

Wound, Heal Thyself.

A New Division of Surgery Tackles One of the Most Daunting Challenges in Medicine

The sore under the patient's big toe didn't hurt, but it wasn't getting better. The 64-year-old woman had been living with type 2 diabetes for many years. She did a good job of keeping her blood sugar under control, but because her nerves had been damaged by diabetic neuropathy, she often didn't notice blisters or sores on the soles of her feet. This one was smaller than a dime and not inflamed, so the woman's doctor reassured her that in time it would heal.

By the time she found Harold Brem, M.D., chief of NYU Langone's new Division of Wound Healing and Regenerative Medicine, an antibiotic-resistant infection had eaten its way down to the bone. Amputation of her toe was a real possibility. Dr. Brem surgically removed diseased tissue from the woman's ulcerated toe and applied human cells, which rapidly began to close the wound. Her toe was saved.

Chronic wounds are a full-fledged epidemic. Wound infections account for some 4.5 million emergency room visits each year, and complications from dia-

betic ulcers result in more than 80,000 lower limb amputations, often because no one recognizes the severity of the wound. "When it comes to diabetic ulcers," explains Dr. Brem, "looks don't matter. A very complex set of molecular abnormalities results in the ulceration."

Dr. Brem's research, funded by six grants from the National Institutes of Health, has pioneered understanding of the cellular and molecular biology of chronic wounds. Among his team's discoveries is that keratinocytes, specialized skin cells that normally multiply and migrate across an open wound as it heals, behave differently in chronic wounds. They multiply but do not migrate, due to overexpression of *c-myc*, a gene that inhibits healing. The result is an abnormally thick margin on the edges of an open wound.

With regard to the three most common types of chronic wounds, Dr. Brem explains that pressure ulcers, or bedsores, cost the most lives; diabetic ulcers claim the most limbs; and venous ulcers, which afflict mostly the elderly, cause the most suffering.

A firm believer that "every wound can and will heal with proper care," Dr. Brem has merged research and clinical efforts in the new division, which is part of the Department of Surgery. "All of our research is translational," he says, "pursued only if the results will directly and significantly benefit the patient." The result is a set of protocols designed to prevent ulcers from developing and to ensure complete healing if they do. These include daily examination and swift treatment of any break in the skin. Wounds are measured, photographed, and tracked using advanced informat-

ics via a Wound Electronic Medical Record. Diseased tissue is removed surgically, leaving healthy tissue at the margins. Cellular and collagen therapy is applied to tap the patient's natural ability to regenerate tissue.

The division's multidisciplinary team of health-care professionals provides same-day coverage for inpatients with a break in the skin and same-week coverage for outpatients. Nurses are specially trained to assess wounds and, if appropriate, refer patients for treatment at Tisch Hospital and NYU Hospital for Joint Diseases.

"NYU has created the best clinical surgical department on the East Coast," says Dr. Brem, who was recruited from Columbia University's Department of Surgery, where he directed the wound-healing program. "By putting all these resources under one roof, we can offer patients a unique set of services with seamless care."

Dr. Brem's research program is focused on the hypothesis that non-healing wounds are a localized biological phenomenon rather than a systemic pathology. An ongoing funded clinical trial is testing a way to deliver a gene that makes a protein that can reverse a non-healing wound. The next step is finding out which genes stop the wound from healing. "We hope to one day just reverse the genes," says Dr. Brem. "Meanwhile, our goal is to return patients to their referring physician, nursing facility, or home in the same condition they were in prior to the wound."

For more information, call (212) 263-7187 or visit NYUWound.org.