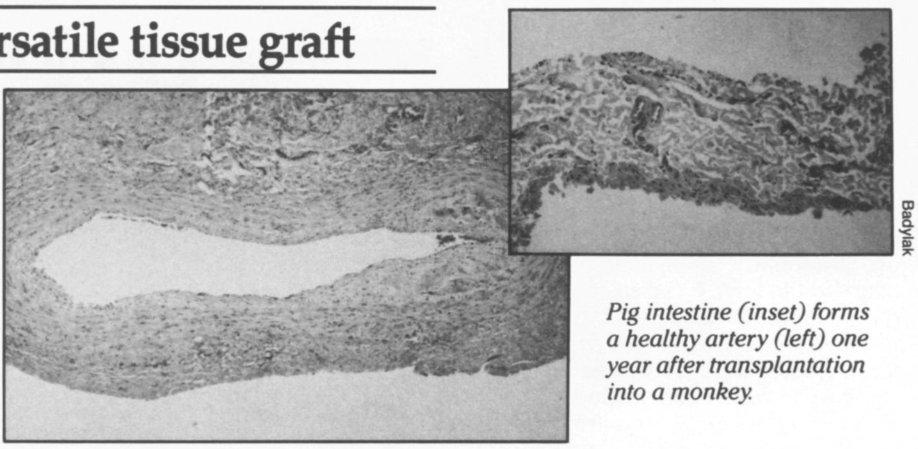
Pig intestine yields versatile tissue graft



Badylak

Pig intestine (inset) forms a healthy artery (left) one year after transplantation into a monkey.

First, there were chitlins. Then, butchers started packaging sausage in the strong but thin casing of pig intestine. Now, tissue engineers are fashioning the proverbial silk purse out of a sow's gut by using a diaphanous inner layer of pig intestine to make tissue grafts for replacing worn-out blood vessels, ligaments and bladders. Their aim: an off-the-shelf graft that can serve as spare parts for any patient, regardless of tissue type.

Veterinarian-physician Stephen F. Badylak and his colleagues at Purdue University in West Lafayette, Ind., have isolated a tissue film the thickness of two human hairs that they can transplant successfully into many other species, including dogs and monkeys. Badylak told a symposium on tissue engineering last week that his team has transplanted the material into more than 600 animals of various species without any signs of immune rejection. The session was part of the Keystone (Colo.) Symposia on Molecular and Cellular Biology.

The researchers call the material SIS, for small intestinal mucosa. Much like the film of jelly between two layers of a jellyroll cake, SIS lies between the outer, muscular intestinal surface and the layer of finger-like villi lining the intestine's inner wall. It consists mainly of collagen, the connective tissue that holds most organs together.

Badylak and his colleagues have a cheap and plentiful supply of SIS from their local slaughterhouse. "It's very similar to what they use for sausage casings," he says. After meticulously scraping off the inner and outer intestinal layers, the researchers place the resulting SIS in a bottle of antibiotic-laced saline solution and store it in a refrigerator, where it keeps for more than a month.

Because of SIS' ability to resist blood clots, the Purdue group first used it in dogs to replace the aorta, the largest artery in most animals. Remarkably, they found that the opaque-white material dissolved over two months and was replaced by the dogs' own blood vessel tissue, a phenomenon that tissue engineers call remodeling. Several of the dogs have lived four or five years since their transplants and have aortas indistinguishable from those of nongrafted dogs, Badylak says.

Following the success of the aorta transplants, Badylak's group tested SIS in dogs as a replacement for the vena cava, the largest vein in most animals' bodies. Unlike arteries, which carry high-pressure blood away from the heart, veins carry blood under lower pressure toward the heart and do not require a layer of smooth muscle to give them extra strength. The SIS vena cava graft adapted to form muscle-less vein tissue, Badylak's group discovered.

Encouraged by SIS' potential, Badylak's team then used the material to replace canine knee ligaments and Achilles tendons. Within weeks, the SIS became fully developed ligament and tendon tissue, they found. Moreover, a tunnel drilled in the dogs' leg bones to accommodate the knee ligaments closed around and fused with the new tissue.

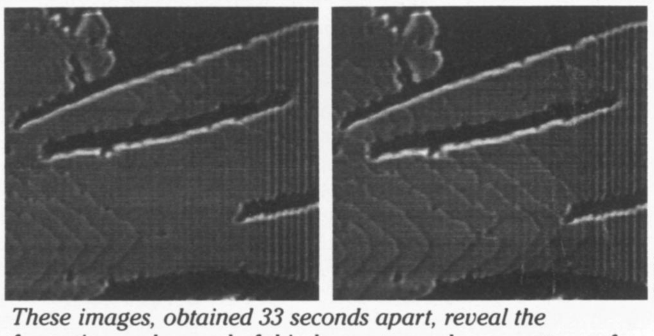
The group hopes to test SIS grafts in humans "within a couple of years," Badylak says. He predicts that orthopedic applications will come first, because of the lack of an adequate number of donor ligaments and tendons from humans. He and his co-workers recently began testing injections of minced SIS as a means to shore up the muscles of leaky bladders.

They also plan to see if SIS will promote wound healing when used as a skin graft. However, Badylak says, "I don't want to oversell this material ... we still don't know how it works."

Eugene Bell, a biologist at the Massachusetts Institute of Technology in Cambridge, calls SIS "extremely promising" as a universal tissue graft. "We are just beginning to probe the regenerative capacities of the human organism," he asserts. Synthetic materials have been "singularly ineffective" as tissue replacements, he says, because they do not serve as templates for the host to regenerate his or her own tissue and are sometimes subject to immune-system attack.

– C. Ezzell

Calcite on the edge of growth, dissolution



Hillner

These images, obtained 33 seconds apart, reveal the formation and spread of thin layers to produce a pattern of V-shaped steps (lower left) on a calcite surface. Each image represents an area 1 micron wide.

Whether incorporated into seashells or deposited as limestone, marble or chalk, the mineral calcite participates in a variety of biological and geologic processes. To help elucidate how calcite fulfills its varied roles, researchers have developed a new technique for observing hitherto hidden details of the way calcite crystallizes and dissolves.

Physics graduate student Paul E. Hillner of the University of California, Santa Barbara, geoscientist Andrew J. Gratz of the Lawrence Livermore (Calif.) National Laboratory and their co-workers use an atomic force microscope to observe the step-by-step addition or removal of calcium and carbonate ions at a calcite crystal surface. Although they can't detect individual atoms, they can clearly see the apparent movement of edges as ions settle into layers to produce characteristic patterns of steps.

These findings represent "extremely important first observations [by atomic force microscopy] of in situ crystal growth ... of a mineral," comments Richard J. Reeder of the State University of New York at Stony Brook, who has also studied calcite growth.

Hillner and his colleagues describe their work in the April GEOLOGY.

The researchers track changes in surface features during crystal growth by passing a concentrated solution of calcium carbonate dissolved in water across the surface of a calcite sample. By making the solution highly alkaline, they slow the deposition process sufficiently to allow time for repeatedly scanning the surface to detect any changes.

"Our growth rate is so small that it would take us years to grow a reasonably