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Y CICATRIZACIÓN DE HERIDAS A.C.
MEXICAN ASSOCIATION
FOR WOUND CARE AND HEALING

Clinical Practice Guideline For The Treatment Of Acute And Chronic Wounds With Maggot Debridement Therapy

CLINICAL PRACTICE GUIDELINE FOR THE TREATMENT OF ACUTE AND CHRONIC WOUNDS WITH MAGGOT DEBRIDEMENT THERAPY

Asociación Mexicana para el Cuidado Integral y Cicatrización de Heridas A.C.
[Mexican Association for Wound Care and Healing]

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CONFLICT OF INTEREST DISCLOSURE

Dr. Sherman declares his potential conflicts of interest in that his laboratory currently provides biotherapeutic supplies including medicinal maggots. However neither he, nor his laboratory either funded or received any revenues to or from the present guidelines.
The rest of the authors hereby declare the absence of any type of conflict of interest in the development of the clinical guideline here presented.
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INDEX

PREFACE

The “Asociación Mexicana para el Cuidado Integral y Cicatrización de Heridas, A.C.”, [Mexican Association for Wound Care and Healing], AMCICHAC, through the Education and Clinical Practice Guidelines Committee, assumes as one of its fundamental purposes facilitating permanent and high level continued education, through top of the line educational material that guides health care professionals dedicated to the care of patients with wounds, in order to facilitate reasoned decision making in specific situations of daily practice, supported by the best possible scientific evidence.

In virtue of the great disparity of criteria surrounding the patients with wounds and re-emerging adjuvant therapies such as maggot therapy (MT), [also known as maggot debridement therapy (MDT), biotherapy, biosurgery, biodebridement or larval therapy], we have considered that one strategy for guaranteeing excellence in application is the development of a Clinical Practice Guideline (CPG) in the treatment of acute and chronic wounds with maggot therapy.

This CPG constitutes a series of recommendations developed methodically and supported by the best scientific evidence available on the clinical diagnosis and treatment of wounds through the use of maggot therapy.

The objective of this CPG is to improve medical attention, decrease the variability in the application of this resource, foment its efficient use, guide the clinician in decision making, and provide valuable continuing education for health care workers and therefore become a tool for the improvement in the care of patients with acute and chronic wounds that could benefit from MT. In this guideline, the healthcare professionals will find answers to a series of questions posed in the daily aiding of this complicated group of patients through an alternative therapy that has proven its efficacy with scientific evidence.

The evidence and recommendations elaborated in this document were developed with the participation of expert clinicians from the diverse disciplines that participate in the care of patients with acute and chronic wounds, each, with maggot therapy experience.

AMCICHAC

SUMMARY OF RECOMMENDATIONS

Recommendations for the use of maggot debridement Therapy (MT)		Evidence Level
Patient evaluation	1.1 Before performing any debridement make sure that it is indicated.	III
	1.2 Evaluate and treat the underlying condition and co-morbidities of the patient.	IV
	1.3 The patient who will receive MT should be well informed and the health care personel worker should document through the patient's consent.	II
	1.4 Consider the shipping times to program patients for MT.	IV
Patient selection and indications	2.1 To perform MT one must have qualified personnel and medical grade maggots.	IV
	2.2 MT is indicated in patients with necrotic tissue where there is no contraindication.	II
	2.3 MT can be used when conventional treatment is not working.	II
	2.4 MT can be used in patients where surgical debridement cannot be performed.	III
	2.5 MT is especially useful in wounds colonized or infected with MRSA	III
	2.6 Patients infected with other bacteria also benefit from MT.	III
	2.7 MT is useful in delineating viable from unviable tissue.	III
	2.8 MT can be an adjuvant in limb salvage.	III
	2.9 MT has been used with success to eliminate necrotic tumor.	IV
	2.10 MT can be used concomitantly with practically any systemic therapy.	IV
	2.11 MT can be used as a debridement method where a surgical closure is being expected.	III
Application procedure	3.1 Check the package containing the maggots upon arrival.	IV
	3.2 Check that the container with the maggots is properly sealed, does not have a strong or fould smell and the maggots are viable.	IV
	3.3 The maggots can be refrigerated if not used on the day of arrival.	IV
	3.4 Make sure the surface of the wound is adequate for MT.	IV
	3.5 Apply MT according to proper methods described in the literature.	III
	3.6 Explain to the patient the necessary recommendations while the maggots are in place and the measures to take in case of emergency.	IV
	3.7 Use an adequate technique for the removal of the maggots 24 to 48 hours (maximum 72) of maggot placement.	IV
	3.8 Dispose of the maggots according to the existing policy for dangerous biological waste.	IV
	3.9 If necessary, re-apply a new MT cycle.	IV
	3.10 Treat adequately any complication associated with the detachment of the cage dressing.	IV
	3.11 Carefully evaluate the border of the wound and take necessary measures not to cause additional damage to existing macerated or partially damaged skin.	IV
Contraindications and Precautions	4.1 MT should not be applied when there is an absolute contraindication (close proximity to large blood vessels or internal organs, patient's denial or refusal of the patient or lack of sterile maggots).	III
	4.2 Carefully evaluate your patient when there are precautions to the use of MT.	IV
	4.2.1 Carefully evaluate ischemic wounds or with arterial insufficiency.	IV
	4.2.2 Carefully evaluate wounds with severe life-threatening infections or those requiring permanent visualization.	IV
	4.2.3 Carefully evaluate non infected wounds with granulation tissue.	III
	4.2.4 Carefully evaluate patients with anticoagulants or coagulopathy.	IV
	4.2.5 Carefully evaluate your patient if superficial or deep infection by *Pseudomonas aeruginosa* is present	III
	4.2.6 Do not apply maggots for the treatment of osteomyelitis in a wound unless no other options exist to treat it.	I
	4.2.7 Be cautious in patients allergic to components used in the nutrition media used for shipping the maggots.	IV
	4.2.8 Carefully consider the use of MT in painful wounds.	III
	4.2.9 Carefully evaluate the use of MT in patients with severe hepatic insufficiency or risk of encephalopathy.	IV

GUIDELINE DEVELOPMENT PROCESS

Evidence search

In a first stage, a review of the existing available evidence, through the use of MEDLINE (PubMed) was performed. The terms utilized for this review were:

skin ulcer AND maggot
skin ulcer AND larval
skin ulcer AND biosurgery
skin ulcer AND larvae
skin ulcer AND *Lucilia sericata*
debridement AND maggot
debridement AND larval
debridement and larvae
debridement AND *Lucilia sericata*
maggot therapy
maggot debridement therapy
larval therapy
surgical maggots

A total of 272 articles were found, 245 of which were relevant to the topic. Thereafter a manual search of references cited in the papers previously identified was performed. Key opinion leaders in maggot therapy were then contacted to request a review of the papers found and whether or not other articles should be incorporated that were not located during the initial search. In total, 279 relevant articles were included for this revision. In the references of the present CPG only those papers that the authors found to be relevant to the present guideline were included.

Evidence Classification

In a second phase, the articles found were divided according to evidence level. The evidence levels used by the AMCICHAC Clinical Practice Guideline Committee are:

I. Meta-analysis and systematic reviews of randomized controlled trials
II. One or more comparative randomized control trials with good methodology
III. Open trials and case series
IV. Case studies and expert opinion

Note: For the purpose of clarity, in this guideline we decided to write the highest level of evidence available, therefore inferring that lower levels of evidence are also present.

After this classification the papers were grouped as follows:
6 Meta-analysis and systematic reviews
3 Randomized controlled trials
8 Open clinical trials and case series
262 Case studies, simple reviews, basic science trials, editorials, others

Delphi Process

In the third phase, concrete clinical questions were constructed on the topics that were considered to be relevant to the care of patients with wounds elegible for maggot therapy (MT). These were:

How do you select an appropriate patient for MT?
In what wounds is MT indicated?
What is the procedure to follow for MT application?
In what type of wounds is MT not recommended?
In what patients is MT contraindicated?
What parameters should the clinician look for to decide a change in therapy?

These questions, expert responses and relevant literature were combined and distributed again to the expert panel to achieve consensus following a DELPHI process[1]

Final version of recommendations
Once consensus was obtained, the recommendations were submitted to our international external expertreviewers for input prior to publication in its final form.

INTRODUCTION

Maggot therapy (MT) is the therapeutic use of larvae of necrophagic/coprophagic flies (that only feed on dead organic material) cultured in a sterile manner for the debridement of wounds.[2-4] The fly most commonly used is *Lucilia sericata* (or green bottle fly) but other species have been used with similar efficacy. [5,6] MT has also been called biosurgery or larval therapy (larval debridement therapy) [7-9] and can be described as a carefully controlled process where an artificial theapeutic myiasis is induced. The health care professional makes use of the natural ability of maggots to ingest necrotic or infected tissue without affecting healthy tissue, reducing bacterial burden locally and promoting wound healing.

Ambroise Paré in the 16th century was the first European to describe that the infestation of wounds with fly larvae was not harmful,[10-12] but he did not use them therapeutically. During the Crimean War (1853-1856) Nikolay Pirogov, a Russian surgeon used MT in the battle field where the technique saved many soldier's lives.[13,14] Based on his observations as a World War I military surgeon, Johns Hopkins Professor of Orthopedics, William S Baer was probably the first therapist to apply maggots to wounds. Beginnin in the year 1928, he successfully treated patients with soft tissue infections and osteomyelitis. [15,16] Within 5 years, MT became a popular treatment for the control of these infections[15] and the treatment of wounds. However, with the arrival of antibiotics and modern surgical techniques, by the beginning of the 40's, MT was quickly substituted and forgotten. [11,17-19] Given the alarming increase in bacterial resistance, and the elevated cost of the care of patients with chronic wounds, Ronald Sherman, re-explored this therapeutic option beginning in 1982. With excellent results and a decrease in costs,[20] soon the technique became popular again in all continents, the treatment is now cleared for marketing by the FDA in the United States of America, and it has benefited thousands of patients all over the world.[21-23] In Mexico it was used for the first time in the Dermatology Division of the "Dr. Manuel Gea González" General Hospital in the year 2000 with excellent results [24] and has remained as part of the therapeutic armamentarium ever since for patients with wounds requiring debridement.

Chronic wounds (leg ulcers, diabetic foot, pressure ulcers, surgical dehiscence, etc.) represent a high percentage of healthcare costs. In the United States, the cost of healing a pressure ulcer varies from $500 to $4000. [2516,17] It is also estimated that 15% of diabetics develop one or more ulcers during the course of their disease.[26]
Chronic wounds require effective debridement in order to heal and it is here that MT can be a useful treatment method.[27-30] Since its renaissance for the treatment of wounds with necrotic tissue, a large number of reports on their efficacy has been published.[9,31,32]
Although MT is primarily used for the debridement of necrotic tissue, other benefits also have been described such as wound disinfection and the promotion of granulation tissue that have popularized its use all over the world. The secretions or excretions of maggots contain powerful enzymes that lyse necrotic tissue, freeing the wound of non-viable contaminated tissue.[7,20,33-37]

Among the degrading enzymes isolated in maggot secretions are trypsin, leucinaminopeptidase, carboxypeptidase, tryptase, peptidase and lipase. [38-41] One of the most studied is larval chemotrypsin I, that has been even been tested as a debriding agent experimentally as a gel applied to venous ulcer eschars with good results.[42]

With those enzymes, the maggots begin to digest the necrotic tissue extracorporially and then they ingest it. [43,44] The main advantage of this method is that these secretions digest the necrotic tissue without harming the viable one. The microorganisms present in the wound bed are also eliminated by competing for the same substrate, by destruction in the digestive tract of the maggot and by substances in the secretions that are bactericidal and capable of destroying biofilms.[8,31,35,45-48] Maggot secretions also contain calcium carbonate, urea, allantoin, ammonia and other less characterized substances that have been described to favor the formation of granulation tissue and cellular migration.[19,29,39,41,49-58] There is evidence that the hormone that aids in the maggot transformation into a fly, 20-hydroxyecdisone, stimulates fibroblast growth, and it has been suggested that the proliferation of tissue inside the wound, stimulated by the presence of growth factors can allow the maggots to become better nourished.[59] The mechanical stimulation of the wound surface by the movements of maggots also could be a factor in the stimulation of tissue growth.

Finally, all this is potentiated by the ability of maggots to debride necrotic tissue in difficult to reach areas such as sinuses, tunnels, wound pockets, etc. The ability of their digestive enzymes to dissolve necrotic tissue wile sparing viable tissue makes maggot debridement of the wound effective and still quite safe.[8,19,54,60,61] This also decreases the need for large incisions. These factors combine to results in less tissue damage and consequently faster wound healing.

Since Sherman re-explored the use of MT, it has been suggested as an excellent alternative for developing countries.[34] This was the case of Mexico where it resulted in an excellent choice for patients that do not have the resources to undergo surgical procedures, when the patient is at high-risk for surgical debridement, when preserving viable tissue is a goal, when there is a need to distinguish between living from dead tissue, while the patient is awaiting other types of more radical debridement, when patients cannot tolerate general anesthesia, or when the infected and/or necrotic tissue is difficult to assess surgically without extensively enlarging the wound. [24]

What is certain is that MT is now widely practiced and it offers great advantages in well selected patients. [47,48] Therefore it is important for the clinician to discriminate between those patients capable of obtaining the greatest benefit with MT, those who would have none to very small benefit, and those were it would be not recommened or even contra-indicated. [62]

JUSTIFICATION

The impetus for CPG was the need to establish criteria for optimal patient selection, increase knowledge about maggot therapy within the medical community, develop standards of care for this treatment modality, and define the level of certainty associated with the clinical practice of MT.

Within this scope, one of the goals of this guideline is the concise criticism of currently available literature. As a result, the recommendations are valid both for private and institutional practice.

PURPOSE

The purpose of this document is to offer a standardized framework with recommendations developed in a systematic fashion that will facilitate decision making for the wound care professional in the treatment of patients with chronic and acute wounds, particularly in the inflammatory and/or exudative phase with the use of MT.

BASIC RECOMMENDATIONS FOR THE CARE OF PATIENTS WITH WOUNDS
Source: AMCICHAC translation and modification of Sibbald et al. 2006.[63]

Recommendations for the general care of the patient with wounds		**Evidence level**
Goals of treatment	1.0 Clearly establish the goal of treatment according to the patient's condition.	IV
	1.1 If the goal is not the healing of the wound, define the treatment plan with the patient and family.	IV
	1.2 In those wounds where there is absence of circulation or palliative care is indicated, avoid moisture and aggressive debridement, and control pain.	IV
Indentify and treat the cause	2.0 Make sure you have a proper diagnosis of the wound being treated.	IV
	2.1 Correct treatable causes of tissue damage.	IV
Patient and family concerns	3.0 Evaluate patient and family concerns	IV
	3.1 Provide necessary education and answer any questions of patients or family	II
	3.2 Adequately control pain in all its dimensions	II
Provide local wound care	4.0 Evaluate and document the wound characteristics (shape, size, wound bed, etc.)	IV
	4.1 Before performing any debridement make sure it is within the limits of your expertise and clinical priviledges.	IV
	4.2 Debride wounds only after you have an adequate diagnosis, when the goal is healing the wound and when you are sure you will not create more damage	IV
	4.3 Debride wounds by eliminating non-viable, contaminated or infected tissue using the appropriate method (surgical, mechanical, maggot therapy, enzymatic, etc.)	II
	4.4 Cleanse the wound with normal saline or water. The use of antiseptics is reserved for infected wounds.	I
	4.5 Evaluate the presence of superficial or deep infection and treat accordingly	II
	4.6 Select the proper dressing for the wound and for each particular patient.	IV
	4.7 Re-evaluate periodically the evolution of the wound. If it is not advancing, re-assess all the previous points.	III-IV
	4.8 When necessary consider the use of adjuvant therapies (biologicals, grafts, negative pressure wound therapy, hyperbaric chamber, etc.)	I-IV
Team support	5.0 Work in teams to provide education, prevention and collaborate with other specialties involved in the treatment of a patient with a wound	III

EVIDENCE AND RECOMMENDATIONS FOR MAGGOT THERAPY

Patient evaluation

1.1 Before performing any debridement make sure it is indicated. (Evidence level III)

Maggot therapy is primarily a debridement technique u used to eliminate necrotic tissue in wounds. [64,65] For this reason there are basic principles that should be considered before performing any debridement.[30,66-68] A proper diagnosis of the wound to be debrided is mandatory since there are wounds that may get worse when debrided (e.g. untreated pyoderma gangrenosum) [69] Before debriding the result of the intervention must be evaluated. Given their size or severity, some wounds will require surgical closure or other treatment after debridement, so those subsequent therapies must be considered and be available before embarking on debridement. Finally, there are wounds with underlying severe ischemia without infection. In these wounds, usually called "stable", the goal is not to heal the wound but to avoid further deterioration or complications before the patient can be re-vascularized. Therefore, one must avoid unnecessarily increasing the size of the defect until the blood flow can be optimized. All other wounds require debridement for the removal of necrotic tissue. There are many methods of debridement (autolytic, enzymatic, mechanical, MT, surgical, etc.) and for that reason the best method should be selected according to its indications and contraindications as well as patient's preference.

1.2 Evaluate and treat the underlying condition and co-morbidities of the patient. (Evidence level IV)

It is fundamental to know the general condition of the patient and the co-morbidities associated. In many occasions the lack of treatment results is due to failure to treat the cause of the ulcer or associated co-morbidities.

1.3 The patient who will receive MT should be well informed and the health care personnel should document through the patient's consent. (Evidence level II)

Before applying MT, it is necessary for the patient to be well informed about maggot therapy, its risks and benefits, and the alternatives. It is also important for the patient to understand why they are a candidate for MT, and how the treatment is to be carried out. Patients should be given enough time to ask questions and feel comfortable with their decision. Patients should not be shown actual maggots or images of maggots (especially those older than 70), as this may generate anxiety[70] Kitching[71] demonstrated that the initial repulsion that patients had to MT disappeared with good communication, patient autonomy, and informed consent. A systematic review on therapies for venous leg ulcers in 2007 found that, despite the fact that there weren't then reviews or solid evidence for their use on venous leg ulcers, the majority of patients with this disease accepted them as therapy.[72] In a series of 103 patients studied between 1990-1995, all but two patients and two surrogate care providers consented to maggot therapy.[73]

The healthcare provider must make sure that the candidate for treatment of MT signs the consent form and that the latter is properly filed in the medical record. study, all patients felt initial natural repulsion to MT that disappeared with proper communication, patient's autonomy and informed consent.

1.4 Consider the shipping times to program patients for MT. (Evidence level IV)

There are few places in each country where maggots are produced adequately and with medical quality. Medicinal maggots are highly perishable, and must be transported quickly by reliable couriers. Therefore, medicinal maggots can be shipped only at certain times, and they must be used shortly after arrival. As a result it is necessary to consider shipping issues when scheduling patients for their treatments.

Patient selection and Indications

2.1 To perform MT one must have qualified personnel and medical grade maggots. (Evidence level IV)

Although MT can be used by health care professionals who are not trained in surgical debridement, it is necessary to be trained in the use of maggots, in their indications and contraindications, and to have performed this procedure under supervision for at least 3 times. There are groups and associations performing courses and workshops regularly for this purpose. The maggots used for MT should be disinfected so that they will not generate infections or endanger the patient. In countries where there is not an established process or committee to certify the laboratories that produce maggots, whoever provides the maggots has quality control mechanisms in place to uphold the highest production standard. Ask for evidence of quality control if in doubt.

2.2 MT is indicated in patients with necrotic tissue where there is no contraindication. (Evidence level II)

The best recognized mechanism of actions of MT is the elimination of necrotic tissue without harming healthy tissue. A Cochrane Collaboration Meta-annalysis[64] reviewed the topic of debridement in the diabetic foot and concluded [74] that MT, may be better than hydrogel. However their findings were based on a single study published as a congress abstract[74] (see below) showing faster debridement and decreased wound size associated with MT. These results have not been confirmed by a larger trial. Published alongside this meta-analysis is a commentary by Sherman, noting that this maggot therapy trial by Markevich et al. used debridement as the primary outcome measure rather than wound healing, and therefore should not be compared to other studies evaluating wound healing. Instead, one should focus on the profund debridement efficacy that was reported in the MT group (60%) compared to the hydrogel group (33.4%).

Another systematic review[75] intended to evaluate the interventions that are useful in the treatment of diabetic feet. In relation to MT they conclude that information is needed to consider it a useful therapy in patients with diabetic foot ulcers.

In another systematic review[76], the authors evaluated the effect of wound debridement and the use of negative pressure wound therapy (NEWT) on wound healing. The authors concluded that there is currently no evidence to support the wound healing benefit of MT or even surgical debridement of diabetic foot ulcers, probably because of a lack of studies rather than a true lack of benefit. The same randomized controlled trial published in two different journals simultanously[77,78], included patients with venous leg ulcers and those with ankle brachial index (ABI) higher than 0.6 with a minimum of 25% necrotic tissue. They compared MT with free larvae, bagged larvae (Biofoam® before Biobag®) and hydrogel alone. They evaluated healing of the largest wound as the primary outcome measure and as secondary variables time to achieve debridement, cost of treatment, quality of life, bacterial burden, presence of MRSA and patient's and health care worker's attitude towards MT. In the study, 267 patients were included finding that there was no significant difference in wound closure in the three groups, but both the MT arms led to faster debridement than did the hydrogel. No significant differences were found in bacterial burden or cost in the three groups. It is important to mention that the cost analysis is published again separately with the same data in a third article.[79] The authors conclude that if the goal is debridement, MT must be preferred to hydrogel even though this will not modify wound's closure. There is a comparative open trial with 69 patients where free maggots were compared to the maggots in a bag. The authors found maggots in a bag required more treatments and are more expensive than free maggots.[80] Other studies did not find real differences between the use of free or bagged maggots.[81,82] There are other open trials and case series documenting the efficacy of MT.[9,19,28,73,83,84] The contraindications to MT are mentioned later in this document (see below).

2.3 MT can be used when conventional treatment is not working. (Evidence level II)

A randomized control trial[85] compared the use of hydrogel with MT. This small trial with 12 patients with non-healing wounds, comparing debridement concludes that MT was faster and more complete than with the hydrogel and at lesser cost. The efficacy of MT was retrospectively analyzed in a cohort of diabetic patients with leg and foot ulcers, followed prospectively after failing conventional therapy.[86] The changes in necrotic tissue and wound size were compared to patients that had only received conventional treatment with surgical and non-surgical debridements. In this cohort of 18 patients with 20 ulcers, 6 of them received only MT and 8 received first conventional and then MT. There was significant debridement when the patients received MT in comparison to the control group or the cross-over period during which the patients used only conventional treatment. After 5 weeks the wounds with conventional therapy still had 33% slough while the MT group after 4 weeks had 100% debridement. They concluded that MT was effective in diabetic patients who are not responding to conventional therapy.

In a prospective case series, in 20 patients with stage III and IV pressure ulcers secondary to spinal cord injury, that had been followed for weeks of conventional therapy decided by the hospital's wound care team[83] , MT was begun. After one week, the majority of the wounds were debrided after receiving MT. Wound healing was faster in the MT period compared with the time they had been treated conventionally. In fact, the wounds were getting larger during the conventional treatment period by 21.8% weekly while they decreased 22% when on MT.

A case series published in Turkish with the experience of 750 wounds commented an efficacy of 80% in debriding wounds that do not respond to conventional treatment.[32]

2.4 MT can be used in patients with wounds where surgical debridement cannot be performed. (Evidence level III)

The majority of authors consider that the best indication for MT is for those patients where surgical debridement may be difficult, contraindicated, a high-risk procedure or when the patient refuses.

Furthermore, MT it has the advantage that it can be used by non-surgical healthcare personnel (i.e. nurses, general practitioners and others not trained in surgical debridement). Even where one systematic review [87] considers there to be insufficient evidence to compare the efficacy of MT to other methods of debridement or wound healing, the author still states that the clinical experience with MT strongly suggests that it is safe and effective to debride well selected patients and that wound care experts use it as a last resource when conservative therapy is not working or when the patient is not a candidate for surgery. In a study[5] evaluating the efficacy of *Lucilia cuprina* (instead of *Lucilia sericata*) in the treatment of the diabetic foot, 29 patients were treated with MT and compared to 30 controls that received conventional therapy and surgical debridement. The authors found no differences and concluded that *Lucilia cuprina* was as effective as conventional debridement. They consider MT a therapy for patients who are high-risk for surgical debridement or those refusing it. In a case report it was illustrated how a Jehovah's witness patient was successfully treated with MT, when surgical debridement was not feasible.[88] In a retrospective trial of patients with diabetic feet, upon whom it was decided that conventional surgery would be of no benefit, MT decreased the time for the wound to heal. It also reduced the number of days that antibiotics were needed.[89]

2.5 MT is especially useful in wounds colonized or infected with MRSA. (Evidence level III)

It has become evident that maggots can rid wounds of Gram positive organisms. This is particularly the case in wounds colonized and infected by MRSA. In a trial, the effectiveness of MT was evaluated[90] in treating colonized wounds with MRSA through the application of 2 to 8 cycles of MT in 13 consecutive patients with MRSA and neuroischemic diabetic foot ulcers. In 92% of the wounds MRSA was eradicated with an average of 3 applications. This phenomenon was also previously reported. [91,92]

2.6 Patients infected with other bacteria also benefit from MT. (Evidence level III)

Many substances with antimicrobial properties have been isolated from maggot secretions. One of the most promising components is a protein now known as "lucifensin" (since it was extracted from *Lucilia sericata*) and it has shown in *in vitro* defensin activity against Gram positive and weaker against Gram negative bacteria. [46,47] At present, a lot of research is being conducted on the presence of biofilms in chronic wounds. These seem to be implicated especially in cases of recurrent infections. A recent article points out that maggots destroy biofilms caused by *Staphylococcus epidermidis*.[31]

An *in vitro* study on the maggot secretions with and without stimulation concludes antimicrobial activity against Gram positives and negative bacteria. [93] In an additional publication, the efficacy of MT in destroying cultures of *Candida albicans*, MRSA, vancomycin resistant *Enterococcus faecalis* (VRE) and *Pseudomonas aeruginosa was reported*.[94] An *in vivo* and *in vitro* study with maggot secretions and live maggots demonstrated high activity against diverse microorganisms.[95]

2.7 MT is effective in delineating viable from non-viable tissue (Evidence level III)

One of the previously described advantages of MT is avoiding damaging healthy tissue. In cases where amputations have been avoided or the efficacy of MT has been proven, it has been also observed that the maggots allow the delineation of viable from non-viable tissue. There are also reports where the authors who were expecting only palliation observed that MT achieved granulation.[96]

2.8 MT can be an adjuvant in limb salvage. (Evidence level III)

In case series it has been documented that MTdecreses the chances of undergoing an amputation in patients where the latter was considered the only option. The efficacy[28] of MT in treating intractable chronic wounds in hospice patients (including leg and pressure ulcers) has been tested. MT was applied up to 5 times a week in 4 different centers. MT achieved a complete debridement in 88.4% of the wounds, significant in 7%, and partial in 2.3% of the cases while this treatment modality was ineffective in 2.3% of wounds. In five patients an imminent amputation was avoided.

In another communication of a series of patients with severe diabetic ulcers, the same authors[19] treated 27 ulcers in 22 patients, who previously were unsuccessfully treated with conventional therapies (including hyperbaric chamber). The patients received MT 2- 5 times per week for a total of 1-23 cycles.

Complete debridement was achieved in 66.7% of the ulcers, significant in 22.2%, partial in 7.4% and none in 3.7%. The 3 patients who did not respond had wounds on their sole or between their toes and were ambulatory. In 5 patients the scheduled amputation was avoided.

In published cases where maggot therapy was used as a last resort to treat patients who would otherwise be treated with amputation, 40-50% of those wounds were healed and avoided amputation.[45,97]

2.9 MT has been used with success to eliminate necrotic tumor. (Evidence level IV)

The intentional use of MT and also accidental infestations in malignant ulcerated and necrotic tumors has been described.[39,98-100] Isolated successful case reporte on the use of MT to remove the necrotic bulk on fungating cancers as a palliative measure have been published. The maggots do not have a pharmacologic effect on the tumor itself, but they debride the necrotic mass decreasing drainage and odor.[101]

2.10 MT can be used concomintantly with practically any systemic therapy. (Evidence level IV)

The clinical experience suggests that maggots are not affected by intercurrent therapies with antibiotics, chemotherapy or radiotherapy.[65,102-104] However no topical antiseptics or antibiotics should be applied on the wound during treatment.

2.11 MT can be used as a debridement method where a surgical closure is being expected. (Evidence level III)

A comparative retrospective study was condicted for a cohort of patients with pressure and leg ulcers who received maggot debridement or surgical debridement of their wounds prior to surgical closure. [105] The purpose of the study was to evaluate whether or not MT increased postoperative complications. Twenty nine wounds in 24 patients were surgically closed, of these, 10 received MT as the debridement method while the rest received surgical debridement. On average 9.7 cycles of MT (1 to 29) were used. None of the MT treated wounds developed infection while 32% of those receiving surgical debridement prior to closure by the same surgical team became infected. The only side effect was pain in 17% of patients receiving MT. The authors concluded that pre-surgical MT did not increase the risk of post-surgical complications; in fact, it decreased the risk. However, they did not recommend maggot therapy should necessarily replace appropriate antibiotic use in patients with wound infections.

Application procedure

3.1 Check the package containing the maggots upon arrival (Evidence level IV)

Maggots are provided in a sealed box or container and are delivered by courier. Upon arrival to the clinic it should be inspected to verify that it was not opened or damaged. If there is evidence of tampering with the package, the maggot provider should be contacted immediately.

3.2 Check that the container with the maggots is properly sealed, does not have a strong or foul smell and the maggots are viable. (Evidence level IV)

Maggots are delivered in a small container with a ventilation filter that allows them to breath but avoids contamination. Within the container there may be moist gauze to supply the maggots with humidity and sustenance. Check the container to ensure that it has not been broken or opened. Occasionally very small maggots cross through the filter and exit the vial. This does not mean that the sterility of the maggots inside has been lost, however any maggots outside the vial are no longer germ-free and should be discarded.[28,39]

3.3 The maggots can be refrigerated if not used on the day of arrival. (Evidence level IV)

If maggots are not used immediately, they can be stored in the refrigerator between 5 to 8º Celsius for up to 48 hours in most countries – in the UK storage is recommended up to 24 hours without a significant loose in their viability. Cold slows down their metabolism[106] The refrigerator must not be in the auto-defrost mode nor produce a vacuum because this would dessicate and kill the maggots. The vial of maggots should be placed in a secondary container that guarantees oxygenation and humidity.

3.4 Make sure the surface of the wound is adequate for MT (Evidence level IV)

Maggots require moisture to be able to perform properly. Therefore dry wounds with hard eschars may impair the efficacy of the maggots. A hydrogel can be used occlusively for some days prior to MT to loosen the eschar and moisten the wound for the maggots. The clinician could cut the surface of the eschar to expose the softer, moist tissue. Finally, humidity should be maintained during the therapy. In cases where the eschar is too dry, one must instruct the patient to carefully and regularly moisten the gauze on the cage dressing (see below) to avoid disecation.[2]

3.5 Apply MT according to proper methods described in the literature (Evidence level III)

There are basically was to apply maggots: using the biobag®, with a cage dressing where the whole hydrocolloid is used like a "doughnut" around the wound and a variation of the latter using hydrocolloid strips rather than the whole dressing. The biobag® is a sealed polyvinyl bag containing the maggots. This dressing is patented and not available worldwide.[80,107] This technique has been described as an effective alternative to traditional application with free maggots (see below), but there are some authors who consider that the benefit of the mechanical movement of the maggots on the wound and the ability to penetrate tunnels and deep necrotic tissue are wasted.

The cage-dressing, modified by Sherman[4,8,29,107] is the most frequently used due to its simplicity, availability, low cost and the best tested in the literature. This dressing is applied as follows:

Step 1.- Make sure you have the necessary material.

For the application of MT you must have all the necessary material. (Figure 1)You will need:

- One or two hydrocolloid adhesive dressings (e.g. Duoderm CGF® Convatec, Ultec Pro® Covidien, Replicare Ultra® Smith&Nephew, Restore hydrocolloid® Hollister, Tegaderm hydrocolloid® 3M, Comfeel® Coloplast, Exuderm® Medline, etc.) that must be at least 1 cm larger than the largest measurement of the wound to be treated (even though you will only use one, it is convenient to have two in case a mistake is made).
- A soft marker that will write on plastic
- A clear plastic sheet the size of the hydrocolloid or, the transparent cover on the hydrocolloid dressing packing.
- Clean (or sterile) scissors to cut the dressings and other materials.
- A piece of fine mesh fabric the size of the hydrocolloid. The authors of these guidelines prefer organza or a contact nylon dressing (e.g. Tegaderm contact® 3M), but there are some that use organdy. The reason is that some organdies come with loose meshing that allows maggots to escape.
- Cyanoacrylate glue and applicator (e.g. Instant Krazy glue®)
- Cotton tipped applicators, tongue depressors or similar (they will be needed to scoop out the maggots from the container and apply them on the wound)
- Hypoallergenic adhesive tape

- Gauze pads
- Non compressive bandages

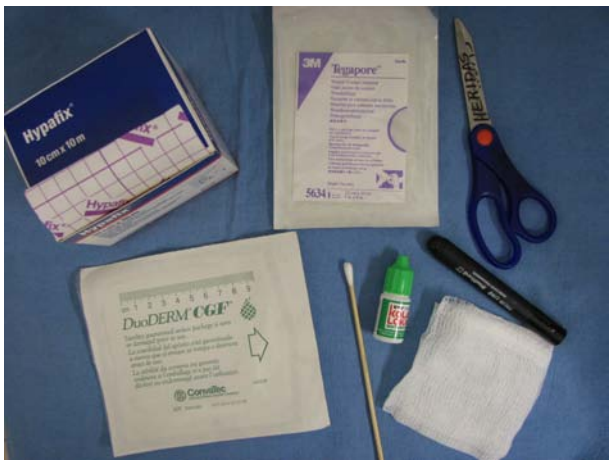


Figure 1.- Necessary material for the application of MT.

Step 2.- Trace the wound and cut and apply the hydrocolloid.
Use the clear plastic to trace the border of the wound as shown in the figure (Figure 2)

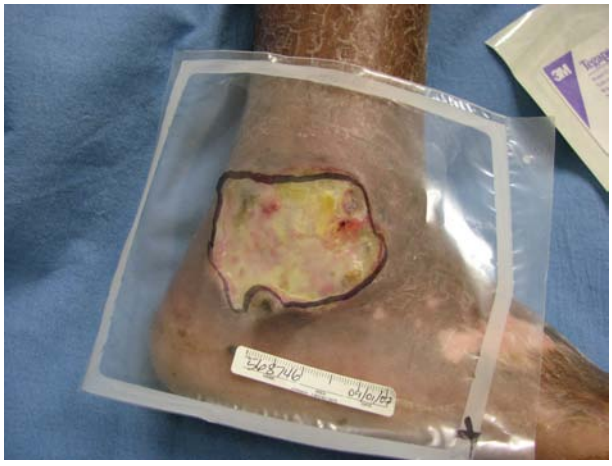


Figure 2

Place this tracing onto the hydrocolloid making sure you that it is not inverted resulting in a "negative" pattern. This could be avoided by using a light source to transilluminate the hydrocolloid and make sure that the adhesive side of the hydrocolloid faces the skin once the right tracing is marked. (Figure 3)

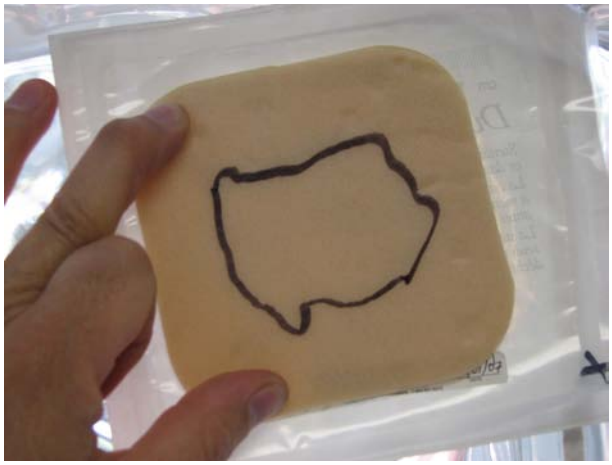


Figure 3

Cut the center of the dressing following the line to make a “doughnut” in order to have a protective border of at least 1 cm around the wound. (Figure 4) This border will protect the skin from the secretions of the maggots and will help for adhesion to the top of the cage dressing.

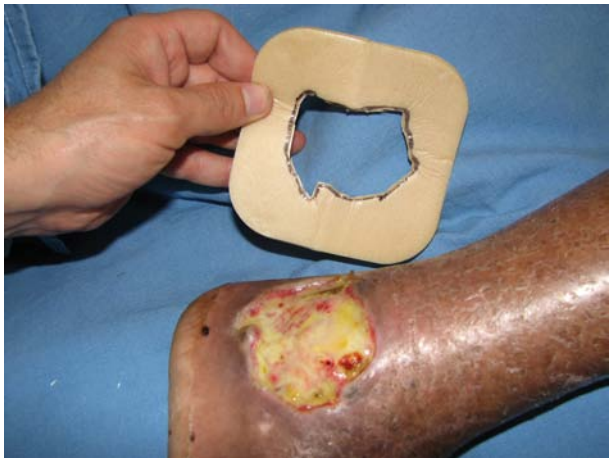


Figure 4

Place the dressing carefully following the border of the wound. Make sure it makes a good seal and there are no places where maggots could escape.

Step 3.- Partial closure of the cage-dressing and maggot placement.

Now take the fine mesh fabric and cut to the size of the hydrocolloid border. Place the fabric on the hydrocolloid and seal 50% of it with the cyanocrylate to the hydrocolloid as shown in the figure. (Figure 5) If time is a limitation you can speed up the process by fixing the fabric with tape first and then applying the cyanocrylate. Open the container with the maggots - if you will be using the totality of the maggots in a single patient you may use clean rather than sterile technique, if you are going to use a single container for more than one patient, you must make sure to use sterile technique, never introducing into the container anything that has previously touched the wound (e.g. a cotton applicator). There are three ways to remove the maggots: a) To remove all of the maggots it is recommend to make a small funnel with the fine mesh or the filter between the index finger and the thumb, put a small amount of saline in the container (it will also help to rinse out the growth media excess), shake it softly

and pour through the funnel to filter out the maggots and concentrate them in a single spot. b) To remove most of the maggots, use forceps to grab the gauze from within the vial and transfer it, with the maggots inside it to the wound (the gause can be cut proportionally if only a fraction of the maggots are needed; C) Using moistened cotton swab applicators to transfer obtain the maggots. This technique is especially useful when only a few maggots are needed using sterile technique for applying for more than one patient with a single maggot container.
In the United States, the FDA regulates medical maggots as a single-use only technique.
Although it cannot be recommended by many maggot providers, the maggots can also be aliquoted into multiple containers in the pharmacy under a laminar flow hood using high sterility standards if only a few per patient are meant to be used.

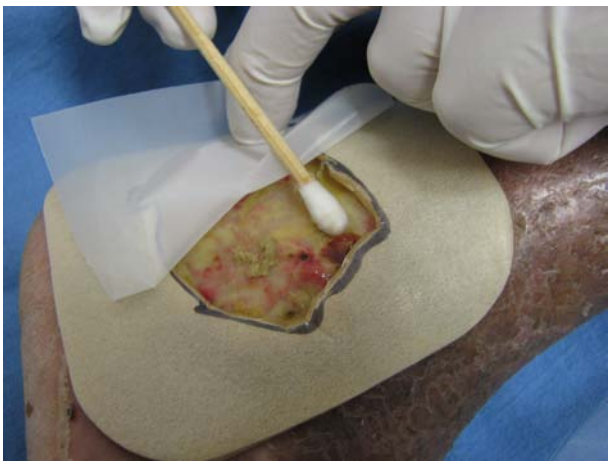


Figure 5

After removing the maggots by any of the previously described techniques, place them on the wound bed. (Figure 6) The amount will depend on the amount of tissue to be debrided. Although literature mentions 3 to 10 maggots per square centimeter, it really is an estimate where one must place many maggots for a large amount of necrotic tissue and a few in the opposite case. Precisely quantifiying the maggots is impractical and very difficult.

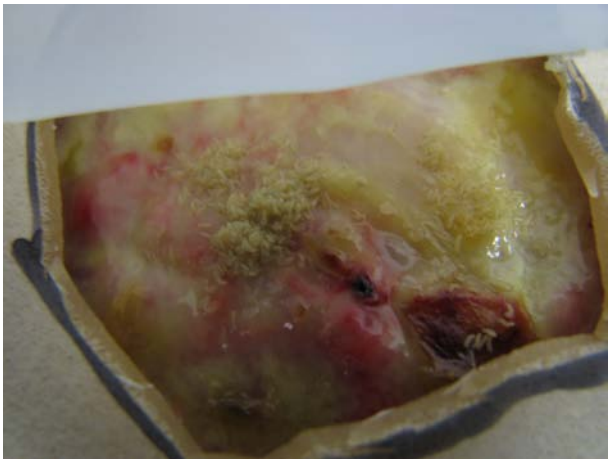


Figure 6

Step 4.- Sealing the cage dressing
Once the maggots are inside, finish sealing the remaining 50% of the fabric on the cage dressing. You may aid yourself again with the adhesive tape or seal and hold in parts. Make sure there are no unsealed spots from which the maggots could escape. (Figure 7)

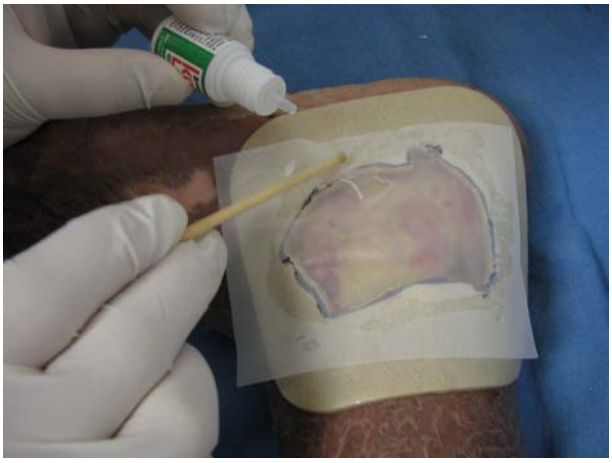


Figure 7

If the adhesive tape has not been applied yet, you can reinforce the borders of the dressing by applying a layer around the edge. (Figure 8)

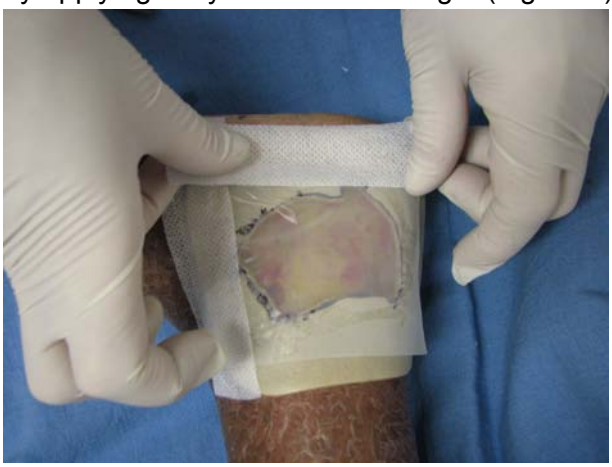


Figure 8

Step 5.- Place the secondary dressing.

Once the dressing is sealed and reinforced, place enough gauze to absorb the exudate that will be draining from the wound and wrap if necessary loosely in order to not squeeze the maggots. (Figure 9)

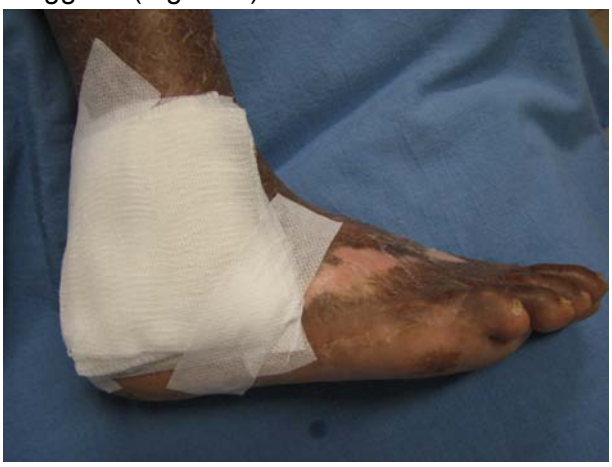


Figure 9

The last method of application is a variant of the previous one where strips of the hydrocolloid are used instead of the tracing on the hydrocolloid. These strips are placed around the border in areas where the placement of the whole dressing is challenging such as between the toes, distally in the foot or creases. (Figures 10 & 11)

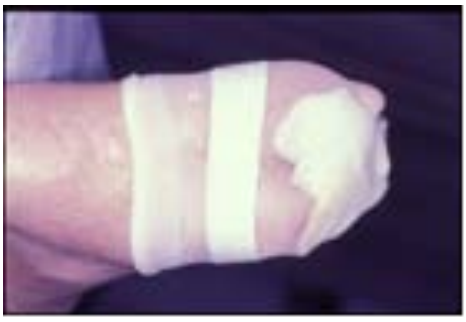


Figure 10. Photo courtesy of Ronald Sherman, MD.

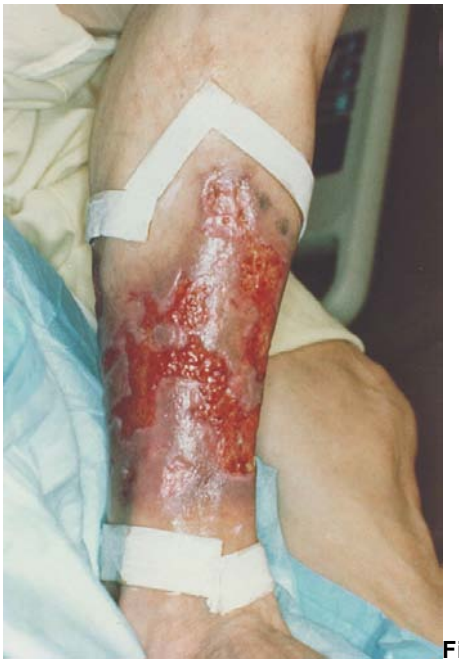


Figure 11. Photo courtesy of Ronald Sherman, MD.

Just recently, a number of dressings for confinement or containment have been developed focusing on decreasing application time and facilitating MT. Some of these dressings are: (Creature Comforts® and LeFlap® by Monarch Labs, BioBag® and BioFoam ® by BioMonde)

3.6 Explain to the patient the necessary recommendations while the maggots are in place and the measures to take in case of emergency. (Evidence level IV)

Previous to discharging the patient home or leaving the patient's bedside make the following recommendations:

- If the patient has uncontrollable pain, bleeding or extreme anxiety within the first few hours, s/he must return to be evaluated. If immediate evaluation is not possible, the patient must remove the maggots with clean water and the maggots disposed of in the toilet. After rinsing with water, the wound should be covered with a dressing or

moist gauze. The patient must return for evaluation as soon as possible with the wound care specialist. If bleeding occurs, the patient must compress the area and go to the emergency department immediately.

- Whenever the gauze on top becomes saturated with exudate, it must be changed to avoid suffocation or drowning of the maggots and maceration of the skin.
- Do not soak the area of the wound. If the patient desires a to bath, a protective bag should be placed over the maggot dressing to prevent it from becoming wet.
- Rest as much as possible during the treatment
- In case of maggot escapes, they must be destroyed immediately (they can be disposed of in the toilet). Do not attempt to place them back into the wound. Re-seal with tape the area from which the maggots escaped, and return for evaluation as soon as possible.
- Do not apply pressure on the area of the wound; avoid squishing the maggots.
- Explain to the patient that during the treatment there will be an increase in exudates and there may be an increase in odor. In case of tachycardia, fever or general deterioration, the patient must seek an emergency consultation for prompt evaluation.

3.7 Use an adequate technique for the removal of the maggots after 24 to 48 hours (maximum 72 hours) of maggot placement. (Evidence Level IV)

The patient must come back for the removal of the larvae after 24 or 48 hours of therapy. Some of the authors mention that they can be removed up to 72 hours after. However, it is the experience of the authors of this guideline that waiting for 72 hours increases the chance of escapes from the cage dressing due to the long exposure of the dressing to the maggot secretions and the instinct of the maggots to migrate far from their host.

Given the life cycle of the flies (Figure 10) there is no problem with them remaining on the wound for this period of time, since pupation will occur after a few more days. Maggots in their initial stages are small and will feed on a small amount of necrotic tissue; it is after the first 24 hours that the maximum amount of necrotic tissue is consumed. When the maggot has reached 1 cm in length they will decrease their feeding needs. This happens around 48 hours.

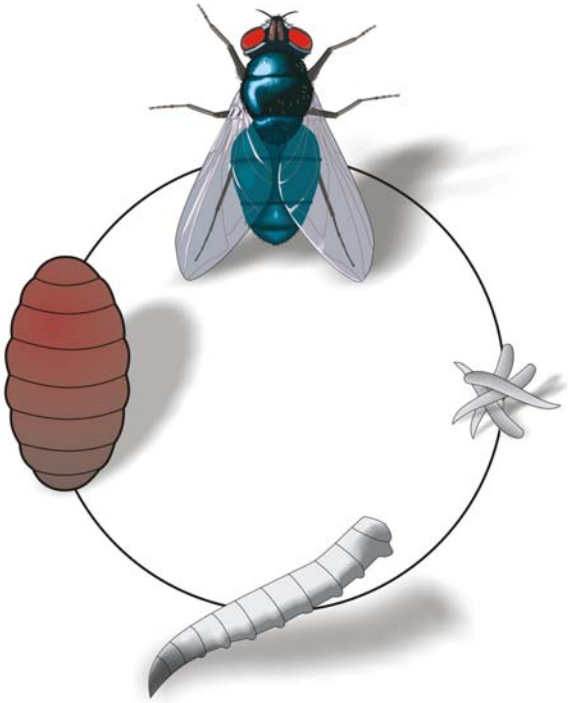


Figure 10.- Life cycle of the *Lucilia sericata* fly. The life cycle of the fly *Lucilia sericata* is significantly influenced by temperature and can last from two to three weeks up until two months. Once the fly lays the eggs, these will hatch in 24 hours. After this the minuscule larvae (1 mm) will start feeding and undergo through 3 larval stages very difficult to differentiate by simple observation (except their size). The maggots feed for 4 to 5 days and when satiated look for a dry and dark place away from the necrotic matter to become pupae. In the pupa stage they will remain for 3 weeks before they emerge as adult flies. The adult fly will live about 3-5 more weeks and will mate for reproduction and consequently closing the reproductive cycle.

Make sure you have a biological waste bag (BWB), saline solution or clean water, gauze, gloves, applicators and forceps.

If the maggots have cleaned the wound completely and there is no more necrotic tissue to debride, maggot removal is simple and quick. After removing the cage dressing the maggots will be exposed and it will suffice to flush them with the saline solution or clean water and if necessary push them with gauze into the BWB.

When there is remaining necrotic tissue on the wound, the maggots have a tendency to seek refuge inside it and therefore applicators and/or forceps may be necessary to remove those not easily flushed out.

If performed properly and the wound is well debrided, a clean wound bed with healthy granulation tissue will be clearly vissible. (Figure 11)

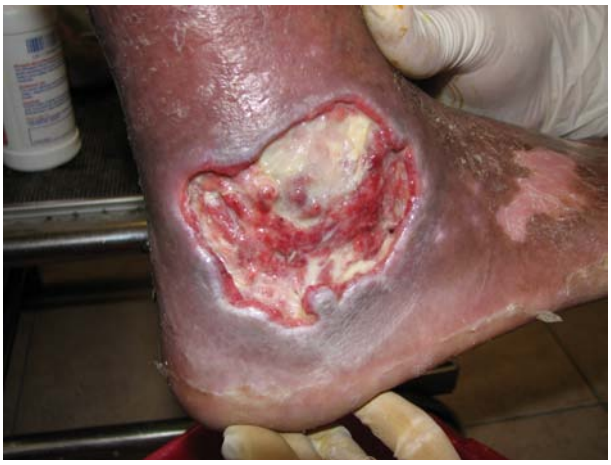


Figure 11

3.8 Dispose of the maggots according to the existing policy for dangerous biological waste. (Evidence level IV)

Maggots will have ingested necrotic material and bacteria from the wound, and for this reason they must be destroyed. Make sure the BWB is properly sealed and that the bag ends up in the designated area in your hospital for their destruction. [108,109] In order to prevent maggots from maturing into flies and distributing potentially resistant organisms through the community, this procedure should be carried out properly.

3.9 If necessary, re-apply a new MT cycle (Evidence level IV)

It is recommended to wait at least 24 hours before re-applying MT since this allows for re-evaluation of the wound once swelling has decreased. This also minimizes the risk of maceration or dermatitis resulting from prolonged exposure to the maggots' proteolytic secretions and wound exudates. Larger sections of the necrotic tissue that are detached/separated from the healthy one could be removed surgically allowing the maggots to concentrate to this more difficult to debride areas of the wound and to accelerate the complete debridement. This period could also be used to control bacterial infections, especially those caused by organisms resistant to MT, using appropriate disinfectants and antibiotics. Re-application of MT is recommended to debride residual necrotic tissue that could not be safely removed using other methods.

3.10 Treat adequately any complication associated to the detachment of the cage-dressing. (Evidence level IV)

Whenever there is detachment of the cage-dressing there may be maggot escapes and the wound edge may become irritated by the secretions. The first situation has no real consequences other than the anxiety in the patient or staff. The patient should know that the maggots can be picked up with a paper towel or tissue and disposed of in the toilet. The patient should re-seal the dressing and seek evaluation as soon as possible, as described above.

The second complication is due to the lytic power of the maggot secretions that may leak through the hydrocolloid seal and produce an irritative type of dermatitis that can, in rare cases, be severe. For its treatment it is necessary to wash several times with saline solution, dry and apply a potent topical steroid and antimicrobial ointment, preferably with activity against Gram positives (e.g. Fucicort®)

3.11. Carefully evaluate the border of the wound and take necessary measures not to cause additional damage to existing macerated or partially damaged skin. (Evidence level IV)

The amount of exudate in the wound during MT will necessarily increase as the secretions of the maggots are produced and the necrotic tissue is liquefied. In the presence of maceration around the wound proper barriers should be instituted and the cage dressing securely adhered to prevent further damage. Consider performing the maggot removal more frequently if necessary although smaller maggots will debride slowlier.

Contraindications and Precautions

4.1 MT should not be applied when there is an absolute contraindication (close proximity to large blood vessels or internal organs, patient's denial or lack of sterile maggots). (Evidence level III)

There are a few absolute contraindications to the use of MT. Maggots should never be applied to wounds involving a major blood vessel (e.g. an area where a previous amputation was performed) nor wounds where they may inadvertently reach internal organs. There have been reports of life threatening hemorrhages when this precaution is ignored.[110] Maggots should also not be applied to a wound within 24-48 hours of surgery because they may disturb the fresh blood clots.

Once the therapy and its benefits have been properly explained to the patient, if the patient refuses the clinician should use a different method for debridement.

Finally since contaminated maggots may generate infections, it is fundamental to only apply disinfected (medical grade) maggots, procured from a trustworthy provider.[111,112] For this same reason maggots coming from the wound of one patient should NEVER be used for another patient.

4.2 Carefully evaluate your patient when there are precautions to the use of MT. (Evidence level IV)

There are conditions that make the use of MT not recommended without a previous thorough evaluation of the patient's case.

4.2.1 Carefully evaluate ischemic wounds or with arterial insufficiency. (Evidence level IV)

As mentioned previously, and as is the case with any other wound healing modality, the debridement, of wounds with maggots may generate serious complications. However, in those cases where the patient is aware of the risks and accepts the therapy with the intention of delineating viable from non-viable tissue, for palliation, or while awaiting a more definitive therapy, they can be applied making sure the informed consent includes these considerations.

4.2.2 Carefully evaluate wounds with severe life-threatening infections or those requiring permanent visualization. (Evidence level IV)

The former must always be debrided surgically since the speed of MT may not be sufficient and the patient continues to deteriorate. They should only be considered in the setting where the surgical option is not available due to lack of resources, lack of personnel, or a medical contrainidication to surgery or its anesthesia. This should be a last resource until the patient can be referred for surgical debridement. Since the cage-dressing does not allow for wound visualization, consideration should be given to opening or changing the dressing every 24 hours in order to visualize the wound.

Patients with septisemia should not be treated with MT until the situation is under control.

4.2.3 Carefully evaluate non infected wounds with granulation tissue (Evidence level III)

The clinician should remember that MT is primarily a debridement method and for that reason granulating wounds may not benefit from it. However there is evidence that there are angiogenic and fibroplastic agents present in the maggot secretions that may act by increasing wound healing so in selected patients, it could be of use. Among the angiogenic factors isolated in maggot secretions are hystidine, valinol and 3-guanidinepropionic acid. [49] Other studies support the fact that they stimulate endothelial migration.[113] The authors of this guideline consider that MT in these patients is justified in those wounds not healing at an expected rate. If maggots are left on fully or almost fully debrided wounds, this should be done only with small numbers as larger amounts of maggots and their secretions could superficially damage the healthy tissue.

4.2.4 Carefully evaluate patients with anticoagulants or coagulopathy. (Evidence level IV)

In these cases the clinician should be very thorough on the explanations on the conduct to follow in case of bleeding. The majority of patients in this situation benefits from MT since one of the advantages of MT is not damaging healthy tissue, thereby avoiding the bleeding that conventional surgery may cause. If maggots erode any minor blood vessel causing bleeding, compression should be applied and evaluation sought immediately.

4.2.5 Carefully evaluate your patient if superficial or deep infection by *Pseudomonas aeruginosa* is present. (Evidence level III)

Controversy still exists on this topic. An experimental randomized trial showed complete lysis of P. aeruginosa, MRSA, C. albicans and VRE in 24 hours with persistence of the effect for 5 days. [94] An in vitro and in vivo case series showed that although MT is effective in treating all types of bacteria, it is less effective in Gram negatives like Klebsiella sp and Pseudomonas sp.[95] Another study, in materials used for orthopedic prosthesis, used the destructive power of the maggot secretions to destroy P. aeruginosa biofilms confirming they are highly effective, particularly the secretions of third stage maggots. [114] An in vitro study on the secretions points out its efficacy against P. aeruginosa and other bacteria.[93] However, another study by the same author concludes that there was no evidence of antibacterial effects of the secretions for any bacteria studied. In fact she describes that the maggots favored the growth of all bacteria analyzed except for P. aeruginosa.[115] Another study of P. aeruginosa with genes of virulence for the formation of biofilms showed that P. aeruginosa secretes virulence factors toxic to maggots rendering them ineffective. [116] Some other authors consider that, since maggots remove dead tissue and therefore there is less nutrition media for bacteria to thrive, maggots would be beneficial. The recommendation of the authors of this guideline is that if a first cycle does not result in benefit for the patient in a patient with *Pseudomonas aeruginosa*, other therapies should be considered.

4.2.6 Do not apply maggots for the treatment of osteomyelitis in a wound unless no other options exist to treat it. (Evidence level I)

The use of MT for the treatment of osteomyelitis dates from the initial descriptions from Baer in times when the options for this ailment were very few.[50,117,118] Although the use of MT for osteomyelitis has been described, it would likely require multiple cycles to achieve results. A systematic review[76] with the purpose of evaluating useful therapies for the treatment of osteomyelitis in the diabetic foot concluded that there is not enough evidence to support the use of MT in osteomyelitis.

Surgery is much quicker and effective in this setting and allows for bone samples to be obtained for diagnostic purposes. Infectious diseases consultation is most of the time mandatory. Maggot therapy is not the recommended treatment for osteomyelitis, and should only be attempted if surgical and medical treatments are unavailable or have failed.

4.2.7 Be cautious in patients allergic to components used in the nutrition media used for shipping the maggots. (Evidence level IV)

Some maggots are transported with nutrient media that may contain chicken egg, soy, yeast and/or other ingredients. Ask your maggot provider to specify the contents of the nutritious transport media, and ensure that your patient is not allergic to these substances. In the opinion of the panel, they can be applied with care performing two or three washes of the maggots using saline solution prior to application. In the reviewed literature, although this recommendation exists, there are no reported cases of allergies to maggots or the nutrient media.

4.2.8 Carefully consider the use of MT in painful wounds (Evidence level III)

5-35% of patients in published reports experienced pain or discomfort. MT-associated pain generally occurs in patients who are already recognized to have painful wounds. It is particularly painful in patients where the wound has exposed nerve endings and maggot movement or secretions irritate them or in those cases where the wound was already very painful. In a randomized controlled trial of Dunville,[77,78] the pain that the patients felt in the MT group was approximately double compared to the hydrogel group, however this study evaluated the pain after 72-96 hours with the maggots on, a practice not recommended. Wollina found in his case series that pain and burning were mild but that patients with pioderma gangrenosum required potent analgesia.[9]

In the Northwest Medical Center in Florida, a scheme for the safe treatment of patients with pioderma gangrenosum was developed and referenced in a review article. [27] In all the cases where the patient complains of pain, the amount or type of analgesics should be increased or consultation with a pain specialist considered. If the pain is strong, MT should be applied for shorter periods of time (e.g. during the day only), in the form of a biobag or discontinued and another debridement method considered.

4.2.9. Carefully evaluate the use of MT in patients with severe hepatic insufficiency or risk of encephalopathy. (Evidence level IV)

One of the compounds isolated in maggot secretions is ammonia. Even though there aren't any reports of patient deterioration in patients at risk of encephalopathy with the use of MT, there is a potential risk of absorption of the ammonia and worsening of encephalopathy. Besides, there is evidence in sheep where maggot infestation produced ammonia toxicity.[119-121]

CONCLUSIONS

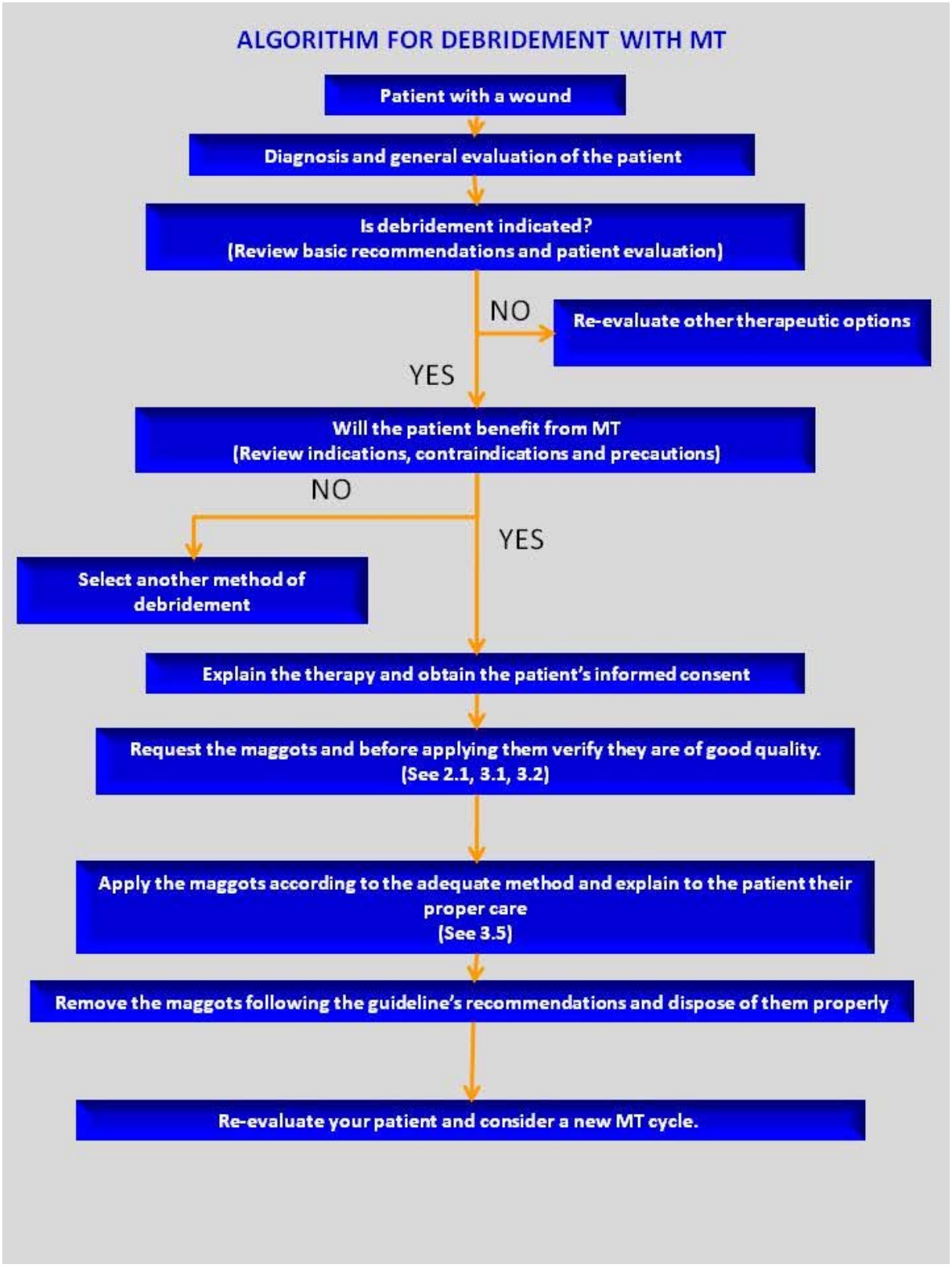
In the adequate preparation of the wound bed it is fundamental to carry out adequate debridement of the necrotic tissue. The latter acts as an obstacle for epithelialization, a foreign body, and is culture media for bacteria commonly infecting chronic wounds. [10,14]

MT is a simple and successful method for the debridement of wounds. The application of sterile larvae of the fly *Lucilia sericata* to a wound with necrotic tissue results in the removal of eschar and slough (debridement), in wound disinfection and in the stimulation of healing; these three actions are important steps in wound bed preparation. [122]

MT is a simple, effective, well tolerated and cost-effective for the treatment of chronic wounds not responding to conventional treatment and surgical interventions.[11,12,53] The emergence of bacteria resistant to antibiotics and the recognition that the surgical and pharmacological tools available are not capable of curing all wounds has made hospitals open their doors to MT again.[19,25,26]

Embedded in the present guideline are recommendations for selecting the patients who would benefit most from with MT and recommendations for methods that minimize inherent risks.

ALGORITHM



ABBREVIATIONS AND DEFINITIONS

ABBREVIATION	MEANING
MT	Maggot therapy
CPG	Clinical Practice Guidelines
BWB	Biological Waste Bag
MRSA	Methicillin resistant *Staphylococcus aureus*
VRE	Vancomycin resistant *Enterococcus faecalis*

A

Antiseptic: product that kills or inhibits bacterial growth designed to be used on the skin or other superficial tissues.

C

Colonization: Term referring to a specie or species populating an area. In relation to wounds it is used to describe the presence of less than 1 X 10^5 colony forming units (CFU) per gram of tissue. In colonization there is no harm to the host.

Contamination: Is the presence of germs or bacteria without signs of colonization. The majority of wounds are contaminated and very few are infected.

Contraindicated: condition or factor that speaks against a certain measure. It is mostly used in medicine, with regard to factors that increase the risks involved in using a particular drug, carrying out a medical procedure, or engaging in a particular activity.

Coprophagic larva: Larva feeding usually on fecal matter.

D

Debridement: Medical removal of a patient's dead, damaged or infected tissues or foreign bodies from the remaining healthy tissue. In wounds it has the objective of improving the healing potential and decrease bacterial burden and the inflammatory response. It can be carried out using several methods, some of those are:

- **Enzymatic:** with the application of exogenous enzymes (collagenase, streptokinase, papain-urea, etc.), that act synergistically with endogenous enymes.
- **Autolytic:** disintegration or liquefaction of necrotic tissues by leucocytes and endogenous enzymes. Their actions depends on the hydration of the tissues though the use of water containing dressings such as hydrogels or occlusive dressings.
- **Surgical:** it is performed with scalpel, scissors or curette. It is indicated in the presence of thick adherent eschars, devitalized tissue over large areas or deep areas, signs of celullitis and urgently in the presence of sepsis, and to eliminate bone or tendon. It can be performed in the operating room under anesthesia or as an outpatient procedure when there is no risk of bleeding, infection and the pain is controlled.

Delphi Method (Process): An interactive and systematic method that depends on an expert panel. The experts respond to questionnaires in two or more cycles. After each cycle a facilitator provides an anonymous summary of the predictions and opinions of the experts and their reasons for their judgment. In this way the experts review their previous answers with this new information. It is believed that during this process, the variation in the answers decreases and the group reaches a "correct" answer or consensus. Finally the process stops when an "a priori" selected criterion is reached and normally this criterion is reaching consensus.

Diabetic foot: Any loss of continuity of the skin below the ankle in a patient with diabetes. It usually is accompanied by one or more of the following: neuropathy, ischemia, or infection.
Disinfection: a set of interventions aimed at eliminating the germs that may exist over a specific site or living being.

E
Epithelialization: cellular regeneration of the epidermis through the surface of a wound.
Eschar: a slough or piece of devitalized, dehydrated, black hard tissue giving the aspect of leather or cardboard that is cast off from the surface of the skin.

H
Healing: repair process of an altered or damaged tissue giving as a result the formation of a scar.
Hydrocolloid (Dressing): An advanced wound care dressing made of adhesive gelatin, and a pectin mass that absorbs exudates from the wound to form a gel. In general it does not allow for the exchange of gases and it exists in the form of diverse shapes, thickness and other presentations such as powder and paste.

I
Infection (Clinical): presence of microorganisms whose amount (burden) and virulence overwhelm the ability of the host to combat them. Usually it is correlated with a bacterial burden of more than $1x10^5$ CFU/g of tissue. It is generally accompanied by fever, pain, swelling and increased temperature.

L
Larva: distinct juvenile form many animals undergo before metamorphosis into adults. In flies, depending on the temperature this form begins after the eclosion (hatching) of the eggs and finalizes when the maggot turns into a pupa around 4 to 8 days after.
Necrophagic larva: Larvae feeding only on dead organic matter.
Lucilia sericata: Mid size fly easily recognizable by the metallic coloration of its body (metallic green), especially on the abdomen. Its life cycle comprises 4 stages: egg, larval (with three larval stages), pupa and adult. This cycle lasts from weeks to months depending on temperature and moisture. Frequently the fly deposits its eggs in feces and decaying matter or cadavers and more seldom on wounds. The eggs are white to light yellow, are about 1 to 2 mm in length and are always grouped in a mass.

M

Maggot: larva of a fly (usually dipteral).

N

Necrosis: The death of a tissue. It is usually of a black or dark brown color. When hydrated it is known as slough. (See slough)

P.

Pupa: the life stage of some insects undergoing transformation. Some pupae remain inside the exoskeleton of the final larval instar (such as flies) and receive the name of puparium. In this stage flies remain in a dark, dry area away from the feeding source where they emerge as adult flies in a period ranging from 2 to 4 weeks (see also life cycle of L. sericata) depending on the temperature.

S

Skin ulcer: loss of the full thickness of the skin that may involve deeper tissues.

Slough: Hydrated necrotic tissue, usually loosely adhered and fibrous of yellowish coloration.

W

Wound: Loss of continuity of a tissue

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