

The evidence for honey promoting wound healing

Molan, P. C. "A brief review of the use of honey as a clinical dressing."

Primary Intention (The Australian Journal of Wound Management) 6 (4) 148-158 (1998).

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Summary

The use of honey as a wound dressing material, an ancient remedy that has been rediscovered, is becoming of increasing interest as more reports of its effectiveness are published. The clinical observations recorded are that infection is rapidly cleared, inflammation, swelling and pain are quickly reduced, odour is reduced, sloughing of necrotic tissue is induced, granulation and epithelialisation are hastened, and healing occurs rapidly with minimal scarring. The antimicrobial properties of honey prevent microbial growth in the moist healing environment created. Unlike other topical antiseptics, honey causes no tissue damage: in animal studies it has been demonstrated histologically that it actually promotes the healing process. It has a direct nutrient effect as well as drawing lymph out to the cells by osmosis. The stimulation of healing may also be due to the acidity of honey. The osmosis creates a solution of honey in contact with the wound surface which prevents the dressing sticking, so there is no pain or tissue damage when dressings are changed. There is much anecdotal evidence to support its use, and randomised controlled clinical trials that have shown that honey is more effective than silver sulfadiazine and a polyurethane film dressing (OpSite®) for the treatment of burns.

Introduction

In 1989 an editorial in the Journal of the Royal Society of Medicine (1) expressed the opinion: "The therapeutic potential of uncontaminated, pure honey is grossly underutilized. It is widely available in most communities and although the mechanism of action of several of its properties remains obscure and needs further investigation, the time has now come for conventional medicine to lift the blinds off this 'traditional remedy' and give it its due recognition." Mostly this was in reference to reports of the use of honey as a wound dressing. The ancient usage of honey as a wound dressing has been reviewed (1-3), but there have been only some very brief reviews, with little clinical detail, of the literature reporting modern usage of this rediscovered therapy for wounds (1, 4, 5). Because of the increasing interest in the use of alternative therapies, especially as the development of antibiotic resistance in bacteria is becoming a major problem (6), and because of the increase in reported usage of honey as a wound dressing in recent times, it was considered timely to review the clinical and experimental findings that have been published on this subject. Pertinent to this are reports of honey being effective on wounds not responding to conventional therapy (7-12).

In many of the reports the effectiveness of honey as a dressing on infected wounds is attributed in part to its antibacterial properties (1, 5, 7, 9, 13-31). But the large volume of published literature from in vitro studies that has established that honey has significant antibacterial activity will not be included in this review as it has been comprehensively reviewed elsewhere (32, 33). However, it is noted here for the interest of the reader that honeys with median levels of antibacterial activity have been found to completely inhibit the major wound-infecting species of bacteria at concentrations of 1.8% - 11% (v/v) (34), and a collection of strains of strains of MRSA at concentrations of 1% - 4% (v/v) (35).

Mode of application of honey

The procedure that is described in most of the reports is to clean the wound first, even though many describe honey as having a cleansing and debriding action on wounds (see next section). Some report abscesses being opened and pockets of pus drained (25, 30, 31, 36), and necrotic tissue being removed (11, 25, 31, 37), before dressing wounds with honey. Some used rigorous cleansing procedures: scrubbing with a soft toothbrush followed by hydrogen peroxide, saline rinse, betadine, and another saline rinse (38); dilute Dakin solution or dilute hydrogen peroxide on the wound bed and alcohol on the surrounding skin (31); or the wounds were cleaned with eusol (30) or aqueous 1% chlorhexidine (10). Some reported cleaning the wounds before dressing, but did not specify with what (10, 11, 25, 30). One cleaned the wounds with gauze (25).

Most report simply washing wounds with saline before dressing with honey (5, 7, 9, 16-20, 39), and when dressings are changed (5, 7, 9, 15-20, 31).

In many of the reports the honey is spread on the wound then covered with a dry dressing, mostly gauze (5, 8-10, 15, 16, 19-23, 31, 38-41). The quantity of honey used varies: one reported using a thin smear of honey (but with relatively poor outcomes); two reported using a thin layer honey (but this was applied 2 - 3 times daily) (15, 36); most just refer to the honey being spread or poured over the wound (9, 16, 19-21, 23, 38); others report using a thick layer of honey (42), soaking the wound generously with honey (25), pouring honey into the wound to three-quarters fill (31), and applying 15-30 ml of honey to ulcers (7, 22). Others have applied the honey to the dressing then placed it on the wound: either the honey was spread on gauze (10, 11, 25, 38) or the gauze was soaked in honey (17, 18, 23), or "honey pads" were used (37). (It has also been reported that covering cracked sore nipples in nursing mothers with gauze soaked in honey can prevent them from becoming infected (43).) Honey-impregnated gauze has also been used to pack cavities of wounds (22). Others have packed cavities of wound directly with honey and then covered the wound (10, 23, 25). Cervical ulcerations stubborn to healing have been treated by inserting 85 ml honey in the vagina and holding this in place with a tampon for 3 days (43).

Mostly the dressings are changed daily (7-11, 16, 23, 25, 40, 42) or every 2 days (17-20, 39): or every 2 - 3 days (41). One paper reported that dressings were changed daily, but that less frequent changes (every 2 - 3 days) were needed if the wounds were clean and dry (42). Another reported dressings being changed once or twice daily until clean granulated wounds were achieved, then once-daily changes (38). Others have reported changing honey dressings twice daily (15, 21, 24), 2 - 3 times a day (36), 3 times daily (30, 37), and 3 times daily if contaminated with urine or faeces, otherwise twice daily (31).

Two papers report mixing lipid material with the honey to make it easier to spread; either castor oil (25) or 20% vaseline or lard (42). Although this was a common form of wound dressing in ancient times, it is not necessary as honey can be made very fluid by warming to 37°C if vigorous stirring is not sufficient. Bulman (23) refers to using liquid honey on large surfaces, or carefully warming granulated honey. (Excessive heating of honey should be avoided because the glucose oxidase enzyme in honey which produces hydrogen peroxide, a major component of the antibacterial activity of honey, is very readily inactivated by heat (44).)

Comment: There is no indication of any of the reported modes of application of honey being decided upon on empirical or theoretical grounds, the large degree of variance in modes appearing to reflect a more notional approach. The spreading of honey on the dressing pad rather than on the wound is much easier to do and is less traumatic for the patient. It also gives a more even coverage of the wound surface. Where deep wounds or abscesses need to be filled with honey the most practicable way of doing this would be to use honey packed in squeeze-out tubes, now available commercially.

Rationally, the amount of honey required per unit area of the wound would depend on the amount of exudation. The various beneficial effects of honey on wound tissues that have been reported (see below) would be expected to be reduced or lost if small amounts of honey become diluted by large amounts of exudate. Likewise the frequency of dressing changes required will depend on how rapidly the honey is being diluted by exudate. The effectiveness of honey in reducing inflammation and exudation (see below) should lead to less frequent changes being required later. There should be no need to change dressing frequently to prevent bacterial growth under the dressing, as the antibacterial activity of honey will prevent this if there is not excessive dilution by exudate, especially if a honey with a high level of activity is selected.

Clinical observations

It has been reported from various clinical studies on the usage of honey as a dressing for infected wounds that the wounds become sterile in 3 - 6 days (21, 36), 7 days (7, 15, 22) or 7 - 10 days (30). Others have reported that honey is effective in cleaning up infected wounds (23, 45). It has also been reported that honey dressings halt advancing necrosis (22, 37).

Honey has also been found to act as a barrier preventing wounds from becoming infected (7, 16, 17, 26, 46), preventing cross-infection (25), and allowing burn wound tissue to heal rapidly uninhibited by secondary infection (7, 43).

It has been reported that sloughs, gangrenous tissue and necrotic tissue are rapidly replaced with granulation tissue and advancing epithelialisation when honey is used as a dressing (7), thus a minimum of surgical debridement is required (21). It has been observed that under honey dressings sloughs, necrotic and gangrenous tissue separated so that they could be lifted off painlessly (7), and others have noted quick and easy separation of sloughs (10, 23) and removal of crust from a wound (10). Rapid cleansing (9) and chemical or enzymic debridement resulting from the application of honey to wounds have also been reported (16, 17, 19, 22, 37), with no eschar forming on burns (20). Several other authors have noted the cleansing effect of honey on wounds (11, 23, 25, 31, 41, 47). It has also been noted that dirt is removed with the bandage when honey is used as a dressing, leaving a clean wound (40). Honey has also been reported to give deodorisation of offensively smelling wounds (7, 15-17, 22, 37, 46).

Honey used as a wound dressing has been reported to promote the formation of clean healthy granulation tissue (7, 10, 11, 20-22, 25, 30, 31, 36, 42, 47). It has also been reported to promote epithelialisation of the wound (7, 18, 20, 22, 37, 42). Dumronglert (31) commented that the rapid growth of new tissue is remarkable. Improvement of nutrition of wounds has been observed (7), also increased blood flow has been noted in wounds (31), and free flow of lymph (23).

Several authors have commented on the rapidity of healing seen with honey dressings. Descottes (39) refers to wounds becoming closed in a spectacular fashion in 90% of cases, sometimes in a few days. Burlando (48) refers to healing being surprisingly rapid, especially for first and second degree burns. Blomfield (41) is of the opinion that honey promotes healing of ulcers and burns better than any other local application used before. Bergman (26) has observed clinically that healing in open wounds is faster with honey, as has Hamdy (49) who also found that it accelerated making wounds suitable for suture.

It has been noted that dressing wounds with honey allows early grafting on a clean clear base (9), with prompt graft taking (11, 25). It has also been reported that it reduces the incidence of skin graft areas (46) and helps skin regenerate, making plastic reconstruction unnecessary (22, 37). Others also have noted that skin grafting is found to be unnecessary (20, 21). It has also been reported that dressing wounds with honey gives little or no scarring (22).

Another effect of honey on wounds that has been noted is that it reduces inflammation (20, 48) and hastens subsidence of passive hyperaemia (42). It also reduces oedema (7, 19, 22, 31, 42) and exudation (7, 22, 48), absorbing fluid from the wound (37). Honey is reported to be soothing when applied to wounds (17, 40, 50)] and to reduced pain from burns (17, 48), in some cases giving rapid diminution of local pain (42).

Honey is reported to cause no pain on dressing (23, 46) or to cause only momentary stinging (23), to be non-irritating (19, 21, 23, 47), to cause no allergic reaction (7, 15, 18, 25), and to have no harmful effects on tissues (7, 15, 19, 23, 25).

It has been noted that honey dressings are easy to apply and remove (11, 25, 41). There is no adhesion to cause damage to the granulating surface of wounds (20, 23, 46), no difficulty removing dressings (17), and no bleeding when removing dressings (17). Any residual honey is easily removed by simple bathing (45).

Comment: These clinical observations provide, in isolation, the lowest level of evidence upon which to base a clinical decision to use honey as a wound dressing. But when compared with the results usually experienced with the more commonly used dressings, they indicate that honey has some actions and attributes that have the potential to make it a very useful wound dressing material. Its physical properties provide a protective barrier and, by osmosis, create a moist healing environment in the form of a solution of honey that does not stick to the underlying wound tissues. The antibacterial properties of honey prevent bacterial colonisation of this moist environment, to the extent that unlike other moist wound dressings it is suitable for use on infected wounds. Its antibacterial components show no impairment of the healing process through adverse effects on wound tissues: to the contrary it appears to have a stimulatory effect on tissue regeneration. In addition there are clear indications of an anti-inflammatory action.

Evidence of effectiveness: animal studies

In one experimental study (28), comparisons were made between honey and silver sulfadiazine, and between honey and sugar, on standard deep dermal burns, 7x7 cm, made on Yorkshire pigs. Epithelialisation was achieved within 21 days with honey and sugar whereas it took 28 - 35 days with silver sulfadiazine. Granulation was clearly seen to be suppressed initially by treatment with silver sulfadiazine. In all honey-treated wounds the histological appearance of biopsy samples showed less inflammation than in those treated with sugar and silver sulfadiazine, and a weak or diminished actin staining in myofibroblasts suggesting a more advanced stage of healing.

In another study on experimental burns (48), superficial burns created with a red-hot pin (15 mm²) on the skin of rats were treated with honey or with a sugar solution with a composition similar to honey. Healing was seen histologically to be more active and advanced with honey than with no treatment or the sugar solution. The time taken for complete repair of the wound was significantly less ($p < 0.01$) with honey than with no treatment or with the sugar solution, and necrosis was never so serious. Treatment with honey gave a clearly seen attenuation of inflammation and exudation and a rapid regeneration of outer epithelial tissue and rapid cicatrisation.

In another experimental study on animals, full-thickness wounds were created by cutting away 2x4 cm pieces of skin on the backs of buffalo calves (51). The wounds were dressed with honey or nitrofurazone, or with sterilised petrolatum as a control. Granulation, scar formation, and complete healing occurred faster with honey than with nitrofurazone and in the control. Histomorphological examination of biopsy samples revealed more marked acute inflammatory changes in the wounds in the control and with nitrofurazone than with honey, and less proliferation of fibroblasts and angioblasts.

In another experimental study on buffalo calves (14) full-thickness skin wounds, 2x4 cm, were made after infecting the area of each wound by subcutaneous injection of *Staphylococcus aureus* two days prior to wounding. Topical application of honey, ampicillin ointment, and saline as a control were compared as treatment for the wounds. Clinical examination of the wounds and histomorphological examination of biopsy samples showed that honey gave the fastest rate of healing compared with the other treatments, the least inflammatory reaction, the most rapid fibroblastic and angioblastic activity in the wounds, the fastest laying down of fibrous connective tissue, and the fastest epithelialisation.

An experimental study carried out using mice (26) also compared honey with saline dressings, on wounds made by excising skin (10x10 mm) down to muscle. Histological examination showed that the thickness of granulation tissue and the distance of epithelialisation from the edge of the wound were significantly greater, and the area of the wound significantly smaller, in those treated with honey ($p < 0.001$). None showed gross clinical infection (honey or control).

In another study, on rats (52, 53), a 10 mm long incision was made in the skin of each rat and the wounds were treated topically or orally with floral honey, honey from bees fed on sugar, or saline. A statistically significant increase in the rate of healing was seen with the treatment with floral honey compared with the saline control, this being greater with oral than with topical administration. The treatment with honey from bees fed on sugar, whilst initially giving a greater rate of healing, after 9 days gave results no better than those obtained with the saline control. The granulation, epithelialisation and fibrous tissue seen histologically reflected the rate of healing measured as decrease in wound length. The infiltration of granulation tissue with chronic inflammatory cells was greatest in the wounds treated with honey from bees fed on sugar, less in those treated topically with floral honey, and least in those treated orally with floral honey.

Oral and topical application of honey were compared in another study on rats (54), in which full-thickness 2x2 cm skin wounds were made on the backs of the rats by cutting away the skin. The rats were treated with topical application of honey to the wound, oral administration of honey, or intraperitoneal administration of honey, or untreated as a control. After seven days of treatment, tritiated proline was injected subcutaneously to serve as an indicator of collagen synthesis in the subsequent 24 hour period. Both the quantity of collagen synthesised and the degree of cross-linking of the collagen in the granulation tissue were found to have increased significantly compared with the untreated control as a result of treatment with honey ($p < 0.001$). Systemic

treatment gave greater increases than topical treatment, the intraperitoneal route giving a better result than the oral route.

In a similarly conducted study following this (55), the rats were treated in the same way, but different parameters were studied to assess healing. The granulation tissue that had formed was excised from the wounds for biochemical and biophysical measurement of wound healing. The content of DNA, protein, collagen, hexosamine and uronic acid, and the tensile strength, stress-strain behaviour, rate of contraction, and the rate of epithelialisation were found to have increased significantly as a result of treatment with honey ($p < 0.05$ - < 0.001). Systemic treatment gave greater increases than topical treatment, the intraperitoneal route giving the best results.

Comment: These animal studies have all clearly demonstrated that honey has beneficial effects on wound healing besides any resulting from its antibacterial properties. Although one of the studies involved infected wounds, the results obtained in this were in line with those obtained in the other studies in which the beneficial effects resulting from the application of honey could not have been secondary to the clearance of infection. There is clear evidence of a stimulatory action on tissue growth, and of an anti-inflammatory action. The experiments showing that these effects were not achieved with sugar demonstrate that it is the chemical constitution rather than the physical properties of honey responsible. That the stimulatory effects were obtained when the honey was administered orally or parenterally suggests that there may be a tissue growth factor involved rather than the stimulation of growth being a consequence of wound acidification or improved nutrition of the tissues. There have been no investigations reported of the component of honey responsible for the stimulation of tissue growth, but one possibility is that it is the hydrogen peroxide produced by honey: the growth of fibroblasts in cell culture has been found to be stimulated by hydrogen peroxide at micro- to nanomolar concentrations (56). Also responsible may be phytochemicals from the nectar source, which would account for the better results seen with floral honey than with honey from bees fed on sugar, although the improved healing from this may have been secondary to the reduction in inflammation that the floral honey effected.

Evidence of effectiveness: clinical study

A study has been reported (7) of the treatment with honey dressings of 59 patients with recalcitrant wounds and ulcers, 47 of which had been treated for what clinicians deemed a "sufficiently long time" (1 month to 2 years) with conventional treatment (such as Eusol toilet and dressings of Acriflavine, Sofra-Tulle, or Cicatrin, or systemic and topical antibiotics) with no signs of healing, or the wounds were increasing in size. The wounds were of varied aetiology, such as Fournier's gangrene, burns, cancrum oris and diabetic ulcers, traumatic ulcers, decubitus ulcers, sickle cell ulcers and tropical ulcers. Microbiological examination of swabs from the wounds showed that the 51 wounds with bacteria present became sterile within 1 week and the others remained sterile. In one of the cases, a Buruli ulcer, treatment with honey was discontinued after 2 weeks because the ulcer was rapidly increasing in size. The outcomes of the 58 other cases were reported as "showed remarkable improvement following topical application of honey". Some general observations reported for the outcomes from honey treatment of these recalcitrant wounds were that sloughs, necrotic and gangrenous tissue separated so that they could be lifted off painlessly, within 2 - 4 days in Fournier's gangrene, cancrum oris and decubitus ulcers (but it took much longer in other types). Sloughs and necrotic tissue were rapidly replaced with granulation tissue and advancing epithelialisation. Surrounding oedema subsided, weeping ulcers dehydrated, and foul-smelling wounds were rendered odourless within 1 week. Burn wounds treated early healed quickly, not becoming colonised by bacteria.

A similar study, but with less detail given, was carried out on 40 patients, half of which had been treated with "the usual topical measures" (another antiseptic) which had failed (9). The wounds were of mixed aetiology: surgical, accidental, infective, trophic, and burns; the average size of the wounds was 57 cm². One third of the wounds were purulent, the rest were red with a whitish coat. The number of microorganism isolates from the wounds dropped from 48 to 14 after two weeks of treatment. Seven of the patients had necrotic tissue excised after treatment with honey, and three of these had skin grafts. It was noted that the honey delimited the boundaries of the wounds and cleansed the wounds rapidly to allow this. Of the 33 patients treated only with honey dressings, 29 were healed successfully, with good quality healing, in an average time of 5 - 6 weeks. Of the four cases where successful healing was not achieved, two were attributed to the poor general quality of the

patients who were suffering from immunodepression, one was withdrawn from treatment with honey because of a painful reaction to the honey, and one burn remained stationary after a good initial response.

In another study honey was used on (12) nine infants with large, open, infected surgical wounds that failed to heal with conventional treatment of at least 14 days of intravenous antibiotic and cleaning the wound with aqueous chlorhexidine solution (0.05% w/v) and fusidic acid ointment. These wounds were still open, oozing pus, and swab cultures were positive. Marked clinical improvement was seen in all infants after five days of treatment with topical application of 5 - 10 ml of honey twice daily. The wounds were closed, clean and sterile in all infants after 21 days of application of honey.

Comment: These three studies are effectively cross-over trials, in that a baseline of non-responsiveness had been established with other forms of treatment before honey was used. Although this form of evidence is less convincing than when there is a simultaneous treated control group of patients, the consistency of the outcome and the numbers of patients involved make it highly improbable that the change from non-healing to healing was just due to chance rather than to the therapeutic effect of the honey. The reports would have been of more value as evidence if more detail had been given, but even as they are they provide good evidence that honey is effective in promoting the healing of wounds that are not responding to conventional therapeutic procedures. They also provide good evidence of the effectiveness of the antibacterial activity of honey on infected wounds.

Evidence of effectiveness: clinical trials

Twenty consecutive cases of Fournier's gangrene managed conservatively with systemic antibiotics (oral amoxicillin/clavulanic acid and metronidazole) in addition to daily topical application of honey were compared retrospectively with 21 similar cases of Fournier's gangrene managed by the orthodox method (wound debridement, wound excision, secondary suturing, and in some cases scrotal plastic reconstruction in addition to receiving a mixture of systemic antibiotics dictated by sensitivity results from cultures) (22). (The microorganisms cultured in both treatment groups were similar.) Even though the average duration of hospitalisation was slightly longer, topical application of honey showed distinct advantages over the orthodox method. Three deaths occurred in the group treated by the orthodox method, whereas no deaths occurred in the group treated with honey. The need for anaesthesia and expensive surgical operation was obviated with the use of honey. Response to treatment and alleviation of morbidity were faster in the group treated with honey. Although some of the bacteria isolated from honey-treated patients were not sensitive to the antibiotics used, the wounds became sterile within 1 week.

The usefulness of honey dressings as an alternative method of managing abdominal wound disruption was assessed in a prospective trial over 2 years compared retrospectively with patients of a similar age over the preceding 2 years (15). Fifteen patients whose wound disrupted after Caesarean section were treated with honey application and wound approximation by micropore tape instead of the conventional method of wound dressing with subsequent resuturing. (The comparative group, 19 patients, had had their dehisced wounds cleaned with hydrogen peroxide and Dakin solution and packed with saline-soaked gauze prior to resuturing under general anaesthesia.) It was noted that with honey dressings slough and necrotic were replaced by granulation and advancing epithelialisation within 2 days, and foul-smelling wounds were made odourless within 1 week. Excellent results were achieved in all the cases treated with honey, thus avoiding the need to resuture which would have required general anaesthesia. Eleven of the cases were completely healed within 7 days, all 15 within 2 weeks. The period of hospitalisation required was 2 - 7 days (mean 4.5), compared with 9 - 18 days (mean 11.5) for the comparative group. Two of the comparative group had their wounds become reinfected, and one developed hepatocellular jaundice from the anaesthetic.

A retrospective study of 156 burn patients treated in a hospital over a period of 5 years (1988-92) found that the 13 cases treated with honey had a similar outcome to those treated with silver sulfadiazine (13).

A prospective randomised controlled trial was carried out to compare honey-impregnated gauze with OpSite® as a cover for fresh partial thickness burns in two groups of 46 patients (17). Wounds dressed with honey-impregnated gauze showed significantly faster healing compared with those dressed with OpSite® (means 10.8 versus 15.3 days: $p < 0.001$). Less than half as many of the cases became infected in the wounds dressed with honey-impregnated gauze compared with those dressed with OpSite® ($p < 0.001$).

Another prospective randomised clinical study was carried out to compare honey-impregnated gauze with amniotic membrane dressing for partial thickness burns (18). Forty patients were treated with honey-impregnated gauze and 24 were treated with amniotic membrane. The burns treated with honey healed earlier compared with those treated with amniotic membrane (mean 9.4 versus 17.5 days: $p < 0.001$). Residual scars were noted in 8% of patients treated with honey-impregnated gauze and in 16.6% of cases treated with amniotic membrane ($p < 0.001$).

Honey was compared with silver sulfadiazine-impregnated gauze for efficacy as a dressing for superficial burn injury in a prospective randomised controlled trial that was carried out with a total of 104 patients (16). In the 52 patients treated with honey, 91% of the wounds were rendered sterile within 7 days. In the 52 patients treated with silver sulfadiazine, 7% showed control of infection within 7 days. Healthy granulation tissue was observed earlier in patients treated with honey (means 7.4 versus 13.4 days). The time taken for healing was significantly shorter with the honey-treated group ($p < 0.001$): of the wounds treated with honey 87% healed within 15 days compared with 10% of those treated with silver sulfadiazine. Better relief of pain, less exudation, less irritation of the wound, and a lower incidence of hypertrophic scar and post-burn contracture were noted with the honey treatment. The honey treatment also gave acceleration of epithelialisation at 6 - 9 days, a chemical debridement effect and removal of offensive smell.

In another prospective randomised controlled trial comparing honey with silver sulfadiazine-impregnated gauze on comparable fresh partial thickness burns (20), histological examination of biopsy samples from the wound margin as well as clinical observations of wound healing were made to assess relative effects on wound healing in two groups of 25 patients. The time taken for healing was significantly shorter with the honey-treated group ($p < 0.001$). Of the wounds treated with honey, 84% showed satisfactory epithelialisation by the 7th day, 100% by the 21st day. In wounds treated with silver sulfadiazine, epithelialisation occurred by the 7th day in 72% of the patients and in 84% of patients by 21 days. Histological evidence of reparative activity was seen in 80% of wounds treated with the honey dressing by the 7th day, with minimal inflammation. Of the wounds treated with silver sulfadiazine 52% showed reparative activity, with inflammatory changes, by the 7th day. Reparative activity reached 100% by 21 days with the honey dressing and 84% with silver sulfadiazine. In honey-dressed wounds early subsidence of acute inflammatory changes, better control of infection and quicker wound healing were observed, while in the wounds treated with silver sulfadiazine sustained inflammatory reaction was noted even on epithelialisation. No skin grafting was required for the wounds treated with honey, but four of the wounds treated with silver sulfadiazine converted to deep and required skin grafts.

Honey was also compared with boiled potato peel as a cover for fresh partial-thickness burns in another prospective randomised controlled trial (19). Of the 40 patients treated with honey who had had positive swab cultures at the time of admission, 90% had their wounds rendered sterile within 7 days. All of the 42 patients treated with boiled potato peel dressings who had had positive swab cultures at the time of admission had persistent infection after 7 days. Of the wounds treated with honey, 100% healed within 15 days compared with 50% of the wounds treated with boiled potato peel dressings. The mean times to heal, 10.4 days with honey versus 16.2 days with boiled potato peel, were significantly different ($p < 0.001$).

Comment: The report on the trial on patients with Fournier's gangrene has been criticised for failing to adequately describe the two patient groups, so that it cannot be known for certain that they were comparable (57). It was also pointed out that statistically there would have been no reliable difference in the mortality rates between the two groups (57). Nevertheless, the trial showed that simply dressing with honey was a very effective treatment for a fulminant, rapidly spreading infection that is usually treated aggressively (37). Although conventional opinion is that necrotic tissue should be removed because it is a source of noxious substance which diffuse into the wound (57), this trial and the trial conducted on infected disrupted abdominal wounds have demonstrated that this is unnecessary when honey is applied to the wound, the slough and necrotic tissue being rapidly removed by the chemical or enzymic debriding action of honey.

The trial conducted on infected disrupted abdominal wounds, with a closely matched control group, showed clearly that dressing with honey was more effective than the conventional treatment of the control group in achieving healing of the wounds, as well as obviating the need for suturing. However, the conventional treatment, using antiseptics which can damage tissues and inhibit wound healing (58), although commonly used, is possibly not the best bench-mark against which to judge the effectiveness of honey. The studies of burn patients treated with honey compared with those treated with silver sulfadiazine, however, showed that

honey is as effective as, or more effective than, the topical burn treatment that is the most widely used in modern times (59). Although the retrospective study did not give details of the cases to allow it to be seen if the cases treated with honey were similar to the ones treated with silver sulfadiazine, the prospective randomised controlled trials were well designed and adequately described, the statistically significant results from large numbers of patients providing convincing evidence that dressing with honey is the best treatment for superficial burns.

Risks and adverse effects

No adverse effects have been noted in any of the studies in which honey has been applied topically to experimental wounds on animals (14, 26, 28, 52, 54, 55). These studies have included histological examination of treated tissues (14, 26, 28, 53). Honey has been used topically on wounds over thousands of years also without gaining any reputation for adverse effects. The many reports published in more recent times on its clinical usage on open wounds mention no more than a transient stinging sensation in some patients (9, 23), other than in 2 cases where the pain persisted for 15 minutes (8) and in 2 cases where the pain was such that the application of honey could not be tolerated (8, 9). There was reported a transient stinging sensation and redness of the eye soon after putting honey in the eye, but never enough to stop the treatment in the 102 cases in a trial of honey for ophthalmological use (60). Generally the topical application of honey on open wounds is reported to be soothing (17), to relieve pain (17), be non-irritating (19, 21, 23), cause no pain on dressing (46), and give no secondary reactions (9).

Allergy to honey is rare (61), but there could be an allergic reaction to either the pollen or the bee proteins in honey (62, 63). In reports of clinical studies where honey was applied to open wounds of a total of 134 patients it was stated that there were no allergic or adverse reactions (7, 12, 15, 18, 25). However, an occurrence of a minor haemorrhage soon after application of honey has been mentioned in reference to an unrecorded case (10). Reference has been made to dehydration of tissues if too much honey is applied to a wound, but it has been stated that the hydration of the tissues is easily restored by saline packs (21, 24). Because honey contains up to 40% glucose there is a theoretical risk of it adversely elevating the blood glucose level of diabetics when applied topically on a large open wound.

Honey sometimes contains spores of clostridia, which poses a small risk of wound botulism. However, in none of the many reports published on the clinical usage of honey on open wounds was the honey that was used sterilised, yet there are no reports of any type of infection resulting from the application of honey to wounds. If spores germinated, any vegetative cells of clostridia, being obligate anaerobes, would be unlikely to survive in the presence of the hydrogen peroxide that is generated in diluted honey. But the use of honey as a wound dressing has been argued against, however, on the grounds that the risk of it possibly causing wound botulism is unacceptable (64). This objection can be overcome by the use of honey that has been treated by gamma-irradiation, which kills clostridial spores in honey (65, 66) without loss of any of the antibacterial activity (65).

The problem of attraction of flies and ants to honey dressings (67, 68), not commonly noted, can be overcome by using effective secondary dressings so that the honey is prevented from leaking out or being exposed to insects.

Advantages of using honey as a wound dressing

Honey provides a moist healing environment yet prevents bacterial growth even when wounds are heavily infected. It is a very effective means of quickly rendering heavily infected wounds sterile, without the side-effects of antibiotics, and it is effective against antibiotic-resistant strains of bacteria (35). Its antibacterial properties and its viscosity also provide a barrier to cross-infection of wounds. It also provides a supply of glucose for leucocytes, essential for the 'respiratory burst' that produces hydrogen peroxide, the dominant component of the antibacterial activity of macrophages (69). Furthermore it provides substrates for glycolysis, which is the major mechanism for energy production in the macrophages, and thus allows them to function in damaged tissues and exudates where the oxygen supply is often poor (69). The acidity of honey (typically below pH 4 (70)) may also assist in the antibacterial action of macrophages, as an acid pH inside the vacuole is involved in killing ingested bacteria (69). Whether it is through this action, or through preventing the toxic unionised form of ammonia from existing that is involved (71), topical acidification of wounds promotes healing (72). The high glucose levels that the honey provides would be used by the infecting bacteria in

preference to amino acids (73) from the serum and dead cells, and thus would give rise to lactic acid instead of ammonia and the amines and sulphur compounds that are the cause of malodour in wounds.

Honey gives a fast rate of tissue regeneration and suppression of inflammation, oedema, exudation and malodour in wounds, as evidenced in clinical observations and the results of animal studies and clinical trials. The antibacterial properties clearing infection could alone account for these effects by preventing the production of the products of bacterial metabolism which are responsible for the contrary conditions. But honey has a direct trophic and anti-inflammatory effect on wound tissues, as evidenced by the results of animal studies in which there was no bacterial infection involved, particularly in those where the honey was administered systemically.

Honey can be expected to have a direct nutrient effect on regenerating tissue because it contains a wide range of amino acids, vitamins and trace elements in addition to large quantities of readily assimilable sugars (70). (The vitamin C content of honey, which is typically more than three times higher than that in serum, and may be many times higher, could be of particular importance as because of the essential role of this vitamin in collagen synthesis.) In addition, the high osmolarity of honey causes an outflow of lymph which serves to provide nutrition for regenerating tissue which otherwise can only grow around points of angiogenesis (seen as granulation): healing is delayed if the circulation to an area is poor, or if a patient is poorly nourished. Also it has been suggested that the decreased turgor resulting from the application of honey may increase oxygenation of tissues (7).

This osmotically induced outflow will also assist in lifting dirt and debris from the bed of a wound. It also ensures that the dressing will not stick to the wound, as what ends up as the material in contact with the wound tissue is a fluid solution of honey, which can be easily lifted off and any residue rinsed away. Thus there is no pain on changing dressings, and no tearing away of newly formed tissue. The cleansing effect of the osmotic flow and the chemical or enzymic debriding effect of honey makes surgical debridement unnecessary, thus saving the patient pain or the risks associated with anaesthesia. It has also been noted that by reducing in surface area oedematous and soggy wounds, or making them more clearly defined, it enables a definite decision on limb amputations to be made, which would be of particular advantage in the case of diabetic and malignant ulcers (7).

There is also an economical advantage to using honey as a wound dressing. This is seen both in the direct cost savings when compared with conventional treatments, and in the savings in ongoing costs when consideration is given to the more rapid healing rates that are achieved. Cost comparisons that have been made are: 480 F for treatment with Debrisan compared with 7.5 F for treatment with honey (39); \$70 for treatment with antibiotics compared with \$2 for treatment with honey (25); \$40 for treatment with Duoderm compared with \$8 for treatment with honey (8). Other observations on cost savings have been: use of antibiotics ceased (30), length of hospitalisation reduced (25, 30, 39) (by at least half (15, 21)). In addition there are the savings in the costs of surgery where debridement and skin grafting become unnecessary when honey is used.

Honey is also an ideal first-aid dressing material, especially for patients in remote locations when there could be time for infection to have set in before medical treatment is obtained: it is readily available and simple to use. It would be particularly suitable for first-aid treatment for burns, where emergency dousing or cooling frequently involves the use of contaminated water which then leads to heavy infection of the traumatised tissue. As well as providing an immediate anti-inflammatory treatment the honey would provide an antibacterial action and a barrier to further infection of the wound.

Acknowledgments

The help of the interloan librarians at the University of Waikato in obtaining copies of reports, and of Anna Blättler, Niaz Al Somai and Paola Galimberti in translating papers is gratefully acknowledged.

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