Back to the Future of Wound Care –
Principles & Practice of Maggot Therapy
Ronald A. Sherman, MD

Medical Surgical Nursing Conference
South San Francisco, CA
April 16 & 17, 2015.

Principles & Practice of
Maggot Debridement Therapy
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Qualifications & Disclosures
Retired, University of California, Irvine, CA
Board of Directors - BioTherapeutics, Education & Research (BTER) Foundation
Co-Founder & Laboratory Director - Monarch Labs, producer of medicinal animals
Staff Physician - Orange County Health Care Agency
Problems:

- Chronic wounds
- Antimicrobial resistance
- Health care costs
- Inadequate staffing

Solutions:

- Many solutions.
- No single solution is best for everyone.
- The more solutions you have available, the more often you will have the right one for the moment.

New Wound-Debriding Device (50 Million years in development)

- Squirts proteolytic enzymes directly into wound bed
- Microscopic rasps loosen & remove necrotic tissue
- Self-propelled; batteries not required
- Guided by internal optics
- 100% disposable and completely biodegradable
**Principles & Practice of Maggot Debridement Therapy**

**Objectives**

- List 4 clinical indications for MDT
- List 3 warnings or relative contraindications
- Describe the metamorphosis
- Explain how maggot biology affects the clinical application of maggot therapy

**Lecture Outline**

- History and Current Status of MDT
- Clinical Data & Review of the Literature
- Maggot Biology 101
- Indications, Contraindications, Warnings
- Conclusions

**History and Current Status of Maggot Therapy**
William S. Baer, MD (1872 - 1931)

Maggot Therapy - 1940's

Popularity decreased because?

- a) improved surgical techniques during WW II;
- b) newly available antibiotics;
- c) reduced incidence of wounds

Maggot Therapy - Current Status

1990 - First modern clinical trials of MDT (UC Irvine / VAMC)

1995 - MDT in U.S., Canada, Israel, U.K., Italy
- MDT discussed at ETR Society Working Party on Debridement

1996 - Founding of International Biotherapy Society (IBS); meeting in Wales

2003 - Founding of the BioTherapeutics, Education & Research (BTER) Foundation in the U.S.
Maggot Therapy - Current Status

2003 – FDA begins regulating medicinal maggots as a medical device

January 12, 2004 - FDA permits production and marketing of Medical Maggots™ brand (510K #K033391) for the following indications:

“... debriding non-healing necrotic skin and soft-tissue wounds, including pressure ulcers, venous stasis ulcers, neuropathic foot ulcers, and non-healing traumatic or post surgical wounds.”

2014 - 24 laboratories world-wide
- Patients treated in > 30 countries
- 50,000+ maggot treatments

Motivation to Re-adopt Maggot Therapy

Why such a rapid adoption of this new / old technology?
Motivation to Re-adopt Maggot Therapy
1. Chronic Wounds still a problem
2. Antimicrobial Resistance
3. Clinical studies now available
4. Personal successes.

Maggot Debridement Therapy
59 year old diabetic man, refused amput’n despite osteomyelitis. Maggot therapy debrided his wounds, including the non-viable big toe; the remains of that toe were removed surgically. He left the facility with his foot fully healed.

Maggot Debridement Therapy
73 yo man with foot ulcer for 3 years; seen here before, 3 days later, and 1 year after MDT.
61 year old diabetic man, receiving surgical and IV antibiotic Rx for 3 weeks, without improvement of foot ulcer. After 3 wks of MDT, his wound was debrided and healing rapidly.

43 year old paraplegic man after IV adrenergic drugs infiltrated during ICU treatment for acute MI. He could not tolerate surgery, so his wound was debrided with MDT. Seen here before, after 1 week of MDT, and 5 weeks following MDT.

67 year old man, who’s ischial pressure ulcer was treated in the hospital for 2 weeks. He was scheduled for surgical resection with flap closure. Instead, he opted for MDT. Seen here before and after 2 cycles of MDT (10 days apart).
46 year old paraplegic man, s/p bilateral gluteal flaps for trochanteric pressure ulcers; 4 months later still has clean but non-healing full-thickness sacral donor site wound. Seen before MT, 1 week into Rx, & 3 weeks later.

55 yo woman treated “conservatively” for 2 months; (still draining, malodorous, painful); then treated with MDT for less than 24 hours.

Principles & Practice of Maggot Debridement Therapy
Clinical Data & Review of the Literature
Maggot Therapy –
Mechanisms of Action

1. Debridement
   ✓ enzymatic
   ✓ mechanical

2. Disinfection
   ✓ kills bacteria
   ✓ dissolves and inhibits biofilm

3. Promotion of wound healing
   ✓ granulation tissue growth
   ✓ epithelial proliferation and migration
   ✓ tissue oxygenation

Studies Demonstrating Debridement

- Baer - 1929
- Hobson - 1931
- Maseritz - 1934
- Ziffren et al - 1953
- Waterhouse & Irzykiewicz - 1957
- Fraser et al: Brookes - 1961
- Pendola & Greenberg - 1975
- Vistnes et al - 1981
- Casu et al - 1994
- Schmidtchen et al - 2003
- Chambers et al - 2003
- Dumville et al - 2009

Proteolytic activity of blowfly larvae secretions in experimental burns

Larry M. Vistnes, M.D., Reza Lee, M.S., and George A. Koulouris, A.M.
Stanford and Palo Alto, Calif.

Secretions of larvae of the blowfly Calliphora erythrocephala digested experimental rat skin burn eschar in vivo and in vitro when applied topically on a subcutaneous wound basis. Debridement was characterized by the liquefication and absorption of denatured collagen in a multifaceted mode over a 5-day period. Analysis of the secretions demonstrated the presence of enzymes with activities characteristic of trypsin, leucine aminopeptidase, and carboxypeptidase A and B. These were not significantly affected. There was no evidence of chymotrypsin, elastase, or collagenase. Preparations of a suitable therapeutic form could result in a preparation useful for enzymatic debridement.


Experimental burns in rats; eschar debrided by larval secretions. Trypsin, leucine aminopeptidase, and carboxypeptidase activities identified; chymotrypsin-like activity and collagenases not identified.
Sir,

For centuries, larval therapy has been recognized as an aid in wound healing. During the 1930s and 1940s, before the antibiotic era, larval therapy was commonly used by surgeons in the USA and Europe when treating various soft-tissue and bone infections. The most commonly used larval species is Lucilia sericata (LS). From a clinical point of view, the two major effects of larval therapy have been ascribed to their antibacterial and debriding mechanisms (1-4). In regard to the latter function it has been speculated that the larvae, when introduced into the wound, secrete proteolytic enzymes that enable them to degrade and ingest necrotic tissue. Here, we address this question and demonstrate that these larvae secrete a group of serine proteases when cultured in vitro. Furthermore, these serine proteases were detected in the wound fluid of a patient with a chronic leg ulcer treated with larvae. The data suggest that serine proteases of LS are released during treatment.

Phaenicia (Lucilia) sericata

Figure 5 from: Fleischmann, Grassberger & Sherman: Maggot Therapy – A Handbook of Maggot-Assisted Wound Healing. Thieme, 2004

Maggot Therapy vs Conventional Therapy for Treatment of Chronic Wounds.

VAMC, Long Beach, CA; 1990-1995

- Pressure ulcers (145)
- Diabetic foot ulcers (31)
- Venous stasis ulcers
- Post-operative wounds
- Burns
**Maggot vs Conservative Debridement Therapy for the Treatment of Pressure Ulcers**

Sherman RA: Wound Repair Regen 2002; 10:208-14

**Maggot vs Conservative Debridement Therapy for the Diabetic Foot Ulcers**

Sherman RA: Diabetes Care 2003; 26:446-51

**Maggot Therapy for Diabetic Neuropathic Foot Wounds: A Randomized Study**

Y.O. Markevich, McLeod-Roberts, M. Mousley, E. Melloy

Lviv Medical University, Lviv, Ukraine
Nene-University College, Northampton, UK

Medical Surgical Nursing Conference
South San Francisco, CA
April 16 & 17, 2015.
The cost effectiveness of larval therapy in venous ulcers

John Weymans¹, Vijaya Nireje², Anne Walker², Adam Sowińska³ and Michael A Walker²

¹Specialist Registrar in Surgery, ²Senior House Officer, ³Trainer, North Staffordshire Health Care Trust, and ³Consultant Surgeon, West Cumberland Hospital, Whitehaven, Cumbria, UK

The treatment of venous ulcers involves considering the timing and expeditious removal of necrotic tissue. A recent meta-analysis involving surgical debridement of venous ulcers demonstrated that debridement was most effective at reducing ulcer size and improving ulcer healing. This study aimed to investigate the cost effectiveness of larval therapy in venous ulcers in a cost-utility analysis. The study compared the cost of larval therapy with that of surgical debridement in a cohort of 50 patients with venous ulcers. The results showed that larval therapy was more cost-effective than surgical debridement, with a cost saving of £200 per patient. The study concluded that larval therapy is a viable and cost-effective alternative to surgical debridement in the treatment of venous ulcers.
Studies Demonstrating Disinfection

- Baer, 1929
- Livingston & Prince, 1932
- Robinson & Norwood, 1933
- Simmons, 1935
- Pavillard & Wright, 1957
- Greenberg, 1968
- Erdmann & Khalil, 1986
- Mumcuoglu et al, 2001
- Armstrong et al, 2005
- Contreras-Ruiz et al, 2005
- Tantawi et al, 2007
- Bowling, Boulton et al, 2008

ABSTRACT

Green fluorescent protein-producing Escherichia coli were used to investigate the fate of bacteria in the alimentary tract of sterile grown maggots, Lucilia sericata (Meigen), using a laser scanning confocal microscope. A computer program was used to analyze the intensity of the fluorescence and to quantify the number of bacteria. The crop and the anterior midgut were the most heavily infected areas of the intestine. A significant decrease in the amount of bacteria was observed in the posterior midgut. The number of bacteria decreased even more significantly in the anterior hindgut and practically no bacteria were seen in the posterior end, near the anus. The viability of bacteria in the different gut sections was examined. It was shown that 66.7% of the crops, 52.8% of the midguts, 55.6% of the anterior hindguts, and 17.8% of posterior hindguts harbored living bacteria. In conclusion, during their passage through the digestive tract the majority of E. coli was destroyed in the midgut. Most of the remaining bacteria were killed in the hindgut, indicating that the feces were either sterile or contained only small numbers of bacteria.

Larval Debridement Therapy in Mexico

The benefit of maggots in wound healing has probably been known for centuries. In the last century, maggots were largely used in Europe to aid in the treatment of chronic wounds. In Mexico, maggots were reintroduced in the late 1970s as a part of the treatment of chronic wounds. These insects were used mainly in the northeastern part of Mexico, where they are still widely used today. The use of maggots in wound care has been reported to be effective in reducing the bacterial load and promoting tissue regrowth.

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Clinical and microbiological efficacy of MDT in the treatment of diabetic foot ulcers

**Objective:** To assess the clinical and microbiological efficacy of maggot debridement therapy (MDT) in the management of diabetic foot ulcers compared to conventional treatment and surgical intervention.

**Patients:** Enrolled patients with foot wounds presenting in the medical surgery ward and working for a period of 16 weeks. The wounds were treated with maggot therapy and compared to conventional treatment and surgical intervention.

**Results:** The results showed significant improvement in wound healing, decreased pain, and improved quality of life for patients treated with maggot therapy compared to conventional treatment and surgical intervention.

**Conclusion:** MDT is an effective and safe treatment option for the management of diabetic foot ulcers.

Larval Therapy: A Novel Treatment in Eliminating Methicillin-Resistant Staphylococcus aureus From Diabetic Foot Ulcers

**Objective:** To evaluate the efficacy of larval therapy in eliminating Methicillin-Resistant Staphylococcus aureus (MRSA) from diabetic foot ulcers.

**Methods:** Larval therapy was administered to diabetic foot ulcers, and the presence of MRSA was monitored using standard microbiological techniques.

**Results:** Larval therapy was effective in eliminating MRSA from diabetic foot ulcers, with a significant reduction in bacterial load observed after therapy.

**Conclusion:** Larval therapy is a promising treatment option for the management of diabetic foot ulcers infected with MRSA.
Maggot Therapy in “Lower-Extremity Hospice” Wound Care
Fewer Amputations and More Antibiotic-Free Days

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Fewer Amputations and More Antibiotic-Free Days

Luciferin, the long-sought antimicrobial factor of medicinal maggots of the blowfly Lucilia sericata

Abstract: A novel homologue of insect defensin designated luciferin (Lucilia sericata) from the extracts of various tissues (gut, salivary glands, fat body, haemolymph) of a blowfly Lucilia sericata larvae and from their excretions/secretions. The primary sequence of this peptide and its intramolecular disulfide bridge was determined by ESI-Q/TOF mass spectrometry and Edman degradation and is very similar to that of luciferin from other insect defensins. We assume that luciferin is the key antimicrobial component that protects the maggots when they are exposed to the highly infectious environment of a wound during the medical process known as maggots therapy. We also believe that luciferin is that long-sought large molecular weight antimicrobial factor of the Lucilia sericata excretions/secretions believed to be effective against pathogenic elements of the wound microbial flora.

Studies Demonstrating Growth Stimulation

- Baer (clinical observations) - 1929
- Robinson (allantoin) - 1935
- Livingston, 1936
- Mumcuoglu et al, 1997
- Prete, 1998
- Markevich et al, 2000
- Wollina et al, 2002
- Horobin et al, 2003-06
- Sealby, 2004
- Armstrong et al, 2005
- Picazo et al, 2005
- Tanyuksel et al, 2005
- Steenvoorde et al, 2007
- Pecivoja et al, 2008
- Dumville et al, 2009
- Bexfield et al, 2010
- Wang et al, 2010
- Zhang et al, 2010, 2010b
- Honda et al, 2011
Maggot vs Conservative Debridement for the Treatment of Pressure Ulcers

- Cohort, 92 PU’s, 63 pts
- MT x 8 wks vs Control x 8 wks

Results:
- Faster 4- and 8-wk healing rates
- Faster wound bed preparation

Sherman RA: Wound Repair Regen 2002; 10:208-14

Table 2: Results of therapy in 40 pressure ulcers treated with conventional therapy or MTT

<table>
<thead>
<tr>
<th></th>
<th>Conventional Therapy</th>
<th>MTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average duration of therapy (weeks)</td>
<td>5.3 (4.9-6.2)</td>
<td>4.5 (4.2-5.1)</td>
</tr>
<tr>
<td>Healing of wounds</td>
<td>78.5% (72.4-84.6)</td>
<td>90.0% (86.6-93.3)</td>
</tr>
<tr>
<td>Percentage of wounds completely healed</td>
<td>55.0% (49.8-60.1)</td>
<td>69.0% (65.0-73.0)</td>
</tr>
</tbody>
</table>

Sherman RA: Wound Repair Regen 2002; 10:208-14
Maggot vs Conservative Debridement Therapy for the Treatment of Pressure Ulcers

- Error bars indicate standard error. * = p<0.05
- Sherman RA: Wound Repair Regen 2002; 10:208-14

Maggot vs Conservative Debridement for Diabetic Foot Ulcers

- Cohort; DM subjects; 20 chronic wounds, 18 Pts; neuropathic and neuro-ischemic foot ulcers

- Results:
  - Faster 4- and 8-wk healing rates
  - Faster wound bed preparation

Sherman RA: Diabetes Care 2003; 26:446-51
Maggot vs Conservative Debridement for Diabetic Foot Ulcers

<table>
<thead>
<tr>
<th>Control</th>
<th>MDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound size and healing</td>
<td>3.5 (3.6-2.5)</td>
</tr>
<tr>
<td>Initial surface area (cm²)</td>
<td>5.0 (4.0-3.5)</td>
</tr>
<tr>
<td>Change in surface area (cm²)</td>
<td>2.5 (2.0-3.0)</td>
</tr>
<tr>
<td>Weekly change in surface area (cm²)</td>
<td>± 5 (15-3.5)</td>
</tr>
<tr>
<td>Hemoglobin at 6 weeks</td>
<td>6.0 (5.5-0.2)</td>
</tr>
<tr>
<td>Healing rate at 6 weeks</td>
<td>6.0 (5.5-0.2)</td>
</tr>
<tr>
<td>Wound completely closed (%)</td>
<td>25 (30-50)</td>
</tr>
<tr>
<td>Number of antemortem amputations (N=14)</td>
<td>30 (35-40)</td>
</tr>
<tr>
<td>Number of autopsies (N=14)</td>
<td>30 (35-40)</td>
</tr>
<tr>
<td>Percent of base covered by granulation tissue</td>
<td>80 (70-90)</td>
</tr>
<tr>
<td>Conventional therapy (N=14)</td>
<td>75 (70-80)</td>
</tr>
</tbody>
</table>

Error bars indicate standard error. * = p<0.05

Sherman RA: Diabetes Care 2003; 26:446-51

Maggot vs Conservative Debridement Therapy for the Treatment of Diabetic Foot Ulcers

Percentage of base covered by granulation tissue over time (in weeks)

Sherman RA: Diabetes Care 2003; 26:446-51

Biopsy of rapidly granulating toe wound in patient undergoing MDT

Sherman RA: Int J Foot Leg Wounds 2002; 1:79-86
Maggots and wound healing: an investigation of the effects of secretions from *Lucillia sericata* larvae upon the migration of human dermal fibroblasts over a fibronectin-coated surface.

Adele J. Mondien, PhD, Kevin M. Shafik, PhD, David E. Frisch, MD

Lucillia sericata larvae, or greenbottle fly maggots, placed within chronic wounds have been observed to remove necrotic tissue and promote granulation. The larvae secrete hydrolytic enzymes and produce large numbers of growth factors which attract fibroblasts to wound sites. Fibroblasts are critical for the repair of wounds, and their recruitment is necessary for proper wound healing. The presence of these factors in the larval exudate may play a role in the proliferation of fibroblasts in the wound. The results of this study suggest that maggot therapy may be a useful adjunct in the treatment of chronic wounds.

Abstract

Biosurgery supports granulation and debridement in chronic wounds – clinical data and infrared spectroscopy measurement

Wolfgang, M.D., Timo Schelting, Michael E. R. G. L. van den Bosch, Jeroen Touw, and Michael van der Meer

Debridement

- enzymatic
- mechanical

Disinfection

- kills bacteria
- dissolves and inhibits biofilm

Promotion of wound healing

- granulation tissue growth
- epithelial proliferation and migration
- tissue oxygenation

Maggot Therapy – Mechanisms of Action

1. Debridement
   - enzymatic
   - mechanical

2. Disinfection
   - kills bacteria
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3. Promotion of wound healing
   - granulation tissue growth
   - epithelial proliferation and migration
   - tissue oxygenation
Principles & Practice of Maggot Debridement Therapy

Maggot Biology 101

Typical Blow Fly Life cycle

- Eggs: 12-24 hrs
- Larva
- Pupa: 16-25 days
- Adult
Myiasis and Maggot Biology

Maggot Therapy is a controlled, therapeutic myiasis (maggot infestation).

The methods of treatment and the potential complications are predicted by studying the natural history of myiasis.

Not all species are therapeutic or safe; not all strains of the same species are equal.

The most successful therapists understand the biology and natural history of their larvae.

Controlled, Therapeutic myiasis

... use only species and strains proven to be safe and effective

Controlled, Therapeutic myiasis

... controlled environments
Controlled, Therapeutic myiasis

... disinfect the maggots ("germ-free")

Controlled, Therapeutic myiasis

... quality control, inspection, testing

Controlled, Therapeutic myiasis

... controlled access to wound - "cage dressings"
Indications & Contraindications

Maggot Therapy - Indications

January 12, 2004 - FDA permits the production and marketing of the brand: Medical Maggots as a medical device (510K #K033391) for the following indications:

"... debrideing non-healing necrotic skin and soft-tissue wounds, including pressure ulcers, venous stasis ulcers, neuropathic foot ulcers, and non-healing traumatic or post surgical wounds."

Maggot Therapy - Warnings

Allergy
Possible pain or discomfort
Ensure sterility; prevent contamination
Single-use only
Prevent escapes
Maggot dressings handled as infectious waste
Thorough evaluation if fever or altered MS
*Pseudomonas* wound infection may not respond
Adverse Events > 1%

- Pain or Discomfort
  Predicted by pre-MDT wound pain
  In published studies, 5 - 30% of patients
- Anxiety
  Not as common as believed; only 5% of studied
  patients declined MDT when offered.
- Inconvenience due to courier-delayed deliveries
  Maggots perishable; must be delivered within 24 hours
  of use; courier industry delays optimally run 1 - 2%

Sherman RA: J Lower Extrem Wounds. 2002;1:135-42
Sherman RA: Wound Repair Regen. 2002;10:208-14

Principles & Practice of Maggot Debridement Therapy

Concluding Remarks

Principles & Practice of Maggot Debridement Therapy

Objectives

- List 4 clinical indications for MDT
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