

Push-Pull Model of Wound Healing Described

BY MARK S. LESNEY
Senior Editor

WASHINGTON — The vascular surgeon insists that revascularization was a success—and there are outcome images to prove it—but the diabetic foot becomes ischemic anyway, and the wound fails to heal.

This is an all too common scenario for physicians who care for these at-risk limbs and problem wounds. Such failures can be explained in a push-pull model of perfu-

sion in these patients, and this model may well indicate what needs to be done for effective treatment, according to Dr. William J. Ennis.

The push-pull model essentially states that despite the “push” of restored macrocirculation from revascularization, the patient still needs the ability to “pull” blood nutrients into all parts of the limb via a functional microcirculation, said Dr. Ennis of the St. James Center for Comprehensive Wound & Disease Management in Chicago.

He spoke at a meeting sponsored by George Washington University Hospital.

But creating “pull” is not an easy task, especially for patients with diabetes. In such individuals, a functional microcirculation may be a problem in its own right because of both physical and physiologic changes in their microvascular system brought on by the long-term chronic disease. In patients with poor microcirculation, successful revascularization of the larger vessels can lead to ischemic reper-

fusion injury in the tissues that they service. White cells stick and create reactive oxygen species that make it almost impossible for wounds to heal.

Damage models in diabetic foot wound responses after revascularization can borrow from cardiology, according to Dr. Ennis—concepts such as tissue “stunning,” whereby tissue is traumatized by the reperfusion injury without being killed and remains capable of recuperating; no reflow, such as that caused by a mechanical obstruction from thrombus; or functional alterations, such as the endothelial dysfunction that is known to occur in diabetics.

It is critical to restore a microvascular “pull” as soon as possible in order for the wound to heal and, in many cases, in order for the limb to survive, according to Dr. Ennis. “It is almost silly for us to think that we can solve the entire process with a simple bypass. We may end up with a mixed pattern, persistent ischemia, and something known as no reflow. These are the patients who get bypass and nothing happens—the wound continues or the open-air site never heals... It is so frustrating for us as wound clinicians to see a great bypass and still lose a limb. It’s not uncommon, and this [microcirculatory problem] is why.”

Angiogenesis agents are one option for restoring microcirculatory “pull.” One such treatment may be ultrasound. Pulsatile flow in tissue pushes and pulls on the endothelium and causes nitric oxide release. Ultrasound can be used to “fake the tissue out that it is receiving pulsatile flow,” according to Dr. Ennis, who along with his colleagues has studied the use of ultrasound to induce angiogenesis, pulsatile flow, and ultimately wound healing.

“We were able to show that there was a difference in angiogenesis at approximately 4½ weeks with ultrasound therapy. ... This was one of the first times we were actually able to quantify the angiogenesis response and correlate it to wound healing,” he explained (*Advances in Skin & Wound Care* 2006;19:437-46).

The future may include novel treatments for reperfusion injury and ischemia such as bone marrow stem cell therapy, which may be available in 5-10 years, and growth factor molecules, many of which are currently being tested in phase I trials, according to Dr. Ennis.

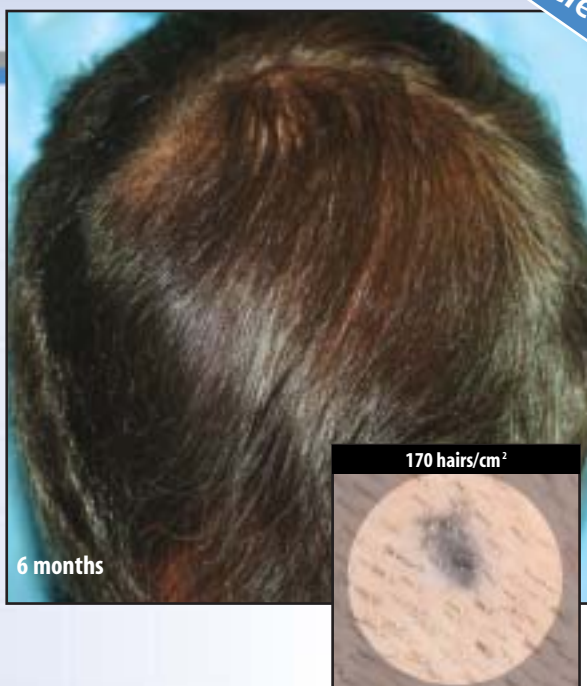
Regardless of which treatment is chosen, it is also important for the vascular and wound-care teams to collaborate on prevention of ischemia after revascularization, Dr. Ennis stated. The certainty of appropriate return of macrovascular circulation must be confirmed, and all other barriers to blood flow need to be addressed.

Preoperatively, it may be possible to use free-radical scavengers or systemic vasodilators. Postoperatively, he advised that tissue-level perfusion be tested for adequacy of revascularization and cautioned against relying on the return of palpable pulse or flow in the bypass graft to do that.

Dr. Ennis disclosed that he was a consultant and received an honorarium from Celleration, which manufactures an ultrasound device for stimulation of wound healing. ■

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