Speeding up wound healing the EGF way

Human skin wounds heal faster when treated with epidermal growth factor (EGF), according to a new study. The finding, which confirms results in pigs, may enable physicians to lower the infection rate of otherwise slow-to-heal wounds and shorten the waiting time between skin grafts in burn victims. In addition, the investigators say their work and follow-up studies now underway suggest that other genetically engineered growth factors, alone or combined with EGF, may speed healing in a variety of skin wounds.

Scientists from Emory University in Atlanta, Vanderbilt University in Nashville and the University of Louisville in Kentucky studied pairs of similar skin regions in each of 12 plastic surgery and burn patients. Using a surgical shaver, they removed patches of epidermis – the top skin layer – and upper layers of the underlying dermis for skin grafts needed by the patients, which created "wounds" they could study. Twice a day they treated one injured region of each patient with antibiotic cream alone and the other site with the cream plus EGF. Photographs and biopsies revealed that EGF-treated wounds healed an average of 1.5 days faster than wounds receiving the cream only.

"A day and a half is not that big a deal *per se*," notes coauthor Gregory L. Brown of the University of Louisville. But if a burn patient has only 20 percent of his or her skin available for grafts, he says, EGF could shorten the healing time required for that skin to yield another graft. The team reports its findings in the July 13 NEW ENGLAND JOURNAL OF MEDICINE.

Brown and Vanderbilt's Lillian B. Nanney, a coauthor of the paper, have separately begun several other wound-healing studies, they told SCIENCE NEWS. In pigs, whose skin resembles that of humans, both are examining the ability of other growth stimulants, including fibroblast growth factor and transforming growth factor-beta, to speed dermal wound healing. In humans, Brown's group is studying EGF's effect on diabetic ulcers – surface wounds that resist rapid healing. Nanney says other Vanderbilt researchers will soon begin a clinical trial using fibroblast growth factor to heal deep, persistent bedsores that can require limb amputation if left untreated. And researchers at several centers are investigating the wound-healing effects of intramuscularly injected human growth factor. "We don't know in wounds what growth factors come into play and in which sequence," Brown says.

Researchers say studies of EGF for treating burned skin await further results of its effectiveness in wounds less infection-prone. Although the Food and Drug Administration so far has approved EGF only for experimental treatment of skin graft wounds, Nanney says she envisions the day when people can routinely obtain an EGF preparation "over the counter for skin wounded during a fall or from a scrape-of-the-knee injury." – *R. Cowen*

Athlete's oxygen just gas

An exhausted football player runs to the sidelines, puts a mask over his nose and mouth and gulps a few breaths of pure oxygen before returning to the field. But time out: This increasingly common practice, rooted in coaches' and athletes' belief that oxygen accelerates recovery from fatigue between bouts of intense aerobic activity, provides no real benefit, according to new research in the July 14 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

David Winter Jr. and his colleagues at Baylor University Medical Center in Dallas compared the effects of 100 percent oxygen versus room air on members of the Dallas Sidekicks, a professional indoor soccer team. The athletes performed a standardized exercise regimen to the point of exhaustion, then received one or the other gas for 4 minutes and resumed exercise. Researchers monitored blood lactate levels (an indication of muscle fatigue), heart rate and oxygen uptake and found no difference between the two groups. Winter doubts there's any harm in the practice, but he says players would do better walking along the sidelines than sitting on a bench sucking oxygen.

The practice may well continue in some sports, he adds, because players think it works – and because companies often provide the oxygen free in exchange for bench seats. □

Stiffened cells lodge in lung capillaries

When bacteria invade the body, white blood cells flock to the infection site, primed to engulf and kill. But getting there is only half the battle. Keeping these cells at the site long enough to conquer the infection is an essential part of the immune strategy.

Focusing on the lungs, researchers have discovered one reason why the body's most abundant white blood cells, called neutrophils, don't desert the battlefield. The finding, they say, might someday yield new ways to move neutrophils along in cases where the cells stay too long or fight too hard.

Too big to travel freely along the average lung capillary, neutrophils normally squeeze through like mice through a chink in a baseboard. When they reach an inflamed area, however, they slow to a standstill, staying where they're needed most. For decades, scientists have explained this ordinarily beneficial slowdown by noting that chemicals released during inflammation increase the cells' stickiness. Now they've added a new mechanism: cell stiffening.

Intrigued by basic research showing that when monoclonal antibodies prevent neutrophil stickiness, they still don't keep the cells from lodging in the lungs, G. Scott Worthen and his colleagues at Denver's National Jewish Center for Immunology and Respiratory Medicine, along with researchers at the Washington University School of Medicine in St. Louis, began looking for another explanation. Following up on a "farfetched" idea that mechanical properties of neutrophils might be important, they discovered that stiffening by itself can cause the cells to lodge in lung capillaries and in capillary-sized filter pores. The group reports its findings in the July 14 SCIENCE.

To stimulate neutrophils to stiffen, Worthen's team used a synthetic chemical with an action similar to certain blood-borne chemical mediators of inflammation. Neutrophils responded by internally assembling microfilaments and becoming stiff. Stimulated neutrophils lodged in the filters, while unstimulated ones squeezed through. When the researchers radioactively labeled the stimulated neutrophils and infused them into rabbits, they could see the cells had pooled in the lungs.

To separate the effects of stiffness and stickiness, the group blocked each effect chemically. Stimulated cells prevented from assembling microfilaments passed through filter pores and rabbits' lung capillaries, but cells prevented from getting sticky still lodged in the filters. "If we prevent the increase in stickiness with a monoclonal antibody," Worthen says, "we still get retention." In addition, the researchers measured cell stiffness directly with a "cell poker," gently denting neutrophils with a fine glass needle. Stiffness increased significantly with increasing chemical stimulation.

When capillary clogging follows severe injury, bacterial blood infections or massive burns, it can lead to adult respiratory distress syndrome – an untreatable and often fatal result of neutrophils run amok. Releasing potent chemicals of their own, the amassed neutrophils can damage lungs so severely that a patient cannot breathe. If researchers can find a chemical that modifies neutrophil stiffening without affecting stickiness or infection-fighting effects, Worthen says, they may be able to produce the first treatment for this syndrome. – *S. Hart*

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