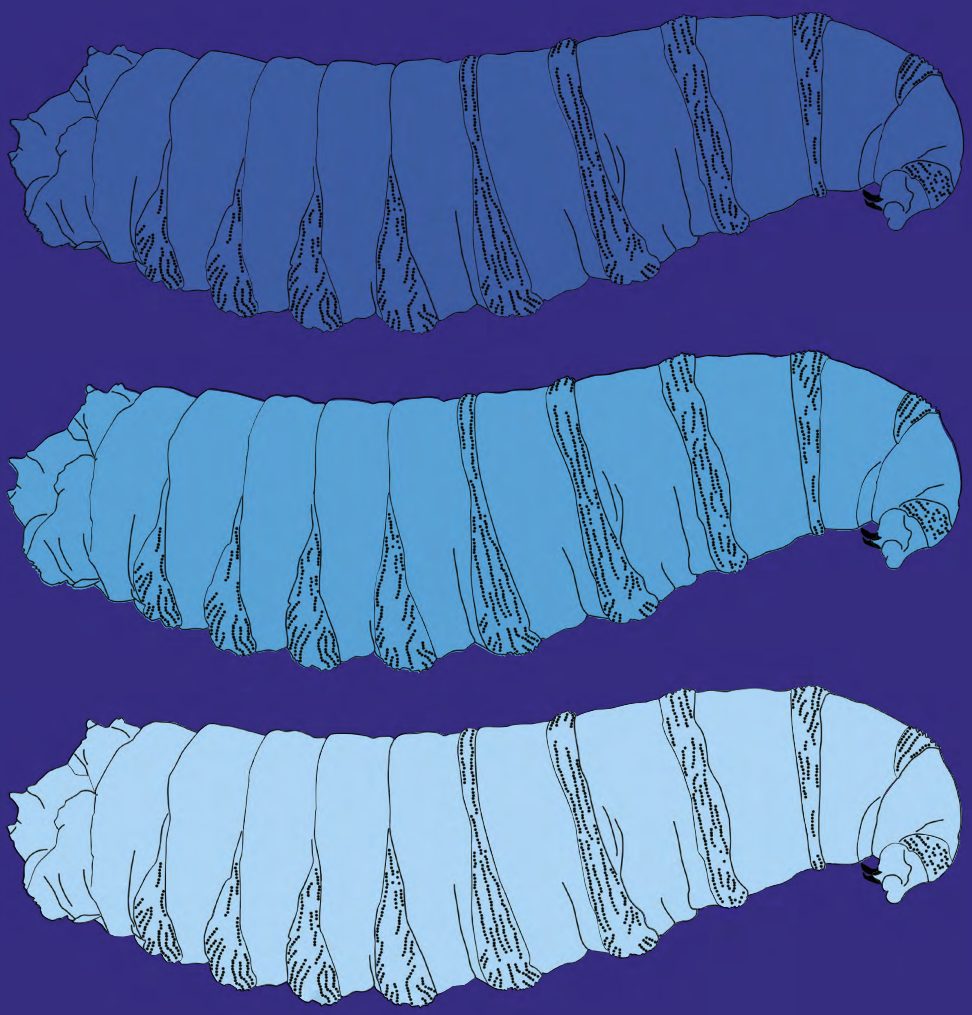
A COMPLETE GUIDE TO MAGGOT THERAPY

Clinical Practice, Therapeutic Principles, Production, Distribution, and Ethics



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Cover image: Line drawing of a green bottle blowfly (*Lucilia sericata*) maggot by Frank Stadler (2022), CC BY-NC. Cover design by Katy Saunders.

4. Indications, Contraindications, Interactions, and Side-effects of Maggot Therapy

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Maggot therapy is not regulated in most countries, but in those countries in which it is regulated, indications authorised by regulating bodies are the law of the land. Irrespective of particular jurisdictional limitations, this chapter describes when maggot therapy can be used, when it can't be used, potential adverse events, and when treatment can proceed with caution. The chapter also examines how medicinal maggots interact with concomitant treatments such as systemic antibiotics, anaesthetics and narcotics, or hyperbaric oxygen therapy. Evidence and expert advice suggest that maggot therapy is a safe and widely applicable wound care modality with few side-effects, most of which can be avoided or successfully managed.

Introduction

The terms "indications" and "contraindications" are short-hand for: when should maggot therapy be used and when should it not be used? When deciding whether or not a medical product should be used, it is critical to keep in mind *who* is issuing the recommendations. For the purposes of the following discussion, two groups of authorities will be referenced: regulators and experts. Maggot therapy is not regulated in

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most countries, but in those countries in which it is regulated (primarily North America, much of Europe, and several countries in the Middle East and Asia), indications authorised by regulating bodies are the law of the land. Indications issued by regulatory agencies tend to be more restrictive, and the use of maggot therapy for anything other than what is specifically authorised is considered "off-label". Off-label use of a product by a licensed care provider is not illegal, but it does put one at legal or professional risk if it is not in keeping with standard-of-care practice by one's peers and licensing boards. In countries where maggot therapy is not formally regulated, therapists are free to follow the advice of experts. In this chapter, indications recommended by experts but not approved by regulatory agencies will be clearly identified.

Indications for Maggot Therapy

As described in Chapters 8 to 10, medicinal maggots have been found to debride wounds, kill microbes, and stimulate wound healing [1–3]. Therefore, many experts around the world use maggot therapy for any or all of those purposes. In those countries where maggot therapy is regulated by health ministries, maggot therapy is approved only for wound debridement. Specific examples will follow.

Debridement

Wound debridement is the removal of dead (necrotic) tissue and debris from the wound. Sharp debridement with scalpels removes dead tissue mechanically, by cutting it out. Enzymatic debriding ointments remove the dead tissue by enzymatically dissolving it [4]. Necrotic tissue can also be removed by blasting it with a jet of water (hydrosurgery) [5] or with pulses of ultrasound [6]. Autolytic debridement involves dressings which potentiate the body's own mechanisms (mostly enzymatic) to dissolve and discharge the dead tissue [7]. Maggot therapy rids the body of necrotic tissue and debris by both mechanical pathways (the physical action of the maggots' cuticular spines and mouth hooks) and enzymatic pathways (liquefaction of the necrotic tissue by the maggots' secreted and excreted digestive enzymes).

In the U.S., where medicinal maggots are regulated by the Food and Drug Administration (FDA), cleared indications are for "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." These indications broadly cover a variety of necrotic and non-healing wounds, such as those described in Chapter 3 [8]. FDA-cleared indications noticeably exclude the debridement of "hard tissue" (bone) as well as the use of maggots for anything other than debridement. Yet, many experts will sometimes resort to maggot therapy when certain modalities fail to achieve adequate disinfection or wound healing, whether or not debridement is also a major goal.

Disinfection

Microbial infection is a common feature of chronic wounds. If not already infected, most non-healing wounds will eventually become infected by invading bacteria or fungi. After all, necrotic tissue, by definition, has no circulation and no defence against microbial invaders, and it provides a moist, nutrient-rich substrate for microbial growth. As has been discussed in Chapter 9 [2], medicinal maggots kill a wide variety of microbes through ingestion and through the secretion of antimicrobial compounds, which is why maggot therapy is commonly used to debride infected necrotic wounds, and to treat chronic wounds whose primary problem is non-gangrenous infection. Chronically infected wounds are typically characterised by drainage, pain, and bad odour. When treated with maggot therapy, all three of these characteristics substantially decrease or resolve.

Examples of infectious complications that are not easily treated with antibiotics include wounds populated by multi-resistant organisms or biofilm. There are now multiple laboratory studies of maggots' antimicrobial activity, but relatively few controlled clinical studies. Still, a few controlled studies and several case series demonstrate clinically relevant antimicrobial effects of maggot therapy [9–18].

Growth Stimulation

For nearly 100 years, maggot therapy has been observed to enhance wound healing, even in apparently clean but stagnant wounds. Clinicians and researchers have described the rapid proliferation of granulation tissue and hastened closing of the wound margins in

previously stagnant, non-healing wounds [19–23]. The mechanisms by which growth stimulation and wound healing are enhanced by maggot therapy are described in Chapter 10 [3]. As a result, some therapists consider non-healing wounds—even those without necrotic tissue or obvious infection—to be appropriate candidates for maggot therapy.

Additional Situations

Maggot therapy is also useful for situations that may not fit neatly into the specific categories of debridement, disinfection and wound healing. Maggot therapy may be used for two or three of these indications simultaneously, and it may be used for non-healing wounds with no obvious infection or gangrene. Often therapists turn to maggot therapy only after conventional therapy has failed or is unavailable. In published studies of patients who failed conventional wound care and were scheduled for amputation but given a trial of maggot therapy instead, at least 50% of those patients healed their wounds and avoided amputation [24]. This has led many therapists to believe that a non-emergency amputation due to a non-healing wound may itself be an appropriate indication for a trial of maggot therapy. Of course, outcomes are even better when wounds are treated with maggot therapy before they progress to the point (and the underlying circulatory status has regressed to the point) that they are earmarked for amputation.

Maggot therapy is useful in treating wounds that are undermined, difficult to visualise, or connected to inner-body cavities [22]. Ordinarily, such wounds might be opened widely ("surgically filleted") to view them completely before cleaning them out. When that is not feasible without significant damage to nearby vital structures, some therapists apply medicinal maggots to the wound entrance so that they will explore the entire inner cavity, looking for and dissolving infected, necrotic tissue. Since medicinal maggots are obligate air breathers and since their natural instinct is to leave the host when satiated or when there is nothing more to eat, they can be considered self-extracting.

Maggot therapy is also indicated for patients who would benefit from surgical debridement but are too frail [22]. Even patients at the end of life or with wounds unlikely to heal can benefit from maggot therapy, if they are suffering from chronic wounds that are painful, draining,

malodorous, or require resource-intense treatments [25]. Since maggot therapy can be applied by non-professionals and outside of medical facilities, many patients with non-healing wounds who lack access to such resources are appropriate candidates for maggot therapy [26–28].

Contraindications and Relative Contraindications for Maggot Therapy

There are relatively few absolute contraindications for maggot therapy. One soft-tissue wound to which they must not be applied is a corneal ulcer, because the maggots' cuticle and mouth hooks are likely to scratch and damage the corneal surface. Maggots are obligate air breathers, so they cannot be placed within a closed cavity, such as an abscess. However, if that abscess is opened and allowed to drain, the maggots could be placed on the surface of the drained abscess, if desired. Maggot therapy is generally contraindicated for sterile cavities, but most sterile cavities should have no reason to undergo maggot debridement.

The anatomy and location of the wound can affect dressing selection, but generally is not itself a contraindication, except as described above. For example, a toe or anterior foot wound cannot easily be covered with a sheet of net fabric to confine the maggots because affixing it to the surrounding tissue would result in multiple wrinkles and tunnels through which the maggots might escape. In this case, a stocking-like dressing might be used instead, and affixed proximally to the foot or ankle. Similarly, a wound very near to an orifice might be of concern if the maggots posed a danger to that particular orifice (mouth or tracheostomy, for example). Again, this may be a contraindication to a dressing that requires a sizeable border to adhere to the periphery of the wound, but need not be a contraindication to maggot therapy in general, because a different dressing could be used: maggots contained within a bag [29].

Rapidly advancing, life- or limb-threatening infections are not appropriate for maggot therapy. In these cases, the standard of care is surgical resection and broad-spectrum antibiotics. Maggot therapy is not appropriate, even in combination with first-line surgical and medical therapy, if it will interfere with the critical close and frequent observation of the wound. Once stabilised, maggot therapy may be

appropriate to debride the necrotic tissue without harming nearby vital structures [22, 30–34].

Maggot therapy is generally reserved for skin and soft-tissue wounds; maggot secretions do not dissolve tendons, fascia or bone efficiently. That said, when surgical resection is not feasible because of patient frailty, or lack of surgical expertise in compromised healthcare settings, maggot debridement of wounds that include necrotic harder tissues can be quite useful [22, 35–37].

Because maggots are aerobic creatures, they are susceptible to drowning and suffocation. Maggot dressings must be highly permeable to air, and allow the efflux of purulent drainage. Medicinal maggots must not be covered by occlusive dressings (i.e., "semi-permeable" transparent membranes, hydrocolloid and hydrogel pads, etc.) or else they will die. They may also suffocate if applied to wounds along with ointments (petroleum jelly, zinc oxide, silver sulfadiazine, triple antibiotic ointments, etc.), if the oily substance covers the maggots' breathing holes (spiracles).

Interactions between Maggot Therapy and Other Treatment Modalities

The viability and debridement capacity of medicinal maggots have been tested under a wide variety of conditions. Under controlled laboratory conditions, medicinal maggots fed increasing concentrations of antibiotics were found not to be affected by pharmacologic doses of any of the tested antimicrobials [23, 38]. Insecticides, however, can be lethal and should not be used during or within two half-lives prior to application of medicinal maggots. Hyperbaric oxygen therapy (HBOT) has been shown to be lethal to very young larvae, but not to older larvae [39]. Therefore, for patients receiving HBOT, maggot therapy should be administered during the non-diving days or else the larvae should be late-second or early-third instars before the patient re-enters the HBO chamber. As discussed in more detail elsewhere in this chapter, bleeding can sometimes occur with maggot therapy. Blood thinning medication puts those patients at increased risk for more significant blood loss (haemorrhage).

Some drugs—especially drugs of abuse—may be present in the blood or tissue without the awareness of the therapist and maybe even without the complete awareness of the patient. Maggot growth and survival has been assessed in the presence of a variety of narcotics and anaesthetics [40–42]. While most of these will have some effect on the larvae, they are generally not lethal in the doses tested, and medical maggots should still do their job.

Most other contraindications are really "relative contraindications". In other words, the benefits of maggot therapy must be weighed against the risks (which we call "adverse events"). Those risks may be greater in some patients than in others... so great as to be considered a contraindication to maggot therapy. We will discuss such relative contraindications within the context of the underlying adverse effects.

Warnings and Adverse Events Associated with Maggot Therapy

All things considered, there are relatively few serious complications associated with maggot therapy (Table 4.1), and they are certainly not as serious nor as numerous as those that can result from the wounds themselves, in the absence of maggot therapy. The best way to avoid these adverse events is to understand the patient and their medical history, understand the nature of maggot therapy, and to read all package inserts carefully *before* using the products. In this way, adverse events can often be avoided or their risks minimised. For example, by reading the package insert it might be discovered that one of the ingredients is something to which the patient may be allergic. This could be a contraindication to therapy. But if the therapist identifies the problem in advance, a special preparation can probably be made to avoid that ingredient, thereby eliminating the contraindication.

The most common adverse event associated with medicinal maggots is wound pain. Discomfort or pain has been reported in anywhere from 5–30% of patients already experiencing wound pain [21, 43–47]. Maggot-associated pain or discomfort usually does not manifest until about 24 hours into the therapy, but then increases as the larvae grow larger. Patients that are at risk of experiencing pain can easily be identified (and prepared) in advance, because they are the patients with painful wounds

Table 4.1 Adverse events and contributing factors (after Sherman [43]).

Adverse Event or Complication	**Contributing Causes**	**Treatment**
Pain	Pre-existing wound pain; large larvae.	Liberal analgaesics; remove the larvae for immediate pain relief.
Infection	Pre-existing wound infection; inadequate maggot dosage; inadequate disinfection of larvae.	Suppress *Pseudomonas aeruginosa* with topical antiseptics prior to maggot therapy; concurrent antibiotics; check adequacy of larval disinfection.
Hepatic encephalopathy or other mental status changes	Underlying hepatic insufficiency; high maggot burden; sepsis.	Check for bacteraemia, serum ammonia; remove maggots.
Excessive bleeding	Coagulopathy; necrosis involving major vessel.	Remove maggots; find and stop source of bleeding.
Hypersensitivity reaction (local or systemic)	Allergy to medicinal maggots (i.e., their media) or the dressings.	Check beforehand; remove immediately and treat reaction.
Tissue invasion	Inappropriate species.	Remove maggots; check species.

who already receive analgaesics during dressing changes or maybe even constantly. Patients should be given liberal access to analgaesics during maggot therapy and offered the opportunity for early removal of dressings upon their request. If systemic analgaesics no longer control the pain, remove the maggot dressing to achieve immediate relief. With these two provisions, patients often cope much better with therapy-related pain and are more satisfied with their experience, even if they do have pain (personal experience).

Patients may be allergic to fly larvae, their media, or the accompanying dressing components. Patients allergic to the maggots or dressing materials may manifest contact dermatitis or more serious immunologic reactions. Patients known to be allergic to media ingredients should not be treated with those constituents; alternatives usually can be substituted. When in doubt, communicate with the manufacturer.

Pseudomonas aeruginosa and some other hardy gram-negative organisms appear to be more resistant to maggot therapy than other microbes [48]. Situations have been reported in which a *P. aeruginosa* infection has actually spread through the wound during maggot therapy. Some experts believe this may occur as a result of maggot-induced killing of the other microbes, leaving the *P. aeruginosa* to grow without competition. When treating wounds with *P. aeruginosa* infection or colonisation, it is recommended that topical anti-pseudomonal antiseptics (i.e., acetic acid, sodium hypochlorite, etc.) be applied for a day or two before maggot debridement, to decrease the *P. aeruginosa* population. Also, a greater density of maggots in the wound is more effective in killing *P. aeruginosa* [48]. Therefore, a high dose of maggots (10+ larvae/cm^2) should be applied when treating wounds suspected of harbouring this organism.

Mild bleeding is common during maggot debridement, and it is common that the wound drainage is blood-tinged. However, patients with coagulopathy (inability to form blood clots and halt bleeding) are at risk of more substantial bleeding. Maggot therapy in such individuals should only be performed under close supervision [22, 49]. Maggot debridement of, or around, necrotic blood vessels may also lead to life-threatening blood loss if and when those vessels dissolve under the influence of maggot excretions and secretions [50]. If maggot therapy is attempted for wounds with uncertain vascular integrity, the patient must receive close and continuous observation for bleeding, infection, or thrombosis.

Large maggot burdens in blowfly-infested sheep (>60,000 maggots per animal) are associated with serious complications ("blowfly strike"), including elevated serum ammonia levels (presumably due to the large protein breakdown in the wound) and encephalopathy. Similar complications in humans were predicted [43] but not seen until 20,000 larvae were applied (against verbal and written advice) to wounds in a patient with underlying alcoholic hepatic insufficiency [51]. Maggot loads over 6,000 should probably be avoided, even in otherwise healthy individuals. Too many maggots in a tight dressing, especially in a patient with insensate wounds, may exert pressure sufficient to compromise circulation and cause further pressure-related necrosis [43].

Patients with fever or changes in mental status should be evaluated for spread of infection (i.e., cellulitis, bacteraemia, sepsis) or hepatic

encephalopathy (check for elevated serum ammonia level). Maggot dressings may need to be removed immediately, even if just to facilitate wound inspection. Patients with infected wounds—especially those with deep or extensive wounds, and those at increased risk of bacteraemia, should receive systemic antibiotic coverage during maggot therapy to prevent sepsis or cellulitis.

The use of maggots that have not been disinfected or were inadequately disinfected has also been found to pose a risk of local and systemic infection [52]. Larvae supplied in a single, primary packaging container are intended for single-use only [53]; they are not to be multi-dosed nor saved for retreatment of the same patient. Firstly, opening and retrieving maggots may contaminate the internal environment and content of the primary packaging container, and secondly, the remaining maggots will have deteriorated beyond therapeutic effectiveness by the time the patient requires a follow-up treatment (usually 48–72 hours later). Medicinal maggots should not be used on more than one patient, nor be allowed to wander away from their host patient. Once they have been applied to a patient, they are contaminated with the patient's wound flora, and must be discarded as infectious ("biohazardous") medical waste.

Summary

Maggot therapy is indicated for the debridement of a wide variety of chronic wounds. Many experts also recommend medicinal maggots for controlling wound infections and the promotion of healthy granulation tissue and reepithelialisation in non-healing wounds. Please refer to Chapter 15, where Takáč and colleagues present examples of successfully treated patients with before-and-after images [54]. Adverse events are very uncommon, with the exception of increased pain in patients with painful wounds. However, a variety of precautions should be taken when treating patients at risk of bleeding, infection, or the complications of liver disease. Patients with inadequate blood flow may never heal their wounds, even if completely debrided by maggot therapy; but we do not yet know how much blood flow is too little because even patients with so little blood flow that they are scheduled for amputation often heal with a trial of maggot therapy.

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