

Take a Biofilm Approach to Wound Infection Tx

BY MARK S. LESNEY
Senior Editor

WASHINGTON — Monotherapy may not be enough in the treatment of diabetic wound infections.

These infections are not caused by the planktonic or individual cellular form of mainly single-species bacteria proliferating in the wound, but rather are caused by a complex, multicell vegetative mixed-bacterial state known as a biofilm, which has to be treated as a unique and dangerous organism in its own right, if treatment is to prove effective, according to Dr. Randall Wolcott, of the department of microbiology and immunology at Texas Tech University, Lubbock.

The medical biofilm concept of infection is a fairly new one, and a recent review noted that almost every bodily system is affected by a biofilm disease, said Dr. Wolcott at a meeting sponsored by George Washington University Hospital.

He estimated that every year, more than 10 million people come down with biofilm diseases, from endocarditis to necrotizing fasciitis, which translates to more than 500,000 people a year who die from the disease.

And if all these infections are really biofilms, then the next therapeutic step is to move from antibiotic monotherapies to include the use of antibiofilm agents and aggressive treatments, Dr. Wolcott said.

His recommended combined treatment is only in its infancy, but it involves frequent, very aggressive debridement, coupled with biocide treatments that include heavy

metal agents such as silver, gallium, and selenium. It is important to rotate treatments in order to prevent selective adaptation of the biofilm, which can happen not in weeks or months, but in days.

It is also critical to include the use of specific antibiofilm agents such as lactoferrin and xylitol, which are approved by the Food and Drug Administration for other purposes. He has even experimentally used predatory bacteriophages and various plant extracts known for their antibiofilm properties. Ultimately, "once you suppress the biofilm below a certain level . . . the wound starts contracting" and normal host healing can begin, he said.

This understanding is very new, and few people are being trained enough to understand it as yet. "I just got a [2007] medical microbiology text and it does not mention biofilms," he said.

However, physicians see biofilms in diabetic foot wounds every day without realizing it: the so-called slough that physicians routinely remove, or not, said Dr. Wolcott. Many physicians believe slough is merely a mixture of white blood cells, protein, and deteriorated host tissue, but it is actually part of a complex biofilm—and one that will return, if even "one cell remains" still virulent, exactly as before without proper treatment.

Once bacteria attach to a wounded surface, "they form a microcolony. Once they reach a critical density, they start form-sensing, and they rise up above the surface and they start forming all these complex structures. One of those structures infests itself around the vasculature and

they invade the host down through the vascular system. [They also] rise up over the surface for community defenses," he said.

This vegetative state behaves like a single organism "made of billions of billions of cells" including multiple bacterial species. A large portion of this "organism"—and he stressed treating it as such—includes gluey, sugar-protein matrices formed within the first 5 minutes of biofilm development. These protect the bacteria from harm by walling them off—not only from the host immune system, but also from many of the treatments that are used, Dr. Wolcott said.

Within 30 minutes, the biofilm is rising from the surface. It is controlled centrally by various intercellular communication molecules that act almost like hormones, and it reproduces by vegetative breaking and single-cell "seeds."

The biofilm components summon white blood cells, with their phagocytic enzymes, which actually can provide nutrients for the biofilm; this explains much of the biochemistry we see, according to Dr. Wolcott.

The bacteria give up their individuality and live for the colony, with different regions producing different proteins. One clinically important factor is that there are portions of the biofilm where the cells upregulate gene transfer to create phenotypic and genotypic diversity to survive. This includes the potential for transferring antibiotic resistance across species.

Dr. Wolcott had no disclosures other than the use of materials that are not FDA approved for these indications. ■

Cutaneous Adhesive Effectively Closes Wounds on Thin Skin

BY JEFF EVANS
Senior Writer

BALTIMORE — The cutaneous adhesive Dermabond can be applied to the margins of a wound to buttress atrophied, thin skin enough to achieve adequate primary closure with sutures, Dr. Michael Bain reported at the annual meeting of the American Society of Plastic Surgeons.

Physicians have always had a difficult time suturing lacerations or defects created from the removal of cancer because sutures tear the skin of older patients with steroid-induced skin atrophy or genetically thin skin, said Dr. Bain, a plastic surgeon in private practice in Newport Beach, Calif.

"There are so many patients out there who in the past have needed skin grafting when they got a bad laceration," he said in an interview. "You could also use this technique in infants who have very thin skin."

After a standard wound preparation, Dermabond is applied 3 mm from the wound

margins. Simple sutures placed either through or behind the Dermabond close the wound without tearing the skin. "You have to make certain that you don't get any Dermabond into the incision or into the wound because that will prevent healing," he said.

Dr. Bain has used the technique on about 15-20 patients without any problems. He said that his colleagues, as well as trauma surgeons, also have begun using the technique successfully.

By allowing the closure of wounds in thin skin, the technique may prevent the need for prolonged wound care, according to Dr. Bain, who presented the method on a poster. He and his coinvestigators have no conflicts of interest with regard to Ethicon Inc., the manufacturer of Dermabond. ■



The cutaneous adhesive, Dermabond, is applied 3 mm from the wound margins.



The healing wound is shown 3 weeks after the graft-sparing procedure.

Split-Thickness Graft Sites Heal In Weeks With Matrix Dressing

BALTIMORE — Oasis wound matrix provides a low-maintenance scaffold for split-thickness skin graft donor sites to grow new epidermis over several weeks without significant pain for the patient, Dr. James C. Yuen said in a poster presented at the annual meeting of the American Society of Plastic Surgeons.

Since Oasis was approved by the Food and Drug Administration in 2000, few articles have been published on its use, none of which describes using it for dressing split-thickness skin graft donor sites, according to Dr.

Yuen of the division of plastic and reconstructive surgery at the University of Arkansas, Little Rock.

Oasis is derived from porcine intestinal mucosa and acts as an extracellular matrix to support cell adherence, he said.

The material contains key components of the dermal extracellular matrix (collagen, elastin, glycosaminoglycans, glycoproteins, proteoglycans, and growth hormones) to promote rapid cellular proliferation and capillary ingrowth.

During 2003-2006, Dr. Yuen and his colleague, Dr. Julio Hochberg, also of the university, used Oasis to reepithelialize split-thickness skin graft donor

sites on the thighs of 131 patients.

Epithelialization was complete after 1-3 weeks in all but two patients who had delayed healing beyond 1 month. Few patients experienced significant pain at the donor site because the material protects nerve endings, the investigators suggested.

Once Oasis is placed directly over the wound, Xeroform (Kendall Inc.) is placed to cover the matrix, followed by nonadherent Telfa gauze (Kendall), 4-by-4-inch dry gauze pads, and then Tegaderm tape (3M Health Care) for smaller donor sites or a circum-

ferential wrap with Kerlix (Kendall) for larger sites. Dr. Yuen said that neither he nor Dr. Hochberg has any conflicts of interest with the manufacturers of any the products used in the procedure.

The investigators typically changed the dressing 4-6 days after surgery, but it was done earlier if there was excessive drainage soaking through the dressing.

Subsequent dressing changes occurred every 2-3 days, leaving the Oasis wound matrix and Xeroform in place each time.

The scab-like wound matrix peels off easily after reepithelialization is complete, Dr. Yuen said.

Of 131 patients receiving the wound matrix to split-thickness skin graft sites on their thighs, epithelialization was complete in 1-3 weeks in all but 2 patients.

—Jeff Evans