

SAVING LIVES AND LIMBS FROM “FLESH-EATING DISEASE”

Even with emergency treatment, this deadly flesh-eating infection kills 20 percent of its victims—and many survivors lose an arm or a leg. But by using NovaBay’s NeutroPhase wound cleanser at Seton Medical Center in California, Dr. John Crew has saved not only the lives of all the patients he’s treated, but also their limbs.

When 51-year-old Lori Madsen fell in a parking lot, her injury hardly seemed serious—just a scrape on her left elbow. But unbeknownst to her, *Streptococcus* bacteria had gotten under the skin and has started a cascade of devastation called necrotizing fasciitis or ‘flesh-eating disease.’ Within three days, she was in shock and being rushed to the emergency room at Seton Medical Center in Daly City, California. She collapsed in the hospital. Her blood pressure dropped so low it was unreadable.

The odds were bad. Even with emergency treatment with antibiotics, 20% of victims of flesh-eating disease die. Many more lose an arm or a leg. Without treatment mortality jumps to 70%.

But Madsen was lucky. She had been taken to the right place, Seton Medical Center, which has a specialized wound care center directed by Dr. John Crew. Moreover, Dr. Crew had been experimenting with a new treatment approach for the life-threatening condition that promised better results than the standard treatment. His key innovation was irrigating the affected area of dying flesh and tissue with NeutroPhase, a FDA-cleared hypochlorous acid (HOCl) product, in conjunction with Negative Pressure Wound Therapy (NPWT). NeutroPhase has been shown in the laboratory to kill many strains of bacteria and to neutralize the toxins that are known clinically to destroy tissue.

Dr. Crew cut away the dead flesh from Madsen’s arm and infused HOCl. His treatment approach worked. Madsen survived, and her arm healed completely. “He saved my arm and my life,” says Madsen.

Madsen is not the only beneficiary.



In 7 recent cases, Dr. Crew has used NeutroPhase as part of the NPWT treatment regimen to successfully manage this devastating infection. The list of these patients includes Michael Meillon, a restaurant manager whose genitals were almost destroyed by the disease.

“This is a whole different way to manage these life-threatening wounds and flesh-eating infections,” says Crew. Crew has published a case study of Madsen’s treatment in the journal *WOUNDS* and has submitted another paper for publication which provides examples of other case studies in which the outcomes appear to be due to Dr Crew’s treatment regimen.

For Dr. Crew, bringing new hope to victims of flesh-eating disease is just the latest advance in a long career on the frontiers of medicine. Yet he did not set out to be a medical pioneer. In fact, as a student and star basketball player working his way through Westmont College in Santa Barbara, the young Crew didn’t

even consider becoming a doctor. But then his two uncles, who had stepped in to advise Crew after his father died, asked him what he was going to do with his life. Crew liked science, so he replied: Maybe a dentist? No, his uncles said, you will be a doctor. “I said, okay,” Crew recalls.

With financial support from his uncles and his wife, who was a teacher, Crew graduated from medical school and trained as a vascular surgeon in San Francisco. “I realized I loved surgery,” he says.

But not just any surgery. Crew was particularly fascinated by new ideas and techniques. He was one of the first surgeons to do balloon angioplasty—inflating a balloon inside an artery to expand the blood vessel. He helped develop a tiny spinning blade that, inserted into a blood vessel, chews up clots that are blocking blood flow. He was a pioneer in using lasers to shoot little holes in hearts to improve blood flow and heart function.

Working in his garage, he even welded together new medical tools, such as a mammary artery retractor. “I’ve been privileged all my life to have tried new things and developed new operations and new kinds of equipment,” he says.

He also became interested in better treatments for hard-to-heal wounds, working with growth factors and other new ideas in the 1980s. As part of that effort, he created a wound care center at Seton Medical Center and was the regional director for a network of about 30 such centers.

So Crew was willing to listen when he got a call out of the blue in 1997 from a chemist named Dr. Ron Najafi. “He told me he had something that might help wounds,” Crew says. “I was the sixth doctor he’d called—and I was the only one who would see him.”

Najafi told Crew about natural substances, such as hypochlorous acid (HOCl), that the body’s immune system produces as a first defense against invaders. These substances are shown in the laboratory to kill bacteria and also to rip apart the biofilms that help protect bacteria from attackers. The problem is that hypochlorous acid is unstable in its natural form.

Najafi’s advance was creating a stable version that he called NeutroPhase, now being marketed by Najafi’s company, NovaBay Pharmaceuticals. An “unstable” and “bleach contaminated” version of hypochlorous acid was invented and used by Professor Dakin and Carrel in 1916. Known as Dakin solution, it was used successfully in acute wounds of soldiers during World War I. Because of tremendous bleach impurity of Dakin solution, though, it had mixed success in more sensitive wounds such as diabetic, pressure and venous ulcers. In contrast, NeutroPhase is stable and contains 0.01% pure hypochlorous acid without any bleach impurities. Pure hypochlorous acid has been shown to be 80-100 times more potent than Dakin solution.

But it wasn’t clear to Crew exactly how much a pure hypochlorous acid solution (NeutroPhase[®]) could contribute to wound care

until the recent cases of flesh-eating disease. A typical doctor doesn’t see many cases of the disease, which is also known as necrotizing fasciitis or toxic inflammatory cellulitis, so it’s challenging to try new approaches or test methods in a controlled manner. The disease strikes about 1,500 Americans every year, according to the Centers for Disease Control, although Crew believes the figure is higher. It typically starts just as a small, seemingly innocuous cut or scrape that gets infected by bacteria. Normally, the infection can be easily fought off by the body’s own immune system or with antibiotics.

But in a small percentage of infections, something goes terribly wrong. The bacteria can hide from the immune system and from antibiotics and spread under the skin, producing toxins and enzymes that destroy cells. Meanwhile, the immune system, attempting to fight the bacteria and clean up the damage, produces chemicals that also can kill normal cells. Together, these toxins cause excruciating pain, dangerously low blood pressure, confusion, high fever, and severe dehydration. Victims can quickly lose an arm or a leg—or their lives. Even with emergency treatment with antibiotics, about 20% of patients die. Without treatment, mortality rises to 70%.

Crew’s treatment regimen, however, is significantly boosting the success rate. The key is pure 0.01% hypochlorous acid in saline, without any bleach impurity. The HOCl doesn’t just kill bacteria (as shown in *in vitro* laboratory studies). It also neutralizes the toxins, as also shown in the lab. That was crucial in Lori Madsen’s case, for instance. Cultures from her wound showed that the bacteria had been quickly killed by antibiotics. Yet the disease continued to eat away at the flesh of her arm and threaten her life, until Crew irrigated the wound with NeutroPhase and used NPWT device to lavage the wound. Combined with surgery to remove the dead tissue, the combination of NeutroPhase cleansing and the NPWT allowed the normal wound healing to progress.

What’s particularly scary about flesh-eating disease is that it often starts with

a seemingly minor cut or illness. It’s a lesson that Michael Meillon, 55, a restaurant manager who lives in Hayward, Calif, also learned the hard way. “I had gotten a flu shot, and a couple of days later, I got sick as a dog,” he recalls. “But I thought it was because of the flu shot.” A couple more days went by, and Meillon felt even sicker. His testicles began to ache. “I was in a lot of pain.” He finally decided he’d better go to the emergency room. The doctors immediately realized that Meillon had gotten a serious infection, possibly because of a hair follicle or a small abscess. Gangrene was already eating away Meillon’s groin area and his kidneys were failing. “They said, ‘Why did you wait so long?’ and they did emergency surgery right then and there,” he says.

Meillon had been infected with flesh-eating *Enterobacter* and *Klebsiella* microbes. The doctors immediately started antibiotics and cut away the necrotic skin. Then Dr. Crew infused the area with NeutroPhase. “It was not fun,” Meillon says. “I was so out of it, I lay there and let them do what they needed to do.”

Fortunately, he quickly responded to the treatment. Now, he’s coping with the aftermath of the infection, which damaged the nerves in his legs and his kidneys. “My balance is off, I walk like a duck and I need kidney dialysis,” he says. “But you deal with it.” He’s just glad to have survived. “You never know what’s going to happen,” he says. “I take one day at a time.”

Having seen the power of this new treatment approach in patients like Meillon and Madsen, Dr. Crew is now anxious to make the medical profession aware of this advance. He is going to meetings, publishing papers and working with other physicians. “We haven’t lost a life or a limb in anyone that we have treated with this new approach,” he says. “I think this approach will make a tremendous difference,” he says.

Necrotizing Fasciitis (Flesh Eating Disease) or Toxic Inflammatory Cellulitis

Necrotizing Fasciitis is a deadly infection and must be recognized early because the body's reaction to the infection can be just as deadly as the bacteria causing the infection. To follow are the step-by-step procedures describing our understanding of the disease and how our proposed surgical procedure and NeutroPhase adjunct therapy can halt the disease in its tracks.

- 1) Bacteria cause the infection which triggers the disease.
- 2) Victims feel excruciating pain in the superficial tissue over the muscle.
- 3) Bacteria begin to secrete their deadly toxins.
- 4) In response body secretes its own equivalent-ly dangerous deadly toxins to kill the bacteria.
- 5) The toxins generated by both bacteria and body begin a cascade of tissue death (flesh eating phase).
- 6) In order to halt the disease, aggressive appropriate antibiotic therapy must be used to immediately eradicate the bacteria.
- 7) In order to save the patient limbs or body parts, toxins must be removed by
 - a. Debridement of the dead tissue surgically with anesthesia.
 - b. Neutralization and removal of all available deadly toxins.
- 8) NeutroPhase is an FDA-cleared wound cleanser. In laboratory testing, NeutroPhase has been shown to kill bacteria and neutralize many toxins (this data has not been reviewed by the FDA, but has been published in the October 2013 issue of the journal WOUNDS).
- 9) This procedure created by Dr. John Crew and NovaBay's team of scientists reduces aggressive surgical therapy and upward of 10-20 surgeries that often end up with amputation (70%

chance) and death (30% mortality).

10) The Crew-NovaBay minimally invasive surgery necrotizing fasciitis calls for multiple small incisions. After suctioning the necrotic tissue, infusion of NeutroPhase through these incisions for 5 minutes is followed by removal of NeutroPhase and all the debris using a wound vacuum down in the incision site. This process gets repeated on an as needed-basis (3-4 times a day) using Negative Wound Pressure Therapy, until the patient is stabilized and wound is showing signs of healing. Then the healing phase can begin.

Disclaimers

NeutroPhase[®] is a FDA 510(k)-cleared wound cleanser and is intended for use under the supervision of healthcare professionals for cleansing and removal of foreign material, including: microorganisms and debris from wounds; cleaning minor cuts, minor burns, superficial abrasions, and minor irritations of the skin; as well as moistening absorbent wound dressings. It is also intended for moistening and debriding acute and chronic dermal lesions, such as: Stage I-IV pressure ulcers, stasis ulcers, leg ulcers, diabetic foot ulcers, post surgical wounds, first and second degree burns, as well as grafted and donor sites. NeutroPhase is a 0.01% pure hypochlorous acid in saline (with no bleach impurities, which is often present in Dakin and Dakin-like solution). FDA has not reviewed NovaBay's data with respect to anti-toxin activity of NeutroPhase in in vitro experiments. In *in vitro* laboratory models, NeutroPhase has shown to be fast-acting against bacteria, biofilm and toxins.

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