

# USING HONEY IN POST-EXCISION MALIGNANT MELANOMA ULCERS

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**M**alignant melanomas are extremely difficult to treat conservatively at primary care level since the precise diagnosis requires a skin biopsy, which then undergoes dermatoscopy or epiluminescence microscopy. The treatment also varies according to the stage of melanoma and whether it is a superficial spreading melanoma or a melanoma *in situ* (Lorentzen et al, 1999). For example, patients with stage 1, 2 and 3 melanomas require excision following biopsy, whereas those with incurable stage 4 melanoma need palliative excision and therapeutic lymph node dissection in order to improve their quality of life (Garcia et al, 1999). These approaches are beyond the scope of most general practice.

Furthermore, most general practices worldwide do not have access to dermatoscopy or staff who are trained in skin biopsy procedures and examination is not a mandatory element of most vocational training. Similarly, it has been shown that 'non experts' demonstrate a decline in sensitivity using dermatoscopy, whereas dermatologists gain from using it (Binder, 1999).

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This article focuses on a new approach using honey-based therapy to manage post-excision malignant melanoma ulcers.

## Background

Although Hippocrates was the first person to describe the condition, it was not until 1806 that Laennec coined the term 'melanoma' to differentiate the disease as a kind of cancer (Baxter, 1939).

Worldwide, there has been a rapid increase in the incidence of malignant melanoma and in the US it is the fifth most common cancer among males (Markovic, 2007). Currently, one in six North Americans will develop melanoma during their lifetime (Jemal et al, 2006).

However, malignant melanoma is quite rare among people of Asian, African and Hispanic background (Euvrard et al, 1997). It is also rare among people of Arab background (Akhtar and Reyes, 1997), and overall incidence of the disease in Caucasians is three to four times greater than in people with darker skin (Anderson, 1941; Morris and Horn, 1951).

Malignant melanoma is the fifth most commonly diagnosed neoplasm in the US and 75% of all skin cancer deaths in the country are associated with it. In the elderly, melanoma is not common in males and is usually discovered later in its development.

Although sun exposure is the main risk (Smith et al, 1993a; Euvrard et al, 2004), the intensity of solar exposure cannot be considered as the sole reason for geographic differences in melanoma incidence. In Europe, for

example, the incidence of melanoma is lower in the southern region, which has a higher solar intensity than the north (Smith et al, 1993b).

The worldwide increase in the incidence of malignant melanoma has been attributed to many factors, including:

- ▶ Prolonged intense exposure to sunlight
- ▶ Occupational exposure, such as polychlorinated biphenyls, petrochemicals, vinyl chloride, ionising radiation (Markovic, 2007)
- ▶ Contraceptive pills (Snell and Bischitz, 1960)
- ▶ Obesity (Naldi et al, 2005)
- ▶ Family history (Cho et al, 2005a, Cho et al, 2005b)
- ▶ Immunosuppression, including HIV, hematological neoplasms and people receiving immunosuppressant agents after solid organ transplantation (Hollenbeak et al, 2005; Smith et al, 1993a; Smith et al, 1993b; Euvrard et al, 1997; Euvrard et al, 2003, Euvrard et al, 2004).

Melanomas are classified conventionally as:

- ▶ Superficial spreading
- ▶ Lentigo maligna
- ▶ Nodular
- ▶ Acral lentiginous (Jemal et al, 2006).

Among people with light skin tone, acral lentiginous melanoma, which is featured in the case discussed here, accounts for 5% of malignant melanomas. However, it is the most common type of melanoma among patients of Asian descent (MacKie, 1985; Kato et al, 1996; Chen et al, 1999; Barnhill et al, 2004; Luk, 2004). Acral lentiginous melanomas often involve the sole of



**Figure 1.** A deep excision to remove a melanoma created an ulcer of approximately 5cm x 5cm in the plantar aspect of the left foot.

the foot and part of the heel (Ferlay et al, 2002; Green and Trichopoulos, 2002; Barnhill et al, 2004; Zhihong et al, 2011).

**Honey**

Honey has a long tradition of use in wound healing, whether for burns, ulcers, acute or chronic wounds. There are many accounts of the use of honey for treating wounds in ancient scripts from Egypt (such as the Edwin Smith Papyrus of 1700BC), Greece and the Ayurvedic traditions of India. The Koran also praises the virtues of honey (Baxter, 1939; Anderson, 1941, Morris and Horn, 1951).

**Case report**

A 75-year-old Arab man with diabetes was referred to the dermatology clinic at the main general hospital in Doha, Qatar, in June 2011. An examination revealed a brown/black flat lesion of the left plantar surface of the foot, measuring 1cm x 2cm. There was no lymphadenopathy and the patient's physical examination was normal.

According to the patient, this lesion had been present for the past 10 years. He denied that there had been recent or old trauma to the site and sought medical advice only when the lesion became painful and enlarged.

Laboratory investigations revealed the following:

- ▶▶ Good blood glucose control (HbA1c < 6.5%)
- ▶▶ Normal lipid profile
- ▶▶ Blood pressure of 130/80mmHg
- ▶▶ Normal liver function test
- ▶▶ Chest X-ray, bone scan and liver computed tomography (CT) scans were all normal.

The dermatologists carried out a complete excision with a 3mm margin and sent it to the laboratory. Histological findings revealed a malignant melanoma of Clark level II. The lesion was 0.5mm thick where neoplastic cells had broken through the basement membrane and extended into the papillary dermis, with a small nest of cells extending to the reticular dermis. According to Clark et al (1969), invading neoplastic cells from the epidermis have their first contact with mesenchymal tissue in the papillary dermis, whereas the presence of melanoma cells in the papillary body is the first evidence of invasion.

The patient then underwent surgery where a deep excision was performed, creating an ulcer of approximately 5cm x 5cm in the plantar aspect, followed by a split-thickness skin graft carried out by the plastic surgery team.

Unfortunately the skin graft did not take as the patient was ambulatory and not off-loading. The patient was offered a second skin graft, which he flatly refused. However, he did continue to present at the health centre for further management.

The consultant family physician, with a special interest in the diabetic foot, was consulted by the attending nurse to examine the patient. On examination, the ulcer revealed a deep lesion which was almost 5cm in length, width and depth (Figure 1).

The patient was educated about the importance of off-loading using a pair of crutches and a simple cotton felt pad to protect the ulcer. He was also introduced to the idea of using commercial honey combined with an alginate Silvercel® dressing (Systagenix).

The patient agreed to the authors' management strategy and daily dressings



**Figure 2.** After two weeks there was a reduction in the size of the wound and granulation tissue had begun to appear.



**Figure 3.** By week six the wound showed rapid healing due to being treated with honey, and had begun to fill from the inside out.



**Figure 4.** By week 10 the ulcer had reduced by 60% in size.

were applied using honey placed inside the cavity, after minimal sharp debridement, which was then covered with alginate packing. Strict off-loading was advised.

After two weeks, there was dramatic improvement in the size of the wound (Figure 2) and granulation tissue started to appear. Betadine solution was applied to the ulcer margins in an attempt to dry up the macerative effect of the honey as it leaked outside the ulcer site.

Off-loading was carried out using a simple incontinence pad, which was bundled in layers and applied around the ulcer in order to redistribute the pressure and mitigate against the weight of the patient's body. At week six the ulcer began to fill from the inside out, indicating a rapid healing process facilitated by honey (Figure 3).

Ongoing daily changes were performed using honey and an alginate dressing and a deep swab was taken. No pathogens were revealed after the swab was sent to the laboratory for culture and sensitivity. A plain film X-ray followed by magnetic resonance imaging (MRI) failed to reveal any signs of osteomyelitis.

By week 10 the ulcer had reduced by 60% in size (Figure 4) and this improvement continued until week 12 where there was an 80% reduction in the size of the ulcer (Figure 5).

However, there were a few islands of granuloma developing in the ulcer bed, which were cauterised using a battery-



**Figure 5.** By week 12 there was an 80% reduction in the size of the ulcer.

operated cautery pen (Bovie Medical). By week 16 the ulcer had completely healed (Figure 6).

### Discussion

Honey is a unique wound dressing component due to its multiple properties. These include a high osmotic gradient, which dehydrates multiple species of bacteria thereby killing them, and its acidic PH of 3.2–4.2, which inhibits the growth of most bacteria in the wound and slowly releases hydrogen peroxide, killing bacteria without causing tissue damage.

Due to its osmotic properties honey also provides a moist wound environment for cells to grow in, drawing out fluid from plasma or lymph in the adjacent tissue.

All of these properties make honey both bactericidal and bacteriostatic. Bacteriostatis means that the agent prevents the growth of bacteria (i.e. keeps it in the stationary phase of growth); while the term bacteriocidal means the agent kills the bacteria (Markovic et al, 2007).

These properties also make honey a powerful chemical debriding agent (Jemal et al, 2006), because of its ability to offer a protective barrier and prevent wounds from becoming infected (Anderson, 1941). This includes necrotic and gangrenous tissue. The continual release of hydrogen peroxide aids in the debridement of wounds without causing damage to normal tissue. This is due to the fact that hydrogen peroxide



**Figure 6.** By week 16 the ulcer had completely healed.

is diluted at 1 000 times more than rinse solutions (Markovic, 2007), thereby enhancing growth and the expression of early growth genes necessary for wound healing (Snell, 1965; Naldi et al, 2005).

Honey also deodorises infected wounds by providing an alternative to the amino acids from dead cells and serum. Elements such as sulphur compounds, ammonia and amines, which are the cause of malodor in wounds, are replaced by lactic acids (Veierod et al, 1997; Cho et al, 2005a).

Furthermore, the hydrogen peroxide released by immune cells may stimulate the growth of fibroblasts at the base of the wound where inflammatory cells are abundant (Naldi et al, 2005).

Finally, honey is thought to possess an anti-inflammatory action according to histological studies although the definitive mechanism is yet to be identified (preliminary data suggest that honey may activate monocytes within the wound) (Cho et al, 2005b; Hollenbeak et al, 2005).

Applying honey to the ulcer provides moisture that:

- ▶▶ Helps cells proliferate
- ▶▶ Prevents cell death
- ▶▶ Accelerates angiogenesis (Charles et al, 1994)
- ▶▶ Initiates the tissue repair process (Molan, 2006)
- ▶▶ Prevents wound infection by producing antibodies to common pathogens, such as *Escherichia coli* (Al-waili and Haq, 2004).

## Recommendation for practice

Currently there is scarce data with regards to the use of commercial honey at primary care level in the management of post-excision malignant melanoma ulceration. In the authors' opinion, this needs to be addressed, especially in the case of general practitioners who are trained in the management of diabetic feet and can provide many services including counselling, metabolic control and wound management, as well as delivering preventive health education, screening for high-risk feet and detecting complications at an early stage.

Honey-based treatment seems to be a cost-effective and viable alternative to commercially available dressing materials, especially in poor countries where diabetes has already reached epidemic proportions.

## Conclusion

This case report clearly suggests the essential role primary care physicians may have in the future when treating diabetic foot ulcers, provided they have adequate training and skills to handle these cases. In summary, to the authors' knowledge this article presents the first case of post-excision malignant melanoma of a diabetes foot ulcer in a patient of Arab descent. **JL**

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## Key points

- ▶ Worldwide, there is a rapid increase in the incidence of malignant melanoma
- ▶ Honey has a long tradition of use for wound healing, whether for burns, ulcers, acute or chronic wounds.
- ▶ Honey provides an alternative to the amino acids from dead cells and serum, thereby deodorising infected wounds.
- ▶ Malignant melanoma is quite rare among Asians, Africans and Hispanics and knowledge of melanoma in Asian patients is scant.

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