,5 This necrotic tissue is a stimulus for inflammation and provides a good environment for bacteria to proliferate. PMNs and macrophages have an important function in removing the debris and cleaning the wound and are regulated by the previously-mentioned cytokines and growth factors.13,14 As mentioned above, macrophages play the most important role by assuring cytokine secretion and secretion of proteases and other substances that digest damaged wound bed matrix and allow migration by other connective tissue cells.
Granulation

The main components of granulation tissue are fibroblasts and capillaries. The capillary network occurs through sprout formation of capillary endothelial cells on the wound surface. Endothelial buds and sprouts are formed through mitosis and these expand and contact other buds or already hollow capillaries. Next, the capillary network is intertwined with fibroblasts. The fibroblasts migrate from the surrounding tissues and develop from fibrocytes, but they also originate from undifferentiated pericapillary cells, mesenchymal cells and monocytes. Fibrin and fibronectin in the wound are important for the formation of granulation tissue because they serve as a framework to support inwardly growing cells. The fibroblasts produce collagen and fibrin is slowly replaced by the collagen deposited. The deposition of collagen is controlled by epithelial cells and fibroblasts themselves, which both have collagenaese activity. Collagen production reaches its maximum on approximately the 9th day of wound healing, but the net collagen synthesis increases up to 4–5 weeks after injury. Endogenously produced vitamin C is essential to the production of collagen. Once the wound is filled with granulation tissue, a reduction takes place of the number of cells and the amount of collagen fibres. Furthermore, the collagen fibres undergo continuous remodelling by breakdown and rebuilding of fibres.

Granulation tissue is characterized by a red, irregular surface because of the newly formed capillary buds. It is fragile tissue that functions as a barrier to infection. A healthy bed of granulation tissue acts not only as a barrier against environmental contamination, but also as a scaffold for migrating epithelial cells. The supply of nutrients, the removal of toxic metabolites and the presence of oxygen are the main factors that determine how the barrier functions. However, hypoxia can stimulate the formation of new capillaries.

Wound contraction

The wound surface and the wound cavity become smaller because of the specific activities of fibroblasts with contractile properties during and after the formation of granulation tissue in the wound. These specialized fibroblasts, called myofibroblasts, are the main contributors, but normal fibroblasts are also capable of aiding wound contraction. Myofibroblasts attach themselves to the dermis under the skin edges and to the underlying fascia or panniculus muscle layer. They orientate themselves parallel to each other on the wound surface. After attaching they contract, pulling the adjacent skin to the centre of the wound. Wound contraction thus involves a process that pulls the borders of the skin adjacent to the wound towards the centre of the wound. When applying a bandage, it is recommended that pressure is kept off the wound by distributing it around the wound. When a bandage is applied, the surrounding skin becomes too high or when the edges of the wound contact each other. If wound contraction is excessive, wound contracture can lead to pressure on the wound, because the wound edges are pushed away from each other. When applying a bandage, it is recommended that pressure is kept off the wound by distributing it around the wound. Wound contraction stops when the tension of the surrounding skin becomes too high or when the edges of the wound contact each other. If wound contraction is excessive, wound contracture can occur. This is a pathological process and results in limited motion of the underlying structures.

Excessive granulation tissue can impede wound healing when it is of poor quality. Another factor that can inhibit wound contraction is pressure on the wound, because the wound edges are pushed away from each other. When applying a bandage, it is recommended that pressure is kept off the wound by distributing it around the wound. Wound contraction, the surrounding skin has been thinned. This will be restored by proliferation of epithelial cells and connective tissue, called intussusceptive growth.
Epithelialization

Epithelialization occurs when there is a partial or full disruption of the epidermis. This process includes proliferation of basal epithelial cells from the adjacent skin edges and their moving over and adhesion to the surface of the wound. The cells fill in the area of the wound that is left after wound contraction, provided the area to be covered is not too large. The epidermal cells make use of the underlying fibroangioblast tissue layer, which needs to be healthy in order for proper epithelialization to occur. The activity of the epithelial cells leads to the formation of granulation tissue. In closed wounds, however, epithelial cells migrate over the exposed dermis and through the fibrin clot.

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Maturation phase

The remodelling or maturation phase is characterized by increasing strength of the scar as a result of remodelling of tissue. Collagen III is replaced by the stronger collagen I, the collagen bundles become thicker and the number of cross-linkages between collagen fibres is increased. The newly formed collagen is arranged parallel to the tension lines of the skin. This phase can take several weeks to 1 year after the traumatic event, but ultimately the healed wound will never regain its original strength. In addition, the newly formed skin has no or insufficient hair follicles, sweat and sebaceous glands, poor moveability and elasticity and an absence of pigment. The signals for the remodelling phase are still largely unknown, but blocking TGF-β activity has been implicated in excessive scarring, suggesting that it may play a role in halting scar formation by encouraging cell apoptosis.

Differences between acute and chronic wounds

As mentioned above, wounds can be divided into acute and chronic wounds. Understanding the differences between these two types of wounds is important for proper wound management. Acute wounds are wounds that heal quickly, while chronic wounds heal more slowly and may not heal at all. The remodelling or maturation phase are still largely unknown, but blocking TGF-β activity has been implicated in excessive scarring, suggesting that it may play a role in halting scar formation by encouraging cell apoptosis.

Differences in wound healing between dogs and cats

For many centuries it was thought that wound healing was the same for all mammals. In the last decades researchers have discovered that although all species follow the same phases of wound healing, they do not all heal in the same way. Differences between horses and ponies and between rabbits and humans were found, and there also seemed to be differences between cutaneous wound healing in dogs and cats. Research into wound management has predominantly been in dogs. Recent studies in cats make previous assumptions that results can be extrapolated to cats questionable.

A few studies have been carried out to investigate the differences between wound healing in dogs and cats. One of these differences is the vascular supply of the skin. One study showed that dogs appeared to have a higher density of tertiary and higher order vessels than cats. This was in accordance with a laser Doppler perfusion study, which concluded that the intact skin of cats was less perfused than the intact skin of dogs. Additionally, the breaking strength of a wound in cats is approximately 30% less than that in dogs 7 days after primary closure. There is also a difference in the rate and pattern of production of granulation tissue. The formation of granulation tissue takes longer in cats compared with dogs. In cats, granulation tissue first appears at the wound edges, in contrast to dogs where it appears simultaneously on the entire exposed surface. The colour of the granulation tissue is paler in cats. Rates of wound contraction, epithelialization and total healing are all reduced in cats compared with dogs. However, the role of subcutaneous tissue in wound healing in the dog and the cat is similar in both species.

Complications in wound healing also differ between dogs and cats. Pseudoeal healing and formation of indolent pockets are much more common in cats. Pseudoeal healing refers to a sutured wound that appears well healed but, after removal of the sutures, dehiscence occurs under normal stresses. Pseudoeal healing is often observed with bite wounds. Indolent pockets, also called indolent ulcers, are chronic pockets in the subcutis that are lined with mature collagen and contain a thin, serosus, modified transudate. Wound contraction does not occur in these wounds.

Because of the lower breaking strength of sutured wounds in cats, some authors have advised leaving sutures for a few days longer in cats after surgery compared with dogs. This is especially important when larger parts of the subcutis have been removed during surgery. More research is needed to better understand the differences in wound healing between the two species and to translate them into practice.

1 A wound showing healthy granulation (red) and advancing epithelialization (pink).
2 A wound that has healed by second intention demonstrating advanced maturation and obvious scar formation.
3 A wound showing healthy granulation (red) and advancing epithelialization (pink).
4 A wound showing healthy granulation (red) and advancing epithelialization (pink).
5 A wound showing healthy granulation (red) and advancing epithelialization (pink).
6 A wound showing healthy granulation (red) and advancing epithelialization (pink).
7 A wound showing healthy granulation (red) and advancing epithelialization (pink).
8 A wound showing healthy granulation (red) and advancing epithelialization (pink).
9 A wound that has healed by second intention demonstrating advanced maturation and obvious scar formation.
10 A chronic nonhealing wound on the hock of a dog.
Wound management

Many of the wounds that the veterinarian is confronted with will heal naturally, but there are wounds that may need intervention (e.g. large wounds or necrotic and infected wounds). In addition, some wounds may heal better, quicker or have a better cosmetic outcome following some kind of stimulation.

In patients presented with acute wounds that are still bleeding, the first step in wound management is to stop the bleeding. With major haemorrhage this can be performed by compression of the wounded area. For minor bleeding, the use of specialized dressings with haemostatic properties is possible (e.g. alginate with calcium, adrenaline-soaked gauzes or gelatin sponges). The second step and primary goal after stopping significant haemorrhage is to try to reduce the level of contamination and prevent further contamination. Contaminated wounds are preferably cleaned within the ‘golden period’. This period of 4–6 hours after wounding is the period in which a contaminated wound can turn into an infected wound because of proliferation of bacteria to more than 10^12 per gram of tissue. Tissue invasion by bacteria after this period makes it almost impossible to remove them by irrigation.

Debridement

Debridement is indicated whenever necrotic tissue or debris exists in a wound and might impede wound healing. Small amounts of debridement may be feasible without sedation or anaesthesia, but generally anaesthesia is required for aggressive debridement. There are several methods of accomplishing debridement of wounds: surgical, mechanical, autolytic, enzymatic, chemical and biosurgical. The objective of debridement is to convert the open contaminated wound into a surgically clean wound, which can be closed primarily or secondarily or treated as an open wound if closure is not possible. The choice of which method to use depends on the wound and the patient. Important factors to consider are the amount of necrotic tissue, the laxity and elasticity of the surrounding tissue, the presence or absence of a clear demarcation line between necrotic and viable tissue and whether or not the patient can tolerate anaesthesia (II). Because of these variable factors, more than one debridement procedure may be necessary before a healthy wound can be created.

Surgical

Surgical debridement is used most commonly and involves the surgical removal of necrotic tissue from the wound (12). It is especially important when considering surgical closure of the wound. The goal is to remove all obvious necrotic tissue and debris. However, during the inflammatory phase of wound healing, it is often difficult to distinguish necrotic nonviable tissue from healthy viable tissue because of incomplete tissue demarcation. The assessment of tissue viability, often based on colour and attachment, is subjective and there is a risk of removing healthy tissue.

Layered approach

The layered approach is the most selective method of debridement and it is painless. Autolytic debridement of devitalized tissue is essential to promote wound healing. It depends on the whole area being kept moist so that natural enzymatic reactions can take place. Wound exudate is preserved on the wound surface and natural components, such as enzymes and leukocytes, remove necrotic tissue. Autolytic debridement can be performed with interactive dressings such as hydrogels, hydrocolloids, hydrofibres and foam dressings. Hydrogels are recognized as the standard treatment in human medicine and are considered to be gentle debriders, promoting rehydration of nonviable tissues. Hydroasorb® and Hydroasorb Comfort® are hydrocellular gel dressings from 60% water and are therefore suitable for keeping granulation tissue and young epithelium moist. Another example of autolytic debridement is the use of honey or sugar, which can be applied as a topical medication. Because of its high osmolality, it attracts fluids and provides a moist environment, which encourages autolytic debridement.

Enzymatic

With enzymatic debridement, proteolytic enzymes are applied to the wound to break down the necrotic tissue. It is a very selective method of debridement and is painless. Proteolytic enzymes or derivatives of bacteria (Bacillus subtilis) can be used in wounds with small amounts of necrotic tissue or debris. The enzymes are processed in powders or creams, which can be applied to the wound. The most commonly used enzymes are trypsin, aprotinin, chymotrypsin, desoxyribonuclease, papain-urea and collagenase.

In animal wounds, enzymatic debridement is sometimes used as an adjunct to mechanical and chemical wound debridement, especially in patients with a high anaesthetic risk. Enzymatic agents break down necrotic tissue, yet leave viable tissue intact, provided they stay in contact with the wound for a sufficient time. However, the effectiveness of enzymatic debridement is questionable and a long exposure time is required to remove the nonviable tissue.

Chemical

Chemical debridement can be performed with antiseptics such as Dakin’s solution (0.25% solution of sodium hypochlorite) or hydrogen peroxide (bisbiguanide chlorhexidine-diacetate solution, 0.05%), povidone-iodine (1%) and hydrogen peroxide. However, it is a nonspecific manner of debridement and cells important for wound healing are also damaged. Chemical debridement is not generally recommended.

Biosurgical

Biosurgical debridement uses the placement of medical maggots (Lucilia sericata) into the wound. The maggots produce enzymes that dissolve the necrotic tissue, but spare healthy tissue. Maggots are therefore selective. The maggots used for this purpose are specially bred and therefore expensive. Maggots may be indicated for management of deep wounds which are difficult to debride by other means.