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# Evidence Summary: Wound management: larval therapy

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## QUESTION

What is the best available evidence regarding the effectiveness of fly larvae for debridement and healing of wounds?

## BACKGROUND

The use of larval therapy, also known as larval (or maggot) debridement therapy (LDT), bio-surgery or bio-debridement, has undergone a revival as a wound management option over the past three decades due to the increasing prevalence of non-healing wounds and the emergence of antibiotic-resistant infections.<sup>1</sup>

Larval therapy involves applying laboratory-raised sterilised fly larvae to the wound bed. The surface sterility of larvae is crucial in ensuring the safe use of LDT.<sup>2</sup> These larvae act by both mechanical and biochemical (secretions and excretions) means to debride necrotic tissue, reduce inflammation, inhibit biofilm and stimulate granulation tissue in wounds.<sup>3,4</sup> The green bottle fly *Lucilia sericata* is the most commonly used species. Several other species, for example, from Malaysia and South America, with similar effectiveness have also been identified.<sup>5,6</sup> Work is progressing on developing a recombinant enzyme from *Lucilia sericata* for inclusion in a topical hydrogel.<sup>7,8</sup>

There are two modes of applying larvae to the wound: contained (bagged) and confined (free to range over the wound but confined by the dressing).<sup>9</sup>

## CLINICAL BOTTOM LINE

### Wound debridement

A multicentre, blinded randomised controlled trial (RCT) of patients with chronic, sloughy wounds compared LDT (n=51) with conventional treatment (surgical debridement three times a week) (n=54) over a two-week period. For the LDT group the contained larval dressings were changed twice a week. On day 8 there was a significant statistical difference (p=0.04) in the percentage of slough between the LDT group (54.5%) and the control group (66.5%). By day 15, however, there was no difference (LDT group 54.4%, control group 53.8%, p=0.78).<sup>10</sup> (Level of evidence 1c)

Two other RCTs (N=267 and N=12) found LDT significantly reduced time to debridement when compared to hydrogel dressings. In the first RCT the rate of debridement in the LDT was about twice that of the comparison group at any point in time [hazard ratio 2.31, confidence interval (CI) 95% 1.65–3.24, p <0.001].<sup>11</sup> (Level of evidence 1c) The second small RCT found that the LDT group only required one confined larval application (i.e. not confined in a bag) for complete removal of slough compared to the hydrogel dressing group who required between 10 and 42 applications.<sup>12</sup> (Level of evidence 1c)

A cohort study evaluated healing-related outcomes in 92 pressure injuries, of which 43 were debrided using larval therapy and 49 debrided using conventional therapy, that is, care by a general practitioner (GP) which did not include larval therapy. Complete debridement was achieved in 80% of larval-treated wounds compared with 48% of wounds debrided with conventional therapy alone (p<0.021). Within three weeks of treatment, necrotic tissue was significantly reduced (p<0.05) and granulation tissue significantly increased (p<0.001) in wounds that were debrided using larval therapy as compared with the conventionally treated wounds.<sup>13</sup> (Level of evidence 3c)

A second cohort study with a control group involving 28 non-healing foot and/or leg ulcers in 18 diabetic patients found that after five weeks of therapy the conventionally treated wounds still had 33% of their surface area covered by necrotic tissue whereas in the LDT group at four weeks all wounds were completely debrided (p=0.001).<sup>14</sup> (Level of evidence 3c)

An observational study of 34 patients with chronic wounds of at least 12 weeks duration also found LDT to be effective method of wound bed preparation. Of the 29 who completed the LDT treatment, all necrotic tissue was removed from the wound and granulation tissue had formed enabling split thickness skin grafting to be done. Following grafting 93% of these wounds healed within seven to 10 days.<sup>15</sup> (Level of evidence 3e)

Another observational study involved 30 patients with chronic leg and foot ulcers. Twenty-eight of the patients received only one application of LDT (confined larvae) lasting 3.3±2.2 days, with the remaining two patients treated for three days, three and four times respectively. Outcomes were assessed by a pre and post wound score tool of four items — sloughy coverage, exudation, malodour, inflammation of surrounding skin and granulation — with the total score range being zero to 15 (worst case). Wound scores improved from 13.5±1.8 to 6.3±2.7 after one application of LDT.<sup>16</sup> (Level of evidence 3e)

A third observational study examined which method of larval therapy — confined or contained — was more effective. Of the 69 wounds (in 64 patients), 54 (78%) were treated with confined LDT while the remaining 15 (22%) received contained LDT. The confined method had significantly better outcomes (p=0.028). This method also resulted in a significantly lower mean number of applications (p=0.028) and the total number of maggots per treatment (p=0.001) thereby reducing costs.<sup>17</sup> (Level of evidence 3e) An RCT, however, found no difference between the two methods in terms of time to healing.<sup>11</sup> (Level of evidence 1c)

### Effectiveness in promoting healing

A systematic review (SR) involving four studies comparing LDT with standard therapy (one RCT and three cohort with

control group studies) with a total of 282 patients with diabetic foot ulcers (DFUs) found that MDT was more effective in achieving complete healing (relative risk=1.80, 95% CI=1.07–3.02, p=0.03). (Note: As one study<sup>5</sup> used a different method of measuring healing from the other three it was not included in the final meta-analysis.) Larval therapy was also reported to be superior in time to healing (no supporting statistical data provided).<sup>18</sup> (Level of evidence 1b)

A second SR included 12 studies: six RCTs and six cohort studies. Eight studies reported on healing rates (total N= 1226) and were subject to a meta-analysis — the risk ratio (RR) for LDT being 1.80 (95% CI 1.24–2.60). A sub-group analysis of patients with DFUs indicated that LDT was more effective than conventional treatment (e.g. hydrogel dressings): RR 1.79 (CI 0.95–3.38). For patients with pressure injuries or venous leg ulcers the RR was 1.70 (CI 1.28–2.27). Time to healing was also significantly shorter.<sup>19</sup> (Level of evidence 1b)

A RCT with blinded assessment had contrasting results (not included in a meta-analysis to date). Although the healing rates between the two groups were not significantly different on day eight, by day 15 the mean wound surface of the LDT group had increased by 14.6% compared to the mean decrease of 8.2% on the surgical debridement group (p=0.02). By day 30 there was once again no significant difference in wound surface area between the two groups.<sup>10</sup> (Level of evidence 1c)

### Effectiveness in reducing bacterial load

In one RCT, LDT was effective in reducing the number of wounds colonised with MRSA whereas in the control group (surgical debridement three times a week) the number of colonised wounds increased. However, the number of wounds colonised by *Pseudomonas aeruginosa* remained the same, leading the authors to suggest that either LDT not be used in the latter case or the number of larvae applied be increased 10 fold and changed more frequently in order to adequately break down biofilm.<sup>10</sup> (Level of evidence 1c) In contrast, another RCT found there was no difference between LDT and hydrogel in eradicating MRSA by the end of the debridement period.<sup>11</sup> (Level of evidence 1c)

A cohort study with comparable groups studied postoperative infection rates in patients who had received pre-surgical LDT. The types of surgery planned included amputations, flaps, split thickness skin grafts and primary closure of non-healing post-surgical wounds. In the 10 wounds debrided with LDT one to 17 days prior to surgery, debridement was effective and there were no postoperative wound infections. However, in the control group (19 wounds) six (32%) developed postoperative clinically significant wound infections with subsequent dehiscence (95% CI, 10–54%; p<0.05).<sup>20</sup> (Level of evidence 3c)

A cohort study with control group of 60 elderly, non-ambulatory patients with diabetic foot ulcers and peripheral vascular disease found that in the case of clinical infection there was no significant difference between the LDT group and the standard care control group (80% versus 60%, p=0.09). However, in the six months of follow-up the LDT group had significantly more antibiotic-free days than the control group (81.9±30.3 versus 126.8±30.3 days; p=0.001).<sup>21</sup> (Level of evidence 3c)

An observational study of 13 diabetic foot ulcers reported that the bacterial load of all ulcers reduced sharply to below the 10<sup>5</sup> CFU per ml wound fluid threshold after the first LDT cycle.<sup>22</sup> (Level of evidence 3e)

## CLINICAL CONSIDERATIONS

### • Patient acceptance

A number of quantitative and qualitative studies have found that the vast majority of patients accept LDT<sup>4,12,13,15,23,24</sup> (Levels of evidence 1c & 3) or even request the treatment.<sup>5</sup> (Level of evidence 3c) Two qualitative studies<sup>23,24</sup> identified a number of factors that influence acceptance: duration or reoccurrence of chronic wounds and impact on quality of life, the patient's negative experience with other treatments, nurse–patient relationship, experience of others and informed choices. A key influence in refusing LDT was the visual imagery that it elicited, particularly in older women aged > 70 years.<sup>23</sup> (Level of evidence 3) Findings in two studies suggest that patient acceptance can be far better than that of health professionals, who frequently disallowed or dissuaded their patients to receive LDT.<sup>13,15</sup> (Levels of evidence 3c & 3e)

### • Suitability of patients

Findings from a case series of 101 patients suggest that LDT results in poor outcomes for patients with the following characteristics: older patients and patients with chronic limb ischemia. Contraindications include open abdominal cavity wounds, pyoderma gangrenosum in patients receiving immunosuppressive treatment and septic arthritis.<sup>25</sup> (Level of evidence 4c)

### • Cost

Two cost-effectiveness studies of LDT have been conducted. The first (n=12) calculated the cost of nursing time and materials involved in LDT compared to hydrogel dressings. Larval therapy was approximately half the cost of hydrogel treatment.<sup>12</sup> A more sophisticated economic analysis involving cost effectiveness and cost utility (n=267), also comparing LDT with hydrogel found the two treatments were similar in costs and health benefits.<sup>26</sup> (Level of evidence 4)

## ADVERSE EFFECTS AND RISK MANAGEMENT

### • Pain

Most studies have reported percentages of participants with discomfort or mild pain ranging from 4% to 40%, with few requiring analgesia. Many had experienced prior pain associated with their chronic wounds.<sup>10,13,14,16,20</sup> (Levels of evidence 1c, 3c, 3e) One RCT, however, did find that the mean ulcer-related pain scores for the LDT group were about double those of the hydrogel group (p<0.001) for the 24 hours before removal of first LDT treatment (mean VAS scores not reported).<sup>11</sup> (Level of evidence 1c) One other study found the peak period for pain was when the larvae were approximately 30 hours old.<sup>20</sup> (Level of evidence 3c)

Several studies reported that participants without neuropathy also reported crawling<sup>5</sup> or tickling<sup>24</sup> sensations in the wound from the larvae but these were not of great concern.

### • Mild bleeding

Mild bleeding can occur with larval debridement therapy; however, it can be significant in patients who take anticoagulant or anti-platelet medication and therefore must be closely monitored.<sup>27</sup> (Level of evidence 4c)

## CHARACTERISTICS OF THE EVIDENCE

This evidence summary is based on a structured search of the literature and selected evidence-based health care databases using the search terms wounds and larval therapy, maggot therapy. The evidence in this summary is derived from:

- Two systematic reviews<sup>18, 19</sup> (Level 1b)
- Three randomised controlled trials<sup>10-12</sup> (Level 1c)
- Five observational studies with control groups<sup>5, 13, 14, 20, 21</sup> (Level 3c)
- Five observational studies with no controls<sup>2, 15-17, 22</sup> (Level 3e)
- Economic study — cost-effectiveness, and cost utility<sup>26</sup> (Level 4)
- Mixed methods study — qualitative data report<sup>23</sup> (Level 3)
- Phenomenological study<sup>24</sup> (Level 3)
- One case series<sup>25</sup> (Level 4c)
- Four laboratory studies: *in vitro*<sup>3,7,8</sup>, *in vivo*<sup>6</sup> (Level 5c)
- Evidence summary (4 studies)<sup>27</sup> (various levels of evidence)
- Three overview articles<sup>1, 4, 9</sup> (various levels of evidence)

## RELATED EVIDENCE SUMMARY

JBI 11561 Wound Management: Overview of Mechanical Debridement

JBI 11563 Wound Management: Overview of Chemical Debridement

## BEST PRACTICE RECOMMENDATIONS

- There is good evidence that larval therapy is an effective means of debridement (Grade A)
- There is good evidence that larval therapy promotes healing and can be more effective than some conventional treatments (Grade A)
- There is some evidence that larval therapy can reduce bacterial burden but its effect is limited against *Pseudomonas* (Grade B)

## REFERENCES

1. Sherman R. Maggot therapy take us back to the future of wound care: new and improved maggot therapy for the 21st century. *J Diabetes Sc Technol* 2009;3(2):336–44.
2. Nuesch R, Rahm G, Rudin W, Steffen I, Frei R, Ruffli T *et al*. Clustering of bloodstream infections during maggot debridement therapy using contaminated larvae of *Protophormia terraenovae*. *Infection* 2002;30(5):306–9.
3. Cazander G, Schreurs M, Renwarin L, Dorresteyn C, Hamann D, Jukema G. Maggot excretions affect the human complement system. *Wound Rep Regen* 2012;20:879–86.
4. Gottrup F, Jorgensen B. Maggot debridement: an alternative method for debridement. *ePlasty* 2011;11:290–302.
5. Paul A, Ahmad N, Lee H, Ariff A, Saranam M, Naicker A *et al*. Maggot therapy with *Lucilia cuprina*: a comparison with convention debridement diabetic foot ulcers. *Int Wound J* 2009;6(1):39–45.
6. Diaz-Roa A, Gaona M, Segura N, Ramirez-Hernandez A, Cortes-Vecino J, Patarroyo M *et al*. Evaluating *Sarconesiopsis magellanica* blowfly-derived larval therapy and comparing it to *Lucilia sericata*-derived therapy in an animal model. *Acta Tropica* 2016;154:34–41.
7. Telford G, Brown A, Seabra R, Horobin A, Rich A, English J *et al*. Degradation of eschar from venous leg ulcers using a recombinant chymotrypsin from *Lucilia sericata*. *Br J Dermatol* 2010;163:523–31.
8. Britland S, Finter W, Vowden K, Telford G, Smith A, Eagland D *et al*. Recombinant *Lucilia Sericata* chymotrypsin in a topical hydrogel formulation degrades human wound eschar *ex vivo*. *Biotechnol Prog* 2011;27(3):870–4.
9. Sherman R. Wound Source. 2015. [cited 2016]. Available from: <http://www.woundsource.com/print/blog/>.
10. Opletalova K, Blaizot X, Mourgeon B, Chene Y, Creveuil C, Combemale P *et al*. Maggot therapy for wound debridement. *Arch Dermatol* 2012;148(4):432–8.
11. Dumville J, Worthy G, Bland M, Cullum N, Dowson C, Iglesias C *et al*. Larval therapy for leg ulcers (VenUS II: randomised controlled trial. *BMJ* 2009;338(b773):1–7.
12. Wayman J, Nirojogi V, Walker A, Sowinski A, Walker M. The cost effectiveness of larval therapy in venous ulcers. *J Tissue Viability* 2000;10(3):91–4.
13. Sherman R. Maggot versus conservative debridement therapy for the treatment of pressure ulcers. *Wound Rep Regen* 2002;10:208–14.
14. Sherman R. Maggot therapy for treating diabetic foot ulcers unresponsive to conventional therapy. *Diabetes Care* 2003;26(2):446–51.
15. Turkman A, Graham K, McGrouther D. Therapeutic applications of the larvae for wound debridement. *J Plast Reconstr Aesthet Surg* 2010;63:184–8.
16. Wollina U, Liebold K, Schmidt W, Hartmann M, Fassler D. Biosurgery supports granulation and debridement in chronic wounds — clinical data and remittance spectroscopy measurement. *Int J Dermatol* 2002;41:635–9.
17. Steenvoorde P, Jacobi C, Oskam J. Maggot debridement therapy: free-range or contained? An *in-vivo* study. *Adv Skin Wound Care* 2005;18(8):430–5.
18. Tian X, Liang X, Song G, Zhao Y, Yang X. Maggot debridement therapy for the treatment of diabetic foot ulcers: a meta-analysis. *J Wound Care* 2013;22(9):462–9.
19. Sun X, Jiang K, Chen J, Wu L, Lu H, Wang A *et al*. A systematic review of maggot debridement therapy for chronically infected wounds and ulcers. *Int J Infect Dis* 2014;25:32–7.
20. Sherman R, Shimoda K. Presurgical maggot debridement of soft tissue wounds is associated with decreased rates of postoperative infection. *Clin Infect Dis* 2004;39(1 October):1067–70.
21. Armstrong D, Salas P, Short B, Martin B, Kimbriel H, Nixon B *et al*. Maggot therapy in “lower-extremity hospice” wound care. *J Am Podiatr Med Assoc* 2005;95(3):254–7.
22. Tantawi T, Gohar Y, Kotb M, Beshara F, El-Naggar M. Clinical and microbiological efficacy of MDT in the treatment of diabetic foot ulcers. *J Wound Care* 2007;16(9):379–83.
23. Spilsbury K, Cullum N, Dumville J, O’Meara S, Petherick E, Thompson C. Exploring patient perceptions of larval therapy as a potential treatment for venous leg ulceration. *Health Expectations* 2008;11:148–59.
24. Kitching M. Patients’ perceptions and experiences of larval therapy. *J Wound Care* 2004;13(1):25–9.
25. Steenvoorde P, Jacobi C, Van Doorn L, Oskam J. Maggot debridement therapy of infected ulcers: patient and wound factors influencing outcomes: a study on 101 patients with 117 wounds. *Ann R Coll Surg Engl* 2007;89:596–602.
26. Soares M, Iglesias C, Bland M, Cullum N, Dumville J, Nelson E *et al*. Cost effectiveness analysis of larval therapy for leg ulcers. *BMJ* 2009;338(b825):1–17.
27. Gray M. Is larval (maggot) debridement effective for removal of necrotic tissue from chronic wounds. *J Wound Ostomy Continence Nurs* 2008;35(4):378–84.