Diabetic Pregnancy Risk Starts Early

Diabetic women who become pregnant typically seek a doctor's advice during the first trimester. They are told to take care of themselves and to be especially careful to keep their blood sugar under control. Not only are they up to four times more likely than nondiabetic women to miscarry, but their babies face three times the normal risk of congenital defects.

A study in mice now suggests that, in some cases, such counseling may come too late. The research indicates that apoptosis—natural cell suicide—often goes awry in a diabetic mouse embryo and wipes out healthy cells. What's more, this damage can occur soon after fertilization, researchers report in the December NATURE MEDICINE.

If the findings translate to humans, those prenatal consultations should become preconception visits, says study coauthor Kelle H. Moley, a reproductive endocrinologist at Washington University in St. Louis.

Apoptosis is a necessary cellular housekeeping process. When cells are no longer needed, become infected, or have damaged DNA, the suicide process dismantles the nuclear material and parcels out DNA fragments to nearby cells for disposal.

Earlier research identified a protein called Bax as a key player in this cascade of events. In people with high blood sugar, such as those with diabetes who don't control their diet or who fail to take insulin, a surfeit of glucose boosts Bax production. Too much Bax induces some cells to kill themselves hastily. Moley and her colleagues suspected that high Bax concentrations might link diabetes to high rates of miscarriage and birth defects.

To find out, the researchers mated male mice with three sets of females: 15 nondiabetic mice, 18 diabetic mice not receiving insulin, and 14 diabetic mice given insulin injections just before and after fertilization.

The team extracted embryos from the female mice 48 to 96 hours after fertilization and found that Bax concentrations in the embryos from insulin-treated females weren't markedly different from those taken from healthy females. However, embryos from the untreated diabetic mice—exposed to an abundance of glucose in the mother's blood—had Bax concentrations nearly eight times as high, Moley says.

To directly assess DNA damage, the researchers used three more sets of pregnant mice. DNA fragmentation in the embryos of untreated diabetic mice was more than six times as prevalent as in embryos of the healthy control mice and nine times as high as in embryos from insulin-treated diabetic mice.

Significant cell death in the embryonic stage may abort a pregnancy—resulting in a miscarriage—while less damage may cause deformities, Moley suggests. The birth defects arising from pregnancies in diabetic women include heart damage, limb deformities, and neural tube defects leading to brain damage.

The new study "is interesting," says David R. Hadden, an endocrinologist at Royal Victoria Hospital in Belfast, Northern Ireland. "They are making a very reasonable case, a good case."

Still, the apoptosis explanation doesn't explain why some diabetic women with high blood sugar go on to have healthy babies, he says. Also, other research indicates that high glucose concentrations later in pregnancy seem to have deleterious effects, he adds.

Fifty years ago in Europe, roughly one in three diabetic pregnancies "ended in disaster of some form," Hadden says. Today, that risk has fallen, indicating that prenatal glucose monitoring reduces the number of developmental problems. Still, 1 in 15 pregnancies in diabetic women results in some type of congenital defect as compared with 1 in 40 among other women.

Since research on human embryos is rare, monkey tests could be the next phase of study. "I think that would really nail down whether [the Bax findings] are a reflection of a human . . . phenomenon," Moley says. —*N. Seppa*

Poor winter homes delay bird nesting

A migratory bird that gets stuck with second-rate winter accomodations will achieve only lackluster breeding success the next summer, hundreds or even thousands of miles away, a new study suggests.

"Making that link before has been impossible to do," says Peter P. Marra of the Smithsonian Migratory Bird Center in Washington, D.C. He and his colleagues established the connection by using a technique that's novel among ornithologists: deducing where a bird has been by the carbon isotopes in its tissue. Isotopes are forms of atoms with different numbers of neutrons.

In the Dec. 4 SCIENCE, the researchers report that American redstarts that reach their New Hampshire summer breeding ground early—a big factor in nesting success—have isotope ratios typical of moist, food-rich winter habitats. Birds that arrive late, however, show ratios typical of poor, dry habitats.

"Things we're seeing in the breeding grounds are caused by events the previous winter," Marra explains.

Monitoring redstarts wintering in Jamaica, the researchers found that dominant males and the tougher females claim forest territories with abundant insects for food. An underclass of smaller, weaker redstarts gets pushed into scrub, which has fewer insects.

The researchers found that birds in prime winter territories increased or maintained their weight, but the birds in the slums lost up to 11 percent of their body mass. Come spring, redstarts in the poor habitat took longer to pack on fat for the flight north, leaving some 10 days later than birds in the forest.

Marra

A female redstart from poor habitat may be late to her breeding grounds.

The researchers could not track those particular birds north—a problem with many such studies. So Marra and his colleagues observed redstarts summering in central New Hampshire. Late-arriving males tended to be high in carbon-13, like the birds in the inferior winter habitats. There, birds ate insects that feed on dry-region plants, which typically build up extra C-13.

Trevor D. Price of the University of California, San Diego welcomes the report as the first evidence tying bad winters and bad summers in a way he and other researchers had suspected. "We've finally got some facts," he says.

Scott K. Robinson of the University of Illinois at Urbana-Champaign points out that the study "certainly indicates there isn't enough good habitat" for wintering redstarts. He predicts the results will bolster claims that problems in the tropics contribute strongly to declines of migratory birds. Some scientists still think breeding-ground problems are more important. However, Robinson says, "I think the jury is still out." —*S. Milius*