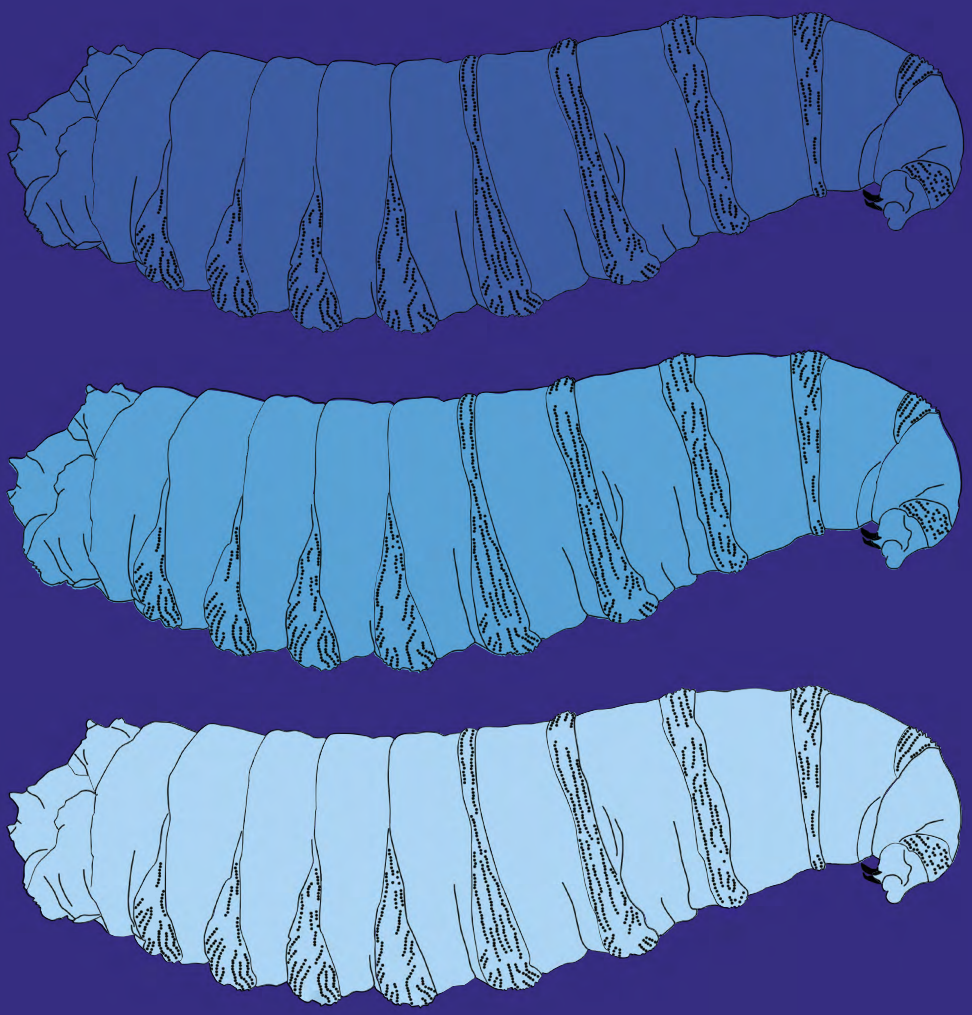
A COMPLETE GUIDE TO MAGGOT THERAPY

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.

1. Introduction

Frank Stadler

The introductory chapter outlines the global wound burden, explains the basics of maggot therapy, and scopes the content covered by the subsequent 18 chapters. Maggot therapy is the treatment of chronic and infected wounds with living fly larvae commonly known as maggots. When applied to the wound, maggots remove dead tissue, control infection, and promote wound healing. This highly efficacious therapy is not widely available around the world due to actual and perceived social, organisational, economic, logistic, and clinical barriers—all of which can be overcome. This is the first comprehensive book on maggot therapy summarising, beyond clinical practice, the principles of therapeutic action, medicinal maggot production and distribution, and ethical considerations regarding the use of living maggots in wound care. The chapter concludes with reflections on the past, present, and future of maggot therapy.

Maggot Therapy and the Global Wound Burden

There is a large and mostly unmet global need for affordable and efficacious wound care, despite modern-day medicine advancing at break-neck speed. Indeed, the tide of chronic wounds is rising. Modern lifestyle changes, particularly in low- and middle-income countries (LMICs), bring a rapid rise in non-communicable disease including cardiovascular disease, obesity, and diabetes, with the latter leading to

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diabetic ulcers at a lifetime incidence of up to 25% [1]. The cities and urban centres in fast-growing parts of the world are also struggling with ever-increasing motorisation and poor road safety standards while local healthcare systems in many LMICs are ill-prepared for the high traffic accident and injury burden [2, 3]. Likewise, due to population growth and urbanisation in disaster prone regions, the number of people exposed to disaster risk and related injuries is also growing. Where there is conflict there is also injury. Due to changes in the nature of warfare there are now far more casualties among the civilian population than among fighting soldiers [4]. People in such conflict zones and complex humanitarian crises are often isolated and are unable to properly care for the many injured due to limited resources. Acute traumatic war injuries therefore lead to infected chronic wounds and ultimately a high burden of amputation and death. To make matters worse, antibiotic-resistant strains of bacteria are highly prevalent in conflict and LMIC environments due to their mis- and overuse in human and veterinary medicine [5, 6].

Irrespective of the healthcare setting patients find themselves in, chronic wounds make life difficult and people living with chronic wounds struggle on a daily basis with social stigma, isolation, poor self-image, depression, and high treatment costs as explained by Ogrin and Elders in Chapter 1 [7].

With this growing wound burden and its social and socio-economic impact in mind, there is now the need for therapies that provide multiple wound care benefits and accessible, affordable, and effective wound care, regardless of where patients live or how wealthy they are. Contemporary care of acute and chronic wounds as it is practised in resource-rich countries relies heavily on the availability of efficacious antibiotics, sophisticated devices, surgical intervention, and advanced wound dressings. However, in compromised healthcare settings there is often limited or no access to these resources and associated basic consumables, which means that wound care options that are relatively cheap, easy to use, and have multiple therapeutic benefits are required. One such treatment modality is maggot therapy. It is the deliberate therapeutic application of living fly larvae (maggots) to remove dead tissue, control infection, and promote wound healing.

All three therapeutic properties are primarily related to the maggots' ecology and evolutionary history as evident in their nutritional preferences, digestive physiology, and immunology [8]. Medicinal maggots consume dead or devitalised animal tissue and wound fluids. Unlike beetle larvae, for example, maggots do not have mouthparts capable of cutting or biting pieces of solid food. While some food manipulation is achieved with a pair of mouth hooks, maggots need to liquefy their food outside their own body before ingesting this nutrient-rich broth [9]. In order to thrive in a microbe-laden environment of decomposing meat, maggots have also evolved ways to protect themselves from their microbe neighbours [10]. Maggots consume and digest many microbes that are suspended in the liquefied necrotic tissue, and their enzymatic excretions and secretions contain powerful antimicrobial compounds. Finally, maggots have a scrambling feeding habit and constantly probe with their two mouth hooks. This disrupts and prevents microbial communities from forming biofilms that stimy wound healing and evade the immune system and antibiotic treatment. The maggot excretions and secretions also contain growth factors that stimulate the regeneration of blood vessels and the growth of granulation tissue, thus supporting the wound healing process [11]. These principles of maggot-assisted wound healing are under active investigation by numerous research groups and their efficacy has been confirmed both at the bedside and *in vitro*.

Maggot Therapy

The human body is fragile and therefore wounds, acute and chronic, have always been part of the human condition since time immemorial. Likewise, flies have evolved to exploit during larval development the ephemeral cadavers and wounds of living animals (humans included), as Michelle Harvey explains in Chapter 7 [8]. So, it must come as no surprise that people through the ages have also noted the beneficial therapeutic effect maggots can have when they colonise a human wound. It is then only a small step to purposely utilise myiasis for wound care in traditional and tribal medicine as practiced by the Aboriginal Ngemba people in Australia, and the Mayan Indians in South America [12, 13], for example.

Nowhere is human fragility more apparent than on the battlefield where soldiers suffer terrible injury and subsequent infections. There, too, flies have been noted for their wound healing and infection control properties. Recorded accounts date back to the Battle of St Quentin in 1557 and other campaigns thereafter, including the Napoleonic Wars and the American Civil War [14]. However, it was not until after World War I that maggot therapy was formally investigated and introduced to modern medicine. William S. Baer, an orthopaedic surgeon, experienced first-hand the therapeutic benefits of maggots during the Great War. Upon returning to peace-time practice at Johns Hopkins Hospital in Baltimore, U.S.A., he revisited his war experience and commenced the first scientific and clinical studies on maggots and their use in wound therapy, in the first instance for the treatment of osteomyelitis [15]. His work spread like wildfire across North America and Europe, with over a thousand hospitals using maggot therapy to treat chronic wounds in the 1930s and early 1940s [16].

The rapid rise of maggot therapy was followed by an equally rapid decline in the 1940s with the advent of penicillin and other antimicrobials to treat wound infection. However, an increasing chronic wound burden, coupled with the emergence of antibiotic-resistant microorganisms, has resulted in a revival of maggot therapy in research and clinical practice over the past three decades. For a more comprehensive history of maggot therapy, please refer to a couple of early papers by Sherman and Pechter [14, 17] and two articles by Kruglikova and Whitaker, and their colleagues [18, 19].

In modern maggot therapy, as established by Baer [15], medicinal flies are reared in insectaries, and medicinal maggots are prepared aseptically under laboratory conditions with quality control procedures in place [20]. These days, maggot therapy is most commonly carried out with the medicinal fly species *Lucilia sericata* and, to a lesser degree, *L. cuprina* [21], but other species are actively being investigated for their therapeutic and commercial potential [22]. Disinfected maggots are placed on the wound either directly or enclosed in a mesh bag [23]. Most wounds treated with maggot therapy are chronic wounds such as diabetic ulcers, but acute wounds requiring debridement, such as infected traumatic and post-surgical wounds or burns, also respond well to maggot therapy [24, 25].

Why a Book on Maggot Therapy?

Although three or so decades have passed since maggot therapy was rediscovered and re-introduced to mainstream clinical practice, there are many barriers still standing in the way of widespread uptake of maggot therapy in modern and compromised healthcare settings alike. Unfortunately, maggot therapy is still not widely understood as a viable alternative to conventional wound care and therefore much underutilised. Many hospital administrators, physicians, nurses, and allied health practitioners still reject maggot therapy due to unfamiliarity, mistrust, or repulsion. There are also regulatory barriers in ministries of health which are made worse by a lack of international harmonisation of maggot therapy and medicinal maggot production regulations. Each jurisdiction repeats lengthy and costly regulatory processes that are blocking implementation, as is evident in the case of Kenya, presented in Chapter 15 of this book [26]. On a practical level, maggot therapy places specific demands on the supply chain with respect to rapid delivery and cool chain requirements, which is particularly the case in low-resource, compromised healthcare settings. [27].

This book fills the information vacuum, and importantly, it makes the current state of knowledge freely accessible to anyone with an Internet connection. It is the first book to provide sound, evidence-based information beyond the much-discussed therapeutic actions and clinical practice. Particular attention has been paid to the challenges encountered in compromised and low-resource healthcare settings such as disasters, conflict, and poverty. Patients in such settings will benefit greatly from affordable, efficacious, and sustainable maggot therapy. This book is as much a practical guide as a summary of the current state of knowledge in the field. The content has been carefully chosen to build global capacity for maggot debridement therapy services including production, distribution, and treatment.

Content

The next 18 chapters are organised into five parts beginning with Part 1, on the clinical aspects of maggot therapy. The behavioural, physiological, biochemical, and immunological principles of medicinal maggots that bring about debridement, infection control, and wound healing are

presented in Part 2. The following three parts are new to the maggot therapy literature as they provide best-practice guidance on medicinal maggot production (Part 3), on medicinal maggot distribution logistics (Part 4), and on the ethics of maggot therapy (Part 5).

Part 1. It is important that we start with the patient. In Chapter 2, Rajna Ogrin and Kylie Elders [7] explain how chronic wounds have a large impact on patients' psycho-social wellbeing. They closely examine what it means to live with a chronic wound. Only if the needs and characteristics of patients and their social environment have been fully appreciated, can medical interventions like maggot therapy be developed and implemented with minimal harm and maximum benefit to the patient. What many clinicians don't realise is that maggot therapy is very versatile and can be used to treat almost any chronic wound. In Chapter 3, Ron Sherman and I [25] present the aetiologies and wound types amenable to maggot therapy. Of course, it is necessary to carefully consider whether patients and their wounds are suitable for maggot therapy. In Chapter 4, Ron [24] develops a typology of factors influencing treatment decisions and explains the recommended indications, contraindications, side-effects, and any interactions between maggot therapy and other treatments or patient behaviour. Practitioners new to maggot therapy will be particularly interested in learning how to apply medicinal maggots to the wound. Ron [23] introduces maggot confinement and containment approaches in Chapter 5 and explains how these dressings are constructed and applied to the wound.

While this clinical knowledge is essential for successful maggot therapy, the biggest hurdle for biotherapists wanting to use maggot therapy is the introduction and integration of the therapy into the healthcare system. To that end, Benjamin L. Bullen, Ronald A. Sherman, Paul J. Chadwick and Frank Stadler [28] explore in Chapter 6 the complexities of such an undertaking and provide guidance on how clinical integration of a maggot therapy programme is best achieved.

Part 2. It is widely acknowledged that medicinal maggots do more than just debride the wound. The second part of this book is concerned with the therapeutic properties of medicinal maggots in the wound. It makes sense to begin this exploration with the natural history of medicinal flies. In Chapter 7, Michelle Harvey [8] scopes the evolutionary history and taxonomic intricacies of calliphorid flies, to which medicinal

and many forensically important fly species belong. Michelle reveals how the therapeutic benefits of medicinal maggots can be traced back to the evolutionary history, life history, and ecology of calliphorid flies. The next three chapters by Yamni Nigam and Michael Wilson provide excellent up-to-date reviews of the therapeutic actions of medicinal maggots [9–11]. Chapter 8 is concerned with the outstanding ability of medicinal maggots to remove dead tissue from chronic wounds, Chapter 9 summarises what is known about the antimicrobial properties of medicinal maggots, and Chapter 10 explains our current understanding of how medicinal maggots support and encourage wound healing.

While most maggot therapy around the world is currently conducted with *L. sericata* and *L. cuprina* blowflies, a wide range of other species have also been used for wound care, with varying degrees of clinical evidence supporting their use [21]. With countless potential species to choose from around the world, it is important to have protocols in place for the bioprospecting and testing of new medicinal fly species to ensure their therapeutic efficacy and safety before they can be approved by regulators and used in wound care. In Chapter 11, Patricia Thyssen and colleagues [22] provide a step-by-step guide to the selection and testing of new medicinal fly species, drawing on their own extensive experience in this field.

Part 3. There are only a few publications fully dedicated to the rearing of maggots for medicinal purposes. The earliest papers on the subject are by the fathers of modern maggot therapy, William S. Baer [15] and Duncan C. McKeever [29]. Subsequent publications on medicinal maggot production lean heavily on these seminal works, and mainly offer methodological improvements (e.g. the refinement of rearing techniques) rather than radical changes [27]. The four chapters in Part 3 provide comprehensive guidance on practical aspects of medicinal maggot production. In Chapter 12, I [30] identify the infrastructure and equipment requirements for medicinal fly insectaries and medicinal maggot laboratories. When it comes to sourcing medicinal flies for the establishment of safe maggot therapy programmes, practitioners may need to collect their own stock from the wild especially in situations where they do not have access to research or medical colonies. Nathan Butterworth and colleagues [21] explain in Chapter 13 how to best collect medical fly species, how to select and identify known safe species

in each of the major zoogeographic regions of the world, and how to set up a breeding colony for sustainable medicinal maggot production. Although the literature on myiasis involving fly species that specialise exclusively in the consumption of necrotic tissue points clearly to the unintended therapeutic benefits of such infestations [31], it is absolutely necessary to produce maggots for clinical application under controlled and hygienic conditions to avoid adverse treatment outcomes and to inspire the confidence of regulators, health practitioners, and patients. Peter Takáč and I [26] outline in Chapter 14 how to maintain fly colonies in the production insectary and how to produce safe and quality-controlled medicinal maggots for wound treatment. Readers who want to start a maggot therapy programme will find Chapter 15 instructive. Peter and colleagues [26] report on their achievements and challenges encountered when establishing a medicinal maggot production facility and a maggot therapy programme in Kenya.

Part 4. The renaissance in maggot therapy over the past twenty years or so has largely taken place in developed countries with excellent logistics infrastructure such as in western Europe, North America and elsewhere. It appears that the lack of maggot therapy in truly compromised healthcare settings is, apart from social factors, largely brought about by supply-chain management challenges. Indeed, the literature on distribution logistics for medicinal maggots and freight packaging is sparse to non-existent, especially when contemplating distribution under extreme climatic conditions [27]. Therefore, Chapters 16 to 18 are concerned with packaging technology, distribution logistics, and innovative forms of transport. In Chapter 16, I [32] provide guidance on how medicinal maggots ought to be packaged to satisfy regulatory requirements and to ensure safe distribution of highly perishable maggots under unfavourable environmental conditions. Viability of any medicinal maggot production programme is dependent on a sufficiently large market which needs to be reached quickly considering the perishability of medicinal maggots. In Chapter 17, I [33] explain the basics of efficient medicinal maggot distribution systems. With rapid advances in the use of unmanned aerial vehicles (drones) in disaster and development, Peter Tatham and I [34] believe that there is great scope to utilise drones for last-mile delivery of medicinal maggots. Chapter 18 describes the various types of drones, how they may be employed,

and what to consider when establishing a distribution partnership with drone operators.

Part 5. While Rajna Ogrin and Kylie Elders [7] begin our complete guide to maggot therapy with a patient's chronic wound journey, the book closes with Chapter 19 where I [35] summarise, for the first time, the ethical dimensions of maggot-assisted wound care from a biomedical and animal ethics point of view. To judge by the animal rights movement and the conscious purchasing choices consumers increasingly make, it is certain that the long-term sustainability and social licence of whole-organism maggot therapy will depend on how producers and health care practitioners treat medicinal flies at all life stages, and their ethical engagement with patients.

Past, Present, and Future

This book was conceived during my research on the supply-chain management for maggot therapy in compromised healthcare settings [36]. It struck me that after almost a hundred years of clinical practice, there was no comprehensive guide on maggot therapy that included guidance on the production of medicinal maggots and maggot therapy supply-chain management. The information that has been published over the years on issues relating to maggot therapy is highly dispersed across a large body of literature and held mostly behind journal paywalls [27]. Consequently, there was a need to both synthesise the literature and make this knowledge accessible to the widest possible readership, including those caring for patients with wounds in low- and middle-income countries, during disasters, and in wartime. It is in these settings where I believe maggot therapy can benefit patients the most because, as Yamni Nigam and Michael Wilson [9–11] explain, medicinal maggots convey several therapeutic properties at once. Besides, maggot therapy itself can be administered in the most austere care settings without diminishing its efficacy.

This book would not have been possible without the contribution of the many expert co-authors and reviewers who followed the highest professional standards. The title of the book claims that it is a complete guide to maggot therapy and related fields. Of course, completeness is wishful thinking and the title has been chosen to tickle the curiosity of

readers, but it also signals our aspiration. While scientific or technical knowledge can never be complete, we must nevertheless strive toward completeness. Indeed, there is much that will need to be added to this book—perhaps in future editions. For example, there is recent research published and in press that explores the sociological and psychological dimensions of maggot therapy and builds on earlier work [e.g. 37, 38, 39]. It seeks to clarify what patients and healthcare practitioners really think about maggot therapy, and how psychological barriers can be overcome [40]. Would early education and sensitisation in schools help to shift attitudes toward maggot therapy [41, 42]? With regard to clinical performance, there has been a successful attempt to boost the therapeutic benefit of medicinal maggots with genetic engineering [43] and from the grey zone between whole-organism maggot therapy and drug development, research is emerging that explores the use of maggot-derived living macrophages for chronic wound care [44].

In conclusion, it is safe to say that the heydays for maggot therapy and maggot-inspired biological therapeutics and drugs are still to come. Meanwhile, this first edition of *A Complete Guide to Maggot Therapy: Clinical Practice, Therapeutic Principles, Production, Distribution, and Ethics* provides clinicians, medical entrepreneurs, health administrators, regulators, supply-chain managers, and isolated communities in compromised healthcare settings with the practical knowledge to treat wounds with maggot therapy.

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