Topical Wound Medications

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KEYWORDS

• Horse • Wound healing • Ointments • Antiseptics • Topical antimicrobials

KEY POINTS

- Topical antiseptics used for wound cleansing should be diluted appropriately to maximize microbial killing and minimize cytotoxic effects to the wound bed.
- When possible, topical antimicrobial medications are recommended in place of systemic antibiotics in the management of equine wounds. Topical antimicrobials can be more effective, because many have the ability to work in the presence of a biofilm or have properties to help eliminate biofilms from the wound bed.
- Topical medications can be used to manipulate the healing process or enhance the wound environment to promote healing. For example, corticosteroids can be used when excessive granulation tissue is present. Other therapies, such as honey or platelet-rich plasma, have various properties that improve autolytic débridement of wounds and provide factors that improve normal wound healing.

LAVAGE SOLUTIONS

Topical cleaning agents should provide antisepsis but should not be cytotoxic to the healthy tissue within a wound. Prior to antiseptic application, a wound should be prepared by applying a water-soluble sterile lubricant, followed by clipping of the wound margins to remove hair. Many equine wounds have substantial contamination with dirt and debris and may have been cleaned by a layperson prior to the arrival of the veterinarian. In these cases, nonsterile tap water may have been used. Although irrigating wounds with tap water does not increase microbial colonization,[1] the use of tap water is reported to be cytotoxic to skin fibroblasts.[2] The cytotoxic effects of tap water are attributed to alkaline pH, hypotonicity, and presence of cytotoxic trace elements.[2] Clinically, however, in humans the use of tap water to clean wound does not delay healing.

The most common agent used by veterinarians to clean equine wounds is 0.9% sodium chloride. Saline provides its antiseptic effects via dilution when used as a lavage. Saline, however, does have mild cytotoxic effects in vitro on canine fibroblasts after 10 minutes of exposure. This results from the slightly acidic pH of normal saline and the lack of a buffering system. Lactated Ringer solution does not result in fibroblast damage[2]; therefore, the use of such isotonic solutions may be preferred over the use of 0.9% sodium chloride.

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Removal of dirt and debris from the wound is important, because soil has been found to have factors that potentiate infection. In the presence of soil, only 100 bacteria are necessary to elicit infection.[3] Therefore, topical cleansing of wounds is an important part of wound management. Pressure lavage can be used to help clean and decontaminate wounds; however, it is important not to be too aggressive. Lavage pressures over 20 psi can damage tissue and drive bacteria deeper into a wound bed. Use of a 35-mL syringe with a 19-gauge needle exerts a pressure of 7 psi to 15 psi at a wound surface (**Fig. 1**).[3,4] Additional cleansing of the wound after the initial treatment may be unnecessary, because it may damage the delicate tissue around the wound margin and remove wound exudate that can have beneficial factors for wound healing.

ANTISEPTICS

Antiseptics can be used alone or added to lavage fluid to reduce microbial content within a wound (**Fig. 2**). Topical antiseptics should have a broad spectrum of activity, controlling both resident and contaminating flora, including bacteria, fungi, and viruses on the wound and surrounding skin. Antiseptics reduce microbial numbers through mechanical and/or chemical properties. The addition of antiseptics, such as povidone-iodine or chlorhexidine, into lavage fluid is a common practice in equine wound management. It is important, however, to dilute these products to appropriate levels (0.1%–0.05% solutions) that minimize deleterious effects to the wound and surrounding tissue prior to use, because many of these antiseptic agents have negative effects on wound healing at higher concentrations.

Fig. 1. Normal saline (0.9% sodium chloride) administered as a pressure lavage using an 18-gauge needle and 35-mL syringe will deliver between 8 psi and 15 psi to the wound surface.

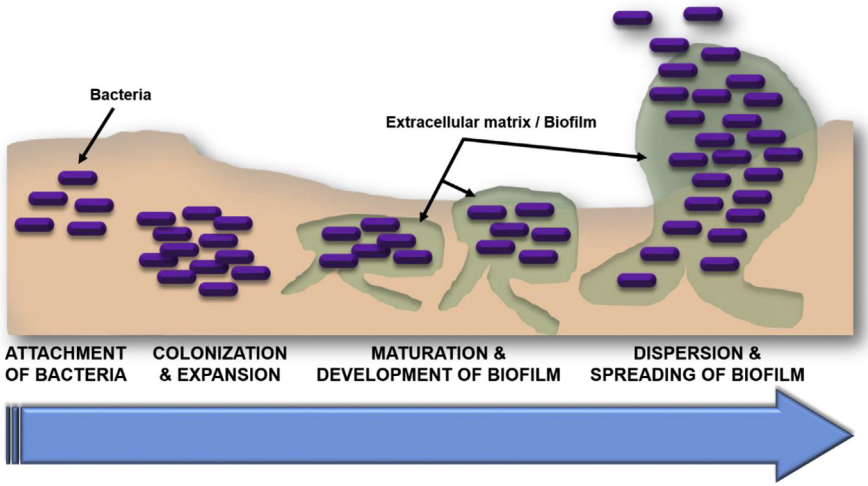

Fig. 2. Development of a biofilm occurs when microorganisms (purple) colonize into communities on the surface of wounds, producing a protective extracellular matrix (green) that encases the organisms, preventing antimicrobial penetration.

Hydrogen Peroxide 3%

Hydrogen peroxide 3% is used to clean wounds, producing an effervescent effect on application. The antimicrobial benefits of hydrogen peroxide in vivo have been questioned because it is rapidly broken down into water and oxygen, via the enzyme catalase, on contact with organic tissue. Bacterial production of catalyze likely limits the microbial killing ability of hydrogen peroxide. Due to its liberation of oxygen, hydrogen peroxide has been recommended for use in deep puncture wounds where *Clostridium* infections may be of concern. Numerous studies suggest that hydrogen peroxide is cytotoxic. Therefore, it is not recommended for use in the general cleaning of equine wounds. Use of a hydrogen peroxide cream has demonstrated improved healing of equine wounds. Experimentally, application of 1% hydrogen peroxide cream (LHP, Bioglan AB, Malmö, Sweden) resulted in faster healing of equine wounds and reduced bacterial colonization compared with controls.[5]

Povidone-Iodine 10%

Povidone-iodine is an iodophor and depends on the release of free iodine to be activated.[3,6] Iodophors were developed to stabilize iodine in solution and subsequently allow the sustained release of iodine. The antimicrobial action of povidone-iodine occurs rapidly, killing a variety of bacterial strains within 20 seconds to 30 seconds. Although the mechanism of action has not been fully elucidated, iodine damages essential cellular structures by attacking intracellular proteins, fatty acids, and nucleotides.[6] Iodine is inactivated by organic material; therefore, removal of dirt and debris is indicated prior to application of povidone-iodine. Prolonged microbial killing is also inhibited by the presence of organic material, such as blood and serum proteins, and effects on microbial killing is short lived. Povidone-iodine reportedly increased damage to vascular endothelium and caused thrombosis in rat wounds compared with other agents, including chlorhexidine.[7] Epithelialization can also be delayed when povidone-iodine is used.[6] Therefore, 10% povidone-iodine should be diluted to concentrations of 0.1% to 0.2% to minimize cytotoxicity to the surrounding tissue. The

addition of 10 mL to 20 mL in 1 L of saline is recommend for cleaning equine wounds. It is important that scrub formulations are not used to clean wounds because the detergent component has increased cytotoxic effects on exposed tissues.

Chlorhexidine Gluconate and Chlorhexidine Diacetate 2%

Chlorhexidine is one of the most commonly used antiseptics in veterinary medicine. It is a biguanide antiseptic that is positively charged and exerts its antimicrobial effects by reacting with the negative cell surface membrane, thereby disrupting and subsequently killing microorganisms. It has a wide antimicrobial spectrum and a prolonged residual effect. Unlike povidone-iodine, the presence of organic material has no effect on the microbial killing ability of chlorhexidine. Bacterial resistance has developed through activation of efflux pumps, which are intermembrane protein channels developed by bacteria to remove various antibiotics and biocides. In particular, some *Pseudomonas* and *Proteus* spp have been found resistant to chlorhexidine.[8] Chlorhexidine can be cytotoxic; therefore, it must be diluted prior to use. A 0.05% solution is recommended for lavage and cleaning of wounds. A 1:40 dilution of chlorhexidine gluconate 2% can be made by adding 25 mL of 2% chlorhexidine to 975 mL of sterile saline. Chlorhexidine should not be used near the eye or open joints, as its use can result in corneal edema and scaring, affecting vision and synovial inflammation and abundant fibrin accumulation, respectively.[9] Overall, chlorhexidine is recommended for use over povidone-iodine, because it is less cytotoxic and has superior bacterial killing.

Dakin's Solution

Dakin's solution or sodium hypochlorite, also known as bleach, is available in varying concentrations ranging from full strength at 0.5% to 1/40 strength of 0.0125%. Sodium hypochlorite exerts its antibacterial effects by liberating chlorine into the tissues. Although bleach has been historically used to clean wounds in battlefield situations, Dakin's solution is cytotoxic; therefore, low dilutions (1:50 dilution resulting in 0.00025% solution) of the 0.0125% concentration are recommended. This solution is not stable and is inactivated by light and heat. Due to the instability and cytotoxic properties, sodium hypochlorite is not commonly used or recommended to treat equine wounds.

Hypochlorous Acid

Similar to hypochlorite, hypochlorous acid exerts its antimicrobial effects through the actions of chloride. Improved microbial killing occurs, however, when chlorine is in the presence of a solution with a low pH (5–6). This makes hypochlorous acid effective as an antiseptic and it is reported be 70 to 80 times more effective than hypochlorite for inactivating bacteria. In evaluation of 19 skin cleansers, hypochlorous acid had minimal cytotoxic effects and demonstrated the most rapid bacterial kill, with various commercial hypochlorous acid products. Application times have ranged between 1 minute to 30 minutes.[10] Although hypochlorous acid has been reported in vitro to achieve bacterial killing within biofilms, the actual biofilm structure was not disrupted by treatment.[11] This suggests that mechanical disruption of the biofilm (see **Fig. 2**) may be necessary when hypochlorous acid is used to treat chronic wounds.

Vetericyn (Innovacyn, Rialto, California) is a commercially available veterinary compound sold in 2 concentrations: (1) as an over-the-counter solution for horse owners and (2) as a veterinarian prescribed solution. The veterinary prescribed compound is comprised of 0.003% hypochlorous acid and 0.004% sodium hypochlorite. It is made by electrochemically treating water resulting in a hypochlorous solution with a neutral pH.[12] Processing has made this product stable, with an average shelf life of 24 months. Vetercyn is supplied as a ready-to-use solution and can be sprayed directly on wounds.

The combination of low cytotoxicity and rapid decontamination of bacteria makes hypochlorous acid a desirable antiseptic. Indications for use include initial wound cleaning of the acute injury and for daily cleaning of chronic wounds.

Tris–Ethylenediaminetetraacetic Acid

The combination of Tris buffer (tris[hydroxymethyl]aminomethane) and disodium-calcium salt of ethylenediaminetetraacetic acid (EDTA) results in microbial death after topical application, particularly to gram-negative bacteria, by increasing microbial cell membrane permeability. Although wounds with reduced pH levels have been associated with improvement in wound healing,[13] some antibiotics, such as aminoglycoside, do not perform well in an acidic environment. Tris-EDTA can be used to alkalize the surrounding tissue environment. This alkalization improves the function of some topically administered antibiotics, such as aminoglycoside. The increase in cell permeability and alkalization of the wound bed further allows Tris-ETDA to potentiate the bactericidal activity of many antibiotics, including aminoglycides, penicillin, and oxytetracycline.[14] Tris-EDTA also has the ability to disrupt biofilms. This disruption results from the chelation of the divalent cations, calcium and iron, by Tris-EDTA, causing bacterial cell detachment, lysis, and destabilization of biofilm.[15] Clinical uses involve the treatment of wounds infected with 4 major bacteria: *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris*, and *Escherichia coli*.[16]

The addition of 0.01% chlorhexidine to Tris-EDTA has been reported to have synergistic effects on microbial killing.[16] Although not commonly used to treat equine wounds, Tris-ETDA has been used in the management of uterine and sinus infections in horses. Indications for use in the horse include lavage solutions for penetrating wounds and fistulous tracts, both with and without the addition of antibiotics. Preparation of a Tris-EDTA solution has been described[16] and can be made from 1.2 g of EDTA and 6.05 of Tris buffer added to 1 L of sterile water (**Box 1**). The pH should be adjusted to 8.0 by adding dilute sodium hydroxide. After it is prepared, the Tris-EDTA solution should be autoclaved for 15 minutes.

Commercial Wound Cleansers

Due to environmental factors, equine wounds are frequently contaminated, resulting in the development of a biofilm that can delay wound healing. Cultures from both acute and chronic equine wounds have isolated multiple bacterial species with varying ability to develop biofilms. Bacterial biofilm formation allows for promotion of antimicrobial resistance and prevents the host immune system from eliciting a productive response.[17] Due to the addition of surfactants, some commercial wound cleansers can help treat bacterial contamination within a biofilm. Shur-Clens (ConvaTec, Oklahoma City, Oklahoma) is a wound cleanser that contains the nontoxic surfactant poloxamer 188.

Box 1
Common antiseptic preparations used in the management of equine wounds

- Povidone-iodine (0.1%–0.2%): povidone-iodine should be diluted to concentrations of 0.1%–0.2% to minimize cytotoxicity. This can be achieved by the addition of 10 mL to 20 mL of povidone iodine into 1 L of sterile saline.
- Chlorhexidine 0.05%: chlorhexidine should be diluted to concentrations of 0.05% to minimize cytotoxicity. This can be achieved by the addition of 25 mL of 2% chlorhexidine gluconate to 975 mL of sterile saline.
- Tris-EDTA: 1.2 g of EDTA and 6.05 of Tris added to 1 L of sterile water. The resulting solution should have a pH = 8.0 and undergo sterilization in the autoclave for 15 minutes.

Mechanical breakdown of biofilm occurs with this product; however, it has been recommended that it be used in conjunction with an antimicrobial agent, because poloxamer alone has no antimicrobial effects.

Many cleansers used for cleaning intact skin, such as shampoos and scrubs (including povidone-iodine and chlorhexidine scrubs), have cytotoxic properties to exposed tissues in wounds and should be avoided.

TOPICAL ANTIMICROBIALS

Topical antimicrobial agents can be useful when treating acute contaminated wounds and when managing chronic granulating wounds. Judicious use of systemic antibiotics for the treatment of equine wounds is strongly recommended, because antimicrobial resistance continues to rise. Many chronic granulating wounds develop a superficial biofilm that can delay healing (see **Fig. 2**; **Fig. 3**). Topical antimicrobials are aimed at treating the local environment and many are efficacious in the presence of a biofilm where systemic antibiotics would have little to no effect. Although some ointments can affect tissue microcirculation and perfusion,[18] their benefits can outweigh the potential negative effects and, in some cases, actually improve wound healing.

Triple Antibiotic Ointment

One of the classic topical antimicrobials used in both humans and animals is triple antibiotic ointment. It is comprised of 3 different antibiotics: neomycin, polymyxin B, and bacitracin. Triple antibiotic ointment has a wide antimicrobial spectrum, but it is ineffective against *Pseudomonas* spp. In people, the use of triple antibiotic ointment results in faster wound healing, reduces the number of colonizing bacteria, and decreases scarring. The zinc compound within the bacitracin component has been reported to

Fig. 3. Wire laceration of 10 days duration. Heavy bacterial colonization and presence of a biofilm is demonstrated by the presence of exudate. Use of topical cleansers with a noncytotoxic antiseptic is indicated in the treatment of this wound followed by the application of a topical antimicrobial.

stimulate epithelialization but may retard wound contraction. In horses, triple antibiotic ointment has been demonstrated to delay wound healing in the distal limb.[19] The mechanism for the delayed healing is believed associated with the petroleum base within the ointment, which can decrease epithelial proliferation. Regardless, the results from this study suggest that other topical therapies may have improved benefits over triple antibiotic ointment, and alternatives should be considered.[19]

Silver Sulfadiazine

Silver sulfadiazine (SSD) 1% ointment is a commonly used topical antibacterial agent for prevention of infection in burn wounds. SSD has a wide antimicrobial spectrum, including both gram-positive and gram-negative bacteria and fungi. Both the silver and sulfa antibiotic components of SSD interact with each other to provide antimicrobial effects. Silver binds to the microbes' DNA releasing of the sulfonamide, which inhibits metabolic pathways within the organism, thereby resulting in microbial death. SSD ointment has been the most effective agent evaluated when treating a multidrug-resistant *P aeruginosa* in full-thickness burn wounds.[20] Although no differences between povidone-iodine and SSD in the healing of distal limb wounds of horses have been identified, the antimicrobial properties of SSD could justify its use in contaminated wounds.[21] SSD should be applied under a light bandage, because it does not adhere well to equine wounds.[12] SSD should also be applied daily, because the silver ions can quickly become inactive once they react with wounded tissue.[12]

Sugar

Antimicrobial effects of granulated sugar on wounds result from the hyperosmolarity of this compound. Other hyperosmolar effects of sugar include wound débridement and a decrease in wound edema, as fluid is drawn out of the wound on application. Sugar is best applied during the early débridement and inflammatory stages of wound healing. It is indicated for use in highly exudative wounds and should be discontinued when a healthy bed of granulation tissue appears.[12] The addition of povidone-iodine to sugar creates a product known as sugardine. This product is commonly used in the treatment of hoof abscesses. Care should be taken when povidone-iodine is added to sugar because high concentrations of iodine can be cytotoxic.

Honey

Although honey has been used to treat wounds for centuries, recent studies have evaluated its effects on equine wounds. In general, honey has several antimicrobial properties. It is hyperosmolar and draws out fluid not only from microbes resulting in desiccation and death but also from the subcutaneous tissue to the wound surface, assisting in removal of debris and necrotic tissue and reducing edema. Honey contains an enzyme that catalyzes the production of hydrogen peroxide in low amounts resulting in microbial death. Manuka honey contains the antibacterial compound methylglyoxal, also known as Unique Manuka Factor (UMF).[22] The antimicrobial effects of Manuka honey are expressed by UMF with higher values demonstrating improved activity. When compared in equine distal limb wounds, Manuka honey with a UMF of 20 was superior in wound healing time compared with honey with a UMF of 5.[23]

Bischofberger and coworkers[24] evaluated the effects of Manuka honey on second intention wound healing in the distal limb of horses and observed that wounds treated with Manuka honey gel healed significantly faster than other wounds (both treated and nontreated) in their study. On average, wounds treated with Manuka honey healed 12 days faster than untreated wounds.[24] Various honey products have been evaluated; however, not all honey is created equal. Veterinarians have suggested that local

produced honey may have improved antimicrobial benefits against resident bacteria versus medical grade honey. Evaluation of different honeys, including locally produced, medical-grade, and store-processed, found that 18 of 29 honeys had positive bacterial or fungal growth before exposure to bacterial isolates from wounds.[25] Nonmedical and processed honeys were more likely to have bacterial contamination. Therefore, the use of locally produced or store-bought honeys for the treatment of wounds may result in inadvertent contamination and are not recommend for wound therapy. When evaluated for their antimicrobial effectiveness on common equine wound isolates, Manuka honey (both medical-grade and store-bought) and heather honey (from a local bee producer) performed best, effectively killing all 10 bacterial isolates studied.[25] Honeys in this study were also compared with sugar solutions of that inhibited bacterial growth of only 5 of the 10 isolates tested.[25] Manuka honey gel (Medihoney, Derma Sciences, Plainsboro, New Jersey) can help decrease the cost of treatment, by eliminating the need for bandaging to keep the medication in contact with the wound. The use of honey seems to have the greatest impact on wound healing during the inflammatory and débridement stages; therefore, it is recommended for use during the first 2 to 3 weeks of wound healing.

Cadexomer Iodine

Cadexomer iodine, a more recently formulated iodophor product, was developed in the 1980s as an antiseptic agent. It is composed of 0.9% iodine mixed with a starch polymer bead that immobilizes the iodine molecules. Once the cadexomer iodine contacts the wound exudate, the polymer bead swells and gradually releases iodine molecules. The slow release of iodine, in cadexomer iodine, provides enhanced microbial killing compared with povidone-iodine. Cadexomer iodine was useful in treating MRSA and *Pseudomonas* infections when present as a biofilm in mice wounds.[26] Cadexomer has also been reported to increase production of proinflammatory mediators and vascular endothelial growth factor by macrophages. This activity can improve wound healing and enhance epithelization in full-thickness wounds.[27] Iodosorb Gel (Smith & Nephew, St. Petersburg, Florida), is a commercially available cadexomer product that can be applied topically to wounds. Although there are no reports of its use in horses, this product may be beneficial in the treatment of contaminated wounds.

Octenidine Wound Gel

Octenidine dihydrochloride is a cationic surfactant and pyridine derivative that was developed in the late 1980s as an antiseptic agent. It has a broad antimicrobial spectrum, including gram-positive and gram-negative bacteria and fungi. It has prolonged activity on skin and has been reported to be present up to 24 hours after application.[12] Octenidine has also demonstrated excellent efficacy for treatment of *P aeruginosa* and *S aureus* infections within biofilms.[8] Treatment of chronic venous leg ulcers in people found that application of an octenidine-based gel resulted in greater wound size reduction and faster healing.[28] Additionally, application of the gel alone had similar results with lower treatment costs, because bandaging was not necessary to have a beneficial effect.[28] Although this compound has not been tested in the horse, it may have several beneficial properties that warrant its use in the treatment of chronic wounds.

Nitrofurazone

Nitrofurazone is an inexpensive broad-spectrum antimicrobial with primary bacteriostatic effects. It is not effective against *Pseudomonas* spp and wound exudate reduces

its potency. Nitrofurazone is available over the counter for owners and farm managers as an ointment. Nitrofurazone can decrease epithelialization and delay wound contraction in horses.[29] It is also believed to promote exuberant granulation tissue formation; therefore, it is not recommended to be placed on distal limb wounds. Nitrofurazone has been reported to cause ovarian and mammary tumors in rodents and suspected as carcinogenic to humans[30]; therefore, it is no longer allowed to be used in food producing animals.[12] Due to its limited antimicrobial activity and potential negative effects in equine wounds, other topical antimicrobials should be preferentially considered.

MANAGEMENT OF EXUBERANT GRANULATION TISSUE

Corticosteroids

The most common topical corticosteroid used in the treatment of equine wounds is triamcinolone used in combination with the antifungal nystatin and the antibiotics neomycin and thiostrepton (Animax (Dechra, Overland Park, KS) or Panalog (Fort Dodge Animal Health, Fort Dodge, IA)). Triamcinolone can suppress the early formation of exuberant granulation tissue in distal limb wounds of horses healing via second intention.[31] The exact mechanism by which corticosteroids decrease the production of exuberant granulation tissue is not known, but is it suspected to be related to a decrease in production of transforming growth factor β1 by monocytes and macrophages.[29] Judicious use of products containing triamcinolone is indicated because negative effects on wound healing are well documented with the use of steroids. Corticosteroids can substantially delay wound contraction, epithelialization, and angiogenesis.[32]

Topical corticosteroids can be beneficial in preparing a wound bed for skin grafting (**Box 2**). It is important, however, that the steroid be discontinued for a minimum of 3 days to 5 days before grafting occurs or success is negatively affected. Corticosteroids are contraindicated in the treatment of infected wounds because the host immune response is dampened, resulting in a decreased ability for the white blood cells to remove bacteria. Care also should be taken when treating extremely large wounds, because systemic absorption of triamcinolone can occur. Although uncommon, high doses of steroids, in particular triamcinolone (40–80 mg), and frequently repeated doses (of 15–20 mg/d of triamcinolone) over days to weeks have been reported to result in laminitis.[33] Although triamcinolone used topically should not be a concern in most horses, those with equine metabolic syndrome and/or pituitary pars intermedia dysfunction may have an increased risk of developing laminitis when large amounts are administered.

Granulex

Granulex is a topical compound comprised of trypsin, balsam of Peru, and castor oil. All 3 ingredients are believed to have an effect on wound healing, particularly in the

Box 2
Preparation of granulated wound bed for skin grafting using corticosteroids

1. Surgically débride the exuberant granulation tissue.
2. Topically apply the corticosteroid 2 days to 3 days post-débridement (only if the granulation tissue is becoming raised above the wound margin)
3. Evaluate the wound every 2 days to 3 days and apply corticosteroid as needed. Most granulation tissue beds require 1 to 3 applications over a 3-day to 9-day period.
4. Once the granulation tissue has uniformly filled the wound bed and is flush with the skin margin, discontinue application of topical corticosteroid.
5. The skin graft can be performed 4 days to 5 days after the last application of corticosteroid.

treatment of exuberant granulation tissue. Trypsin is a protease enzyme that débrides necrotic tissue; balsam of Peru is a local irritant that is believed to result in improved blood flow; and castor oil may offer some protective effects to the wound bed, promoting epithelialization.[29] Anecdotally, Granulex V (Pfizer Animal Health, New York, NY) has been used to débride exuberant granulation tissue in equine wounds. In December 2015, production of Granulex was discontinued.[34] Alternative products for the aerosol spray include TBC Spray (Delta Pharmaceutical, Irmo, South Carolina), which is a prescription-only product that contains all 3 ingredients present in Granulex, and Proderm (Bertek Pharmaceuticals, Morgantown, WV), which is an over-the-counter aerosol that only contains balsam of Peru and castor oil.[35]

MISCELLANEOUS TOPICAL THERAPIES

Platelet-Rich Plasma Gel

Platelet-rich plasma (PRP) has been used in various medical conditions to improve healing since the late 1980s.[36] Platelets are essential in the initial response to wounding because they promote hemostasis, and, in the later hours to early days of wound healing, they provide growth factors and hydrolytic enzymes (see Linda A. Dahlgren's article, "Regenerative Medicine Therapies for Equine Wound Management", in this issue). Because PRP is made from a patient's own plasma, it is considered safe.[37] One limitation in the use of PRP is the variable presence of white blood cells within the preparation. High white blood cell concentrations in PRP are believed proinflammatory, which could be desirable or detrimental, depending on the phase of wound healing. The development of exuberant granulation tissue on distal limb wounds of horses may result from a retarded inflammatory response. This suggests that the use of leukocyte-rich PRP could have beneficial effects in the treatment of wounds with exuberant granulation tissue. Depletion of leukocytes in PRP preparation, however, does not affect the healing ability of fibroblasts.[38] PRP gel is created by the addition of calcium gluconate plus thrombin to the plasma. The calcium gluconate and thrombin combination can be a platelet activator, thereby mediating growth factor release. When evaluated in experimental models of equine wounds, PRP gel improved epithelial differentiation and collagen organization.[39,40]

Oxygen Therapy

Oxygen is essential to the healing of wounds. Optimization of wound perfusion and oxygenation of tissues are essential for prevention of wound infection. Appropriate oxygen levels, measured by the partial pressure of oxygen surrounding the wound, are essential for normal cellular functions and the ability to generate proper healing responses.[41] Although oxygen is important for wound healing, some level of hypoxia is necessary to promote angiogenesis. The ideal oxygen concentration likely varies with the stage of wound healing and level of damage to the affected tissue. This makes determining correct protocols for topical oxygen therapy difficult. Oxygen delivery via hyperbaric chambers has been used to promote healing for numerous conditions in horses. Hyperbaric chambers allow for the exposure to 100% oxygen in a pressurized environment. Hyperbaric oxygen is used in humans to treat crush injuries, compartment syndrome, diabetic chronic wounds/ulcers, and necrotizing soft tissue infections with varying results.[42] In horses, hyperbaric oxygen therapy is particularly useful in the treatment of clostridial myonecrosis allowing for direct inhibition of the clostridial alpha-toxin and improved microbial killing.[42] Topical oxygen therapy via an electrochemical oxygen concentration device (EPIFLO Transdermal Continuous Oxygen Therapy; Ogenix Corporation, Beachwood, Ohio) has been evaluated in experimental

wounds of the distal limbs of horses; however, no difference in wound healing rates or in histologic assessments were noted between the treatment and control groups.[43] Although no differences in wound healing were seen in this study, oxygen therapy could be indicated for some chronic or nonhealing wounds. Ideal application methods and timing of delivery remain to be determined.

Ozone delivery is used to promote oxygenation within the wound bed. Ozone promotes wound healing by increasing fibroblast migration, decreasing inflammation, and up-regulating the production of growth factors.[44] Ozone can inhibit the growth of several common equine wound isolates, such as *E coli*, *S aureus*, and *P aeruginosa*, in culture.[12] Application of topical ozone can occur via 2 methods: (1) by placing the affected region in a sealed, ozone-resistant bag followed by insufflation and (2) by applying ozonized oil directly to the wound (ozone can be stabilized when placed in olive oil).[45] Ozone therapy has not been evaluated in horses. Like oxygen therapy, some equine wounds may benefit from ozone application; however, ideal case selection and timing of administration remain to be determined.

Aloe Vera

Aloe vera is a plant-derived product that is used topically for the treatment of abrasions and wounds. Soothing effects after topical application has been reported in humans. Multiple compounds within the aloe plant provide the benefits seen with its use; however, the main active compound seems to be acemannan. Acemannan stimulates the production of proinflammatory cytokines by macrophages resulting in fibroblast proliferation, epithelialization, and angiogenesis. Numerous human and veterinary products containing acemannan exist, including wound cleansers (EquineVet Acemannan Wound Cleanser, Medline (Carrington Labs, Irving, TX)), sprays, and impregnated gauze dressings. Although no studies have been performed in horses, dog wounds treated with acemannan hydrogels demonstrated improved wound contraction and epithelization.[46]

Scarlet Oil

Scarlet oil is composed of mineral oil, pine oil, eucalyptus oil, isopropyl alcohol 30%, benzyl alcohol 3%, methyl salicylate, parachlorometaxylenol, and scarlet red.[29] Although this compound has been used in the treatment of equine wounds, there is no experimental evidence determining positive or negative effects on wound healing. Scarlet oil is used by veterinarians to hopefully promote the production of granulation tissue, particularly in wounds of the upper body. Some antimicrobial effects may be obtained through the properties of the pine and eucalyptus oils. The use of scarlet oil in horses, however, can result in a substantial contact dermatitis requiring discontinuation of use.[12]

SUMMARY

In conclusion, numerous topical therapies exist for the management of equine wounds. Overall, wounds should be reassessed frequently. The decision of which topical therapies to use should be made based on the stage of wound healing, appearance of the wound, and level of contamination or infection. Combination therapies to enhance healing can be applied where indicated. Topical cleansers and antiseptics are important when treating an acute wound, minimizing bacterial colonization, and with chronic wounds, to prevent infection that can delay wound healing. Topical antimicrobials can be added with or without the addition of a bandage. Continual development of resistant microorganisms demonstrates the importance of minimize systemic antibiotic therapy and controlling local bacterial colonization and infection

with topical antimicrobial products, such as honey and octenidine gel. Other topical medications, such as corticosteroids or PRP gels, can be used during specific phases of wound healing to manipulate the wound environment and promote improved and more rapid healing.

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