The wound to accomplish any necessary fine debridement, control infection, and facilitate healing.

Maggot therapy all but disappeared during the 1940s, with the advent of modern antibiotics and improved surgical techniques. But it is now making a comeback. This year, an estimated 50,000 bottles of medical-grade maggots will be distributed by 12 laboratories to patients in 20 countries.

In 2004, Medical Maggots (Monarch Labs, Irvine, CA) became the first live animal to be cleared for marketing in the United States by the Food and Drug Administration (FDA).

Approved indications are for debriding nonhealing necrotic skin and soft tissue wounds including pressure ulcers, venous ulcers, neuropathic foot ulcers, and nonhealing traumatic or postsurgical wounds. These were the uses for which efficacy and safety data were available, and they remain the most common applications of maggot therapy today.

However, maggot therapy was used in wound care long before the FDA marketing clearance, and some of its applications have been outside these specific indications. It was hypothesized that there may now be frequent off-label uses of maggot therapy. If this is true, there may be a need to evaluate the safety and efficacy of maggot therapy for such indications.

To explore this hypothesis, the authors describe their own off-label experience and that of other surveyed clinicians.

METHODS
Survey Participants and Case Selection
Between 1990 and 1995, 101 wounds in 70 patients were treated with maggot therapy at the Veterans Affairs Medical Center in Long Beach, CA, and the University of California Irvine Medical Center in Orange, CA. Most of these individuals had pressure ulcers or diabetic foot ulcers, and their outcomes were reported elsewhere. Larvae were also distributed to more than 500 hospitals and wound care centers.

In 2005, approximately 350 of those clinicians were asked to complete a brief survey describing the indications for which they used the treatment. Invitations and surveys were distributed with the BioTherapeutics, Education and Research (BTER) Foundation newsletter to nearly 400 therapists. The survey

Seventy years ago, maggot therapy was used by more than 1000 surgeons in North America. More than 90% of them were satisfied with these wriggling surgical assistants. At that time, maggot therapy was most often used for controlling soft tissue infections and as an adjunct to surgical resection for osteomyelitis. One or 2 days following surgical debridement—or as soon as bleeding was controlled—maggots would be placed within

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ABSTRACT
OBJECTIVE: To identify off-label uses for maggot therapy that may be worthy of further clinical evaluation.
DESIGN: Clinician surveys and invitations to submit unusual and off-label uses of maggot therapy.
SETTING: All levels of inpatient, outpatient, extended care, and home care.
PARTICIPANTS: More than 350 clinicians known to use maggot therapy were invited to participate in the survey. Twelve returned the survey.
MAIN OUTCOME MEASURE: Indications for maggot therapy other than simple debridement of wounds listed on product labeling.
MAIN RESULTS: A total of 544 wounds were treated by the 12 respondents; 131 (24%) were rare or off-label applications, including stimulation of epithelialization in clean but nonhealing wounds; disinfection, odor, and drainage control; determination of tissue viability; debridement of acute burns, necrotic tumors, and ischemic ulcers; and debridement of unusual sites (ie, glans penis, joints, pleural space, and peritoneal cavity). Noted drawbacks included the time and effort needed to train personnel and convince administrators of the need for treatment.
CONCLUSION: Medicinal maggots are frequently being used as an adjunct to other methods of surgical and nonsurgical wound care and often for off-label indications, including debridement, disinfection, and stimulation of healing. Further study is warranted to evaluate the efficacy and safety of maggot therapy for these indications, and better education is needed for administrative and clinical staff to make maggot treatment more accessible.

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form was also posted on the Internet. E-mail was the preferred route of contact when addresses were available; otherwise, therapists were contacted by fax or post. Approximately 5% were undeliverable due to inaccurate addresses.

**Preparation of Disinfected Larvae**

Larvae were prepared from a laboratory colony of *Phaenicia (Lucilia) sericata*, as previously described.16 Eggs were collected from gravid females and disinfected with dilute phenol (3% Lysol brand phenol disinfectant; Sterling Drugs, NJ) or 0.525% sodium hypochlorite. Disinfected eggs were then transferred to sterile vials and left at room temperature such that 500 to 1000 healthy larvae would hatch overnight in each vial. After ensuring that overnight aerobic and anaerobic quality control cultures were without microbial growth, the larvae were used locally or shipped to the requesting therapists via overnight courier.

**Method of Dressing Application**

The objective of the maggot dressing was to create a porous cage of maggots over the wound, with the wound bed as the floor of the cage. The porous top of the dressing prevented the maggots from escaping but allowed air to reach the oxygen-dependent maggots and liquified necrotic tissue to drain out. Dressings were constructed as previously reported, with Dacron chiffon,8 nylon stockings,9 or similar porous fabrics affixed directly to the skin or preferably to a hydrocolloid pad covering the periwound skin. Light gauze was placed on top of the netting to absorb the exudate and was changed when soiled. Maggot dressings were removed after 24 to 72 hours, by which time the larvae reached about 1 cm in length and were fully satiated. These 24 to 72 hours applications were referred to as cycles of therapy; patients received 1 or more cycles during a full course of maggot therapy.

**Data Analysis**

Further information was sought for cases associated with previously unreported or off-label indications. Cases were grouped according to indication and subjected to simple descriptive statistical analysis.

**Author Selection**

Therapists who submitted cases used in this study were acknowledged for their contributions, if they were available and agreeable at the time the manuscript was submitted for publication. Those who both submitted case narratives and participated in the writing and/or review of this report were listed as coauthors.

**RESULTS**

Twelve therapists (8 surgeons, 2 nurses, 1 internist, and 1 physical therapist) completed the survey. Together they treated 544 wounds with maggot therapy; 131 (24%) of those wounds met the inclusion criteria for this study. The unusual and off-label indications for using maggot therapy are listed in Table 1. The reasons most often given for including maggot therapy in the care plan were (a) the wound or infection was not responding to conventional surgical and medical therapy, (b) the proximity of vital structures made surgical debridement technically difficult, or (c) underlying medical conditions put patients at unacceptably high risk for complications of anesthesia and/or surgical treatment. In short, surgeons and clinicians with surgical support were most often using maggot therapy in situations where surgical debridement was considered too risky or thus far ineffective.

Several representative cases are described in Table 2 and detailed as follows.

**Case 1: Stimulation of Healing in a Clean, Nonhealing Wound**

A 45-year-old hemiplegic man had been in the hospital for several months following bilateral gluteal flaps to repair his right and left trochanteric pressure ulcers. A 6-cm² clean but nonhealing wound remained over the sacral donor site (Figure 1). Already scheduled for a split-thickness skin graft, the patient requested a trial of maggot therapy to stimulate epithelialization. After the first 2 treatment cycles, the thick peripheral scar dissolved, and 2 abscesses were uncovered, each containing a nylon suture. In addition, new epithelial tissue had grown over 5% of the wound surface. After 4 more 2-day cycles of maggot dressings, the wound was covered with healthy, supple epithelium.

**Table 1.**

**OFF-LABEL INDICATIONS FOR MAGGOT THERAPY REPORTED BY SURVEY RESPONDENTS**

<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic wound</td>
<td>30</td>
<td>23</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Clean but nonhealing wound</td>
<td>26</td>
<td>20</td>
</tr>
<tr>
<td>Debridement of acute burn</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Debridement and/or disinfection of necrotic tumor</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Debridement in the peritoneal or pleural cavity</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Joint infection</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Vasculitic/arterial ulcer</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Wound disinfection other than listed above</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total cases</td>
<td>131</td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>Patient Age, y</td>
<td>Gender</td>
</tr>
<tr>
<td>------</td>
<td>----------------</td>
<td>--------</td>
</tr>
<tr>
<td>1</td>
<td>45 Male</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>42 Male</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>30 Female</td>
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<td>8</td>
<td>29 Male</td>
<td></td>
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<tr>
<td>9</td>
<td>79 Male</td>
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</tr>
</tbody>
</table>

ABX indicates antibiotics; BKA, below-knee amputation; CADz, coronary artery disease; MI, myocardial infarction; PRN, as needed; PVDz, peripheral vascular disease; SCI, spinal cord injury; S/P, status post; STSG, split-thickness skin graft.
Case 2: Debridement of Radiation Necrosis Wound for Odor and Drainage Control
A 42-year-old man was left paralyzed from the waist down after resection and radiation therapy for a sacral chordoma. His course was complicated by radiation colitis requiring colostomy and radiation necrosis of his sacrum and lower back. The back wound failed to heal, despite multiple surgical debridement and flaps. Two years following treatment, he was still lying prone in a long-term-care bed, too embarrassed by the foul-smelling wound drainage to allow his friends or family to visit. By that time, there was no viable tissue left to transfer or graft, so maggot therapy was attempted with the simple goal of decreasing exudate and controlling odor. After a few treatment cycles, the wound color had improved, drainage substantially decreased, and the odor was gone. The patient entertained visitors for the first time in years. Maggot therapy treatments were repeated every few weeks, whenever the drainage and odor recurred. During maggot debridement, a brown mass protruded from the lower margin of his wound. Biopsy identified the tissue as recurrent chordoma, by now also metastatic to his liver.

Case 3: Intra-abdominal Debridement of Necrotic Peritonitis
A 30-year-old woman with colonic inertia was treated with ileoanal bypass. The anastomosis leaked, and necrotizing peritonitis ensued, a complication seen in 4% to 6% of cases. Subsequently, approximately 3000 larvae were introduced deep into the abdominal cavity with the patient under anesthesia, and the abdominal contents were replaced and lightly packed. Two days later, upon removal of the larvae with the patient under anesthesia, the abdominal cavity appeared well debrided. No further debridement was required. The patient healed well without further complications and was discharged.

Case 4: Debridement of Empyema Cavity
A 53-year-old smoker was diagnosed with bronchogenic carcinoma of the right upper lobe in March 2003. He underwent a right pneumonectomy with intercostal muscle flap reinforcement of the stapled bronchial stump, in anticipation of postoperative radiotherapy for tumor involvement of soft tissue margins. During combined chemotherapy and radiotherapy, he developed a right chest empyema in May 2003. Open drainage with posterior rib resection preceded multiple additional surgical debridements with enlargement of the thoracostomy and parietal decortication. No bronchial stump leak was ever demonstrated. In February 2004, thoracoplasty was undertaken with complete resection of ribs 1 to 6, partial resection of inferior ribs, and aggressive sharp debridement of fibrotic and calcific plaques on parietal pleura and diaphragm. Multiple office procedures using a variety of rongeurs, curettes, and enzymatic preparations applied with bronchoscopic visualization of the empyema cavity were all unsuccessful.

On April 14, 2004, sterile maggots were introduced through thoracostomy, but few were alive when dressings were removed.
48 hours later. The following day, another batch of maggots was introduced, with special care taken to ensure adequate aeration of the cavity through the dressings and drainage of empyema fluid. Two days later, the patient was seen in the emergency room because maggots had been escaping. Remaining larvae were removed, and endoscopic inspection of the empyema cavity revealed complete disappearance of all fibrotic and calcific plaque and necrotic fascia. A vacuum-assisted closure device was applied to the wound and complete healing observed, with epithelialization of shallow residual sinus tract by June 2004.

Case 5: Debridement of Gangrenous Penile Glans
A 56-year-old man with diabetes, neuropathy, and vasculopathy and who was also on hemodialysis for chronic renal failure developed ischemia and gangrene of the penis. This was accompanied by ischemia of the left lower extremity and several fingers of the right hand. Multiple amputations, surgical debridement, topical and systemic antimicrobials, topical proteolytic enzymes, and conventional wound care failed to halt the progression of necrosis (Figure 2). The patient readily accepted the suggestion of maggot therapy and anticipated the treatments with confidence and hope. The nursing staff and hospital administration, however, were not supportive of the idea. Maggot treatment was delayed by fears that flies would infest the hospital, by requirements that such a nonformulary treatment would first require executive committee legislation, and by threats that nurses would not be able to care for patients with maggot dressings. Ultimately, a multidisciplinary policy and procedure were written to address and allay the concerns of the staff. Subsequently, maggot dressings were applied to the penis and necrotic stump and kept in place by taping the mesh to a hydrocolloid collar on the skin proximal to the wound. The patient felt no pain with the maggot dressings, and intraurethral migration—if it occurred at all—proved not to be a problem. One 2-day cycle of maggot debridement resulted in significant debridement of both wounds; however, the underlying arterial disease progressed, and peripheral ischemia prevented any of his wounds from healing. Ultimately, the patient became apathetic, discontinued dialysis, and died.

Case 6: Limb Salvage in the Face of Osteomyelitis
A 59-year-old diabetic man refused amputation, despite watching the toes on his right foot necrosed, one by one, over the course of 6 months. By July 1993, only his big toe remained. The second to fourth metatarsal heads protruded through his foot wound, already with radiologic evidence of osteomyelitis (Figure 3). He requested a trial of maggot debridement to save his foot. Medical and surgical staff believed that maggot therapy would be futile but agreed to a trial of maggot debridement because the gangrenous foot was stable. Over the next several weeks, necrotic tissue was replaced by healthy red granulation tissue. The big toe was surgically resected to expedite its debridement; the remainder of the foot wounds slowly healed without further surgical intervention. Every few weeks when wound healing ceased or the wound became purulent, maggot therapy was resumed with a 2- to 4-cycle course until the wound healed. He remained clinically free of osteomyelitis for 1 year but was then lost to follow-up.

Case 7: Debridement of Soft Tissue Necrosis Immediately Following Myocardial Infarction
Following acute myocardial infarction, a 45-year-old paraplegic was admitted to the intensive care unit. Failing to find peripheral
when his medication infiltrated into the neighboring soft tissue, the resulting ischemia caused more than 70 cm² of pretibial necrosis that extended down to the tibial crest (Figure 4). Fearing cardiac instability, the wound care team decided to treat him with antibiotics, topical dressings, and gentle bedside debridement; however, these were ineffective at controlling the infection beneath the eschar. Maggot therapy quickly debrided the eschar; the wound extended down to the periosteum. With continued maggot dressings, the wound was soon covered with healthy granulation tissue that grew to fill the defect within 6 weeks. The patient then received a split-thickness skin graft.

**DISCUSSION**

The approved clinical indications for Medical Maggots are limited to the handful of debridement scenarios where controlled comparative studies have shown safety and efficacy, including use on pressure ulcers, venous ulcers, neuropathic foot ulcers, and nonhealing traumatic or postsurgical wounds. The widespread belief that maggot therapy is useful only for debridement of necrotic tissue and only for wounds on the surface of the body has led many to refer to all forms of maggot therapy as maggot debridement therapy (MDT). Yet there are many accounts in both the clinical and basic science literature of 3 distinct but often simultaneous actions of medicinal maggots on wounds: debridement (liquefaction of necrotic tissue), disinfection, and stimulation of healthy tissue growth. This study revealed that some therapists—whether prompted by the literature or by desperation—are using maggot therapy off-label to debride ischemic wounds, osteomyelitis, and acute burns; to treat infection without necrosis; and to stimulate healing in chronic wounds without overt signs of infection or necrosis. Therefore, it seems prudent to establish controlled clinical studies to evaluate the efficacy and safety of maggot therapy for these additional conditions.

This study also highlights the fact that maggot therapy is not just a surgical alternative for nonsurgeons. The majority of therapists responding to this survey were surgeons who used maggot therapy as another tool in their repertoire, especially when surgical resection was technically difficult, ineffective, or of questionable need. Additional reasons for selecting maggot therapy included infections that were difficult to control, limited time or access to the operating room, and adverse reactions or patient objections to alternative treatments.

It is not possible to determine the exact frequency of off-label usage of maggot therapy, given the small response to the survey; however, a reasonable range can be estimated with relative accuracy. If the responding population is typical, then off-label usage may account for a similar proportion of cases, or 24% of all cases. Off-label usage is unlikely to exceed this level. The minimal level of off-label usage can be estimated by assuming that no other therapist had any off-label cases to report. For this calculation, the denominator would be the total number of wounds treated during this study period, or approximately 3050 (based on the total number of treatments distributed during the study period, divided by an estimated 2.5 treatments per patient). Thus, the minimum level of off-label use would be at least 131/3050, or 4%. The true frequency of off-label use might be near the middle of this range, say 14%. Had the intention of the survey been to identify the frequency rather than the diversity of off-label use, the investigators should have made this apparent in their survey. Some therapists may not have responded to the survey simply because they had no off-label cases; others may not have wanted to reveal their off-label use. Either situation could have contributed to the low survey response rate.

The majority of cases reported here were applications of maggot debridement to conditions not previously evaluated in controlled clinical studies such as debridement of acute burns, debridement of internal body cavities, and debridement of ischemic ulcers. The pleural and peritoneal cavities have long been considered off-limits for maggot therapy, but cases 3 and 4 demonstrate the potential utility of maggot therapy for debridging these internal sites. Therapeutic myiasis had been described only once before for empyema but never before for
necrotizing peritonitis. In both cases, medicinal maggots apparently reached areas of necrosis that were inaccessible surgically and provided the necessary and sustained debridement.

Case 5 demonstrated another off-label use of medicinal maggots for debridement; however, the maggots were given full access to the urethra in this case. This has not been previously reported and is not widely accepted as a reasonable location for applying maggot therapy. When treating similar cases of necrotizing glans penis, some authorities believe that aggressive penile resection is required,21 others support conservative management22 unless the infection progresses rapidly. Case 5 suggests that maggot debridement may have been the ideal compromise: aggressive local debridement without resection of viable tissue. Theoretically, migration of larvae through the anuric urethra could have led to additional problems, but no such complications occurred. This is the first reported use of maggot therapy for this serious condition but is likely not to be the last.

Maggot therapy is commonly used as a last-resort alternative to amputation. Reported rates of limb salvage in these cases are around 40% to 50%.23,24 In this report, 2 unusual cases of preamputation maggot therapy were included. Case 6 was complicated by osteomyelitis, but the wound healed completely without any evidence of infection 1 year later. Although osteomyelitis is not an approved indication for maggot therapy, this case is a reminder that maggot therapy was commonly used for osteomyelitis 70 years ago,2 and some believe that it may still be appropriate for some cases of osteomyelitis when surgical resection is impractical and antibiotics are inadequate.25 The patient described in case 9 was also being considered for amputation, but his vascular surgeon believed he might be able to save the limb with a vascular bypass. In this case, maggot therapy was used as a diagnostic procedure to define the level of viability before placing the graft. Unfortunately for the patient, the larvae quickly dissolved extensive amounts of nonviable tissue from the foot, allowing the surgeons to soon observe that there was little worth saving.

The FDA has not yet approved the marketing of maggots as an anti-infective or growth-stimulating modality as they were used in cases 1 and 3. Published studies that support maggot-induced wound healing include evidence of fibroblast proliferation in response to maggot extracts,26 enhanced migration of secretion-fed human dermal fibroblasts in vitro,27 and increased oxygenation in the periwound tissue of patients undergoing maggot treatment.28 In the reported patients, it is also possible to argue that wound healing could have been stimulated by the removal of biofilm that was too thin to see with the naked eye. The mechanical stimulation and rasping effect of these spined larvae as they crawl over the wound may help dislodge biofilms and may even trigger the formation of granulation tissue.4

Figure 4.

Case 7

After admission to the intensive care unit for acute myocardial infarction, intravenous vasopressors infiltrated the pretibial soft tissue of this paraplegic man (A). Shown during maggot debridement down to periosteum (B) and filled with granulation tissue 6 weeks later (C).
Clearly, maggots was inconsistent. The procedures of maggot dressing application and removal are generally reimbursed in accordance with other procedures classified under CPT codes 97597 and 97598 (selective debridement of devitalized tissue, without anesthesia) for wounds less than or greater than 20 cm², respectively. Reimbursement of the maggots was inconsistent though, since the Center for Medicare and Medicaid Services still requires each subcontractor to make its own reimbursement determination under HCPCS code A9270 (no national coverage policy). This meant that some therapists were initially denied reimbursement for the maggots until they appealed that local decision.

Acute and nonacute burns occasionally have been debrided with maggots, and laboratory data demonstrate that maggot digestive extracts effectively dissolve rat burn eschar. No controlled clinical studies of maggot debridement have been done for burn wounds. Several characteristics of maggot therapy suggest that it would be well suited for burn treatment, especially when the burns are extensive, when the patient is not a good surgical and/or anesthesia candidate, when the wounds are not responding to conventional therapy, or simply when experienced burn surgeons are not readily available. The microdebridement that is achieved with maggot therapy, removing infected and necrotic tissue without loss of viable structures, may be valuable in these patients, especially those with little soft tissue left to spare. As the mass of the wounds increases, the total healing time and the risks of bleeding, infection, and fluid loss also increase. Often, debridement is painful unless done under local or general anesthesia, further adding to the emotional and physical stress and adding to the overall risks of therapy. All of these reasons have been offered to support the use of maggot therapy in burn wounds; however, clinical efficacy and safety data that are objectively collected and analyzed are missing.

It is noteworthy that MDT for burn treatment was reported most often by specialized burn centers, well equipped and staffed with the most experienced trauma and burn care surgeons. Maggot therapy was being used as an adjunct to state-of-the-art surgical and medical care rather than as an alternative when conventional modalities were unavailable.

Some drawbacks of maggot therapy were identified by surveyed therapists, including the need to educate patients and family members about the therapy, many of whom were unfamiliar with the concept. Once the procedure was explained, patients were reportedly agreeable, if not enthusiastic, about maggot therapy. On the other hand, it was more difficult to educate and convince hospital staff and administrators that the treatment would not put the safety of other patients or the reputation of the facility at risk. When the staff and administration saw the results of treatment, however, they usually became supportive. Some survey respondents recommended formal training programs for medical and nursing staff to avoid the technical, logistic, and political problems occasionally associated with maggot therapy.

The time and effort needed to institute policies and procedures before beginning therapy were also noted to be a frustration. This obstacle has since been addressed by the BTER Foundation, which posted a maggot therapy policy and procedure template on its Web site. Also, reimbursement of medicinal maggots by third-party payers in the United States was inconsistent. The procedures of maggot dressing application and removal are generally reimbursed in accordance with other procedures classified under CPT codes 97597 and 97598.

REFERENCES