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- Objective** To review the current evidence on the mechanism of actions and clinical applications of maggot debridement therapy.
- Data sources** Literature search of PubMed and Medline was performed up to January 2007.
- Study selection** Original and major review articles related to maggot debridement therapy were reviewed. Key words used in the literature search were 'maggot debridement therapy', 'wound healing', and 'chronic wound management'.
- Data extraction** All relevant English and Chinese articles.
- Data synthesis** The mechanism of such maggot therapy was shown to be due to the debridement, disinfection, and wound healing enhancement actions of maggot excretions/secretions. The efficacy of maggot debridement therapy in chronic wound management has been demonstrated in chronic venous ulcers, pressure ulcers, and diabetic ulcers. There is also a new delivery system for the excretions/secretions, which has been shown to be as effective as using live maggots.
- Conclusions** Maggot debridement therapy has been shown to be a safe and effective means of chronic wound management. However, there are a number of limitations when considering its local applicability. Future development of the delivery system may help to overcome some of these limitations and improve its acceptability.

## Introduction

As the population ages, the number of patients suffering from chronic wounds attributable to diseases such as diabetes mellitus and peripheral vascular disease is on the rise. This poses a significant impact on the health care system, because of the chronicity of care required and the associated costs. A chronic wound does not progress through the four overlapping phases of wound healing. Instead, it is commonly arrested at the inflammatory phase, due to the presence of slough, necrotic debris and infection. Traditionally, the principles of treatment for acute and chronic wounds include debridement and the application of dressings. Wound debridement involves removing necrotic tissue, exudates, foreign material and bacteria, so that the normal stages of wound healing can take place. The use of dressing materials prevents local contamination of the wound site, facilitates exudate removal, and prevents infection.<sup>1</sup> In addition, much research has been devoted to developing new techniques to enhance and hasten the process of wound healing, including adjuvant growth factors, tissue-engineered products, hyperbaric oxygen and negative pressure wound therapy.<sup>1,2</sup> As an alternative to surgery, maggot debridement therapy (MDT) has been shown to provide rapid and effective wound debridement, thus hastening the process of wound healing and lowering the overall costs of management.<sup>3-7</sup>

### Key words

Debridement; Diptera; Larva; Wound healing; Wounds and injuries

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## Historical perspective

The utilisation of larvae for wound healing has been well-documented across the centuries in different cultures, including the Chinese. The beneficial effects of using larvae in wounds were first noticed by Ambrose Paré in 1557.<sup>8,9</sup> While treating battle wounds in Napoleon's army, Baron Larrey observed that maggots enhanced granulation formation.<sup>10</sup> The first clinical application of maggot therapy was performed by JF Zacharias and J Jones during the American Civil War.<sup>11</sup> Later, William Baer refined the technique by using sterile maggots to prevent maggot-induced wound infection. The therapy became increasingly

more popular and was widely used for the treatment of chronic or infected wounds across North America and Europe during the 1930s. With the introduction and the widespread use of antibiotics in the 1940s, the popularity of MDT gradually declined and became largely forgotten by the medical community. However, with the rising incidence of antibiotic resistance in the late 1990s, there is renewed interest in maggots and their potential use in chronic wound management.<sup>11,12</sup>

### The larvae—green-bottle fly *Lucilia (Phaenicia) sericata*

The larvae of the green-bottle fly *Lucilia (Phaenicia) sericata* are the most commonly used for wound management. This fly belongs to the Diptera order of insects, which are known to be able to infest living hosts and parasitise host tissue. The 1-2 mm long larvae hatch from their eggs in 12 to 24 hours.<sup>13</sup> Feeding on necrotic tissue in the moist environments of wounds, they grow rapidly and mature in 4 to 5 days, measuring around 10 mm in length. Later they pupate and become adult flies.<sup>13</sup>

### Maggot debridement therapy

Larvae used for MDT need to be sterile to prevent contamination, and therefore must be bred in a controlled sterile, moist environment.<sup>7,13</sup> Newborn larvae should be used within 8 hours or stored in a refrigerator at 8° to 10°C, so as to slow their metabolism.<sup>7</sup> To maximise debridement, it is important to ensure an optimal body temperature, adequate oxygen supply and moisture, though too much moisture may kill the larvae.<sup>2,13</sup> The use of occlusive dressings should be avoided, as larvae require oxygen to survive.<sup>13</sup> Propylene glycol from hydrogel dressings can limit the growth and viability of larvae, while systemic antibiotics do not affect larval development.<sup>13</sup>

### Mechanisms of maggot debridement therapy

#### Debridement

Scientists first postulated that the debriding action of maggots was due to their mechanical wriggling.<sup>14</sup> Maggots use a pair of mandibles/hooks for movement and attachment, and it was believed that the probing from the hooks may facilitate wound debridement. Recently, three proteolytic enzyme classes have been identified in the maggot excretions/secretions (ES).<sup>15</sup> These enzymes effectively degrade extracellular matrix components, including laminin and fibronectin. The ES could thus assist in the digestion of the wound matrix, leading to effective debridement.

### 蠅蛆治療法對長期創傷的護理

**目的** 探討蠅蛆治療法的原理和醫學應用。

**資料來源** 於PubMed及Medline資料庫內搜索直至2007年1月的文獻。

**研究選取** 以‘maggot debridement therapy’「蠅蛆治療法」、「wound healing」「創傷治療」、「chronic wound management」「長期創傷護理」搜索關於蠅蛆治療法的論著和綜述。

**資料選取** 回顧所有有關的中英文文獻。

**資料綜合** 蠅蛆治療法的原理在於蛆蟲的分泌物能清理傷口、消毒及提高癒合的效率。文獻亦證實蠅蛆治療法在治療靜脈瘀血性潰瘍、壓力性潰瘍和糖尿病潰瘍上均有顯著的功效。目前有一種運用蛆蟲分泌物的新治療法，效果與利用活生生的蠅蛆同樣有效。

**結論** 文獻顯示蠅蛆治療法是一種既安全，又能有效護理長期創傷的方法，但使用時須考慮其限制。而在將來結合最新科技的蠅蛆治療法則有望能克服這些限制，並在本港更被普及應用。

### Disinfection

The presence of antibacterial substances has long been identified in maggot ES. Thus, ES has an inhibitory effect on Gram-positive and Gram-negative bacteria, including methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *S. aureus* (MRSA), *Escherichia coli* and *Pseudomonas aeruginosa*.<sup>16</sup> This activity of the ES was thermally stable and protease-resistant. Using ultrafiltration, the latter study identified two fractions with inhibitory effects on *S. aureus* and MRSA. It was also believed that ammonia excreted by maggots increases wound pH, thereby creating an unfavourable environment for bacterial growth.<sup>17</sup>

According to another hypothesis, maggots ingest bacteria and kill them within their alimentary tract. Mumcuoglu et al<sup>18</sup> investigated the fate of *E. coli* after ingestion by *L. sericata*. It transpired that the proximal alimentary canal was more heavily infested, with 67% of the throat harbouring live bacteria. The figures dropped dramatically as the bacteria moved distally along their alimentary canal. Only 18% of the posterior hindgut was found to contain live bacteria.

### Enhancement of wound healing

It was believed that the enhancement in tissue growth was due to an increase in fibroblast proliferation brought about by the ES.<sup>19</sup> Horobin et al<sup>20</sup> demonstrated that the ES altered fibroblast adhesions to collagen and fibronectin, and it was subsequently shown that it increased the migration (but not proliferation) of fibroblasts. This was attributed mainly to the action of serine and metallo proteinases. These

BOX. Types of wounds/lesions for which maggot therapy may be used

Diabetic ulcers<sup>4,13,25-27</sup>  
 Venous ulcers<sup>4,23,27</sup>  
 Neuropathic ulcers (non-diabetic ulcers)<sup>4,13</sup>  
 Arterial/ischaemic ulcers<sup>4,13,28</sup>  
 Pressure sores<sup>3,24,28</sup>  
 Thromboangiitis obliterans<sup>4,13,27</sup>  
 Post-traumatic wounds/ulcers<sup>3,13,28-30</sup>  
 Necrotising fasciitis<sup>31-33</sup>  
 Pyoderma gangrenosum<sup>4,13</sup>  
 Excised abscess on malleolus<sup>3</sup>  
 Pilonidal sinus<sup>3</sup>  
 Grossly infected toe<sup>3</sup>  
 Osteomyelitis<sup>27,34</sup>  
 Infected wound after forearm replantation<sup>35</sup>  
 Wound of exposed knee prostheses<sup>36</sup>  
 Wound infection after breast surgery<sup>30</sup>  
 Infected gun shot wound<sup>27</sup>  
 Malignant wounds<sup>4,37</sup>  
 Burns<sup>28,38</sup>  
 Non-healing surgical wound<sup>28,40</sup>  
 Methicillin-resistant *Staphylococcus aureus*-infected wound<sup>12</sup>  
 Mixed arterial-venous ulcer<sup>4</sup>  
 Subacute mastoiditis<sup>39</sup>

investigators then developed a three-dimensional model to better simulate a human wound.<sup>21</sup> Their results were consistent with the previous studies and supported by later investigators.<sup>22</sup> An upregulation of tyrosine phosphorylation was also detected, which possibly enhanced the motility of the fibroblasts.<sup>22</sup> Others have postulated that maggots secreted cytokines, which help wound healing. High levels of gamma-interferon and interleukin-10 (IL-10) were found in the ES, but as to whether these cytokines are responsible for increasing granulation requires further investigation.<sup>19</sup>

### Indications for maggot debridement therapy

Maggot debridement therapy is mainly used for the cleaning and disinfection of chronic wounds that are sloughy, necrotic, and infected. Various clinical studies have demonstrated the efficacy of MDT in treating wounds that fail to heal following alternative forms of treatment. Wollina et al<sup>4</sup> demonstrated that MDT could rapidly reduce a mean±standard deviation wound score of 13.5±1.8 to 6.3±2.7 (P<0.001) with only a single application of maggots for 1 to 4 days. The wound score was determined by and proportional to slough coverage, exudation, malodour, granulation and inflammation of surrounding skin. Larvae were effective in removing necrotic tissue and exudation without damaging adjacent healthy tissue. This action stimulated tissue granulation and reduced offensive odours brought about by infections.

The benefits of MDT have been reported for a variety of chronic wounds (Box<sup>3,4,12,13,23-40</sup>). With the emergence of antibiotic resistance, MDT has

been demonstrated to be useful in surgical wounds infected with MRSA.<sup>12,40</sup> Compared to conventional hydrogel therapy, MDT was more effective for chronic venous ulcers, diabetic ulcers, and pressure ulcers.<sup>23-25</sup> In a controlled study on diabetic foot ulcers, 14 patients were randomly allocated to receive MDT and another 14 to conventional therapy. There was no significant debridement after 14 days in the conventional therapy group. Whereas, after 14 days there was a mean decrease in necrotic tissue of 4.1 cm<sup>2</sup> (P=0.02) in the MDT group, and complete debridement was achieved in 4 weeks.<sup>25</sup> In another study on venous ulcers, 12 patients were randomised to receive MDT or conventional therapy. Complete debridement was achieved in the MDT group with one application for 3 days, while only two out of six patients in the conventional therapy group achieved complete debridement after 1 month. The other four patients required repeated changes of dressing.<sup>23</sup> As for pressure ulcers, a study was performed with 103 patients randomly assigned to MDT or conventional therapy; 80% of patients in the MDT group achieved complete debridement within 5 weeks, while only 48% did so after conventional treatment (P=0.021).<sup>24</sup>

### Contra-indications and side-effects

Dry wounds are a relative contra-indication as maggots require a moist environment. The use of maggots should also be avoided in open wounds of body cavities or wounds in close proximity to large blood vessels so as to facilitate the removal of the larvae.<sup>7</sup> Also, maggots should not be used in patients who are allergic to eggs, soybeans, or fly larvae.<sup>41</sup>

Maggot debridement therapy has not been associated with major adverse effects or complications, but has been reported to cause mild discomfort, malodour at the first change of dressing, and escape of larvae.<sup>13</sup> Excessive pressure applied on to parts of the wound may also kill maggots in that area, leading to uneven wound debridement. Despite these shortcomings, even patients experiencing pain during treatment tend to report improved appearance.<sup>6</sup> Five bloodstream infections attributed to contaminated larvae of *Protophormia terraenovae* have been reported, but provided that the maggots have been effectively disinfected, their use on chronic ulcers appears to be safe.<sup>42</sup>

A major obstacle to the utilisation of MDT appears to be its poor acceptance by both patients and health care professionals. Social and cultural beliefs and the so-called 'yuk' factor may initially hinder its use, but studies have shown that patients who receive adequate psychological preparation and relevant information from health care professionals are more likely to accept the initial therapy and further treatments.<sup>7</sup> Thus, experience of MDT tends to be less 'frightening' and more beneficial than imagined. It is

nevertheless important that health care professionals address and attempt to alleviate patient concerns and respect their wishes at all times.

### Is maggot debridement therapy cost-effective?

Waymen et al<sup>23</sup> demonstrated the cost-effectiveness of MDT in patients with chronic venous ulcers. In their study, the median cost of treatment per patient in the larval group was £79 compared to £136 for the hydrogel controls ( $P < 0.05$ ). The MDT group required fewer visits to achieve debridement than the controls (median number of visits: 3 vs 19;  $P < 0.05$ ). According to Thomas and Jones,<sup>3</sup> when nursing costs were included, the total expenditure on materials to successfully debride one wound was £82 versus £503, in favour of MDT. The reduction in total costs could be attributed to reduced debridement times as well as reduced number of hospital visits or bed days, all of which resulted in significant savings for the health care system.

### The future for maggot debridement therapy—a new delivery system

Studies have shown that the action of ES is concentration-dependent, with efficacy peaking at a certain dosage.<sup>18,19</sup> There is thus an established need for a method of delivery, which can keep its concentration around the wound relatively constant.

There are other problems concerning the use of live maggots for MDT. Repeated changes are necessary because the life cycles of larvae are relatively short. Moreover, their limited 'shelf-life'

means that they need to be used soon after delivery. Smith et al<sup>22</sup> recently experimented with a prototype hydrogel wound dressing containing *L. sericata* larval ES. Their study on a wound model demonstrated a statistically significant difference between the ES-impregnated hydrogel and the buffer-only control group; mean wound areas remaining after a 12-hour treatment were 40 vs 120 megapixels. These results indicated that the new delivery system could increase the wound healing rates in the experimental model.

### Conclusions

Maggots have been used since antiquity to treat chronic wounds. With proper sterilisation and refinement of delivery techniques, they have proven to be a safe and effective method of debridement, for a variety of notoriously difficult-to-treat wounds. Although MDT is not without limitations, it remains a viable option for wounds or ulcers that fail to respond to conventional therapy. In Hong Kong, local experience of MDT is lacking with only individual cases reported.<sup>40</sup> Although alternative methods such as ultrasound and waterjet debridement are available and yield results that are at least equivalent if not better than conventional therapy, whether MDT can be introduced for local patients will depend on the availability of sterile maggots. Use of maggots requires facilities to breed and produce them in sterile conditions. The therapy can then become both accessible and cost-effective. Overcoming political and administrative obstacles may also pose challenges, and include concerns with sterility and acceptance by nurses and patients. Meanwhile, new delivery systems may emerge and provide more promising, acceptable, and popular means of garnering the benefits of MDT.

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