Medical Xpress

Maggots in medicine: Ancient therapy making comeback as wound-healing option

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A VA study in Florida on healing diabetic foot wounds is using maggots that

come contained in a fine mesh bag. Credit: Photo used with permission of BioMonde

These aren't your grandfather's maggots. Maggot, or larval, therapy has been around since ancient times as a way to heal wounds. Now, the method has gone high-tech—in some ways—and it's being tested in a rigorous clinical trial at the Malcom Randall Veterans Affairs (VA) Medical Center in Gainesville, Fla. Recruitment is now underway.

The study involves veterans with chronic diabetic ulcers on their feet. The maggots feasting on the dead or dying tissue in their wounds—and eating germs in the process—have been sterilized in a pristine, pharmaceutical-grade lab. Instead of roaming free over the wounds, they are contained in fine mesh bags, and removed after a few days.

Welcome to maggot therapy, 2015.

"There's an eight-step quality-control process to how these medicinal maggots are produced," notes lead investigator Dr. Linda Cowan. "Every batch is quality-tested."

Cowan has a Ph.D. in nursing science and is a wound-care specialist with VA and the University of Florida. She has studied maggots in the lab, combed through the available research on them, and seen firsthand what they can do in wounds.

"As a clinician, I was very impressed by the literature on larval therapy. And sometimes we would have patients come into the clinic with what I call 'free range' maggots—they're not sterile, they're not produced specifically for medicinal purposes—the patients got them at home, unintentionally. But they really clean out the wound nicely."

Cowan, like other researchers, tends to prefer the scientific term "larvae" over "maggots," but they mean the same thing. The whitish worm-like creatures are young flies, before they mature into pupa and then into adults. For therapy, in most countries, the green bottle fly is the insect of choice.

Co-investigator Dr. Micah Flores, whose background is in entomology—the study of bugs—admits that "maggot" does have a negative connotation for most folks. "It can be a scary word," he says.

Cowan points out that in the study's recruitment flyer "we use the term 'medicinal maggots.' We want people to know these are not home-grown on somebody's windowsill."

The VA study will involve up to 128 Veterans. It's comparing maggot therapy with the standard of care for diabetic wounds—a treatment called sharp debridement, in which a health care provider uses a scalpel, scissors, or other tool to cut or scrape away dead or unhealthy tissue. The procedure promotes wound healing.

Nearly a quarter of VA patients have diabetes, and about a quarter of these will have foot wounds related to the disease. In many cases, the hard-to-heal ulcers worsen to the point where gangrene develops and amputation is required.

The Gainesville researchers will examine how well the wounds heal in each study group. They'll also look at maggots' effects on harmful bacteria. In addition to clearing out dead tissue, maggots disinfect wounds by ingesting bacteria and secreting germ-killing molecules. They also eat through biofilm—a slimy mix of micro-organisms found on chronic wounds.

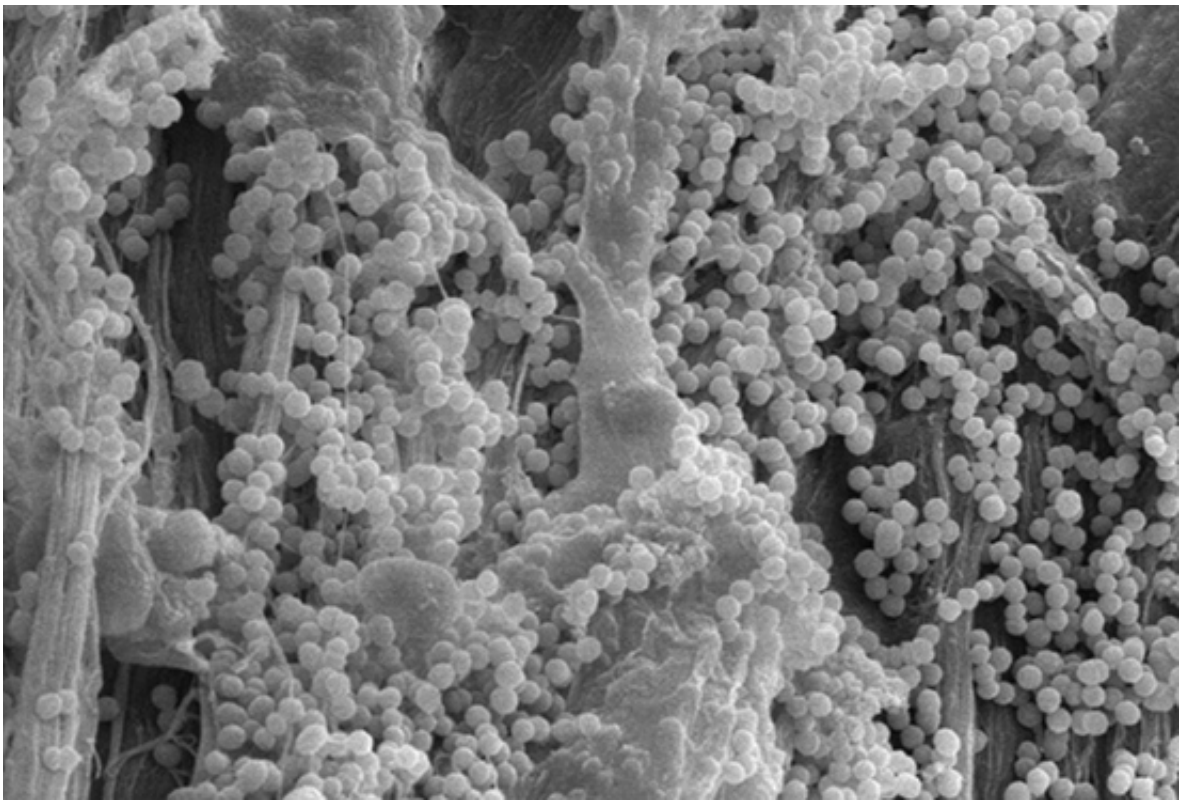
Turn back the clock about 90 years, and there was a researcher who grew

maggots on a hospital windowsill, as unscientific as that sounds. Dr. William Baer had treated U.S. soldiers in France during World War I and noticed that large, gaping wounds that were swarming with maggots—sometimes thousands of the creatures—didn't get infected, and the men survived.

Baer came back to Johns Hopkins University and experimented with the therapy, only to realize that maggots could spread disease as they devoured decaying tissue. Two of his patients died of tetanus. He made some progress with using sterilized maggots, but soon antibiotics would come on the scene and maggot therapy—with its high yuck factor—fell into disregard.

"Antibiotics were the new cure-all, and so we didn't need the maggots around too much anymore," says Cowan. "But they've never gone away completely."

A few studies took place in the U.S. in the ladder half of the last century, including some at the VA Medical Center in Long Beach, Calif. But it wasn't enough to place maggots in the pantheon of modern medical miracles. Meanwhile, the therapy continued to attract interest in the United Kingdom, where a game-changer occurred a few years ago. A Wales-based company called BioMonde came out with the bag concept, which caught Cowan's attention right away.



This photo, from a VA-UF study published in the journal Ulcers in 2013, shows a microscopic view of a biofilm, grown in the lab on a piece of pig skin. This "before" image is teeming with microbes.

She had been interested in studying maggot therapy. But she also realized that many clinicians, as well as patients—and their caregivers at home, who would have to change dressings—might have a hard time warming up to the idea.

"When we started talking about doing this study," says Cowan, "we were interested in the yuck factor. One of my concerns was other clinicians. They have to deal with this. They may be turned off by what I call the squirmy wormies."

Cowan recalls one nurse colleague who would recoil when patients

showed up in the clinic with wounds that had attracted a few maggots.

"She just had an aversion to larvae of any kind. When a patient would come in, and they would have these free-range maggots, she would not want to deal with them. She would come and get me, and I would take care of it.

"I realized she wouldn't be the only clinician out there who would feel like this. So I thought this product would really make a difference."

That said, Cowan believes many patients are undeterred by the insects, bags or no bags. She tells of one veteran who has been struggling with a non-healing diabetic ulcer for three years. "He said he is willing to try anything that might work."

That attitude is not uncommon among those with diabetic sores, says Cowan, although she senses that veterans, as a group, may be a bit less squeamish than the general population, and thus even more receptive to the therapy.

"When we go through the informed consent form with them, we explain the study and we tell them they could be randomized to the 'sharp' group, which is the standard of care, the same kind of debridement they've gotten in the past—or they could get the maggot therapy. We've done about 21 informed consents so far. Overwhelmingly, people have been disappointed if they weren't randomized to the maggot group."

BioMonde, the company sponsoring the trial, has said it will provide maggots for up to two weeks of treatment for any patient who did not receive the therapy during the study but wants it, and whose physician believes it would be appropriate.

Both groups in the study will receive treatment over the course of eight

days. Along with studying the veteran patients and their wounds, the researchers will survey their caregivers and clinical providers. "One thing we want to find out," says Cowan, "is whether this yuck factor is really an issue. And who is it the greatest issue for? Patients? Clinicians? The wife or husband who has to change the dressing?"

To examine the main study outcome, the team will photograph each wound before and after each treatment. Then, wound-care experts who are blinded to which therapy was used—maggots or sharp debridement—will visually assess how much viable versus non-viable tissue remains.

Just as important, the team will study the therapies' effects on biofilms. A biofilm is not a movie about someone's life—it's a soupy mix of bacteria and other germs that resides on or in a wound. Experts believe it may be part of why some wounds—such as diabetic ulcers—are so difficult to heal. Cowan's group has studied biofilms in the lab, grown on pieces of pig skin, and she says the maggots are the only therapy that appears to completely eradicate them.

"A biofilm is a party of poly-microbial organisms," explains Cowan. "It could be bacteria, fungus, virus—all of them. They spit out a protective coating that protects them from things you would put on the wound, like an antiseptic gel. Also, it protects them from things you might take inside the body systemically, like antibiotics. So it's tough to get rid of these biofilms.

"You can debride with a scalpel, and you can cut away what looks like dead or unhealthy tissue, but you can't see biofilm. And if you don't completely get rid of a biofilm growth, within 24 to 72 hours it can completely regenerate, with its protective coating."

Cowan collaborated with Dr. Gregory Schultz on numerous studies

involving biofilms at UF's Institute for Wound Research.

"Both independently and collaboratively, we tested quite a number of products," says Cowan. "We tried all kinds of expensive things. There were some that were more promising than others. We would get some good, favorable results. But there was nothing that was getting rid of everything—until we tested the maggots."

The group published a 2013 study in the journal Ulcers that included before-and-after pictures, taken with an electron scanning microscope, attesting to the maggots' handiwork.

"The results were mind-blowing," says Cowan. "The photos show the difference with the larvae at 24 and 48 hours. At 24 hours there were hardly any [bacteria] to count, and at 48 hours the biofilm was completely gone. Not one organism left."

She points out another benefit of the maggots, versus drug treatment: "It's hard for bacteria or other organisms to develop a resistance to something that's going to eat them." Drug-resistant bacteria are a huge problem in U.S. heath care.

Flores, the entomologist, wants to peek inside the maggots, to see what they've ingested. After they are removed from a wound, the bagged maggots are being frozen for later analysis. (Not in the same freezer where the lab crew keeps their Haagen-Dazs, by the way.)

"My background is studying insects—flies in particular," says Flores. "So I'm very interested in what's inside the larval gut, what they've been feeding on. Are they picking up the same organisms we're seeing growing on the wound? Does it match up?"

Flores and Cowan say theirs is the first study to do this type of analysis.

And there should be plenty to look at: Between dead tissue, bacteria, and biofilm—an all-you-can-eat buffet for maggots—they take in enough grub to noticeably blow up in size.

"They do a great job," says Cowan. "They plump up to the size of a small jelly bean, whereas when they go in, they're smaller than a grain of rice. So it's pretty impressive."

The team is also looking at biomarkers of wound healing as another study outcome. Enzymes known as MMPs, for example, rise in response to inflammation. Levels drop as a wound heals.

Pending the study results, Cowan hopes to see maggot therapy catch on in the U.S. as an evidence-based way to treat wounds—not just diabetic ulcers, but other types as well. One example might be deep skin wounds in combat veterans. She's already gotten calls from plastic surgeons interested in the therapy.

"If the maggots can clean up a wound, they can possibly make advanced therapies more effective so you don't have to repeat them. For example, if you take a skin graft from the leg and put it on the belly, if that wound has a chronic biofilm, that graft is not going to take. But if you clean it up and then do the skin graft, it may take. What a win-win that would be."

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