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Maggots and Leeches and Bees . . .

Oh my!

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Credentials & Disclosures

Retired, University of California, Irvine, CA

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Clinic Physician – Orange County Health Care Agency

What is Biotherapy?

The use of live animals
(including microbes)
to diagnose or treat illness.

How many Biotherapeutic modalities can you think of?

(give examples of medicinal animals)

Examples of Biotherapy:

Guide Dogs
Maggot Therapy
Bee Venom Therapy
Helmintherapy
Leech Therapy
Phage Therapy
Canine Olfactory Detection
Fecal Microbiota Transplants
Ichthyotherapy
Service animals
Hippotherapy

Objectives -

Attendees should be able to:

Give four examples of medicinal animals

List 2 indications for bee venom therapy

Describe the mechanism of action for phage therapy

Describe the differences between the way leech therapy works and the way maggot therapy works

Outline

- BioTherapy
  - Definitions & Examples
- BioTherapy for Wound Care
  - Leech Therapy
  - Phage Therapy
  - Bee Venom Therapy
  - Maggot Debridement Therapy (MDT)

Hirudotherapy (Leech Therapy)

- ✓ Oldest biotherapy (along with honeybees)
- ✓ Leeches suck blood
- ✓ Leeches secrete anticoagulants & anesthetics

Hirudotherapy (Leech Therapy)

Apply leeches

Leeches suck blood for 30-90 min

Leeches fall off, but the bleeding continues for hours

Hirudotherapy (Leech Therapy)

FDA-cleared:

Venous congestion in soft tissue wounds (reconstructive surgery)

Not FDA-cleared:

Venous stasis; congestive heart failure; PVDz; ischemia; dentistry; arthritic pain; . . . .

Leech Therapy Research Center, Irvine, CA

Bacteriophage - Definition

Bacteriophages are viruses that invade bacterial cells and, in the case of lytic phages, disrupt bacterial metabolism and cause the bacterium to lyse.

Bacteriophage - Characteristics

- ✓ Highly specific
- ✓ Lyse the targetted host bacteria
- ✓ Relatively safe
- ✓ Can be delivered via multiple routes

Phage Therapy – History

1896 - Ernest Hankin, British bacteriologist, reported antibacterial activity against *Vibrio cholerae* observed in India.

1898 – Gamaleya, the Russian bacteriologist, observed similar phenomenon while working with *Bacillus subtilis*.

1914 - Frederick Twort, a British bacteriologist, proposed that the antibacterial activity was the results of a virus. For various reasons, including financial difficulties, Twort did not pursue this work.

Phage Therapy – History

1930's - Several labs produced therapeutic phage products commercially, including

Eli Lilly Company; Dr. d'Herelle in Paris.

Efficacy of phage preparations controversial; no controlled trials.

1940's – With the advent of antibiotics, commercial production of therapeutic phages ceased in most of the Western world.

Phage Therapy - Current status

Thousands of patients treated; but few scientifically rigorous studies.

Modern, controlled clinical studies are now underway.

Example: Topical application of mixed phage for diabetic foot ulcers (Kutter [Evergreen, WA], Wollcott [Lubbock, TX], et al)

Apitherapy


#31515
Dressing with Active Leptospermum Honey
WOUND & BURN DRESSING
MEDIHONEY™
#31222
2" x 2"
Honeycolloid™ Dressing
with Active Leptospermum Honey
WOUND & BURN DRESSING
MEDIHONEY™
• The MEDIHONEY™ Dressing contains 80% Active Leptospermum Honey.
• Helps maintain moist environment conducive to wound healing.
• For lightly to moderately exuding wounds.
10 dressings
DERMA SCIENCES
#31222

Bee Venom Therapy

Alexander the Great – BVT for pain

Charlemagne - BVT for gout

1858 C. W. Wolf of Berlin wrote book: *The Poison of the Honey Bee considered as a Therapeutic Agent*

1800's - Austrian physician, Phillipp Terc, treated thousands of arthritic patients for more than 40 years

Bee Venom Therapy

Modern BVT "formulations:"

1) Live bees

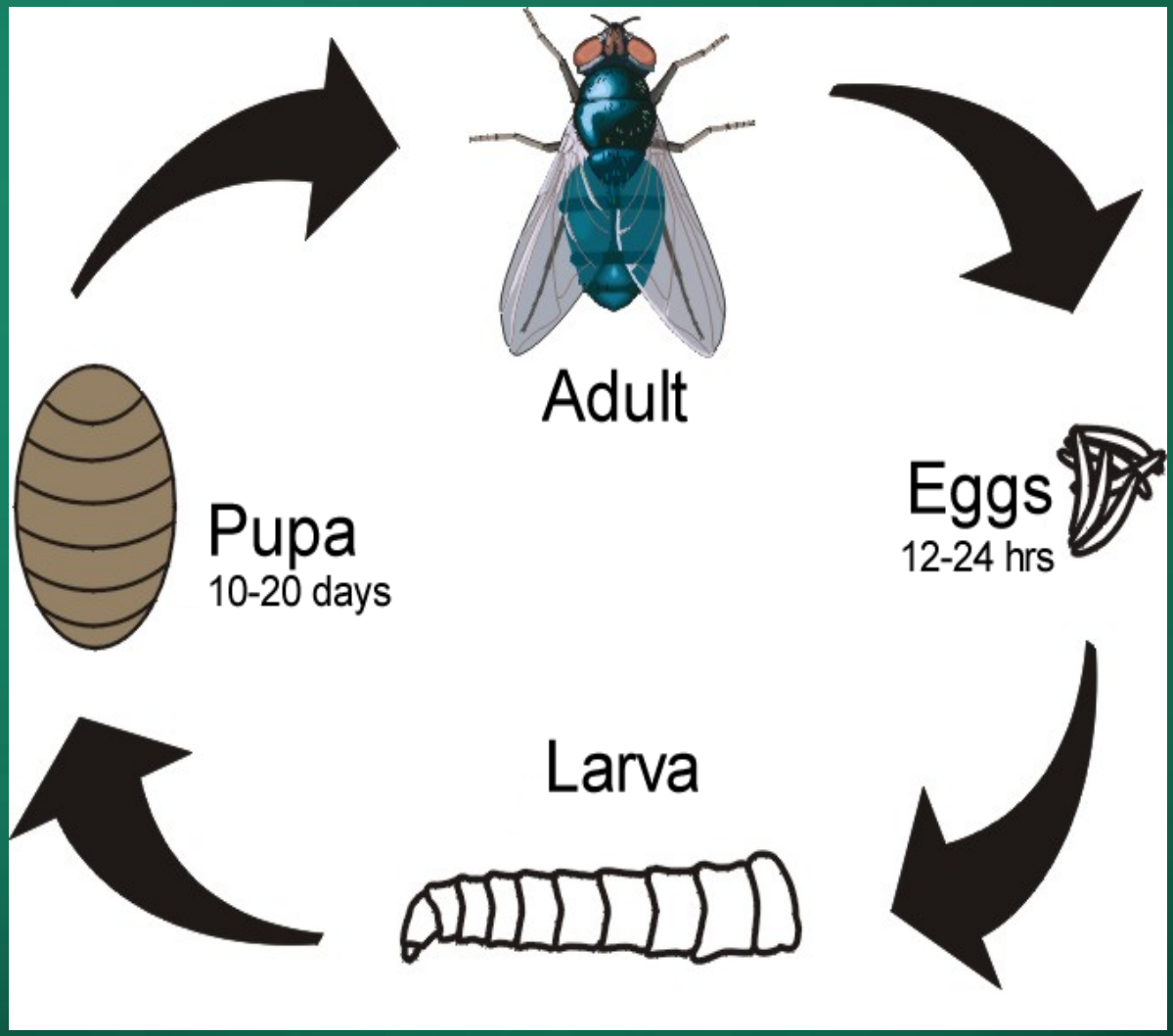
2) Purified venom extract

Bee Venom Therapy

Effective for a variety of pain, immunological, and neurological maladies.

Not used significantly for wound care, so will not be discussed here any further.

Maggot Debridement Therapy



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.

Maggot Debridement Therapy

History and Current Status of Maggot Therapy

Maggot Debridement Therapy

1930's – Used by over 1,000 doctors and surgeons in North America

1990 – First controlled clinical trials

2003 – FDA regulates medicinal maggots

2004 – FDA grants marketing to the first live medicinal animal: Medical Maggots™

Maggot Debridement Therapy

2004 – FDA permits marketing of first live medicinal animal (Medical Maggots™) for:

" . . . 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."

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

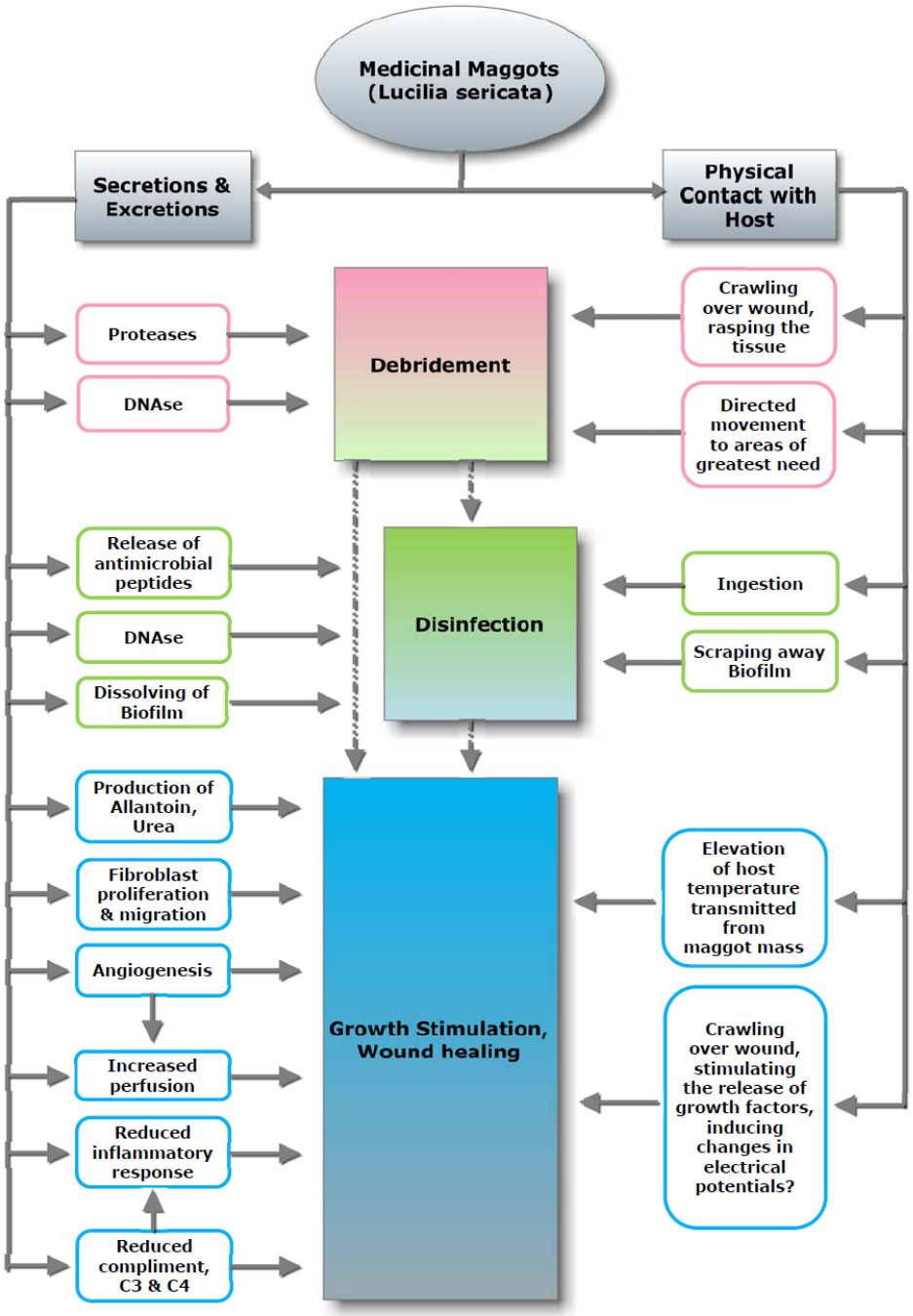
- Squirts proteolytic enzymes directly into wound bed
- Microscopic raspers loosen & remove necrotic tissue
- Self-propelled; batteries not required
- Guided by Internal optics
- 100% disposable and completely biodegradable

Maggot Therapy - Current Status

- ✓ 23 laboratories
- ✓ Patients treated in 30 countries
- ✓ 50,000+ treatments/yr

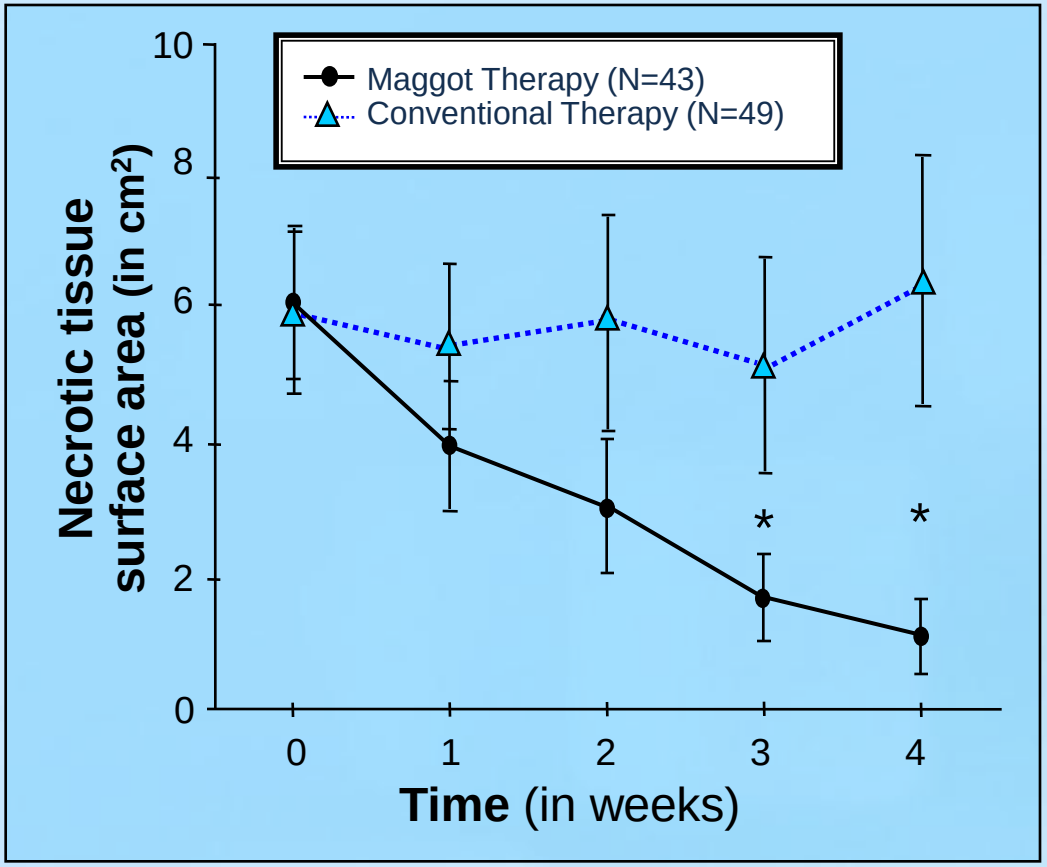
Maggot Debridement Therapy

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



Sherman RA: Mechanisms of maggot-induced wound healing. Evid Based Complement Alternat Med. 2014;2014:592419.

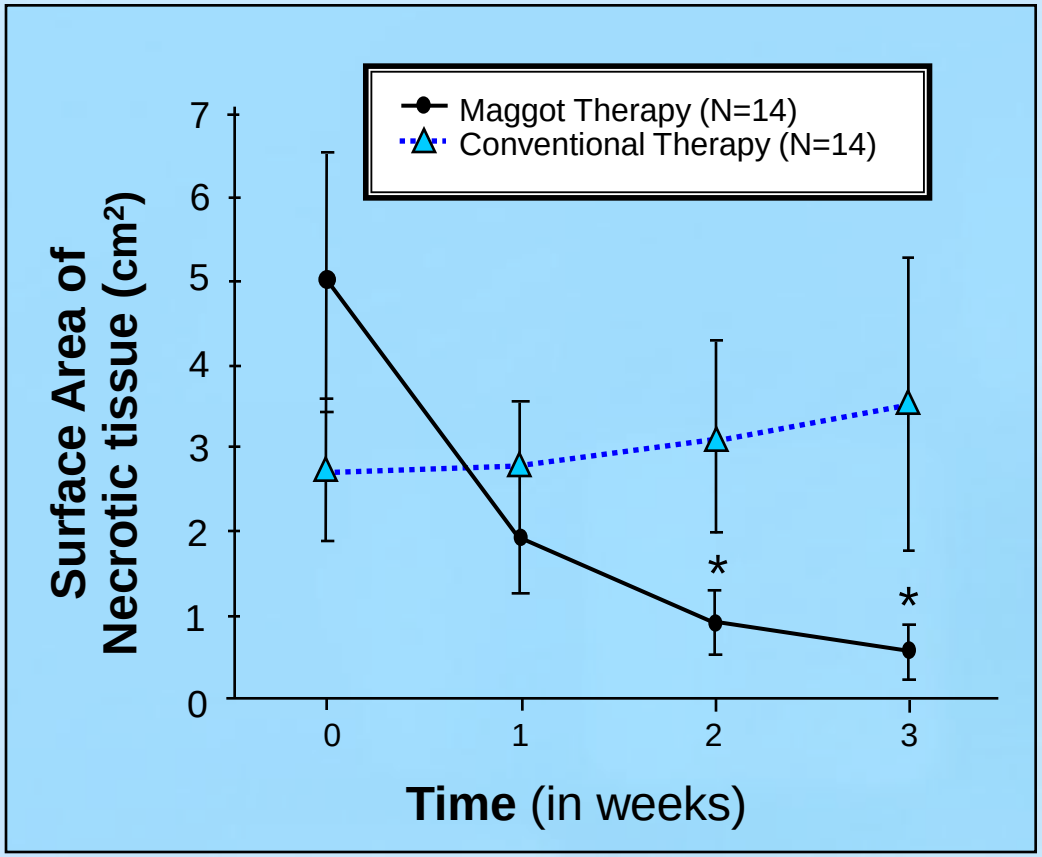
Maggot vs Conservative Debridement Therapy for the Treatment of Pressure Ulcers



Error bars indicate standard error. * = p<0.05

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

Maggot vs Conservative Debridement Therapy for the Diabetic Foot Ulcers



Error bars indicate standard error. * = p<0.05

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

Maggot Therapy - Indications

2004 – FDA permits marketing of first live medicinal animal (Medical Maggots™) for:

" . . . 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."

Warnings / 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 delayed deliveries
  - Maggots perishable; must be delivered within 24 hours of use; courier industry delays optimally run 1 - 2%

Sherman RA:Int J Lower Extrem Wounds. 2002;1:135-42
Sherman RA: Wound Repair Regen. 2002;10:208-14
Sherman RA: J Diabetes Sci Technol. 2009;3:336-44

Maggots and Leeches and Bees ? . . . Oh Yes!

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