Diabetes as a smoldering disease

Antibodies directed against insulin-manufacturing cells of the pancreas can cause insulin-dependent diabetes, some studies have suggested. Moreover, the antibodies are present before diabetes actually occurs, European investigators recently reported. And now a progressive decline in pancreatic manufacture of insulin between the time of antibody appearance and the arrival of diabetes has been found by George S. Eisenbarth and colleagues at the Joslin Diabetes Center in Boston.

This result, they conclude in the Feb. 10 New England Journal of Medicine, further implicates pancreas-directed antibodies as a cause of insulin-dependent diabetes. It also suggests that the disease does not necessarily come on abruptly, as scientists used to think, but may first smolder for many years, and that, after further study, antibodies might be used to predict which persons will eventually succumb to insulin-dependent diabetes. In an accompanying editorial, Aldo A. Rossini of the University of Massachusetts Medical School in Worcester agrees with these conclusions.

Eisenbarth and his co-workers followed, for 17 years, the health status of two triplets and one twin who did not have insulin-dependent diabetes at the start of the study but whose identical triplet and identical twin, respectively, did. (They followed these particular subjects because genes as well as autoimmunity seem to be implicated in the disease.) One triplet was found to have pancreatic-reactive antibodies at the beginning of the investigation; he developed full-blown insulin-dependent diabetes eight years later—indicating that insulin manufacture by his pancreas had become so deficient that there was not enough to regulate the amount of sugar and fat breakdown in his bloodstream.

The twin was found to have pancreatic-reactive antibodies eight years after the study was underway; he came down with full-blown insulin-dependent diabetes five years after that. What's more, these two subjects had shown a progressive decline in pancreatic manufacture of insulin with a concomitant rise in blood sugar between the time of antibody appearance and the arrival of diabetes. The other triplet developed neither antibodies nor diabetes during the study.

These findings, Rossini points out, will probably encourage clinical investigators to use immunosuppressive therapy to treat insulin-dependent diabetes and perhaps even to try to prevent diabetes in healthy persons with pancreatic-reactive antibodies. Yet "this prospect," he contends, "raises a number of ethical and scientific issues." For instance, immunosuppressive therapy has already been used to treat patients with insulin-dependent diabetes, and it has produced no cures. (However, Rossini hopes that more extensive, aggressive immunosuppressive therapy than that used to date might eventually do so, because other researchers have found that immunosuppressive drugs prevented and reversed diabetes in rats.) What's more, such therapy can exert serious toxic side effects such as arrested growth, high blood pressure, cataracts and behavioral changes. It's even possible, he conjectures, that if a virus helps cause the disease, as some evidence suggests, immunosuppressive therapy might encourage rather than counter it.

Indications that pancreatic-reactive antibodies might be capable of conspiring with a virus to trigger diabetes can be found in the triplet whose diabetes developed eight years after antibody appearance. Although his insulin production generally slacked off gradually after the appearance of antibodies, once he came down with infectious mononucleosis, which is caused by a herpes virus, it plunged drastically. Five months later he was diabetic. —*J. A. Treichel*

Viking: Still no word from Mars

Hope faded a little more this week at Jet Propulsion Laboratory in Pasadena, Calif., as the Viking 1 landing craft on Mars failed once again to respond to engineers' efforts to end the baffling silence that has afflicted the spidery device for the last three months.

The lander, sole survivor of the four-spacecraft fleet that reached the planet in the summer of 1976, is programed to take pictures and monitor the weather automatically through 1994. After spending its first four years obediently following complex commands from the JPL control center, the craft's computer was instructed in 1980 to continue on its own, with JPL merely signaling it about once a week to transmit its findings. Last Nov. 19, however, Viking's messages stopped coming.

Trying to understand the problem has been a frustrating experience for the engineers. If the lander's transmissions were reaching earth totally garbled, at least there would be something to work with. But there has been nothing—not so much as an unmodulated carrier wave (a smooth signal carrying no data) even to reassure the engineers that the craft is still "alive." Instead, the skeleton Viking crew at JPL (aided by consultants from Martin-Marietta Corp. in Denver, where the lander was built) have been working blind—or deaf—with only their own powers of deduction to help them decide what radioed instructions might be able to end the silence.

The Nov. 19 "downlink," or message from the lander, was to have come just after the JPLers had "uplinked" a signal requesting it, and the uplink also included some commands for the lander to change its battery-charging procedures. The engineers soon concluded that those commands had apparently been sent in a way that caused them to garble or erase the vital data that the lander had been using to keep its movable antenna aimed toward earth. After figuring out the probable changes in the antenna's movements, the engineers tried several more times to get a message through, but no answering downlink was received (SN: 1/8/83, p. 20). On Jan. 11, an uplink was sent to restore the lander's computer memory (which had held the now-garbled antenna data) to its former condition, but still to no avail.

This showed that there must be more to the problem than just the antenna data, says George Gianopulos of JPL. The leading candidate was the possibility that the craft's batteries (which had been having trouble even before the downlinks stopped) had gotten weak enough to trip a built-in switch designed to save power by shutting off everything but the receiver. Everything — including the antenna-pointing motor and the all-controlling computer, which in turn was necessary to recharge the batteries. Fixing all this would require uplinking a much more elaborate set of commands, about 20 times as many as the standard Viking uplink system could handle, so the engineers devised a method of translating Viking commands for the more recently developed system used to communicate with such sophisticated craft as Voyager. On Feb. 1, the lander was asked to reactivate its computer and start recharging its batteries, and after four days of charging time, a second uplink ordered the power-saving switch to be reset and the antenna to be moved to its proper position. (The command sequences take only minutes, but the engineers sent each one for hours to improve the chances of getting through, so the second uplink was actually completed on Feb. 10, five days after it began.) The third uplink, sent on Feb. 11, was the acid test: the order for the lander to reply.

Silence.

On Wednesday, yet another uplink was sent, but it marked a radical departure from its predecessors: Ordering the lander to switch to its backup transmitter, in case it had actually been receiving all of JPL's commands but was unable to say so, it was the first formal acknowledgment of possibly malfunctioning parts, vastly multiplying the range of the engineers' potential worries.

Again, no response. More strategies and uplinks are planned, but they can't be carried on forever. "We're feeling lower around here," Gianopulos says.

—*J. Eberhart*