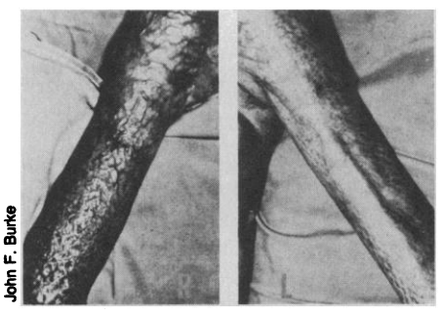
A New Treatment for Burn Victims

A polymeric synthetic skin has proved useful in limited trials on the severely burned; a newer version looks even better

When part of the body is damaged, says Ioannis V. Yannas of the Massachusetts Institute of Technology (MIT), "what we would like to do is use the patient as a bioreactor and provide that bioreactor with the catalytic device that will allow it to regrow what was lost." As he told the 28th Macromolecular Symposium of the International Union of Pure and Applied Chemistry*: "I think we have accomplished that for skin."

Yannas and John F. Burke of Massachusetts General Hospital have, in fact, devised two different forms of artificial skin. The first and simpler version, called stage I, is now being used on severe burn patients by Burke and his colleagues as quickly as Yannas and his graduate students can make it. The more advanced version, stage II, has proved very successful in animals and will be submitted to human trials soon.



John F. Burke

Conventional versus artificial

The left arm and shoulder of this patient received conventional skin grafts (left). The right received stage I skin (right).

An estimated 130,000 people are hospitalized in the United States each year because of burns, and some 10,000 of them die. The burned area must be covered quickly, both to inhibit infection and to prevent fluid loss. An autograft of the patient's own skin is a nearly ideal covering: an epidermal layer and part of the dermal layer can be removed from an unaffected area and placed over the wound. This creates two scars instead of one, however, and severely burned patients generally do not have enough unaffected skin to meet this need.

Homografts from cadavers can be used, but such skin is generally in short supply and there is a persistent problem with graft rejection. Heterografts of animal skin, typically from pigs, can also be used, but they must be removed between 3 and 9 days after application. "Our synthetic skin offers the best hope for saving most of these severely injured patients and for preventing disfigurement in those injured less severely," says Yannas.

The template Yannas has constructed is a highly porous polymer of collagen fibers (obtained from cowhide) covalently bound to chondroitin-6-sulfate, a major polysaccharide of cartilage, which they obtain from sharks. This polymer is covered with a sheet of medical-grade silicone rubber that serves as a barrier to infection and fluid loss and that provides mechanical strength when the graft is sutured into place.

After the graft is in place, mesodermal cells begin to migrate into it and to make more collagen, synthesizing a new dermal layer or "neodermis." Epidermal cells also begin to grow inward from the edge of the graft. The synthetic skin, meanwhile, is slowly biodegraded. After 20 days, the silicone layer is removed and epidermis from elsewhere on the patient's body is transplanted in its place. This procedure is much less traumatic than an autograft because no dermis is moved. New epidermis grows back over the source area in 7 to 10 days "rather like a sunburn healing." Eventually, patients are able to distinguish heat and cold and experience pain. The main difference between the new skin and the rest of the patient's skin is that it doesn't have hair follicles or sweat glands.

Burke and his colleagues have used the stage I skin successfully on 35 severely burned patients ranging in age from 3 to 85. "Several of these would probably have died without the artificial skin," says Yannas. "Burke is very pleased and his main complaint is that my students don't have time to make a lot more of the material."

Part of the reason they don't have more time is that they are working on a more advanced skin called stage II. The basic structure of the stage II material is the same as that of stage I. In this case, however, Yannas, Eugene M. Skrabut, and Dennis P. Orgill take a small graft of skin from the subject and isolate basal cells, the most immature skin-forming cells. The basal cells are then seeded into the polymer network by centrifugation. An autograft about the size of a quarter provides enough basal cells to cover an entire guinea pig, for example, so that scarring and trauma are minimal.

The seeded material is then sutured over the wound. "There is no culturing of the cells, as is the case with some other proposed skin substitutes, so there is no delay in covering the wound. The whole process takes less than 4 hours." Again, mesodermal cells form a neodermis, but the basal cells also proliferate to form a new epidermis. "By day 14 after the graft, the epidermis is confluent, which is very desirable clinically, and the silicone layer can be removed. By day 30, there is almost intact skin." Again, there are no hair follicles or sweat glands, but the wound shrinkage is less than 25 percent of the original wound area. "One of our major achievements is that we have separated the contraction process from the scarring process."

Yannas and Burke have so far used the stage II skin only on guinea pigs, and hope to begin trials on humans within the next year. Meanwhile, the MIT patent for stage I has been licensed to Marion Laboratories of Kansas City, Missouri. Marion is now working to find ways to make the polymer in larger quantities and to lay the groundwork for the further trials that will be necessary before stage I is approved by the Food and Drug Administration.

Yannas's material is unique, but it is not the only skin substitute under development. Abe Widra of the University of Illinois College of Medicine has developed a glycoprotein that protects the injury while providing a template for fibroblasts to attach to. It has not been tested in humans. Eugene Bell of MIT, Howard Green of the Harvard Medical School, and Magdalena Eisinger of the Memorial Sloan-Kettering Cancer Center have independently developed techniques to culture sheets of epidermal cells that can be applied to the wound. The culturing process can take several days, however. These materials have had very limited trials in humans. For the time being, Yannas and Burke appear to be well out in front in both the commercial race and the race to save patients' lives.—THOMAS H. MAUGH II

*Held at the University of Massachusetts, Amherst, 12 to 16 July 1982.

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