

Maggot therapy in Pretoria, South Africa: an update

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Abstract

Maggots are known to clean wounds by removal of slough and dead tissue. This was put to therapeutic use in the last century between the great wars, where it was in use in at least 300 hospitals in the United States being prescribed by at least 1 000 physicians. Antibiotic use replaced it for a while, but resistance caused a renewed interest in maggot debridement therapy.

Maggot treatment works on three levels by debriding dead and necrotic tissue with a process of 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.

Since a private company became interested in rearing maggots, the treatment is now also available to a wider group of patients who may need debridement.

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Introduction

Maggot therapy was frequently mentioned in historical papers by surgeons caring for soldiers in battle circumstances. Ambroise Pare in the 16th century, and Baron Larrey, Napoleon's surgeon, and others^{1,2,3} mentioned the fact 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 quoted¹ 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". 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^{4,5} on the effect of maggot therapy came from Professor William Baer, an orthopaedic surgeon, who saw the effect

of maggots on wounds during the First World War. 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 was presented in 1929,⁵ and published in 1931,⁴ and started the widespread use of maggots in North America. Within 10 years maggots were being used by at least 1 000 physicians in over 300 hospitals³ spread over the USA and Canada. 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,^{3,14} until the therapy was rediscovered in the 1980s, when microorganism resistance against antimicrobial therapy became a problem. A study done in 1989 at the VA Medical Centre at Long Beach, California, and the University of California, Irvine,⁶ with maggots on lower leg ulceration showed its efficacy in this group of patients, and renewed interest in maggot therapy⁷ began. 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 FDA⁸ since January 2004 for “debriding of non-healing necrotic skin and soft tissue wounds ...”, and also in the UK since February 2004 for use in the NHS. It is also used in Israel, Sweden, Germany, Switzerland, Austria, Thailand and Canada.⁹ 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 can be a simple process like washing of the wound with water or saline or, with dead tissue present, debridement may be needed. This can be done surgically with scalpel and scissors (and may need analgesia or anaesthesia of some sort), mechanically (irrigation with water or with the Versa jet), chemically (with enzymatic ointments), or with wet to 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 indicated 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, *Phoenicia* or *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 of 1–2 mm. 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 comes from the pupa in 10 to 20 days, and the cycle repeats itself (Fig 1).

The flies can be kept in a laboratory environment in isolation cages¹¹ 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.

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 extra-corporeal 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 needed. 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, phenyl acetic acid, phenyl acetaldehyde, calcium carbonate and other enzymes, which are antimicrobial, especially against MRSA (the most common organism in wounds).^{8,14,15,16,17}

Other organisms are also killed by these acids and chemicals.¹⁵ Even the biofilm created by *Staphylococcus 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 IL 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 (Fig 2).

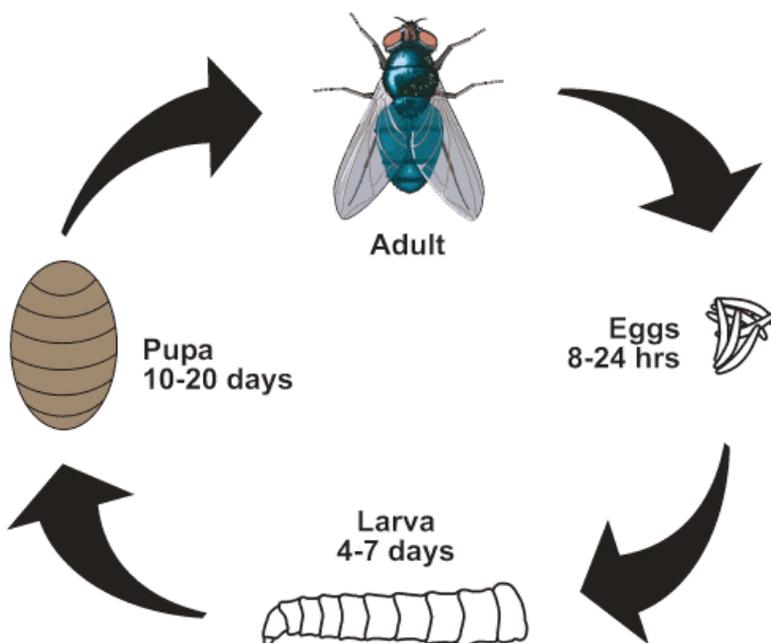


Figure 1. Life cycle of the green bottle blowfly (Credit: Dr R Sherman, Director of BTER Foundation)



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 Maggot Laboratory was taken over by Dr Frans Cronje in 1999 and moved to the Eugene Marais Hospital as part of the Wound Care Unit that was established there (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 use by patients in this institution. The laboratory functioned under the guidance of Professor Jan Pretorius (a surgical intensive care specialist and head and neck surgeon) until a Wound Care Division was formed in the Department of Surgery in 2010.

The flies of our colonies are of two different species of *Lucilia 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 species living in the wild, probably because of a long period of inbreeding (Figs 3 and 4). *Lucilia 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 fly-strike in sheep, a form of massive myiasis that can kill sheep. A recent paper from Malaysia shows that *L. cuprina* can 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 maintains the colony by feeding and caring, and stimulation to lay eggs when needed. She isolates the eggs and sterilises them before hatching, gets the maggots together, places them on the wounds and places the covering dressing. Wounds remain closed for three to four days, and dressing changes are done at the hospital in the Wound Clinic during follow-up. At dressing change, the covering dressing is removed, the wounds are washed to remove the residual maggots. If necessary, new maggots are placed on the prepared wound for a further period of three to four days, 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.



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



Figure 4. Flies feeding on whey protein

Maggot debridement therapy is not painful. On the contrary, patients frequently mention that the pain in the infected wound clears up during treatment. Some of them note "awareness" of the maggots with a tingling sensation in the wound area. One can 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 done. 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 (Fig 5).

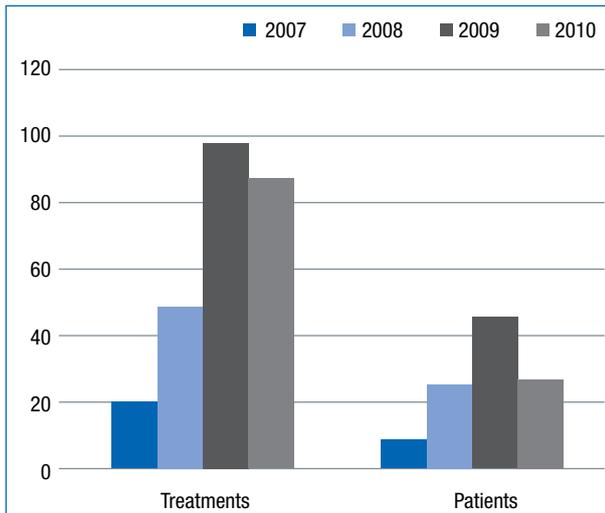


Figure 5. Numbers of maggot treatments at Steve Biko Academic Hospital since 2007, per year

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} where the prospective studies usually compare different modalities. The VenUS II study²³ compared maggots with hydrogel, and found no difference in cost or healing time, even though the maggot debridement time was shorter. Another study²⁴ showed a success rate of 67% in high risk patients (ASA grade III and IV) with infected gangrenous wounds. 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 or 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.

Contra-indications were stated as any rapidly advancing infection (that would need close observation or surgery) or inability to obtain informed consent. Relative contra-indications were osteomyelitis (even though Professor Baer used maggots on these patients in the 1920s) and arterial insufficiency. The indications used 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 comorbidities 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.

Developments in the past five years

We lost our fly colony on two occasions during the past five years after some fly wasps found access to them. Once the colony was replaced from flies accessed by Dr Cronje, and the second time we had pupae donated from Dr Ron Sherman from Monarch Laboratories in Davis, California. As *Lucilia sericata* is endemic worldwide, we did not need permission from the government to import the pupae. They survived the 48 hour flight and thrived in our environment. We had to close and sterilise the laboratory before starting afresh. During these periods without larvae we could not treat any patients.

A private company, Inqaba Biotechnical Industries, which specialises in biological products, became interested in the maggots, and started to produce maggots commercially to supply to the private sector. Through a cooperative agreement between the University of Pretoria,

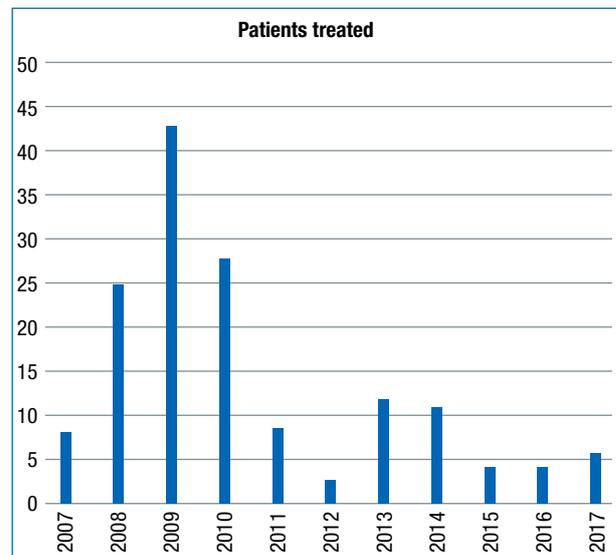


Figure 6. Patients treated with maggots over 11 years. In 2012 and 2015 the colony died and we did not have any maggots for treating patients.

Inqaba Biotech and Entomos (a Swiss company that supplies maggots in Europe) they are rearing maggots at their facility in Pretoria, and distribute them through their channels to whoever needs them in South Africa. They were also able to register the maggots with the NAB (NAPPI Advisory Board) for a NAPPI (National Pharmaceutical Product Index) code to enable billing for the supply of the maggots to patients. Some of the larger medical funds are prepared to pay for maggot debridement therapy since the registration. Their maggots are produced under the name SURGIMAGGS.²⁵

A recent review article²⁶ looked at 93 published papers to assess the validity of claims that were anecdotally made. The evidence shows that maggots do debride wounds efficiently, but the claims for improved wound healing need further study.

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 comorbidities that make them a high risk for general anaesthesia.

Maggot debridement therapy is now also available on a much larger scale to any patient in South Africa for treatment of difficult wounds. This is true for both private and public sector patients as Inqaba can supply the whole of Southern Africa.

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