

Case Series

Natural Honey as a Safe and Efficacious Alternative to Skin Grafting Post-Surgical Excision for Necrotizing Fasciitis at Primary Care Level: A Preliminary Study

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ABSTRACT

Necrotizing fasciitis is a soft tissue bacterial infection that spreads rapidly resulting in the destruction of muscles, skin, and underlying tissue. Necrotizing fasciitis is defined as a fast and progressive inflammatory infection of the fascia leading to secondary necrosis of the subcutaneous tissue moving along the facial plane. Fournier gangrene is a type of necrotizing fasciitis involving the scrotum and perineal area. Patients suffering from acute necrotizing fasciitis require an effective regimen which includes surgical removal of devitalized tissues, systemic antimicrobials and mitigating underlying systemic disease processes. The burden of treating wounds following surgical debridement, on the other hand, can be challenging especially in the third world where resources are scarce resulting in suboptimal wound coverage and function. At primary care level we had the opportunity of using natural honey in 5 patients with non-healing wounds in either the lower limb or scrotum due to acute necrotizing fasciitis. This natural non-invasive approach offers a cost-effective and efficacious alternative to dermatotraction, skin grafting and negative pressure wound therapy. In these patients, the use of natural honey led to the restoration of the appearance and function of the fasciotomy wound especially in patients with co-morbidities or those refusing skin grafting due to cost, religious factors, etc. The authors present the clinical results followed by a discussion on the therapeutic properties of natural honey. This case series demonstrates the efficacy of topical raw honey as a catalyst for speeding the healing process by secondary intention thereby offering a safe and efficacious alternative for managing various wounds resulting from acute necrotizing fasciitis.

Keywords

Natural honey; Necrotizing fasciitis; Primary care; Wounds.

INTRODUCTION

Necrotizing fasciitis is considered a life-threatening situation for patients with diabetes and presents a clinical challenge for clinicians worldwide. Necrotizing fasciitis is defined as a fast and progressive inflammatory infection of the fascia leading to secondary necrosis of the subcutaneous tissue moving along the facial plane. Fournier gangrene is a type of necrotizing fasciitis involving the scrotum and perineal area.¹ The main feature of necrotizing fasciitis include an aggressive progressive inflammatory infection involving the fascia complicated by a secondary necrosis of the subcutaneous tissues.^{1,2} A variety of surgical procedures and or medical conditions can lead to necrotizing fasciitis including cardiac catheterization³ and vein sclerotherapy⁴; or it may be idiopathic,

as in penile or scrotal necrotizing fasciitis or secondary to contaminated skin wounds. Bacteria responsible for necrotizing fasciitis include aerobic bacteria, anaerobes, or mixed flora.⁵ The incidence of necrotizing fasciitis has been increasing due to an increase in patients with immuno compromised status such as those with diabetes mellitus, alcoholism, cancer neutropenia, etc. Patients with diabetes are more prone to have local ischemia, hypoxia and compromised host defenses favoring the development of necrotizing fasciitis. Patients with diabetes are at risk in more than 90% of cases for life-threatening progressive bacterial gangrene. Diabetes is associated with around 20-40% of patients with necrotizing fasciitis and around 80% of those who suffer from Fournier gangrene are people with diabetes. Delayed diagnosis and surgical debridement can lead to huge open wounds, amputations, and even death.

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Standard management entails surgical debridement of necrotic and de vascularized tissue, intravenous antibiotic treatment, and hyperbaric oxygen.^{6,7} After the necrotizing fasciitis is tackled and the patient is stabilized medically, attention of health care professionals can then focus on promoting the healing process of the debrided wound. Various options are available for wound closure which include, healing by secondary intention, delayed surgical closure or split-thickness skin grafting. At times some patients may refuse surgical intervention, advanced wound products due to high cost or religious and cultural reasons and as a result they may opt for alternative therapies. This case series demonstrates the efficacy of topical raw honey as a catalyst for speeding the healing process by secondary intention thereby offering a safe and efficacious alternative for managing various wounds resulting from acute necrotizing fasciitis.

CASES

Case I

History and diagnosis: A 45-year-old Egyptian man with type II diabetes mellitus, presented to the accident and emergency department complaining of a swelling and blistering of posterior neck region. He was afebrile on admission and did not report any history of fever or chills. Outpatient medications included Metformin 500 mg three times a day, Aspirin 100 mg and Esomeprazole 40 mg. On physical examination, the patient had a temperature of 99 °F and the posterior neck region showed a dusky bullous lesions and erythema of 6×7 cm. His fasting glucose was 10 mmol/L, creatinin 95 mmol/L, Glycosylated haemoglobin 7% white blood count was 11.4 with a differential of 89% neutrophils, 11% lymphocytes, 2% monocytes, and 3% bands. An X-ray of the posterior neck region did not demonstrate any presence of subcutaneous air. Based on the clinical examination he was diagnosed as having necrotizing fasciitis and received IV ceftriaxone and clindamycin and the surgical team was consulted.

Treatment: The patient was immediately taken to the operating room for surgical management. Post-operatively, a wet-to-dry dressing was applied to the wound bed and the patient was admitted to the main surgical ward with intravenous ceftriaxone 1 gram daily. When offered a split-thickness skin graft, the patient refused the procedure. Five days later the patient discharged with amoxicillin-calvulanate 625 mg tid for one-week and the patient was told to continue dressing at the health center. On presentation the patient had a wound of 12×10×3 cm with necrotic base (Figure 1A). The decision was made to debride the wound and apply honey impregnated cotton gauze packing into the deep wound space on a daily basis. Basis this amounted to 10 gram per change of dressing. Daily fasting blood glucose levels remained in the range of 7-8 mmol/L during the dressing period Four-weeks later the wound size area decreased by 90% (Figure 1B). Six-weeks later the wound almost healed by 98% (Figure 1C). Post treatment six weeks later the glycosylated haemoglobin level remained at 7% with a fasting glucose level of 7.5 mmol/L.

Figure 1. A) On Presentation B) Four-Weeks Later Area is Reduced by 90% C) Six-Weeks Later Wound Area is Reduced by 98%

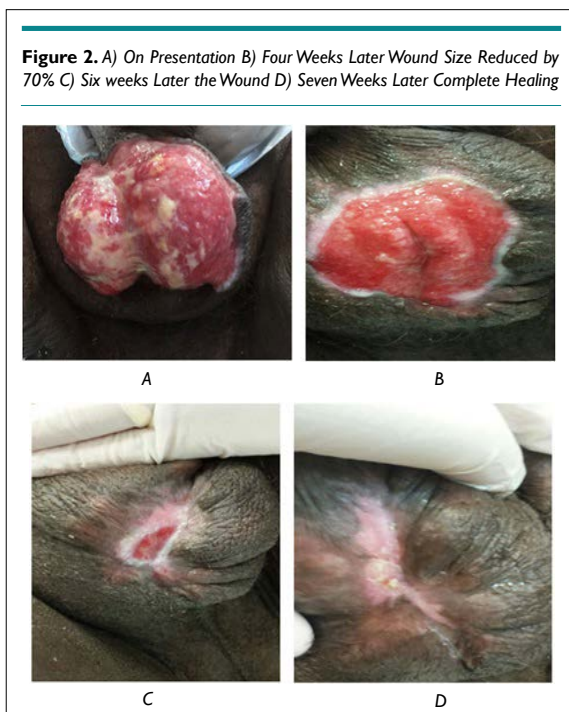


Case 2

History and diagnosis: A 55-years-old male Sudanese patient, with type II DM, coronary artery disease, morbid obesity, chronic renal impairment, presented to A/E with fever, myalgia, pain and swelling of his scrotum. The patient denied any history of recent travel, intercourse, preceding genitourinary injury or symptoms or any notable lapses in personal hygiene. The patient was fully conscious but looked ill and in pain, with chills and rigors along with a rectal temperature of 104.3 °F. His blood pressure was 85/50 mmHg, heart rate was 116 beats/min, and respiratory rate was 22 breaths/min along with an oxygen saturation of 99% on room air. His biochemical profile was as follows: fasting glucose level of 12 mmol/L, glycosylated haemoglobin of 11%, creatinin 154 mmol/L. The patient medication to control blood sugar included, Gliclazide 120 mg daily, Pioglitazone 30 mg daily and Glargine basal insulin of 16 units subcutaneously at evening time.

Treatment: On physical examination there was significant erythema, edema, and calor of the scrotum. A provisional diagnosis of Fournier's gangrene was provided, surgical team on call was consulted, followed by rapid intravenous (IV) fluid resuscitation with 5% dextrose normal saline was started along with, IV clindamycin, and ampicillin/sulbactam. His initial A/E investigations were significant for leukocytosis of 13,000/mm³ and a lactate of 2.3 mEq/L. Subsequently he was transferred to the operating room where anoscopy and cystoscopy showed source of infection or signs of gangerous extension from the bladder or rectum. He underwent surgical debridement of the scrotum with good post-operative recovery. Blood cultures were positive for strains of *Streptococcus pyogenes* and *Staphylococcus aureus*. During his hospital stay the wound was dressed with Betadine solution and dry gauze on a daily basis. The wound was not improving in a satisfactory fashion despite his long stay in the hospital which was around three months!. As a result the patient has asked to be discharged home. He was given a follow-up appointment in outpatient clinic after one-week with the option of skin grafting. The patient refused skin grafting and came to Um Gwailinah Health Center for dressing. On presentation the wound was 5×8 cm showing slough and necrotic tissue (Figure 2A) with no signs of infection such as fever, swelling, redness or pain at the wound site. The wound was cleaned with normal saline, natural honey was applied directly on the wound and covered with a petroleum jelly based barrier dressing adaptic be-

fore being covered by cotton gauze. His fasting glucose level values were in the range of 9-12 mmol/L despite educating him about his diet and exercise and intensifying his basal insulin to 32 units in the evening. The idea of introducing a glycerin based dressing is to prevent natural honey from coming off the wound and being absorbed on the secondary cotton gauze. The honey dressing was changed on a daily basis meanwhile the patient was warned against the possibility of mild stinging sensation due to the acidic nature of honey. Four-weeks later the wound has decreased in size by 70% with healthy granulation tissue and normal skin (Figure 2B). The patient and staff both expressed satisfaction at the level of progress including the hospital surgeons and advice the patient to continue with the honey dressing. Six-weeks later the wound has healed by 98% (Figure 2C) and one week later there was complete healing (Figure 2D) with no scar formation. His glycosylated haemoglobin level was 11% at the end of the treatment.



Case 3

A 72-year-old male Sudanese patients with type II diabetes mellitus, hypertension, obesity presented to the accident and emergency department complaining of a swelling and blistering of the dorsum of the right foot. His medications included Gliclazide 60 mg, Atorvastatin 40 mg, Aspirin 100 mg and Sitagliptin 100 mg. On examination the patient had a body temperature of 36.6 °C, blood pressure of 113/70 mmHg, heart rate of 93 beats/min and a respiratory rate of 18/min. Right foot examination revealed a swelling and redness on the dorsum of the foot with palpable crepitus. laboratory findings revealed a white blood cell (WBC) count of 440/mm³ with 32% polymorphonuclear cells and platelet count of 140,000/mm³. Serum lactate was 5.8 mmol/L; sodium, total protein/albumin, 3.9/1.6 g/dL; 29 mmol/L; and random blood glucose of 15 mmole/L. The patient had no evidence of coagulopathy with international normalized ratio 1.1 and a prothrombin time of 11.5 seconds. His glycosylated haemoglobin level was 13%

at the time of admission to the hospital.

An intensive care unit (ICU) admission was arranged with basal bolus insulin comprising Glargine insulin 32 units subcutaneously at night and rapid acting insulin Aspart 10 units subcutaneously prior to main meals. This was coupled with fluid resuscitation and intravenously administered broad-spectrum antibiotics including teicoplanin (400 mg), metronidazole (1,500 mg) and meropenem (500 mg). The patient was rushed to the operating room, where an incision was made over the dorsum of the right foot and exploration of the fascia revealed an inflamed and necrotic tissue with collection of pus. At the time aerobic and anaerobic cultures were sent for sensitivity and biopsy. Fasciectomy was performed and the fascia was excised sharply, exposing the underlying muscles and tendons (Figure 3A). The patient was stabilized over night and was discharged next day and given an appointment for skin grafting on the 10th post-operative day. Upon presentation the right dorsum of the foot showing extensor digitorum longus tendon, rolled under edges of the wound and blood clots (Figure 3C). On presentation to our health center the wound was cleaned with normal saline, dressed with a total of 20 grams of natural honey and covered with adaptic a petroleum jelly impregnated gauze and a cotton gauze was placed to secure the wound. Fasting glucose level was 9 mmol/L on his first visit. After wards the wound was wrapped and secured with cotton bandage. One-week later the wound started to fill from down upwards with healthy granulation tissue covered with a thin layer of serous fluid with the wound edges attaining a well-defined, attached tissue (Figure 3B). Two -eeks later, the wound reduced by 50% in size with healthy granulation tissue covering the extensor digitorum longus (Figure 3c). The wound has completely healed with no contracture at 4-weeks (Figure 3D). During daily dressing his average fasting blood glucose level was around 8 mmol/L, and his glycosylated haemoglobin levels were 12%.



Case 4

A 58-years-old male with type II diabetes, hypertension, obesity, diabetic retinopathy, peripheral neuropathy and chronic heavy smoker smoking 20 cigarettes per day for the last 30-years. The patient was diagnosed with necrotizing fasciitis and had surgery performed on his right lower limb and had been dressing his wound in the main hospital inpatient wound clinic for the last three-months prior to his presentation to our health center. On presentation to our health center the patient had a fasting glucose level of 12 mmol/L, creatinin 170 mmol/L and a glycosylated haemoglobin of 10%. His daily regimen included, Gliempiride 6 mg daily, Pioglitazone 15 mg daily and Vildagliptin 50 twice daily, Clopidogrel 75 mg and Rosuvastatin 10 mg daily. The attending family physician looking after the wound had decided to intensify his medications by introducing basal insulin (Glargine) 14 units subcutaneously at night and introducing bolus insulin 10 units subcutaneous before each main meal. On examination the wound had a lot of necrotic tissue, slough and was extending from above the medial malleolus and extending down to the dorsal aspect of the right foot (Figure 4A). The whole lower limb was washed with the antiseptic solution Chlorhexidine Gluconate 4% from the anterior tuberosity to the toes. Afterwards the wound was washed with normal saline and necrotic tissue was debrided using a surgical blade (Figure 4A). Post-debridement the wound had around 10 gram of natural honey applied to it and covered with (Adaptic™) which is a primary non-adhering dressing composed of petroleum jelly impregnated knitted cellulose acetate fabric. This dressing works as a barrier keeping honey in the wound bed and preventing it from being absorbed onto the secondary cotton gauze which is directly applied over it to secure the wound. Thereafter, the wound was covered with

th cotton bandage and the patient was scheduled for daily change of the dressing. One month later the wound had reduced by 50% in size (Figure 4B). The patient had continued to attend on a daily basis, however on one occasion the wound has developed a greenish color discharge which was considered *pseudomonas aeruginosa* and a swab was taken and sent for culture and sensitivity which was positive for *pseudomonas aeruginosa*. Meanwhile the wound was irrigated on a daily basis with 1% acetic acid in order to clear the contaminated wound bed followed by normal saline. *Pseudomonas aeruginosa* is inhibited by the application of 1-5% acetic acid concentration *via* lowering the pH of the wound thereby inhibiting the growth of bacteria including *pseudomonas aeruginosa*. The acetic acid irrigation was continued for another week till no more green discharge is seen. Post-irrigation another wound swab was taken which showed no growth. Two-months later the wound has reduced by 75% (Figure 4C). The patient started to come only once every three-days as his work was not allowing him to go for daily dressing. Three months later the wound has almost healed with 97% reduction in size and normal skin formation with no contracture (Figure 4D). The patient managed to attain a glycosylated haemoglobin of 8% and an average fasting glucose of 8 mmol/L after intensifying his therapy at the three-month follow-up appointment but unfortunately, the patient did not show up for further inspection and dressing.

Case 5

A 62-years-old male with hypertension, type II diabetes, diabetic nephropathy, obesity, hyperlipidemia, diabetic retinopathy, peripheral neuropathy presented to our health center after being discharged from the main hospital. His medications were as follow Metformin-Sitagliptin 100/50 mg twice daily, Pioglitazone 15 mg daily and Dapagliflozin 10 mg daily, Atorvastatin 80 mg daily and Aspirin 100 mg daily. His biochemical profile was as follows: fasting glucose level of 7.5 mmol/L, glycosylated haemoglobin of 8%, creatinin 100 mmol/L. The patient was diagnosed with necrotizing fasciitis and had surgery performed on his left lower limb extending from above the ankle joint anteriorly down to the dorsum of the left foot. The patient left the hospital and was asked to do daily dressing at the health center with the plan of having a skin flap in two-weeks time. On inspection the wound is showing lower, extensor retinaculum and anterior tibial tendon, and extensor digitorum brevis, slough, necrotic tissue, extending down to the dorsal aspect of the left foot (Figure 5A). The wound did not show any signs of infection such as erythema, foul smell, swelling, tenderness and as result no antibiotics were prescribed. The wound was irrigated with normal saline followed by debridement of necrotic tissue using a surgical blade followed by application of natural honey to the wound area and covered with (Adaptic™) a petroleum jelly impregnated dressing. Thereafter, the wound was covered with cotton bandage with a daily change schedule. One-month later the wound had decreased in size by 90% in size (Figure 5B) with complete healing achieved six-weeks later (Figure 5C). Post-healing his average fasting glucose was 7% and his glycosylated haemoglobin remained at 8%.



Figure 5. A) A Wound Showing Extensive Slough Necrotic Tissue and Exposed Tendons B) 90% Reduction in 4-Weeks C) Complete Healing without Contracture



Mechanism of Action of Honey

A broad spectrum of wounds including burns, acute and chronic wounds, psoriasis, pressure ulcers and chronic diabetic foot ulcers have been successfully treated by honey.⁸⁻¹² Although, in the medical literature, its wound healing properties is exclusively related to its antibacterial activity, nonetheless honey has anti-inflammatory as well as immunomodulatory properties which clearly aids in the healing process of various types of wounds and skin conditions including being an efficacious alternative to skin grafting.¹³ Depending on wound conditions, honey being present in the wound environment is able to either stimulate or inhibit the release of the various cytokines including tumor necrosis factor- α , interleukin-1 β , interleukin-6) from macrophages and human monocytes.¹⁴ Additionally, in the presence of honey fibroblasts, human keratinocytes, are positively affected leading to cell-proliferation and migration, chemotaxis and collagen matrix production, ultimately leading to reepithelization and wound closure. Honey also releases H₂O₂ at 1:1000 concentration adequate enough to kill pathogens without compromising the healthy granulating cells, provides adequate amount of moisture without leading to dryness or maceration, vitamins and provides a sound barrier against external pathogens.¹⁵⁻¹⁷ Honey also aids in wound healing by providing a low pH, anti-inflammatory action and an osmotic gradient just enough to dehydrate the bacterial cell wall without compromising the cellular matrix of wounds.^{18,19} The amount of honey placed on various wounds depended on the size of the wound, however, the investigator applied enough amount to cover the whole surface area of the wound. The purity of honey was established through the food laboratory of the Ministry of Health which confirmed its purity, lack of bacterial spores (including botulism toxins), fungi and viruses. The water content was 14% with 35% fructose, 25% glucose and 26% sucrose.

Necrotizing fasciitis is characterized by lack of specific symptoms and lack of reliable laboratory parameters therefore it is imperative that patients with suspected signs and symptoms of necrotizing fasciitis be rushed to the operating room. Mortality rate varies from 6% when patients undergo operation within 12 h of onset of signs and symptoms, but rises to 30% after 24 h.²⁰ It is recommended that the first surgical intervention should aim at removing all of the necrotic tissue.²¹⁻²⁵ However, at times

several surgical debridement may be necessary with the use of a vacuum-assisted closure device (VAC) in between where the patient is possibly booked for a flap surgery at alter stage.²³ Various alternative therapeutic options have been including intravenous immunoglobulin and hyperbaric oxygen, however, their efficacy remains controversial.²² Unfortunately not every patient can afford to have the commodity of a skin flap surgery especially in the World and War III stricken regions where resources are scarce and plastic surgery is considered a luxury. In these circumstances natural honey can replace flap surgery since it stimulates the growth and proliferation of fibroblasts even on fibrous tissues such the plantar aponeurosis.¹³ Furthermore, honey exerts its action primarily by two actions. First, it increases vascularity and wound bed cell growth through angiogenesis acting as a Natural VAC System whereby it speeds the healing process especially in deep wounds. Honey used in deep wounds must be used *via* impregnating cotton gauze with it and the clinician must make sure the wound dressing material (honey impregnated cotton gauze) fills the wound bed in order to stimulate cells to grow against resistance.¹³ Second, honey may act as natural skin flap offering a viable alternative to classical skin flap especially when patients cannot afford it, refuse having operation, or have multiple comorbidities precluding them from benefiting from it. Honey's ability to replace skin flap is related to its ability to stimulates angiogenesis, epithelial cell growth, fibroblast growth and ultimately tissue regeneration with minimal hypertrophy and scarring. The majority of surgical incisions heal by primary intention, i.e. stitches or clips are used to close together the edges of a surgical incision until the cut edges merge. Healing by secondary intention is said to occur when an open wound begins to heal from the base upwards, through the formation of new tissue. Many types of dressings and topical agents are available in the market but few have been rigorously evaluated in randomized clinical trials. Many clinical studies have demonstrated the efficacy of honey in the treatment of a variety of wounds including burns,²⁶ diabetic foot ulcers,²⁷ pressure injuries,²⁸ ostomy wounds,²⁹ cancerous wounds,³⁰ radiation burns³⁰ along with dermatological cases including palmo-plantar psoriasis,²² seborrheic dermatitis,³¹ and acne vulgaris.³² Recent meta-analysis has shown the superiority of honey compared to conventional therapies in relation to burns³³ and diabetic foot ulcers specifically.³⁴ Healing by secondary intention is an often underused and underestimated reconstructive modality. Spontaneous healing versatility becomes ostensible when it is adopted to heal previously repaired wounds complicated by infection, dehiscence, and graft loss or flap necrosis.

Zitelli³⁵ has confirmed statistically through his clinical trial that moist environment accelerates re-epithelization which is the main component of healing by secondary intention, as a result he suggested the use of antibacterial ointment to minimize desiccation, pain and necrosis. Raw honey offers a safe and efficacious alternative to antibacterial ointments and petroleum based products since it has almost 16% of its content as water produces hydrogen peroxide, flavanoids, minerals, vitamins, stimulates angiogenesis *via* its osmotic gradient and promotes epithelization.

Limitation of the Studies

Most studies addressing the use of honey in clinical settings had

small number of participants, lacked double blinding, originated from single centers and lacked long-term follow-up. These factors can be attributed to the fact that health establishments are used to utilizing advanced wound products much of which lack rigorous scientific basis for their efficacy and depend on intensive marketing targeting health professionals mainly wound care specialists worldwide. Additionally, health care professionals are usually skeptic about the use of complementary and alternative medicine (CAM) due to the fact that most medical and nursing schools fail to include (CAM) into their curricula and worse still health care professionals utilizing (CAM) are not supported with grants when it comes to undertaking multi-center randomized clinical trials.

CONCLUSION

Natural raw honey use in wounds post-fasciotomy may offer a viable alternative especially in the third world where resources are scarce, however, a randomized controlled trial involving a comparative group with the use of advanced wound product is needed to confirm such a conclusion.

CONSENT

The authors have received written informed consent from the patient.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

- Misiakos EP, Bagias G, Patapis P, Sotiropoulos D, Kanavidis P, Machairas A. Current concepts in the management of necrotizing fasciitis. *Front Surg*. 2014; 1: 36. doi: [10.3389/fsurg.2014.00036](https://doi.org/10.3389/fsurg.2014.00036)
- Hakkarainen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: Review and current concepts in treatment, systems of care, and outcomes. *Curr Probl Surg*. 2014; 51(8): 344-362. doi: [10.1067/j.cpsurg.2014.06.001](https://doi.org/10.1067/j.cpsurg.2014.06.001)
- Federman DG, Kravetz JD, Kirsner RS. Necrotizing fasciitis and cardiac catheterization. *Cutis*. 2004; 73(1): 49-52.
- Chan HT, Low J, Wilson L, Harris OC, Cheng AC, Athan E. Case cluster of necrotizing fasciitis and cellulitis associated with vein sclerotherapy. *Emerg Infect Dis*. 2008; 14(1): 180-181. doi: [10.3201/eid1401.070250](https://doi.org/10.3201/eid1401.070250)
- Kihiczak GG, Schwartz RA, Kapila R. Necrotizing fasciitis: A deadly infection. *J Eur Acad Dermatol Venereol*. 2006; 20(4): 365-369. doi: [10.1111/j.1468-3083.2006.01487.x](https://doi.org/10.1111/j.1468-3083.2006.01487.x)
- Urschel JD. Classic diseases revisited: necrotizing soft tissue infections. *Postgrad Med J*. 1999; 75: 645-649.
- Perry B, Floyd WE. Gas gangrene and necrotizing fasciitis in the upper extremity. *J Surg Orthop Adv*. 2001; 13(2): 57-68.
- Mohamed H, Salma MA, Allenjawi B, Barakat N, Gouda Z, Abdi S, et al. Natural honey as an adjunctive alternative in the management of diabetic foot ulcers. *Wound Practice and Research*. 2012; 20(4): 212-216.
- Mohamed H, El Lenjawi B, Salma MA, Abdi S. Honey based therapy for the management of a recalcitrant diabetic foot ulcer. *J Tissue Viability*. 2014; 23(1): 29-33. doi: [10.1016/j.jtv.2013.06.001](https://doi.org/10.1016/j.jtv.2013.06.001)
- Mohamed H, Salma MA, Al-Lenjawi B, Mohammad A, Jouda Z, Abdi S, et al. Enhancing primary healing post ray amputation in a diabetic patient: Efficacy of natural honey. *The Journal of Diabetic Foot Complication*. 2014; 6(2): 13-18.
- Mohamed H, Salma MA, Al-Lenjawi B, Abo Gouda Z, Hussain Z, Al-Majid S, et al. Efficacy of natural honey in the management of second degree burn complicated by acute dermatitis in a diabetic patient. *J Diabetes Metab*. 2014; 5: 5.
- Salma MA, Abo Salama M, Al-Lenjawi B, Hassan I. Using honey in post-excision malignant melanoma ulcers. *Journal of Lymphoedema*. 2012; 7(1): 41-44.
- Majtan J. Honey: An immunomodulator. *Wound Repair Regen*. 2014; 22: 187-192. doi: [10.1111/wrr.12117](https://doi.org/10.1111/wrr.12117)
- Mohamed H, Salma MA, Al-Lenjawi B, Abdi S, Gouda Z, Barakat N, et al. The efficacy and safety of natural honey on the healing of foot ulcers: A case series. *Wounds*. 2015; 27(4): 103-114.
- Mohamed H, Abo Salama M, Al-Lenjawi B, Abo Gouda Z, Hussain Z. The efficacy of natural honey in the management of second degree burn complicated by acute dermatitis in a diabetic patient. *J Diabetes Metab*. 2014; 5(373): 1000373. doi: [10.4172/2155-6156.1000373](https://doi.org/10.4172/2155-6156.1000373)
- Al-Lenjawi B, Mohamed H, Salma MA, Gouda ZA. Natural honey in the management of thermal burn of the foot in a type 2 diabetic patient: A case report. *Dermatol Open J*. 2016; 1(1): 14-18. doi: [10.17140/DRMTOJ-1-105](https://doi.org/10.17140/DRMTOJ-1-105)
- Mohamed H. Successful healing of diabetic foot ulcers and various etiology ulcers with natural honey: An alternative paradigm in wound healing. *J Diab Rel Dis*. 2016; 1(1): 107. doi: [10.5812/ircmj.41939](https://doi.org/10.5812/ircmj.41939)
- Samarghandian S, Farkhondeh T, Samini F. Honey and health: A review of recent clinical research. *Pharmacognosy Res*. 2017; 9(2): 121-127. doi: [10.4103/0974-8490.204647](https://doi.org/10.4103/0974-8490.204647)
- Al-Meslamani L, Al-Lenjawi B, Al-Majid S, Mohamed H. Palmoplantar psoriasis successfully treated with raw natural honey: A case report. *Dermatol Open J*. 2019; 4(1): 1-6. doi: [10.17140/DRMTOJ-4-133](https://doi.org/10.17140/DRMTOJ-4-133)
- Wong C-H, Chang H-C, Pasupathy S, Khin L-W, Tan J-L, Low

- C-O. Necrotizing fasciitis: Clinical presentation, microbiology and determinants of mortality. *J Bone Joint Surg Am.* 2003; 85-A: 1454-1460.
21. Elliott DC, Kufera JA, Myers RA. Necrotizing soft tissue infections. Risk factors for mortality and strategies for management. *Ann Surg.* 1996; 224: 672-683. doi: [10.1097/0000658-199611000-00011](https://doi.org/10.1097/0000658-199611000-00011)
22. Anaya DA, Dellinger EP. Necrotizing soft-tissue infection: diagnosis and management. *Clin Infect Dis.* 2007; 44: 705-710. doi: [10.1086/511638](https://doi.org/10.1086/511638)
23. Heitmann C, Pelzer M, Bickert B, Menke H, Germann G. [Surgical concepts and results in necrotizing fasciitis]. *Chirurg.* 2001; 72: 168-173. doi: [10.1007/s001040051287](https://doi.org/10.1007/s001040051287)
24. Nagoba B, Wadher B, Kulkarni P, Kolhe S. Acetic acid treatment of pseudomonal wound infections. *Eur J Gen Med.* 2008; 5: 104-106. doi: [10.29333/ejgm/82586](https://doi.org/10.29333/ejgm/82586)
25. Greener B, Hughes AA, Bannister NP, Douglass J. Proteases and pH in chronic wounds. *J Wound Care.* 2005; 14: 59-61. doi: [10.12968/jowc.2005.14.2.26739](https://doi.org/10.12968/jowc.2005.14.2.26739)
26. Zbuche A. Up-to-date use of honey for burns treatment. *Ann Burns Fire Disasters.* 2014; 27(1): 22-30.
27. Shukrimi A, Sulaiman AR, Halim AY, Azril A. A comparative study between honey and povidone iodine as dressing solution for wagner type II diabetic foot ulcers. *Med J Malaysia.* 2008; 63(1): 44-46.
28. Jull AB, Cullum N, Dumville JC, Westby MJ, Deshpande S, Walker N. Honey as a topical treatment for wounds. *Cochrane Database Syst Rev.* 2015; (3): CD005083. doi: [10.1002/14651858.CD005083.pub4](https://doi.org/10.1002/14651858.CD005083.pub4)
29. Lund-Nielsen B, Adamsen L, Gottrup F, Rorth M, Tolver A, Kolmos HJ. Qualitative bacteriology in malignant wounds—a prospective, randomized, clinical study to compare the effect of honey and silver dressings. *Ostomy Wound Management.* 2011; 57: 28-36.
30. Shoma A, Eldars W, Noman N, Saad M, Elzahaf E, Abdalla M, et al. Pentoxifylline and local honey for radiation-induced burn following breast conservative surgery. *Curr Clin Pharmacol.* 2010; 5(4): 251-256. doi: [10.2174/157488410793352021](https://doi.org/10.2174/157488410793352021)
31. Mohammed HA, Al-Lenjawi B, Mendoza D. Seborrhic dermatitis treatment with natural honey. *Wounds International.* 2018; 9: 36-38.
32. Eady EA, Layton AM, Cove JH. A honey trap for the treatment of acne: Manipulating the follicular microenvironment to control. *Propionibacterium acnes in Human Health and Disease [Special Issue]. Bio Med Research International.* 2013; doi: [10.1155/2013/679680](https://doi.org/10.1155/2013/679680)
33. Wijesinghe M, Weatherall M, Perrin K, Beasley R. Honey in the treatment of burns: a systematic review and meta-analysis of its efficacy. *N Z Med J.* 2009; 122(1295): 47-60.
34. Wang C, Guo M, Zhang N, Wang G. Effectiveness of honey dressing in the treatment of diabetic foot ulcers: A systematic review and meta-analysis. *Complement Ther Clin Pract.* 2019; 34: 123-131. doi: [10.1016/j.ctcp.2018.09.004](https://doi.org/10.1016/j.ctcp.2018.09.004)
35. Zitelli JA. Wound healing by secondary intention. A cosmetic appraisal. *J Am Acad Dermatol.* 1983; 9(3): 407-415. doi: [10.1016/s0190-9622\(83\)70150-7](https://doi.org/10.1016/s0190-9622(83)70150-7)