Beta-cell break benefits diabetics

Patients with insulin-dependent diabetes mellitus (IDDM) gradually lose their ability to produce insulin, a hormone required for proper maintenance of blood sugar levels. But a two-week treatment with very large doses of insulin can delay for more than a year the demise of insulin-producing pancreatic beta cells in patients newly diagnosed with IDDM, researchers report.

Increasingly, scientists believe IDDM results from an immune reaction against some part of the insulin-making machinery in beta cells or against insulin itself. Indeed, treatment with immunosuppressive drugs has proved useful in delaying IDDM progression in some newly diagnosed diabetics (SN: 11/7/87, p.292). But the new research suggests the beneficial effects of this immunosuppressive therapy may result not from the drugs themselves but from the large doses of insulin routinely administered along with those drugs. Physicians typically give large amounts of insulin with immunosuppressive steroids because these drugs tend to raise blood sugar concentrations to dangerous levels.

Shirish C. Shah and his colleagues at the University of South Florida Health Sciences Center in Tampa treated two groups of newly diagnosed IDDM patients for one year. They kept 14 patients on conventional doses of insulin to hold blood sugar levels under control. But they hospitalized 12 other new patients and gave them insulin doses four times higher than normal for two weeks, before sending them home and putting them on conventional insulin therapy for the rest of the year. Tests showed that during the two-week period of high-dose insulin therapy, the hospitalized patients' beta cells got a "rest," producing only one-seventh the amount of insulin produced by the patients on normal insulin doses.

After one year, the experimental group's beta cells were producing almost twice as much insulin as those of the conventionally treated group. Reporting in the March 2 New England Journal of Medicine, the researchers attribute the difference to the rest period granted beta cells during the two weeks of megadose insulin therapy. They hypothesize that too much beta-cell activity early in the disease process somehow triggers or exacerbates the body's autoimmune reaction. By giving the cells a rest during that critical period, they say, a full-blown autoimmune reaction can be set back by as much as a year or more.

"We think it is insulin itself that is the antigen that causes the immune system to attack the beta cells," says Shah. "And when we give megadoses of insulin . . . you can produce tolerance in the body." Immune tolerance is a poorly understood mechanism by which the body, when exposed to large amounts of foreign material, comes to accept it rather than reject it.

Shah says unpublished follow-up studies with 12 other patients indicate the autoimmune process eventually comes back, necessitating repeat megadoses of insulin every six to 12 months. The treatment is not simple: While being treated with the abnormally high doses of the sugar-lowering hormone, patients must remain on an "artificial pancreas" to keep their blood sugar levels normal. However, Shah says, the results are striking. "We have one girl who has been treated three times now and she's beyond two years [since diagnosis] and she can make more insulin now than she was making three months after she was diagnosed." The girl is scheduled for a fourth treatment this summer, Shah says.

"Our ultimate goal is to try this treatment before they become insulin dependent," he adds, noting it's now possible to predict "with reasonable certainty" those who will develop diabetes. "If we treat prediabetic high-risk individuals and if we can stop the progression, then they may never have to take [daily] insulin. That's what we'd like to achieve."

Getting to the heart of the Chinese

Chinese men are more sensitive than Caucasian men to a widely prescribed heart drug, according to a new report. The finding underscores the importance of adjusting drug dosage to the individual patient, and it raises questions about the way companies test drugs.

Hong-Hao Zhou, Alastair J.J. Wood and their colleagues at Vanderbilt University in Nashville, Tenn., studied 10 men of Chinese descent who had lived in the United States an average of 1.6 years and compared them with 10 U.S.-born white males. The researchers gave the men a range of propranolol doses and then measured their heart rate and blood pressure. Propranolol, a beta-blocker drug, slows heart rhythm and reduces blood pressure.

To get the same heart-rate reduction, the Chinese men needed only half as much of propranolol in their blood as the Caucasians, the research team reports in the March 2 New England Journal of Medicine. To get the same blood pressure drop, Chinese men needed one-tenth the propanolol blood levels required by Caucasians.

Wood says the team started the study after hearing anecdotal reports that doctors in China prescribed less propranolol than their Western counterparts. Their results suggest the need for additional research to see whether racial differences in drug response are common. Many firms test products primarily on Caucasians, then market the drugs worldwide with no effort to identify ethnic differences, Wood notes.

"For the physician, the lesson of the Zhou study should be the importance of increased awareness of the possibility of differences in drug response and in dose requirements among patients from various ethnic and racial groups," writes Werner Kalow of the University of Toronto in an accompanying editorial.

Lollipop draws consumer group's ire

Public Citizen Health Research Group (HRG) wants the Food and Drug Administration to halt clinical trials of a grape-flavored lollipop laced with a powerful narcotic called fentanyl. HRG is a Washington-based consumer organization.

Anesta Corp. of Salt Lake City has tested the product as a presurgical sedative on more than 180 children. Doctors give the product to anxious children before surgery, says Brian Hague, Anesta's director of research and development and co-inventor of the bullet-shaped candy-narcotic on a stick. Hospitals now may give pediatric patients a fentanyl injection before an operation, a practice that unnecessarily frightens children, Hague says.

But HRG Director Sidney M. Wolfe contends the narcotic lollipop sends the wrong message to children. "A potent narcotic in a candy matrix clearly targeted at children is inappropriate," he says in a letter sent to FDA Commissioner Frank Young. Wolfe believes hospitals can calm children without drugs by using hypnosis or by letting parents stay with the children during preoperative anesthesia.

Wolfe also expresses concern about the product's potential for abuse. "Fentanyl, the active ingredient in the lollipops, is already a leading drug of abuse among health professionals and street users," he says. Anesta officials label that worry groundless, saying their product would be available only to anesthesiologists. In addition, it does not produce the "high" sought by drug users, Hague says. The product also leaves a telltale purple stain on the tongue as a deterrent to pilfering, Hague notes.

FDA officials are considering HRG's petition, but have not decided whether to allow clinical testing of the product to continue. FDA's Bill Grigg says the product has some merit, especially for children who need repeated painful procedures.