ABSTRACT: Large, contaminated wounds are difficult and expensive to treat. Honey contains many nutrients and minerals and has a bactericidal effect due to hydrogen peroxide liberation and a phytochemical constituent. The use of honey in the management of wounds enhances healing and eliminates invading bacteria without the use of systemic antibiotics. Honey also decreases inflammatory edema. Thus the use of honey can be an effective and economical approach to managing large wounds.

Contaminated wounds, especially large wounds (e.g., major degloving injuries, burns), and conditions such as necrotizing fasciitis acquired through infections with Pseudomonas species, Escherichia coli, or streptococci, can be difficult and expensive to treat using conventional methods. As a result, owners whose pets have extensive wounds often opt to have the affected limb amputated or the animal euthanized. Honey has been shown to be effective against the growth of bacteria, and its use enhances wound healing. Thus it is an inexpensive topical treatment that is extremely effective in wound management and its use makes management of large, open wounds financially feasible.

HISTORY OF THE USE OF HONEY IN WOUND CARE

The use of honey to treat wounds dates back to 2000 BC. Numerous reports document the efficacy of honey in wound healing, and several studies even indicate that honey appears to be superior to many modern methods of treatment. Honey has been used for cleansing and accelerating the healing of wounds for centuries; however, the scientific basis for its success was not elucidated until the twentieth century. Honey is currently used worldwide to treat human patients with contaminated wounds or infected body cavities. The use of honey to treat wounds on animals has been slow to come into acceptance.

HEALING PROPERTIES OF HONEY

Mechanisms associated with wound cleansing and healing properties of honey include decreased inflammatory edema, attraction of macrophages to further cleanse the wound, accelerated sloughing of devitalized tissue, provision of a local cellular energy source, and formation of a protective layer of protein over the wound and a healthy granulation bed. Honey also has a deodorizing
action; this may be due to its rich supply of glucose, which would be used by the infecting bacteria in preference to amino acids, resulting in the production of lactic acid instead of malodorous compounds.\(^6\) The cleansing and healing properties of honey are not widely known in veterinary medicine.

Honey also has antibacterial properties that have been attributed to its high osmolarity, acidity, and hydrogen peroxide (\(\text{H}_2\text{O}_2\)) content.\(^2\) The effects of osmolarity in contaminated wounds is based on the low water content (or high osmolality) created in the wound.\(^24\) As the high osmolarity of honey draws lymph from a wound, dissolved nutrients within the lymph provide nutrition for regenerating tissue.\(^9,4\)

The antibacterial factor inhibitine has been isolated from honey produced from several different plant sources.\(^3\) Inhibite, which was determined to be \(\text{H}_2\text{O}_2\), is produced by the natural glucose oxidase in honey. Glucose oxidase produces gluconic acid (which is the principal acid in honey) and \(\text{H}_2\text{O}_2\) from glucose. Although \(\text{H}_2\text{O}_2\) is primarily responsible for the antibacterial properties of honey, it is present at harmlessly low levels. \(\text{H}_2\text{O}_2\) is continuously produced by the activity of the glucose oxidase enzyme, which is only activated when diluted.\(^3-7\) The concentration of \(\text{H}_2\text{O}_2\), that accumulates in 1 hour is approximately 1000 times less than that found in the \(\text{H}_2\text{O}_2\) solution (3%) that is commonly used as an antiseptic.\(^7,8\)

In addition to its inhibitine component, pure, unpauseder, commercial honey is composed of approximately 40% glucose; 40% fructose; 20% water; and trace amounts of amino acids, vitamins (i.e., biotin, nicotinic acid, folic acid, pentotenic acid, pyridoxine, and thiamine), enzymes (i.e., diastase, invertase, glucose oxidase, and catalase), and minerals (i.e., potassium, iron, magnesium, phosphorus, copper, and calcium).\(^6,18\) The rate of granulation tissue formation and epithelialization of wounds may be enhanced by the various constituents of honey.\(^18\) Honey is an excellent cellular energy source, provides a viscous barrier to wound invasion, and has a hygroscopic effect, which reduces edema.

Honey also has high levels of antioxidants,\(^9\) which protect wound tissues from oxygen radicals that may be produced by the \(\text{H}_2\text{O}_2\).\(^7\) \(\text{H}_2\text{O}_2\) has been shown to be more effective against bacteria when it is continuously generated.\(^5-7\) The generation of low levels of \(\text{H}_2\text{O}_2\) stimulates angiogenesis and the growth of fibroblasts.\(^8\) This increased angiogenesis increases oxygen delivery to tissues, which is a limiting factor for tissue generation.\(^6\) Topical acidification of wounds has been shown to promote healing\(^11;\) therefore, honey’s low pH (3.6 to 3.7) will accelerate healing as well as increase antibacterial effects.

\(^{11}\)For more information, see the companion article entitled “Wound Management Using Sugar” on page 41.

**VARIATIONS IN THE ANTIBACTERIAL ACTIVITY OF DIFFERENT HONEYS**

Two millennia ago, it was recommended that honey be collected in specific regions and during certain seasons (presumably from different floral sources) to be used for the treatment of different ailments.\(^13\) Today, honey is produced from many sources of plants and its antimicrobial activity varies greatly with origin and processing.\(^12\) Honey used to treat wounds must be unpasteurized and ideally should not be heated above 37°C. However, the honeycombs have to be heated to get the honey out, and sometimes heating the honeycombs to 39°C is necessary to do this (although not ideal, this temperature has not caused any problems). To assess the variation in antibacterial activity of honey, numerous varieties of New Zealand honeys were tested in vitro against *Staphylococcus aureus* in an agar well diffusion assay.\(^14\) This study demonstrated a highly significant difference in the antibacterial activity of honey from different floral sources. Kanuka, manuka, heather, and ling kamahi were shown to be sources likely to produce honey with high antibacterial activity. When antibacterial activity was assayed with catalase added to remove \(\text{H}_2\text{O}_2\) liberated into the agar, most of the honeys showed no detectable antibacterial activity. However, manuka and vipers bugloss honeys retained their antibacterial activity in the catalase environment, indicating that these honeys also contained a nonperoxide component of activity. This activity stems partly from a phytochemical component.\(^12\) When manuka honey and pasture honey were tested against 58 strains of coagulase-positive *S. aureus* isolated from infected wounds, the minimum inhibitory concentrations were between 2% to 3% for manuka honey and 3% to 4% for pasture honey.\(^12\) This activity is beyond the point at which the osmolarity would have had an antibacterial effect; therefore, it was concluded that the previously identified phytochemical components of honey and the low pH are also active components.

Another study\(^15\) showed that *E. coli, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhimurium, Serratia marcescens, S. aureus* (including methicillin-resistant strains), and *Streptococcus pyogenes* were all susceptible in vitro to a manuka honey and a *Knightia excelsa* honey. In quite dilute solutions, both types of honey completely inhibited growth of all bacterial strains over an incubation period of 8 hours.\(^15\) The antimicrobial effects of honey are also effective against *Candida albicans*. The susceptibility of 72 isolates of *C. albicans* to a honey distillate fraction and several antifungal agents showed all the isolates to be sensitive to the honey distillate, although 10% were variably resistant to nystatin, miconazole nitrate, and...
The potency of the antibacterial activity of honey can vary by as much as 100-fold. It is believed that any locally produced honey with high levels of antibacterial activity will achieve good results when used to treat infected wounds. To assess this, the minimum inhibitory concentration or zones of inhibition in an agar diffusion assay can be used. A simpler method to assess the antibacterial activity of honey is to compare the amount of honey that has to be added to milk to prolong souring times. In practice, any unpasteurized honey would be effective in treating wounds.

**Case 1—Dog with Second- and Third-Degree Burns**

An 8-month-old beagle mix presented with second- and third-degree burns to 20% of its body. The referring veterinarian debrided the third-degree burns and treated the area topically with silver sulphadiazine for 9 days prior to presentation to the Ontario Veterinary College. At this time, a healthy bed of granulation tissue had formed over the dorsum of the anterior thorax. The remainder of the dorsum of the torso and rump had an odorous, purulent discharge under a thick loose eschar. Oxymorphone, ketamine, and diazepam were administered, and the area was further debrided and lavaged with tap water (A).

Although the dog appeared to be adequately anesthetized, it vocalized when the honey was applied to the granulation tissue and area under the previously removed eschar. Within 24 hours after the application of honey, the wound was no longer odoriferous and the appearance of the tissue was dramatically improved (B). Oxymorphone followed by propofol was used as an anesthetic to facilitate a bandage change. The dog was quiet until the honey was applied to both the areas of full thickness burn and the granulation bed, at which time it again started to vocalize. Within 48 hours of honey treatment, a clean, healthy appearing granulation bed of tissue was present in the area previously under the eschar, which could not be discerned from the early granulation bed. Isoflurane anesthesia was used for subsequent bandage changes and application of honey. At 72 hours, a healthy granulation bed was forming and most of the debridement was complete.

Due to the potential for further discomfort with the application of honey, sugar was used to complete the debridement. Once a healthy granulation bed was formed (C), Furacin ointment was used to keep the wound clean during epithelialization. Primary closure of the wound was performed when the wound had contracted sufficiently.

Because of this dog’s severe injury and inability to control its pain adequately prior to admission, the potential for a hyperalgesic state was high. This resulted in a very low threshold to pain; therefore, the painful response to the honey dressing may not be typical for the average wound. Pain has not been reported to occur in any human study.

For more information, see the companion article entitled “Wound Management Using Sugar,” which appears on page 41.
HONEY VS. CONVENTIONAL TREATMENT

In a mouse model, unpasteurized honey or saline was applied to open, clean wounds. Wound healing was quantified by the area of the wound at 3, 6, and 9 days after injury, the degree of epithelialization from the periphery inward, and the thickness of granulation over time. In all cases, the area of the wound was less and the depth of granulation was deeper in wounds treated with honey; and acceleration of epithelialization was seen at 6 and 9 days when honey was used. Wounds treated with honey healed much faster than wounds in the control animals. In addition, honey had no adverse effect on tissues.18

In many clinical trials in humans, honey has been used instead of standard or conventional methods19–24 to treat contaminated wounds, most notably vulvectomy wounds.19 The use of honey to treat large, open, infected postoperative wounds in human neonates resulted in complete healing in 7 to 21 days. The wounds of these infants had failed to heal with conventional treatment that included a systemic antibiotic combination (i.e., vancomycin and cefotaxime), topical treatment, and cleansing of the wound twice daily (with chlorhexidine 0.05% w/v in aqueous solution and fusidic acid ointment).20

In a study by Efem21 and colleagues, 59 patients with wounds and ulcers that had failed to heal by conventional methods were treated with unprocessed honey; wounds healed in all but one patient. Fifty-one of these patients had wounds that were contaminated with bacteria; eight had wounds that were not contaminated. Wounds were sterile within 1 week after beginning treatment with honey. In all patients, sloughing, necrotic, and gangrenous tissues gradually separated from the floor and wall of the ulcers and could be lifted with a pair of forceps without the patient experiencing pain. The surrounding edema subsided, weeping ulcers dehydrated, and foul-smelling wounds were rendered odorless within 1 week of dressing with honey. Because of the chemical debridement action of honey, these patients did not need surgical debridement of the wounds, which would have otherwise been required. The sloughing and necrotic tissue were rapidly replaced with granulation tissue and advancing epithelialization. Incidentally, diabetes that had been hard to control in four patients became controllable following successful sterilization of their ulcers with honey. In this study, in vitro sensitivity testing was performed by placing a drop of honey on culture plates containing pure bacterial cultures obtained from these wounds. This test indicated that complete inhibition of Pseudomonas pyocyanea did not occur in vitro, yet all wounds containing this organism were completely sterile within 1 week of therapy. The study21 concluded that honey may have greater activity in vivo than in vitro.

Honey has been used successfully to treat burn wounds. In a prospective, randomized study22 of 92 human patients with partial thickness burns, the wounds treated with honey-impregnated gauze showed earlier healing and significantly less infection than did those treated with polyurethane film (OpSite® Smith & Nephew, London). The honey-impregnated gauze was prepared by dipping sterile gauze in unprocessed, undiluted honey obtained from hives. After washing the wound with normal saline, the gauze was placed over the burn and covered with pads and bandages. Bandages were changed daily if infection was present. When no infection was evident, bandage changes were performed on alternate days until the wound was healed (mean 10.8 days). In the control group, a bioocclusive, moisture-permeable, polyurethane dressing (OpSite®) was placed on the wound after cleansing with normal saline. The wounds were observed for evidence of infection, excessive exudates, or leakage. If none of these factors were present, the dressings were removed on day 8 for inspection of the wound. If infection was present, a new covering sheet was applied after cleansing. Healing occurred at a mean of 15.3 days.

A similar study23 of burn wounds in humans that compared honey treatment with silver sulfadiazine (SSD) gauze dressings showed a more rapid rate of healing in patients treated with honey. Of the 52 patients (43 were infected at admission) with burns that were treated with honey, 33 had granulation tissue within 10 days compared with 3 of 52 patients (41 infected at admission) that were treated with SSD. All wounds in the honey-treated patients healed within 31 to 40 days; the wounds of the patients in the SSD group required 51 to 60 days to heal. In the group treated with honey, the infected wounds in 39 of 43 patients were sterile at 7 days compared with those treated with SSD (only 3 of 41 patients had sterile wounds). One patient treated with honey had hypergranulation and one experienced postburn contracture. Three patients treated with SSD had hypergranulation, six had postburn contracture, and seven had hypertrophic scarring. It was the author’s impression that the patients treated with honey experienced less pain and irritation than those treated with SSD. In the treatment of superficial burns, the use of honey is cost effective because it shortens the duration of treatment.

Another study24 conducted several years later showed a similar healing rate. Of the 25 human patients whose burns were treated with honey, 21 healed in 7 days compared with 18 of the 25 patients treated with SSD.24 There was no eschar formation in wounds treated with honey, and the margins of the wounds were free of...
edema, whereas the wounds of patients treated with SSD formed an eschar, which had to be surgically removed. Histologic examination of the burn tissue treated with honey showed early attenuation of acute inflammatory changes, control of infection, and early reparative activities when compared with those treated with SSD. The author concluded that honey seemed to function better as a topical treatment for superficial burns than did SSD because honey appeared to promote fast reepithelialization and decreased the inflammatory reaction.

In a subsequent study\textsuperscript{25} by the same author, early tangential excision and skin grafting were found to be superior to honey dressings. The author concluded that when facilities and expertise are available, prompt surgical wound excision and immediate autologous skin grafting are superior to the management of burns with honey.

Honey-impregnated foam has been used as a stent in oral cavity reconstruction.\textsuperscript{26} Foam packs were kept in place for 72 hours, at which time the oral cavity graft appeared viable. Honey has also been used as a storage medium for skin grafts.\textsuperscript{29}

There are no reports of infection resulting from the application of honey to wounds.\textsuperscript{3} Because the use of raw honey is advised, it is assumed that unsterilized honey was used in all trials; in fact, this was specifically stated in some studies. It is recommended that honey should not be heated above 37°C to prevent the inactivation of glucose oxidase, which is an essential enzyme in the liberation of H$_2$O$_2$.\textsuperscript{6} Honey sometimes contains clostridia spores, which may be problematic; however, this has not been reported or mentioned (even in babies and young children) in any of the studies reviewed in this paper or by Vardi\textsuperscript{20} and colleagues.

**DRESSING TECHNIQUE USING HONEY**

Similar techniques are used to manage various types of injuries, burns, and infected or necrotic wounds. Initially, grossly contaminated wounds should be lavaged with body temperature tap water using a kitchen-type spray nozzle over a grating to allow drainage. If the wound requires irrigation, using tap water under pressure may be a reasonable alternative to saline irrigation.\textsuperscript{30} In large breeds of dogs, large, dirty-infected wounds may require up to 50 L of lavage fluid. Once the wound is lavaged, it should be patted almost dry with sterile towels. Resection of necrotic tissue or debridement of traumatic or surgical wounds should be performed prior to the application of honey. The amount of honey required varies with wound size. Generally, 30 ml of honey is used on a 10 x 10 cm dressing. It has been suggested that soaking a piece of gauze or an absorbent dressing pad (e.g., Gamgee dressing) in honey prior to application makes wound dressing simpler than pouring the honey directly onto the wound. Honey does not reduce the absorbency of the dressing material; therefore, large amounts of wound exudates can still be contained within the dressing.\textsuperscript{3}

In our experience with a dog with second- and third-degree burns (see Case 1), small sterile laparotomy sponges were used initially; however, this process was cumbersome. Strips of bandage, which adhered to the wound, were then used (Figure 1). This proved to be an excellent method of debriding dead skin from the large area of the burn. Within 2 days as the granulation tissue formed, the bandage adhered to the granulation bed and caused bleeding. Subsequently, Telfa\textsuperscript{®} pads (Kendall Healthcare, Mansfield, MA), which are less adherent, were used. Deep wounds or abscesses can easily be filled by applying the honey using a large Toomey\textsuperscript{®} syringe (Bard, Inc., Covington, GA). The honey that we used had been heated to 39°C (slightly above the ideal temperature). Occlusive or absorbent secondary dressings are needed to prevent honey from oozing out from the wound dressing. The frequency of dressing changes will depend on how rapidly the honey is
REFERENCES


CONCLUSION

Honey offers an alternative to the more expensive products available for managing contaminated wounds. Although the current focus is on wound management, many animals with these wounds have associated problems, such as shock or sepsis, and these must be treated appropriately prior to and during wound management. It is also important to remember that these patients are in pain; therefore, general or local anesthesia and/or the administration of a pure opioid is required to render the animal pain-free during surgical resection, wound cleaning, and debridement.


1. A major antibacterial action of honey is
   a. the production of inhibine from the action of glucose oxidase.
   b. its low level of H₂O₂.
   c. its low osmolarity.
   d. its rare phytochemical component.

2. H₂O₂ in honey
   a. has an equal concentration to commercially available H₂O₂ solution (3%).
   b. is liberated by glucose oxidase, which is activated only when diluted.
   c. requires a high pH for activity.
   d. is detrimental to the formation of granulation tissue.

3. The rapid rate of granulation and epithelialization of wounds after the application of honey is
   a. due to inhibine.
   b. due to the concentration of glucose oxidase.
   c. enhanced by various constituents of honey.
   d. due to the low pH.

4. When used to treat contaminated wounds, honey
   a. compared poorly to SSD.
   b. was unable to control infection caused by bacteria.
   c. caused eradication of infection when compared with various systemic antibiotic combinations.
   d. was unsuccessful in eradicating infection in deep wounds.

5. When necrotic tissue is present in wounds,
   a. honey has a debridement action.
   b. honey delays sloughing of tissue.
   c. honey has no effect on the removal of tissue.
   d. the wound also requires surgical debridement to facilitate removal of all necrotic tissue.

6. Ideally, honey should not be heated above ___˚C to prevent the inactivation of glucose oxidase.
   a. 28 c. 37
   b. 35 d. 42

7. Honey is an excellent source of
   a. protein.
   b. cellular energy.
   c. amino acids.
   d. minerals.

8. Which of the following statements regarding the antimicrobial activity of honey is false?
   a. The antimicrobial activity of honey varies greatly with origin and processing.
   b. The antimicrobial activity of honey is effective against *C. albicans*.
   c. H₂O₂ is primarily responsible for the antibacterial property of honey.
   d. A study of New Zealand honeys showed no significant difference in the antibacterial activity of honey from different floral sources.

9. The ________ effect of honey reduces edema.
   a. hypoglycemic c. hyperglycemic
   b. hygroscopic d. hypokalemic

10. The pH of honey is
    a. 3.6 to 3.7. c. 2.1 to 2.3.
    b. 5.2 to 6.2. d. 7.1 to 7.3.