Biomedicine

Islet-cell transplants *sans* rejection

Since 1973, researchers have attempted to cure insulin-dependent (Type I) diabetes by substituting healthy, insulin-secreting islet cells for nonfunctioning ones in the pancreas. But the body rejects these grafts within six months, even with the use of immunosuppressive drugs. A new study now suggests the key to successful islet-cell grafts may involve their implantation in the thymus.

Researchers at the University of Pennsylvania in Philadelphia found that the thymus — a gland that lies just above the heart and gives white blood cells the ability to attack foreign antigens — can be manipulated to remove or inactivate certain white blood cells, known as T-lymphocytes, that might otherwise destroy islet-cell grafts placed in the gland. They triggered this unusual thymus response in diabetic rats with the injection of antibodies programmed to eliminate the graft-destroying lymphocytes. When healthy islet cells were subsequently implanted into the thymus of those animals, blood sugar levels returned to normal within three days. The cells survived for more than 200 days. Further, test implants of islet cells in the kidneys of the same rats survived without rejection, even after removal of grafted islet cells from the thymus, reports Andrew M. Posselt, one of the study's authors.

Thymus implantation could establish islet-cell grafts as a key therapy for Type I diabetes, the researchers say, if human studies — which may not begin for several years — show similar success. However, Posselt cautions that he and his co-workers limited their work to rats whose diabetes had been induced by an islet-cell toxin. He hopes the new technique also proves useful in helping the thymus establish similar transplant tolerance in animals with naturally occurring Type I diabetes — in which the immune system is believed to kill the body's own islet cells, as well as foreign grafts.

Runner's HDL: Former fatties finish first

Among runners, "Tis better to have been fat and lost than never to have been fat at all," says Paul T. Williams of the University of California, Berkeley — at least when it comes to boosting blood levels of high-density lipoprotein (HDL) cholesterol, the so-called "good cholesterol."

He and his colleagues from Berkeley and Stanford University studied 33 middle-aged male joggers who ran at least 20 miles a week. Five who had been overweight, and who had lost the greatest number of pounds, exhibited the highest levels of HDL cholesterol, with an average of 83 milligrams per deciliter (mg/dl) — greatly exceeding the levels of runners who had started out lean. HDL levels found among the other runners averaged 61 mg/dl, a level that the researchers note is still well above the 45 mg/dl typical of adult U.S. men.

Williams notes that shedding pounds shrinks the size of fat cells, which boosts activity of lipoprotein lipase, an enzyme that clears fats from the bloodstream. He speculates that more rapid fat clearance leads to HDL accumulation, accounting for its heightened levels in formerly overweight joggers. Williams also observes that even men with the same weight may have different cholesterol levels, depending on their previous weight history.

Several factors other than weight loss — including increased muscle mass, weekly running mileage, current weight and calorie intake — did not correlate with HDL levels among the joggers, the researchers report in the recently released May INTERNATIONAL JOURNAL OF OBESITY. They plan a similar study with overweight women joggers.

Citing known health benefits of staying lean, Williams says he doesn't advocate putting on extra pounds before starting to jog. But he says these data do imply "some additional compensation for [overweight men] who become runners."

Earth Sciences

Underneath an early continent

The wind-scoured plains of northwest Canada above the Arctic circle present an image of primeval times. So it seems fitting that geologists have traveled there to probe eons back into Earth's history. After studying the ancient rocks preserved in this barren landscape, two scientists conclude that the lithosphere — Earth's hard, outer skin — underlying this region was far thinner 1.9 billion years ago than it is today.

Like a cracked eggshell, the lithosphere is broken into more than a dozen rigid plates that slowly rearrange their positions over the planet. The brittle lithosphere covers a hotter, more ductile mantle that can flow over geologic time. In the modern world, the thickness of the lithosphere measures about 100 kilometers under continents and up to 40 km under oceans.

To estimate the thickness of the ancient Canadian lithosphere, John Grotzinger and Leigh Royden of the Massachusetts Institute of Technology in Cambridge studied a basin created when two large continental blocks collided 1.9 billion years ago. In the crash, one block rode over the other. The thickness of the basin sediments revealed how much the lower block warped under the weight of the top one, allowing the researchers to calculate that the continental lithosphere in this region once measured less than half its present thickness. They report their findings in the Sept. 6 NATURE.

The lithosphere's shallow depth is important, say the researchers, because this indicates the ancient continent was sitting over hot mantle rock. Geophysicists believe that in the modern world, continents have thick "roots" of relatively *cold* mantle material extending down to a depth of 300 to 400 km (SN: 12/13/86, p.380). But Grotzinger and Royden believe no such mantle root existed 1.9 billion years ago under the ancient continental block they studied.

These findings bear on a hot debate among geophysicists concerning how and when mantle roots formed. Because there are rocks in South Africa indicating that region had a root as far back as 3.2 billion years ago, some scientists have suggested all roots formed during the earliest era of Earth's history. But Grotzinger says the new work suggests instead that roots continued to form during more recent periods.

When feet had seven toes

Paleontologists have discovered something unexpected at the end of a 360-million-year-old leg: two extra toes. Since the 1930s, scientists have believed that *Icthyostega,* one of the earliest known amphibians, crawled around on five-toed feet. But fossil finds from Greenland now indicate that *Icthyostega* had seven toes on each hind foot. What's more, fossils from *Acanthostega,* another primitive amphibian, reveal it had eight fingers on each forelimb, according a report in the Sept. 6 NATURE by Michael I. Coates and Jennifer A. Clack of the University of Cambridge in England.

These early amphibians lived at the end of the Devonian period — a time when vertebrates were first making the transition from water to land. In fact, the *Acanthostega* fossil is the most primitive known limb. Judging from their skeletons, these amphibians spent most of their time in the water, Coates says.

Paleontologists have traditionally held that all land vertebrates followed a five-digit or pentadactyl pattern. Though many vertebrates, such as horses, have fewer than five digits, they evolved from pentadactyl forms. The new fossil finds complement a previous discovery by Soviet scientists of another six-digited Devonian amphibian. Taken together, these fossils indicate that development in early land vertebrates followed a more flexible pattern. While some amphibians had seven-toed feet, other members of the same species might have sported feet with six or eight toes, Coates says.