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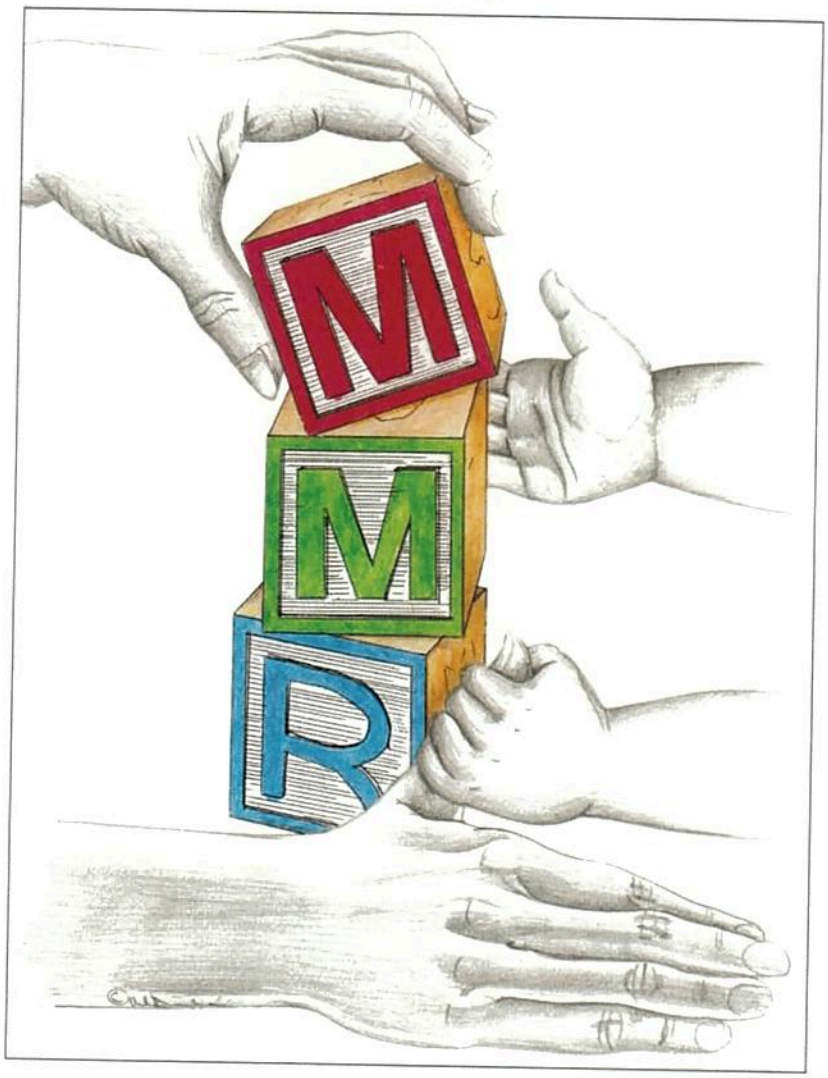


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# THERAPEUTIC USE OF HONEY FOR RESISTANT GENITAL/VULVO — PERINEAL HERPETIC ULCERS IN AN IMMUNOCOMPROMISED PATIENT

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A case of resistant herpetic ulceration is reported in a 30 year old Ugandan female 'J' with known immunodeficiency (HIV antibody positive). She presented with a large herpetic ulcer in the vulvo-vaginal and perianal areas, resistant to aciclovir. The use of valaciclovir, topical and oral aciclovir, silver sulphadiazine cream, hydrogen peroxide and teatree oil did not cause any improvement and there was no sign of any skin regeneration.

The ulcer responded remarkably to the topical application of honey, with obvious skin regeneration by the third week. Local wound care was also achieved with daily sitz baths, and saline irrigation followed with the direct use of oxygen (on weekly visits to the Mildmay Centre).

This case highlights the difficulties faced with the conventional treatment of resistant herpetic ulcers and introduces an inexpensive and effective approach, by the use of fresh pure honey.

Herpetic ulcers usually start with a group of tiny papules which are irritant or painful. The papules develop into vesicles, which eventually erode, forming ulcers.

Herpetic ulcers are often resistant to treatment and recurrence is quite a problem with genital herpes, (the re-occurrence rate is greater in herpes simplex virus II (HSV II )(80%) than in herpes simplex virus I (50%) (HSV I). An association has been made between (HIV) human immunodeficiency virus and HSV II.

It has been noted that plasma HIV viral load rises when HSV II infection reactivates in persons with HIV infection,[1] suggesting that herpes may adversely affect the course of HIV disease. Also the prevalence of HSV II infection in populations at risk of HIV is extremely high, and subclinical shedding of HSV is almost certainly present, even when cutaneous or mucosal ulceration is not apparent. The size of the lesion rarely exceeds 2cm, but very large forms occasionally occur, as in the case of J (14cm x 25cm). The lesion usually develops 4 -7 days after contact, and the condition tends to re-occur because the virus establishes latent infection of the sacral sensory nerve ganglia, from which it reactivates to re-infect the skin.[2] Severe and persistent reoccurrence of herpes infections are common in the immunocompromised patient. Chronic herpetic ulcers vary in appearance and may resemble a traumatic lesion. It is also essential to exclude syphilis.

Treatment for genital herpes (in the immunocompromised patient) is aciclovir 400mg, five times daily for five days, with the addition of topical aciclovir applied five times daily for five days. Intravenous administration has been suggested in severe cases in the immunocompromised patient (5mg/kg tds for five days). It is advised that early treatment increases the efficacy of aciclovir, though it should be noted that aciclovir does not eradicate the virus.

Valaciclovir and famciclovir may be used as alternatives, and foscarnet sodium, if introduced at an early stage, has also been found to be effective,[3] but is not generally available in resource poor settings.

However, some cases are resistant to the above treatments, and healing may not always follow, even when there is no obvious activity of HSV.

## BACKGROUND

J, a 30 year old Ugandan female schoolteacher presented at the Mildmay Centre on the 8th November 1999, with an eight month history of a painful ulcerating lesion of the genital area, which was becoming progressively larger. J also had a cough of 10 months duration with associated nightsweats and generalised weakness.

## HISTORY

Past medical history revealed that J had once been pregnant in 1992 (unfortunately the baby died at 5 months of age).

In 1993, J developed herpes zoster of the left thorax. She had also been treated for recurrent chest infections. J lived with her sister, who was the main carer.

On the 5th November 1999, three days prior to her presentation at the Centre, J had been diagnosed HIV positive at a private clinic. Her haemoglobin was 5.5g/dl.

## EXAM

On examination she was observed to be depressed, pale, weak, and markedly wasted (she had lost >10% of her body weight). The ulcer involved the vulvo-vaginal and perianal area, spreading from the mons pubis to the gluteal folds. It was 14 x 25cm in size, wet, and had an offensive odour. Swabs for

culture were taken at that time, and repeated when indicated.

A chest X -ray was consistent with the clinical findings and sputum tests for acid fast bacilli were positive on three occasions. Diagnoses of pulmonary tuberculosis and infected herpetic ulcer of the vulvo --perianal area were made.

J was started on a course of ethambutol, isoniazid, rifampicin, pyrazinamide (2 months) and isoniazid/rifampicin (6 months), topical aciclovir (applied 5 times/ day), oral aciclovir (400mg 5 times/ day). She was also prescribed Septrin 960mg (as prophylaxis for Pneumocystis carinii), Periactin 4mg daily, antibiotics (depending on growth from swab culture), Fefol and Flagyl powder (applied to the ulcer on initial visit).

On subsequent visits, J developed recurrent episodes of fever over a period of 4 months, which were controlled with paracetamol tablets. During these febrile episodes, a blood culture, malaria parasite screen, Widal test and Treponema pallidum haemagglutination test (TPHA) were done, but all were negative.

Pain control at the ulcer site had been initially achieved with regular intake of paracetamol, but with increasing intensity of pain, this was changed to morphine (5mg 4 hourly and 10mg nocte). J was subsequently maintained pain free on morphine for three months.

Antiretroviral therapy, Combivir (zidovudine + lamivudine) was introduced on the 17th February. Her CD4 count was 2cells/cu.ml, CD8 125cells/cu.ml, viral load 84,125 RNA Copies/ ml and haemoglobin 6.9g/dl. Nelfinavir was later introduced on the 13th April 2000.

In addition to both topical and oral aciclovir, J was treated with teatree oil, silverdiazine cream (for 2 weeks), valaciclovir (for 2 weeks), daily sitz baths and air drying by use of a fan at home, for over a period of five months.

On the 2nd March 2000, the direct use of oxygen at the ulcer site after saline irrigation was introduced. However the wound continued clean but with no signs of skin regeneration until the 16th March 2000 when honey was introduced and applied as a dressing to the wound. Epithelialization occurred by day 7 while remarkable skin regeneration was observed by day 21.

In April 2000, circulating CD4 count was 73cells/cu.ml, CD8 423cells/cu.ml while the HIV RNA levels were less than 400 copies/ ml.

In addition J received intermittent counselling sessions, which helped her through her depression. She had physiotherapy sessions and she and her sister were referred for nutritional advice.

## DISCUSSION

### ACICLOVIR

Both topical (applied 5 times/ day) and oral aciclovir (400mg, five times/ day) had been introduced at the onset of management (05/ 11/ 99). Subsequently, longer courses of aciclovir (or valaciclovir) were prescribed.

A. A study done by the Royal Infirmary, Glasgow, on therapy for genital herpes in the immunocompromised patient concluded that aciclovir treatment failure is more common than hitherto recognised and it is recommended that there should be wider awareness of the use of Foscarnet at an earlier stage in management of resistant herpes simplex virus infection.[3]

B. A study in Australia where valaciclovir was compared to aciclovir in the treatment of recurrent herpes simplex, concluded that valaciclovir maintains the established efficacy and safety of aciclovir but offers a much more convenient twice-daily dosing regimen. Valciclovir is an ester of aciclovir.[4]

### OXYGEN/SALINE IRRIGATION

The use of oxygen on the ulcer was introduced on the 2nd March, 2000. This was applied after a saline irrigation (once a week at the Centre). She had been having daily sitz baths for 3 months at home.

One week later (9/03/2000), it was observed that the edges were dry, but the ulcer remained painful. However by the second week (15/03/2000), the wound looked wet again.These were continued for a further four months and the wound was maintained clean, although healing did not take place.

A. A study in Spain aimed to investigate the use of saline irrigation on the bacterial load on wound surfaces and wound infection rate in an animal model. The study found that after contaminating the wound with Bacillus fragilis and Escherichia coli, aerobic bacterial counts in the wound margins were reduced with saline irrigation.[5]

B. Another study by the University of New York comparing normal saline with tapwater for wound irrigation found that there was a mean reduction in bacterial counts of 86% with saline and 65.3% with tap water.[6]

### FRESH PURE HONEY

On the 16th March 2000, topical application of fresh honey was introduced. It was applied twice a day, starting with the edges first.

By day 7 - the ulcer had shown some epithelialization especially around the mons pubis. It was relatively dry with no signs of inflammation.

By day 14 satisfactory epithelialization was observed all over the ulcer site but for a few septic areas. A swab for culture was taken.

By day 21 -the ulcer had healed remarkably with signs of skin regeneration. Culture of a previous swab revealed Staphylococcus aureus; the patient was commenced on amoxycillin. Topical and oral aciclovir were now stopped.

A. A comparative study on the effect of topical honey and local antiseptics on post operative wound infections

due to gram negative and gram positive bacteria following caesarean sections, revealed that for the patients treated with honey, 84.4% showed complete wound healing without wound disruption or need for resuturing. Only 4% of patients showed mild dehiscence. In the group of patients treated with local antiseptics (ethanol 70% and povidone-iodine) 50% showed complete wound healing, 12 patients showed wound dehiscence and 6 needed suturing.[7]

B. Another study was done on the local application of honey for treatment of neonatal post operative wound infection. Findings revealed the wounds were clean, closed and sterile in all infants after 21 days of honey application. They concluded that honey is useful in the treatment of post surgical wounds that are infected and do not respond to conventional systemic and local antibiotics.[8]

C. A prospective randomised study of wound healing was made on comparable fresh partial thickness burns with honey dressing or silver sulphadiazine in two groups of 25 allocated patients. In the group treated with honey, 100% showed satisfactory epithelialization with histological evidence of reparative activity by day 21. In the group treated with silver sulfadiazine 84% showed epithelialization with reparative activity by day 21. They concluded that with honey dressed wounds, there was early subsidence of acute inflammatory changes, better control of infection and quicker wound healing.[9]

D. A study on the effect of gamma irradiation on the antibacterial activity of honey revealed that there was no significant change found in the anti bacterial activity following sterilization. The sterilization was also sufficient to eradicate clostridia spores, allaying fears of wound botulism.[10]

## CONCLUSION

In conclusion we discuss the topical application of fresh honey in resistant herpetic ulcers and on any ulcer/ wound that may have proven difficult to treat or slow to heal irrespective of the cause.

The use of aciclovir is virostatic and suppresses the resurgence of the virus, but whilst this is being achieved, it is necessary to facilitate the healing process of the ulcer.

In this patient, the topical use of honey achieved rapid epithelialization, no inflammation and obvious skin regeneration by the third week, indicating the remarkable healing qualities of honey.

It is noteworthy that the acute - phase rapid increase in circulating CD4 cells occurred within eight weeks of antiretroviral therapy.

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