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Honey has proved to be such a useful medicine in my practice that I wanted to provide you with a copy of these very comprehensive articles by Dr. Molan. Honey was also widely used in traditional medical systems as a food, wound dressing, and preservative for herbal medicines.

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Honey as a Dressing for Wounds, Burns, and Ulcers: A Brief Review of Clinical Reports and Experimental Studies

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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 polyurethane film dressings (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 (7-10).

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, 11-29). 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 (30, 31). 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) (32), and a collection of strains of strains of MRSA at concentrations of 1% - 4% (v/v) (33).

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 (23, 28, 29, 34), and necrotic tissue being removed (23, 29, 35, 36), 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 (37); dilute Dakin solution or dilute hydrogen peroxide on the wound bed and alcohol on the surrounding skin (29); or the wounds were cleaned with eusol (28) or aqueous 1% chlorhexidine (10). Some reported cleaning the wounds before dressing, but did not specify with what (10, 23, 28, 35). One cleaned the wounds with gauze (23). Most report simply washing

wounds with saline before dressing with honey (5, 7, 9, 14-18, 38), and when dressings are changed (5, 7, 9, 13-18, 29).

In many of the reports the honey is spread on the wound then covered with a dry dressing, mostly gauze (5, 8-10, 13, 14, 17-21, 29, 37-40). 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) (13, 34); most just refer to the honey being spread or poured over the wound (9, 14, 17-19, 21, 37); others report using a thick layer of honey (41), soaking the wound generously with honey (23), pouring honey into the wound to three-quarters fill (29), and applying 15-30 ml of honey to ulcers (7, 20). Others have applied the honey to the dressing then placed it on the wound: either the honey was spread on gauze (10, 23, 35, 37) or the gauze was soaked in honey (15, 16, 21), or "honey pads" were used (36). (It has also been reported that covering cracked sore nipples in nursing mothers with gauze soaked in honey can prevent them from becoming infected (42))

Honey-impregnated gauze has also been used to pack cavities of wounds (20). Others have packed cavities of wound directly with honey and then covered the wound (10, 21, 23). 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 (42).

Mostly the dressings are changed daily (7-10, 14, 21, 23, 35, 39, 41) or every 2 days (15-18, 38): or every 2 - 3 days (40). 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 (41). Another reported dressings being changed once or twice daily until clean granulated wounds were achieved, then once-daily changes (37). Others have reported changing honey dressings twice daily (13, 19, 22), 2 - 3 times a day (34), 3 times daily (28, 36), and 3 times daily if contaminated with urine or faeces, otherwise twice daily (29).

Two papers report mixing lipid material with the honey to make it easier to spread; either castor oil (23) or 20% vaseline or lard (41). 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 (21) 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 (43).

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 (19, 34), 7 days (7, 13, 20) or 7 - 10 days (28). Others have reported that honey is effective in cleaning up infected wounds (21, 44). It has also been reported that honey dressings halt advancing necrosis (20, 36). Honey has also been found to act as a barrier preventing wounds from becoming

infected (7, 14, 15, 24, 45), preventing cross-infection (23), and allowing burn wound tissue to heal rapidly uninhibited by secondary infection (7, 42).

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 (19). 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, 21) 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 (14, 15, 17, 20, 36), with no eschar forming on burns (18). Several other authors have noted the cleansing effect of honey on wounds (21, 23, 29, 35, 40, 46). It has also been noted that dirt is removed with the bandage when honey is used as a dressing, leaving a clean wound (39). Honey has also been reported to give deodorisation of offensively smelling wounds (7, 13-15, 20, 36, 45).

Honey used as a wound dressing has been reported to promote the formation of clean healthy granulation tissue (7, 10, 18-20, 23, 28, 29, 34, 35, 41, 46), allowing early grafting on a clean clear base (9). It has also been reported to promote epithelialisation of the wound (7, 16, 18, 20, 36, 41). Dumronglert (29) 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 (29), and free flow of lymph (21).

Several authors have commented on the rapidity of healing seen with honey dressings. Descottes (38) refers to wounds becoming closed in a spectacular fashion in 90% of cases, sometimes in a few days. Burlando (47) refers to healing being surprisingly rapid, especially for first and second degree burns. Blomfield (40) is of the opinion that honey promotes healing of ulcers and burns better than any other local application used before. Bergman (24) has observed clinically that healing in open wounds is faster with honey, as has Hamdy (48) who also found that it accelerated making wounds suitable for suture.

It has been noted that dressing wound with honey allows early grafting on a clean clear base (9), with prompt graft taking (23, 35). It has also been reported that it reduces the incidence of skin graft areas (45) and helps skin regenerate, making plastic reconstruction unnecessary (20, 36). Others also have noted that skin grafting is found to be unnecessary (18, 19). It has also been reported that dressing wounds with honey gives little or no scarring (20).

Another effect of honey on wounds that has been noted is that it reduces inflammation (18, 47) and hastens subsidence of passive hyperaemia (41). It also reduces oedema (7, 17, 20, 29, 41) and exudation (7, 20, 47), absorbing fluid from the wound (36). Honey is reported to be soothing when applied to wounds (15, 39, 49) and to reduced pain from burns (15, 47), in some cases giving rapid diminution of local pain (41).

Honey is reported to cause no pain on dressing (21, 45) or to cause only momentary stinging (21), to be non-irritating (17, 19, 21, 46), to cause no allergic reaction (7, 13, 16, 23), and to have no harmful effects on tissues (7, 13, 17, 21, 23).

It has been noted that honey dressings are easy to apply and remove (23, 35, 40). There is no adhesion to cause damage to the granulating surface of wounds (18, 21, 45), no difficulty removing dressings (15), and no bleeding when removing dressings (15). Any residual honey is easily removed by simple bathing (44).

Evidence of Effectiveness: Animal Studies

In one experimental study (26), 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 (47), 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 (50). 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 (12) 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 (24) 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 (51, 52), 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 (53), 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 (54), 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.

Evidence of Effectiveness: Clinical Study

What was effectively a form of cross-over trial was conducted in a study (7) 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 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.

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) (20). (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 (13). 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 (11).

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. 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 (16). 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 (14). 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 (18), 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 (17). 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 ($p < 0.001$).

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 (12, 24, 26, 51, 53, 54).

These studies have included histological examination of treated tissues (12, 24, 26, 52). 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, 21), 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 (55). Generally the topical application of honey on open wounds is reported to be soothing (15), to relieve pain (15), be non-irritating (17, 19, 21), cause no pain on dressing (45), and give no secondary reactions (9).

Allergy to honey is rare (56), but there could be an allergic reaction to either the pollen or the bee proteins in honey (57, 58). In reports of clinical studies where honey was applied to open wounds of a total of 125 patients it was stated that there were no allergic or adverse reactions (7, 13, 16, 23). 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 (19, 22). 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 (59). This objection can be overcome by the use of honey that has been treated by gamma-irradiation, which kills clostridial spores in honey (60, 61) without loss of any of the antibacterial activity (60).

The problem of attraction of flies and ants to honey dressings (62, 63), 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 (33). 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 (64).

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 (64). The acidity of honey (typically below pH 4 (65)) may also assist in the antibacterial action of macrophages, as an acid pH inside the vacuole is involved in killing ingested bacteria (64).

Whether it is through this action, or through preventing the toxic unionised form of ammonia from existing that is involved (66), topical acidification of wounds promotes healing (67). The high glucose levels that the honey provides would be used by the infecting bacteria in preference to amino acids (68) 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 (65). (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 (38); \$70 for treatment with antibiotics compared with \$2 for treatment with honey (23); \$40 for treatment with Duoderm compared with \$8 for treatment with honey (8).

Other observations on cost savings have been: use of antibiotics ceased (28), length of hospitalisation reduced (23, 28, 38) (by at least half (13, 19)). 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.

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Selection and Use of Honey on Wounds

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Honey is one of the oldest known medicines that has continued to be used up to present times in folk-medicine. Its use has been "rediscovered" in later times by the medical profession, especially for dressing wounds. The numerous reports of the effectiveness of honey in wound management, including reports of several randomised controlled trials, have recently been reviewed, rapid clearance of infection from the treated wounds being a commonly recorded observation.

In almost all of these reports honey is referred to generically, there being no indication given of any awareness of the variability that generally is found in natural products. Yet the ancient physicians were aware of differences in the therapeutic value of the honeys available to them: Aristotle (384-322 BC), discussing differences in honeys, referred to pale honey being "good as a salve for sore eyes and wounds"; and Dioscorides (c.50 AD) stated that a pale yellow honey from Attica was the best, being "good for all rotten and hollow ulcers".

Any honey can be expected to suppress infection in wounds because of its high sugar content, but dressings of sugar on a wound have to be changed more frequently than honey dressings do to maintain an osmolarity that is inhibitory to bacteria, as honey has additional antibacterial components. Since microbiological studies have shown more than one hundred-fold differences in the potency of the antibacterial activity of various honey, best results would be expected if a honey with a high level of antibacterial activity were used in the management of infected wounds.

Other therapeutic properties of honey besides its antibacterial activity are also likely to vary. An anti-inflammatory action and a stimulatory effect on angiogenesis and on the growth of granulation tissue and epithelial cells have been observed clinically and in histological studies. The components responsible for these effects have not been identified, but the anti-inflammatory action may be due to antioxidants, the level of which varies in honey. The stimulation of tissue growth may be a trophic effect, as nutrition of wounds is known to hasten the healing process: the level of the wide range of micronutrients that occur in honey also varies.

Until research is carried out to ascertain the components of honey responsible for all of its therapeutic effects it will not be possible to fully standardise honey to obtain optimal effectiveness in wound management. However, where an antiseptic wound dressing is required then standardisation for this effect is possible. Several brands of honey with standardised levels of antibacterial activity are commercially available in Australia and New Zealand, but even where these are not available it is possible to assay the level of antibacterial activity of locally available honey by a simple procedure in a microbiology laboratory.

The antibacterial activity of honey is due primarily to hydrogen peroxide generated by the action of an enzyme that the bees add to the nectar, but there are some floral sources that provide additional antibacterial components. The body tissues and serum contain an enzyme, catalase, that breaks down hydrogen peroxide - how much of the honey antibacterial activity is lost through this is not known. The antibacterial components that come from the nectar are not broken down by this enzyme. Until comparative clinical trials are carried out to determine which type of antibacterial activity is the more effective, it may be best to use manuka honey, as this contains hydrogen peroxide activity as well as the component that comes from the nectar.

Because the enzyme in honey that produces hydrogen peroxide is destroyed by heating and exposure to light, unpasteurised honey should be used, and it should be stored in a cool place and protected from light. If it is necessary to warm honey to liquefy it, it should be heated to no more than 37°C. If it is considered necessary to sterilise honey, this can be done by gamma-irradiation without loss of antibacterial activity. Gamma-irradiated manuka honey is available commercially. (In none of the clinical reports of use of honey on wounds was the honey used sterilised. No case of infection resulting from the use of honey has been reported.)

Manuka honey can have a uniquely high level of an antibacterial component from nectar that is not broken down by catalase. This antibacterial component is particularly effective against *Staphylococcus aureus*. Like all honeys, manuka honeys vary very much in their potency. A 'UMF' rating ('Unique Manuka Factor', equivalent to the % phenol with the same activity against *Staphylococcus aureus*) is being used by producers of manuka honey to show the potency of this antibacterial component, as more than half of the manuka honey on sale does not have any significant amount of this component present.

Some practical considerations are:

Ensure that there is an even coverage of the wound surface with honey. Honey can be made fluid by stirring or warming. Cavities may be filled by pouring in fluidised honey, or more conveniently by using honey packed in squeeze-tubes. (Gamma-irradiated manuka honey in tubes is available commercially.)

Spread honey on the dressing pad rather than on the ulcer - it is much easier to do and causes less discomfort for the patient.

The amount of honey needed depends on the amount of fluid exuding from the wound - the benefits of honey on wound tissues will be reduced if honey becomes diluted a lot: typically, 20 ml of honey is used on a 10 cm X 10 cm dressing.

Cover with absorbent secondary dressings to prevent honey oozing out from the dressing. Change the dressings more frequently if the honey is being diluted a lot - otherwise change every day or two.

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Honey Bee Lore

Honey bees have been closely associated with human beings for a long time. More than 9000 years ago, in a rock shelter in the mountains of eastern Spain, an early artist recorded the exploits of a brave individual surrounded by bees reaching inside a cavity to steal honey. Robbing honey from the nests of wild bees is still practiced by some Asian cultures. The oldest alcoholic beverage, mead, a drink made from fermented honey and water has been found in an Iron Age tomb in Scotland.

Honey bees appear in the temple and tomb art of Egypt as far back as 2400 B.C. The honey bee was the symbol of Lower Egypt. In the solar cult of Ra, the tears of Ra were honey bees.

Bee-keeping shows up in Greek mythology. Aristaeus, a keeper of bees who lost his hives to disease, compelled Proteus, a shape-changer who was also the wise god of the sea, to tell him how to avoid such a loss in the future. More diseases have been described for honey bees than any other insects. The earliest written descriptions were made by Aristotle around 325 B.C.

The honey bee, a sacred symbol of Artemis, was an important design on Ephesian coins for almost 6 centuries. (Ephesus was the center of worship of Artemis.)

After his death in 323 B.C., Alexander the Great was embalmed in a coffin filled with honey.

Over the centuries, bees have been used many times as weapons of war. In the thirteen century, residents of the Aegean island of Astipalaia hurled beehives onto pirates storming the castle gates. During W.W. I, Belgians trapped in an apiary used bees against the Germans.

Honey, too, has been used as a weapon. Certain members of the heath family produce grayanotoxins, chemicals that act as breathing inhibitors and hypnotics. Honey from these plants is referred to as toxic or "mad" honey. Three squadrons of Pompey's Roman troops were slain while under the influence of toxic honey provided by local tribesmen. In small amounts, toxic honey has been used in alcohol, as an additive to increase its punch, and in medicine.

Honey bees are not native to the Americas, Australia or New Zealand. Settlers had established colonies in Virginia by 1622, but California had to wait until the 1850s. Because of their close connection with the advancing colonists, Native Americans referred to honey bees as the "white man's flies".

Today, honey bees perform a vital role in agribusiness, pollinating many of our food crops. The honey and wax produced are significant. According to May Berenbaum in her book "Bugs in the System", it takes 130,000 loads of nectar or about 10 million flower visits to produce one kilogram of honey (about 2.2 pounds).

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