CPD article

Wound management part one: topical treatments

Several topical solutions and preparations are available for the treatment of wounds in veterinary patients. Topical preparations can be used to help create a favourable healing environment, with some products having additional antimicrobial properties. With many products available, it can be difficult to decide which topical treatment is most appropriate for the individual wound. This article will discuss the most commonly used wound cleaning solutions and topical products currently available in veterinary practice.

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Joanna McCagherty BVMS, PGcert Small Animal Surgery, MRCVS; **Samantha Woods** BSc MA VetMB CertSAS DipECVS MRCVS. Royal (Dick) School of Veterinary Studies, Division of Veterinary Clinical Sciences, The University of Edinburgh, Hospital for Small Animals, Easter Bush Veterinary Centre, Roslin EH25 9RG. samantha.woods@ed.ac.uk

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Wound management is a common aspect of companion animal veterinary practice. Most wounds occur as a result of trauma, or following surgery if superficial dehiscence and/or surgical site infections have occurred. Regardless of the cause, the general principles of wound management can be applied to all types of wounds, with the overall aim of supporting progression to healing. Recently, there has been a move towards the use of topical preparations as a key component of wound management, either solely or alongside systemic antibiotic therapy.

With the increasing concerns of antibiotic resistance in veterinary patients, the use of topical therapy is becoming more important. A key component of the development of antibiotic resistance is the ability of some bacteria to form biofilms in which the organisms can evade the effects of systemic antibiotics and continue to proliferate. Topically applied antimicrobials can provide high concentrations of active ingredients at the target site. This may not be achievable with systemic therapies, because of side effects and/or selection pressure for antibiotic resistance, and some antibiotics may not be available in systemic formulations.

This article discusses commonly used and licensed topical products (including irrigation solutions and topical preparations), and their applications for wound management. The second article will discuss wound dressings and their appropriate clinical applications.

Initial wound preparation and assessment

When first evaluating a wound, it is important that the wound is prepared and decontaminated appropriately, while preventing further soft tissue trauma. The wound should be covered with a sterile dressing until thorough irrigation and appropriate debridement can be performed.

First, the hair of the surrounding skin should be widely clipped to reduce the risk of ongoing wound contamination. During the clipping process, the wound should be covered or filled with a sterile water-based lubricant (such as KY jelly), which is subsequently removed by lavage once the clipping process is complete. Good clipper care and maintenance is vital — clean, sharp blades should be used in each case. Prior to every use, the blades are checked, and replaced if there are missing teeth or if they are visibly blunt or damaged. Blunt or damaged clipper blades can cause further trauma to the skin surrounding the wound. The wound should be photographed at this point, with the image kept to document progress over time.

Following clipping, the wound should be irrigated with large volumes of sterile saline solution to remove any surface exudate and debris. A one-litre saline bag is connected to a standard intravenous giving set with a hypodermic needle at the end and is pressurised to 300 mmHg. This delivers a consistent pressure of between 7–8 PSI, which is the currently recommended wound irrigation pressure (Gall et al, 2010). Alternatively, if a pressure bag is unavailable, a 20 ml syringe can be used with an 18-gauge needle to achieve 8–12 PSI (*Figure 1*); however, the generated pressure is less consistent (Gall et al, 2010; Hosgood, 2018). During lavage, it is important to monitor the wound to ensure that bubbles are not forming on the surface; this indicates that the pressure is too high and could potentially force surface contaminants deeper into the wound (Anderson, 2009).

The skin surrounding the wound is cleaned using a 2% chlorhexidine gluconate solution (Swales and Cogan, 2017). Good aseptic technique is required when managing wounds — gloves should be worn when handling or treating all wounds — and absorbent pads should be placed underneath the patient. The wound and surrounding skin should be gently dried using sterile swabs in a dabbing action; a wiping action is inappropriate as this will cause unnecessary soft tissue trauma.

The wound should be assessed to determine which stage of healing it is in (inflammatory, proliferative or maturation), as wounds will have differing requirements depending on the stage

Figure 1. Volume lavage (a) may be used for highly contaminated wounds or pressure lavage (b) can be provided using a giving set, syringe and hypodermic needle. Notice that the hair surrounding the wound has been clipped, the surrounding skin has been cleaned, the patient is lying on clean, absorbent pads and that gloves are being worn to maintain asepsis.

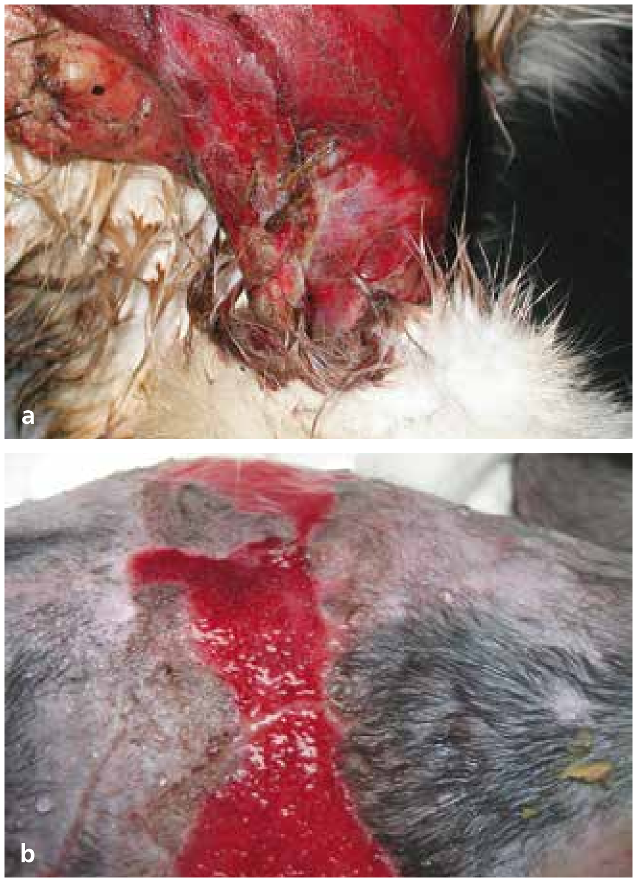

Figure 2. Assessing the stage of wound healing: (a) This pelvic limb wound has organic and necrotic debris on the surface. The wound is in an early inflammatory state and requires active wound management including debridement to progress to healing; (b) This flank wound is covered in healthy granulation tissue. The wound is now resistant to infection and the surface requires protection to allow epithelialisation and wound contraction to progress.

of healing. For instance, during the inflammatory phase wounds may require debridement to enable wound healing to progress, while proliferative wounds require protection and support during granulation and early epithelialisation (*Figure 2*) (Anderson, 1996). Evaluation of the wound to establish the stage of healing will enable appropriate selection of topical preparations and dressings. It is important that any surface debris or necrotic tissue that has not been removed by irrigation should be debrided at this point using scalpel excision; abrasion with a dry non-woven swab; or mechanically using a wet-to-dry dressing (Anderson, 2009). An alternative product for wound debridement (Debrisoft® debridement pad, Pioneer Veterinary Products, Canterbury) has become available — it is a polyester pad that removes slough, debris and non-viable tissue from the wound, while preserving granulation tissue and epithelium (Pioneer Veterinary Products, ND). Whichever method is used, care should be taken to avoid excessive debridement, and only clearly devitalised tissue should be removed. Remaining tissue should be monitored at each dressing change and can subsequently be debrided if necessary. Following debridement and irrigation, a tissue sample or swab should be taken for bacterial culture and sensitivity (Hosgood, 2018). Broad-spectrum antibiosis should be instigated where appropriate, and subsequently modified based on bacteriology results. Minimally contaminated wounds and those without necrotic material generally do not require systemic antibiosis and can be managed solely with topical antimicrobial products (Anderson, 2017). Antibiosis should be instigated in patients with immunocompromise or systemic disease. Once a healthy granulation bed has formed, antibiosis can be stopped as healthy granulation tissue is highly resistant to subsequent bacterial colonisation (Anderson, 2017).

At every assessment, the stage of wound healing should be documented. This will enable early identification and intervention should wound healing become arrested or delayed. A useful method to aid wound assessment is to photograph the wound at each dressing change; this enables direct comparison of the wound appearance and is invaluable when more than one person is managing the wound. Ideally, a scale marker (such as a wound measure or a ruler) should be included in the photographs to allow objective comparisons (*Figure 3*). Alternatively, the wound can be measured and its dimensions documented in the patient's clinical record.

Factors affecting wound healing

Systemic diseases such as organ failure and endocrinopathies that can alter wound healing should be ruled out with screening blood tests. Any local factors that will affect healing should be identified and addressed. Typically, wound healing will become arrested if the local environment is inappropriate. This can be due to presence of foreign material, infection, excessive moisture, dessication, excessive movement or patient-induced trauma.

A favourable environment for wound healing can be achieved using a combination of topical treatments and dressings. Dressings will be covered in the second article.

Commonly used topical antimicrobial solutions

Topical antimicrobial solutions are typically used following initial saline lavage (+/- wound debridement) to reduce the surface bacterial load and remove any biofilm that may have formed on the surface of the wound (*Figure 4*). Their use following saline lavage has been demonstrated to achieve thorough wound irrigation (Finnegan and Percival, 2015; B. Braun, ND; Uri et al, 2016). Topical antimicrobial solutions are frequently used in human patients, and some demonstrate no known microbial resistance. The most commonly used antibacterial solutions in veterinary patients are chlorhexidine, iodine-based solutions, hypochlorous acid, tris-ethylenediaminetetraacetic acid (tris-EDTA) and polyaminopropyl biguanide, although other products such as octenidine and quarternary ammonium compounds are also available. It is important to stress, however, that these products are used alongside, rather than in place of, good wound management.

Chlorhexidine

Chlorhexidine is a broad-spectrum biocide with fungicidal and concentration-dependent bacteriostatic or bactericidal properties. It acts by destabilising the cell wall and disrupting osmosis of micro-organisms (Swales and Cogan, 2017; Boucher, 2018). It is typically diluted with water to create a 2% solution for surgical skin preparation and for cleaning the skin surrounding open wounds. It can be further diluted to a 0.05% solution for wound irrigation, however this application should be used with caution as it may affect wound healing through induction of fibroblast apoptosis and necrosis (Faria, 2009). Chlorhexidine gluconate is the most commonly used antimicrobial product in veterinary practice (Evans, 2009). Bacterial resistance to chlorhexidine is becoming an increasing concern. Resistance has been documented with *Proteus* spp.; *Pseudomonas* spp.; *Klebsiella* spp.; *Bacillus* spp.; *Escherichia coli* and *Shigella* spp. in human and veterinary patients, which could have serious implications for the development of surgical site infections (Dance et al, 1987; Levy, 2002; Evans et al, 2009; Swales and Cogan, 2017).

Figure 3. Objective wound assessment. The wound is measured using a clean ruler, the ruler on the dressing packet or a sterile wound probe. Documenting wound measurements allows for comparison of progress between dressing changes, and makes it easier when multiple clinicians are managing the wound.

Figure 4. In chronic wounds, bacteria often form a protective polysaccharide coating called a biofilm. These biofilms allow a persistent bacterial population to reside within the wound bed, leading to delays in wound healing and resistance to the innate immune response and many systemic and topical antimicrobials (Westgate et al, 2011). For a wound to progress to healing, the biofilm must be disrupted using appropriate methods of debridement to allow the host response and topical therapies to permeate the wound surface (Sood et al, 2014). (a) This wound is covered in necrotic debris and areas of biofilm. Debridement of the debris and biofilm is necessary to allow the wound to continue to heal; (b) biofilm on a swab (courtesy of T Nuttall).

Iodine-based solutions

Either 1% or 0.1% povidone-iodine solutions are often used for wound lavage, because of their wide-spectrum antibacterial activity and their action against spores, fungi, yeasts, viruses and protozoa. Unlike chlorhexidine, povidone-iodine has a short residual activity and frequent re-application is necessary due to inactivation by organic matter (Sanchez et al, 1988). More concentrated solutions of povidone-iodine are cytotoxic to fibroblasts, leading to delayed wound healing (Anderson, 2009).

Hypochlorous acid

Hypochlorous acid is endogenously produced by neutrophils and has oxidative and proteolytic effects. It is commercially available as an oxychloride-based topical veterinary biocide solution (e.g. Vetericyn ®, Innovacyn Inc, California; RenaSan®, Renapur Ltd, East Sussex; Leucillin®, Lyvlee Ltd, Dorset) that is capable of killing 99.9999% of known pathogens (Eryilmaz, 2013). It is a potent broad-spectrum non-toxic solution that can be applied around the mouth and eyes. Its use has been associated with improved wound healing in human patients (Robson et al, 2007). Hypochlorous acid also has actions against biofilm, with microbicidal effects (Sakarya et al, 2014).

In the commercially available products, hypochlorous acid is present at a concentration of 110 mg/l. At this concentration, it has been shown to reduce the minimum bactericidal and fungicidal concentration of microorganisms within 3 and 10 minutes of application respectively, in vitro (Uri, 2013). This property would suggest its clinical use could potentially reduce the required tissue concentration of systemic and topical antibiotics; however, further research is required to determine this effect in vivo. Hypochlorous acid can be applied using a spray bottle to liberally coat the surface of the wound and surrounding skin, or can be drawn up in a syringe and applied directly or through a plastic cannula or a hypodermic needle. A hypochlorous acid product can be used during all stages of wound healing (Sakarya et al, 2014).

Tris-ethylenediaminetetraacetic acid (Tris-EDTA)

Tris-EDTA is commercially available as an ear flushing solution for veterinary patients (Trizaural, Dechra Veterinary Products, Putney). It contains disodium-EDTA, which is responsible for its antimicrobial and anti-biofilm effects.

Disodium-EDTA potentiates and is synergistic to the effects of other antimicrobial products, by removing magnesium and calcium ions from the outer cell membrane of Gram-negative bacteria, to expose the inner cell membrane (Finnegan et al, 2015). This action allows other antimicrobials to directly access the inner cell membrane, enhancing their efficacy.

The anti-biofilm effect of disodium-EDTA is achieved by preventing the bacteria from forming adhesions, necessary to create the biofilm (Finnegan et al, 2015). It also acts to prevent proliferation of the bacteria within an established biofilm, and has been shown to disrupt the biofilm structure itself, which may increase the susceptibility of the encased bacteria to other antimicrobials (Finnegan et al, 2015).

Tris-EDTA can be mixed with injectable antibiotic solutions — the most frequent application of this in veterinary patients is for the management of *Pseudomonas aeruginosa* otitis externa, where it is combined with gentamicin. Topical application of antibiotics in this way can provide a means of achieving a high local tissue concentration of antibiotic, which would otherwise be unattainable with systemic antibiotics, or in cases where a systemic antibiotic product is not available. It is important to note that this method of delivering local antibiotic therapy is not licensed and should only be prescribed in accordance with the veterinary Cascade guidelines.

KEY POINTS

- Ensure that the hair of the surrounding skin remains clipped and clean throughout the entire wound management process.
- Regularly evaluate the wound to identify which stage of healing it is in and adapt treatment accordingly.
- If wound healing has arrested, identify and treat the cause to allow wound healing to progress.
- Where topical wound treatments are used as part of wound management, the wound should be re-evaluated at every dressing change to determine its requirements. Always assess whether or not the wound environment has changed, making other topical treatments more appropriate.
- Topical treatments can have a significant impact on the level of wound exudate produced. Ensure that an appropriately absorbent dressing is applied and that dressing changes are performed frequently enough to avoid strike-through.

Polyaminopropyl biguanide 0.1%

An irrigation solution is available containing polyaminopropyl biguanide plus a betaine surfactant (Prontosan®, B Braun, Sheffield). This effectively lifts surface debris and microorganisms from the wound surface and suspends them in solution so that they cannot re-contaminate the wound (B.Braun, ND; Wolcott et al, 2014). With continued irrigation, the suspended microorganisms are removed from the wound surface. The product does not inhibit formation of granulation or epithelial tissue.

Acute wounds can be irrigated directly with the solution, whereas chronic wounds should be covered in a sterile swab soaked in the solution and left for at least 15 minutes, to ensure appropriate penetration of the wound bed, before irrigation with the solution. The solution should be re-capped immediately after use and can be stored at room temperature for 8 weeks after opening. This product has demonstrated efficacy for removing and preventing formation of biofilm on wound surfaces, making it superior to a purely saline lavage; however, it should be used following initial saline lavage to achieve thorough wound irrigation (Wolcott et al, 2014; Bellingeri et al, 2016). The product is also available in a gel form that can be used in conjunction with a dressing to help maintain wound surface moisture levels and deliver ongoing wound decontamination between dressing changes. In order for this formulation to maintain efficacy, the gel must remain moist — this will influence the type of dressing selected and the required frequency of dressing changes, but these choices will vary between individual wounds.

Topical antimicrobial agents

Application of an appropriate topical antimicrobial agent has multiple benefits when managing wounds in veterinary patients, including creation of a favourable environment for wound healing; destruction or inhibition of the growth of surface microorganisms; and provision of a source of moisture to the wound. Such agents should be used in conjunction with an appropriate contact layer dressing that will protect the wound surface but also absorb any exudate, to prevent maceration (Anderson, 2009). It is important that wounds are thoroughly lavaged at each dressing change to ensure removal of the topical preparation, preventing them from drying out and acting as foreign material on the wound surface, thereby negatively impacting healing.

Medical-grade manuka honey

Medical-grade manuka honey (e.g. Activon®, Advancis medical, Nottingham; Manuka Fill®, Pioneer Veterinary Products, Canterbury; Kruuse Manuka Honey, Kruuse, Denmark; Medihoney®, J.A.K Marketing Ltd, York; Henry Schein veterinary wound gel, Henry Schein, Paisley) differs from raw manuka honey in that it has been filtered and irradiation-sterilised, making it appropriate for topical application. It has multiple antimicrobial mechanisms (Cooper et al, 2011; Molan and Rhodes, 2015): it has a high sugar content, which will draw out water molecules from micro-organisms, causing their death or disrupting growth; it has an acidic pH (around 3.2–4.5), which inhibits growth of many bacteria; and it produces hydrogen peroxide at a low concentration (0.003%), which undergoes oxidation to produce free radicals that are toxic to microorganisms. Medical-grade manuka honey has been shown to inhibit formation of biofilms and reduce the mass of existing biofilms within wounds in human patients (Cooper et al, 2011), however this has not yet been demonstrated in veterinary patients.

Manuka honey also exhibits wound debridement activity. The mechanism of this activity is not fully known, but is partially attributed to plasmin stimulation within the wound, which causes denaturation of fibrin and thus releases any adherent surface debris (White, 2016). Manuka honey also aids wound debridement through its osmotic activity, as exudate containing necrotic tissue is transferred to the contact layer dressing through the osmotic gradient created by its application (Bardy, 2008).

When using medical-grade manuka honey, it is important that an appropriate contact layer dressing is used, as a significant amount of exudate is produced by the wound, in addition to moisture from the honey (White, 2016). If sufficiently absorbent dressings are not used, this can lead to maceration of the wound and surrounding skin (Hollis, 2017) Medical-grade manuka honey-impregnated alginate dressings are commercially available and will be discussed in the second article.

Silver sulfadiazine

Silver sulfadiazine is available as a 1% ointment (e.g. Flamazine, Smith and Nephew, London). It has an acidic to neutral pH (3.5–6) and, as it is water-based, it provides a source of moisture to the surface of the wound. It causes bacteriostasis in susceptible organisms, via the sulfadiazine component. The product also induces structural changes within bacterial cell membranes, ultimately causing weakening of the membranes (Smith & Nephew, NDb). When used as a topical wound treatment, silver sulfadiazine should be used with an appropriate contact layer dressing that will absorb any wound exudate in addition to moisture from the silver sulfadiazine ointment itself (Hosgood, 2018). Silver sulfadiazine can be used in combination with a contact layer dressing such as a foam dressing, or, alternatively, slow-release silver impregnated dressings can be used. Silver sulfadiazine can be used as a delivery vehicle for antibiotic preparations, although, once again, this is not licensed and should only be prescribed in accordance with the veterinary Cascade guidelines. The use of silver sulfadiazine ointment appears to be being replaced in favour of slow-release silver dressings (Hosgood, 2018) — these dressings will be discussed in the second article.

Fusidic acid

Fusidic acid is an antibiotic that has proven in vitro activity against coagulase-positive staphylococci including methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) (Clark et al, 2015). Use of fusidic acid is common in cases of canine pyoderma, and its use may be warranted in some cases of more superficial wound infections. It is worth noting that the break-points quoted for fusidic acid on sensitivity panels are extrapolated from systemic doses, so often, where resistance is suggested, topical use is nevertheless likely to be effective.

Topical preparations

Hydrogels

There are multiple hydrogels available for use in veterinary patients. These provide a source of moisture to the surface of the wound, so are mostly applicable to dry and potentially dessicated wounds, where provision of moisture will keep granulation tissue hydrated and allow migration of epithelial cells from the wound edges (Smith & Nephew, ND; Harrison and Spada, 2018). They have no antimicrobial effect of their own, and if not thoroughly removed from the wound by irrigation at every dressing change, the gel can dry out and act as foreign material on the wound surface, delaying wound healing and potentially acting as a nidus for infection. Hydrogels should be used in conjunction with a contact layer dressing to protect the wound and absorb any wound exudate (Sood et al, 2014). They can be used to hydrate necrotic tissue to aid debridement through moisture-facilitated cell migration, and may also be combined with antibiotics, making them a topical delivery system (Harrison and Spada, 2018). The process of wound debridement with use of hydrogels is slow (Milne et al, 2012). For necrotic wounds, medical-grade manuka honey may provide superior debridement through provision of an osmotic gradient, in addition to its antimicrobial properties.

Conclusions

The use of topical antimicrobial preparations for management of wounds in veterinary patients is gaining popularity in the face of increasing antibiotic resistance. Antimicrobial solutions can be used to complement the effects of saline lavage to further reduce the surface microbial burden while also having demonstrated efficacy against biofilm formation. Topical preparations can help create wound environments that favour healing, with some having concurrent antimicrobial and wound debridement effects. They should routinely be used in conjunction with an absorbent contact layer dressing to provide protection for the wound and to absorb surface exudate. CA

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