The utilisation of maggot debridement therapy in Pretoria, South Africa

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Keywords: maggot debridement therapy, wound care, Pretoria

Abstract

Maggots are known to clean wounds by removing slough and dead tissue. This was put to therapeutic use in the last century, between the world wars, when it was in use in at least 300 hospitals in the United States and being prescribed by at least 1 000 doctors. Antibiotic use replaced it for a while, but the emergence of antibiotic resistance has led to a renewed interest in maggot debridement therapy.

Maggot treatment works on three levels: debriding dead and necrotic tissue by extracorporeal digestion, disinfection by the secreted enzymes and the stimulation of wound healing.

We have access to a maggot laboratory at the Steve Biko Academic Hospital in Pretoria, where maggot therapy is frequently used to debride and clean wounds. The results are at least comparable to other modalities of wound debridement, and can be used on patients who are high-risk candidates for general anaesthesia, and also when a shortage of beds in the hospital prevents admission for inpatient treatment.

℗ Peer reviewed. (Submitted: 2011-05-31, Accepted: 2011-09-15). © Medpharm
Wound Healing Southern Africa 2011;4(2):80-83

Historical overview

Maggot therapy was frequently mentioned in historical papers by surgeons caring for soldiers in battles. Ambroise Pare, Baron Larrey, Napoleon's surgeon, and others[1,2,3] noted that wounds infested by maggots on arrival at the treatment facility looked healthy and clean, compared with other wounds which were frequently septic and draining pus. The treatment of these septic wounds was amputation of the limb proximal to the injury, to control the infection before it killed the patient. During the American Civil War, a Confederate medical officer, Dr Joseph Jones, was quoted as saying "I have frequently seen neglected wounds … filled with maggots … as far as my experience extends, these worms only destroy dead tissues, and do not injure specifically the well parts. I have heard surgeons confirm that a gangrenous wound which has been thoroughly cleaned by maggots heals more rapidly than if it had been left to itself."[1] Another Confederate surgeon, J Zacharias, observed that "maggots … in a single day would clean a wound much better than any agents we had at our command … I am sure I saved many lives by their use."[1, 3]

The first publications on the effect of maggot therapy came from Prof William Baer, an orthopaedic surgeon, who saw the effect of maggots on wounds during the First World War.[4, 5] When he was appointed at the Johns Hopkins Hospital in Baltimore, Maryland, he used maggots to treat some children with osteomyelitis. The wounds were cleared of infection and healed within six weeks. This finding, which was presented in 1929[5] and published in 1931,[4] started the widespread use of maggots in North America. Within 10 years maggots were being used by at least 1 000 doctors in over 300 hospitals, across the USA and Canada.[3] Some hospitals had their own maggot laboratories, but maggots were also commercially available from a pharmaceutical company, Lederle, at the grand fee of $5 for 1 000 maggots (equivalent to $100 in 2000).[3] Maggot therapy became so popular that more than 100 scientific papers were published on the subject in the decade 1930 to 1940, mostly anecdotal cases on the efficacy of maggot treatment.

With the development of antibiotics during and after the Second World War, maggots fell into disuse for a period, until the therapy was rediscovered in the 1980s, when microorganism resistance against antimicrobial therapy became a problem. A study conducted with maggots on lower leg ulceration at the VA Medical Centre at Long Beach, California and the University of California, Irvine in 1989,[6] showed its efficacy in this group of patients, and a renewed interest in maggot therapy began.[7] Once again a need for maggots stimulated the development of a commercial venture, and medicinal maggots are now produced in the USA by Monarch Laboratories.

Maggot therapy has been registered in the USA by the Food and Drug Administration[8] since January 2004 for "debriding of non-healing necrotic skin and soft tissue wounds," and also in the United Kingdom since February 2004 for use in the National Health Service. It is also used in Israel, Sweden, Germany, Switzerland, Austria, Thailand and Canada.[8] There is no formal registration in South Africa for the use of maggots on wounds.

Wound debridement

All chronic and infected wounds need to be cleaned before healing can take place. This may be a simple process like washing of the wound with water or saline but, with dead tissue present, debridement may be needed. This can be done surgically with scalpel and scissors (and patients may require analgesia or anaesthesia of some sort), mechanically (irrigation with water or with the Versajet®), chemically (with enzymatic ointments), with wet or dry dressings or maggot therapy.[9] The latter has distinct advantages over the others, but also limitations on its use. The advantages are that debridement can be done very accurately as no normal tissue is injured or removed,[10] and it can be done on an outpatient basis. The disadvantages are that it takes time and is not appropriate when a large volume of dead tissue is present.

Maggot production

The fly species most commonly used for maggot therapy is the green bottle blowfly, *Phaenicia* (syn. *Lucilia*) *sericata*, as the maggots live only on dead and necrotic tissue. The larvae of some other species also digest living tissue, which can lead to the destruction of normal host tissue. This fly lays its eggs on carrion (or special feeds) in a warm, dark, moist environment where they hatch in 18 to 24 hours, producing larvae 1–2 mm in size. They immediately start feeding on the food available and grow to a length of 8–10 mm in four to seven days, when they form pupae in a dry area. If circumstances allow, the adult fly emerges from the pupa in 10 to 20 days, and the cycle repeats itself (Figure 1).

The flies may be kept in a laboratory environment in isolation cages,[11] and can be stimulated to lay eggs when fed a special diet of liver (to simulate carrion). The eggs are isolated and sterilised with an antiseptic before hatching to ensure that no infection is transferred to the wound. After hatching, the maggots can be put on the wound directly, or in a cage to confine them to the wound area.

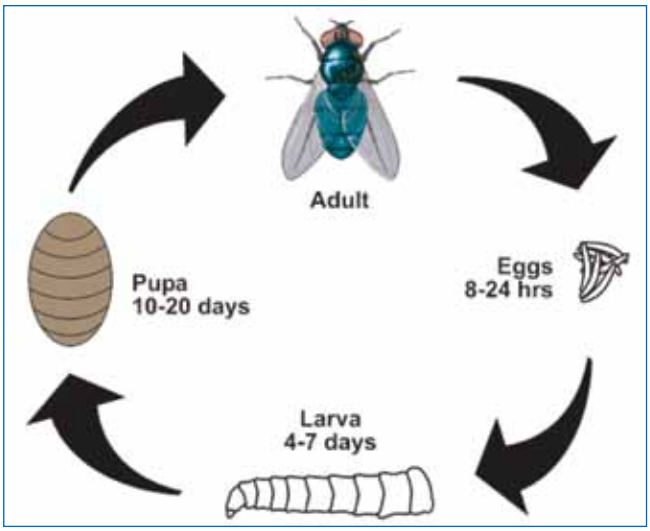

Figure 1: The life cycle of the green bottle blowfly

Mechanism of action

The maggots have an effect on the wound on three levels, namely debridement of necrotic tissue, bactericidal action on microorganisms present in the wound, and stimulation of wound healing.[2,3,8,12]

The *debriding action* on the wound is caused by the extracorporeal secretion of digestive enzymes by the maggots, which digest the carrion or dead tissue before it is ingested by the larvae. These enzymes contain carboxypeptidases A and B, leucine aminopeptidase, collagenase, serine proteases and metalloproteinases, which break down different components of the dead tissue present. These enzymes are resistant to protease inhibitors secreted by the wound,[13] thereby allowing debridement and digestion to take place. The volume of dead tissue present will have an effect on the speed of this process, and on the frequency of larval changes required. As the larvae live for only four to seven days, dressing changes are scheduled twice weekly or every third or fourth day. As soon as the wound is clean with no slough present, other dressings are used until the wound has healed.

The *bactericidal action* of the maggots is caused by the secretion of allantoin, urea, phenylacetic acid, phenylacetaldehyde, calcium carbonate and other enzymes, which are antimicrobial, especially against methicillin-resistant *Staphylococcus aureus* (MRSA, the most common organism in wounds).[8,14–17] Other organisms are also killed by these acids and chemicals.[15] Even the biofilm created by *S. epidermidis* is disrupted by the secretions from the maggots.[18] Furthermore, bacteria are ingested by the maggots and killed in the foregut and midgut by the proteolytic enzymes secreted in the gut.[19]

Wound healing is promoted[12,14] by the secretion of ammonium bicarbonate, creating an alkaline environment that stimulates the *formation of granulation tissue.* The secretion of ammonia, urea and allantoin also has a stimulatory effect on the host epidermal growth factor and interleukin 6, which in turn promotes the growth of fibroblasts, chondrocytes, type II collagen and the formation of granulation tissue. These substances may have a vasodilatory effect on the blood vessels as well, because the tissue oxygenation is improved and wound oedema is decreased, probably by improving the blood supply and venous drainage to the wound area (Figure 2).

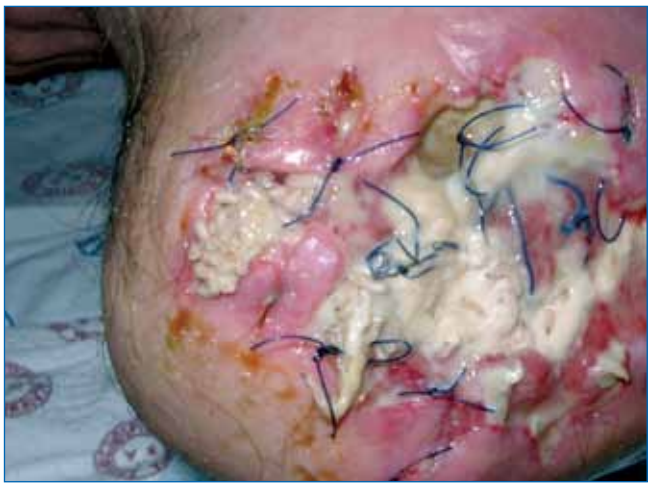

Figure 2: Septic below-knee amputation stump undergoing maggot therapy

Maggot therapy in Pretoria

Maggots were first kept in Pretoria by a private laboratory for use on a very small scale. The laboratory was taken over by

Figure 3: A fly cage covered with nylon netting to prevent the flies from escaping

Figure 4: Flies feeding on whey protein

Dr Frans Cronje in 1999 and moved to the Eugene Marais Hospital as part of the Wound Care Unit that was established there, and which included hyperbaric oxygen facilities. When Dr Cronje left Pretoria in 2007, the laboratory was donated to the Department of Surgery, University of Pretoria, at the Steve Biko Academic Hospital for the use by patients in this institution. The laboratory functioned under the guidance of Prof Jan Pretorius (a surgical intensive care specialist and head and neck surgeon) until the Wound Care Division was formed at the Department of Surgery in 2010.

The flies of our colonies are of two different strains of *L. sericata*,[20] also known as Welkom 1 and 2. They are kept apart in different glass cages, but the maggots are used in similar fashion. The flies are slightly smaller than the those of the wild species, probably because of a long period of inbreeding (Figures 3 and 4). *L. cuprina* is very similar in appearance to *L. sericata,* but also feeds on live tissue, and is known as the "sheep blowfly" because it is responsible for flystrike in sheep, a form of myiasis that can kill sheep. A recent paper from Malaysia shows that *L. cuprina* may be used on patients without untoward effect.[21]

The technologist looking after the flies and maggots is Ms Johanna Legodi, who started with the private laboratory in the 1990s, and moved with the flies until they ended up at Steve Biko Academic Hospital. She still takes care of her flies, feeds them and stimulates them to lay eggs. She isolates the eggs and sterilises them before hatching, gathers the maggots together, places them on the wounds and applies the covering dressing. The wounds remain closed for three to four days, and dressing changes are carried out at the hospital at the Wound Clinic during follow-up. At dressing change, the covering dressing is removed, the wounds are washed to remove the residual maggots, new maggots are placed on the prepared wound for a further period of three to four days if necessary, and the wound is covered with a fresh dressing. The dressing should exclude light but must not be airtight, as the maggots need oxygen to survive. Occlusive dressings with plastic sheeting are therefore not indicated.

Maggot debridement therapy is not painful. On the contrary, patients frequently mention that the pain in the infected wound disappears during treatment. Some of them report "awareness" of the maggots with a tingling sensation in the wound area. One may also see the improvement of the cellulitis around the wound, even after a single maggot application. If the wound remains painful during treatment, one must look for another cause, such as ischaemia, neuropathy or underlying osteomyelitis.

Maggot debridement is used only until the wound bed is cleared from all necrotic tissue. Thereafter other dressings are used until healing is complete, or a split skin graft is performed. In our experience, very few patients are grafted and most continue with dressings until the wound has healed.

Results

Since the initiation of maggot therapy at our hospital, a total of 255 treatments have been applied to 108 patients. Therapy started slowly but gradually increased as personnel became aware of the existence of the Maggot Laboratory. In 2010 a total of 87 treatments were applied to 27 patients, with an average of three applications per patient, but it varied between one and eight applications (Figure 5).

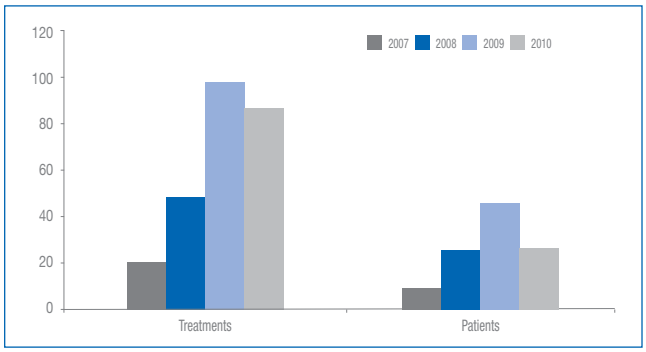

Figure 5: Annual numbers of maggot treatments at Steve Biko Academic Hospital since 2007

A large number of our patients suffered from concomitant diseases, such as diabetes (66%) and hypertension (30%). A third (35%) had had a previous amputation of a toe with wound sepsis, needing maggot debridement because of being a poor risk for anaesthesia. One of five (18%) such patients ended with a higher level of amputation where maggot debridement therapy was not effective in controlling the infection. A further 20% of patients died during or after treatment, mostly from cardiac complications. Two patients developed septic wounds following mastectomy and were successfully treated with maggots.

Our success rate in cleaning the wounds is 80%, which is comparable to the figures in the literature. We measured success as the removal of at least 80% of the slough that was present when therapy was initiated. When the wounds were cleaned, we changed to standard dressings to continue treatment until wounds were healed or skin-grafted. Reports in the literature are mostly case studies,[6,8,10,16,21,22] with the prospective studies usually comparing different modalities. The VenUS II study compared maggots with hydrogel, and found no difference in cost or healing time, even though the maggot debridement time was shorter.[23] Another study showed a success rate of 67% in high-risk patients [American Society of Anesthesiologists (ASA) grade III and IV] with infected gangrenous wounds.[24] They defined success as complete and almost complete healing of the wounds. They found that the outcome was influenced by the degree of chronic ischaemia, depth of the wound and age of the patient. The factors that did not influence healing were gender, obesity, diabetes, smoking, ASA classification, wound location, wound size and duration of wound.[24]

Our failure rate was 20%, and was made up of patients that had to be amputated proximal to the wound. Causes for failure were mostly chronic ischaemia (inadequate blood supply to sustain healing) and chronic osteitis.

Indications for maggot debridement therapy

The initial indication for the use of maggot debridement therapy was for any open wound failing two or more conventional treatments. Contraindications were stated as any rapidly advancing infection (that would need close observation or surgery) or inability to obtain informed consent. Relative contraindications were osteomyelitis (even though Prof Baer used maggots on these patients in the 1920s) and arterial insufficiency. The indications for registration in the USA are "for the debridement of non-healing necrotic skin and soft tissue wounds, such as pressure ulcers, neuropathic foot ulcers, chronic leg ulcers, or non-healing traumatic or post-operative wounds." This is stated on the package insert of Monarch Laboratories.[9]

We use maggots in Pretoria on selected wounds that need debridement. The therapy is especially useful in patients who can be treated as outpatients, when a shortage of beds precludes admission for in-hospital treatment, and also in patients having co-morbidities that make them high-risk candidates for anaesthesia. A large percentage of diabetic patients fall into this category and we have found it easy to manage them on an outpatient basis. Maggot debridement will not replace surgical debridement, as surgery will still be needed when the wounds are large, the volume of necrotic material is high, or when amputation is indicated.

Conclusion

We have an asset in the Maggot Laboratory at Steve Biko Academic Hospital, which gives us the ability to treat patients with maggots to debride certain septic wounds. This therapy is a cost-effective alternative available to our patients who can be treated as outpatients, saving on hospital admissions and bed space. It is also an effective alternative to surgical debridement in patients with co-morbidities that make them a high risk for general anaesthesia.

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