Spina bifida: Paralyzing fluid in the womb?

Amniotic fluid would seem a safe haven for the developing fetus. But scientists report evidence that within this fluid may float substances that, while safe for the skin, sabotage the spinal cord. If verified, the new findings could explain the paralysis and bladder dysfunction associated with the most serious form of spina bifida, the researchers say.

No current treatment can reverse the damage suffered by those born with myelomeningocele, the most common birth defect in North America and the most severe form of spina bifida. In this congenital neural-tube defect, some as-yet-unidentified initial assault causes abnormal development of the spinal cord and the overlying bone and skin, leaving the cord in an exterior position and exposed to the amniotic fluid, explains Dan S. Heffez, a pediatric neurosurgeon at Johns Hopkins University School of Medicine in Baltimore. It is this secondary exposure to the amniotic fluid that causes much of the spinal cord injury borne by human infants with myelomeningocele, the new research suggests.

Heffez and co-worker John Aryanpur removed and operated on about 50 fetuses from 20 pregnant rats, removing the bone and skin over the cord. In half the fetal rats – their control group – they closed the skin. All fetuses were replaced in the mothers' wombs. At birth, all of the 14 live-born experimental rats had paralyzed hind limbs and deformed spines, but none of the six live-born control pups with healed wounds displayed these abnormalities, Heffez reported last week at the Johns Hopkins Centennial Science Writers Seminar.

Using a light microscope, the researchers found extensive tissue damage at the surface of the spinal cords of the open-wound rats, while the spinal cords of the closed-wound controls appeared normal. The pathology looks "extremely similar" to that of human children with myelomeningocele, Heffez says. In addition, the microscope revealed scarred and distended kidneys in eight of 14 experimental rat pups. Heffez says this is exactly what would be expected in human infants with myelomeningocele, whose malfunctioning bladders cause urine to back up, harming the kidney, Heffez says.

While the new results are compelling, not all experiments support Heffez's "two hit" theory for the cause of myelomeningocele. Neurosurgeon David G. McLone of Children's Memorial Hospital in Chicago says his mice with genetic myelomeningocele do not show any destruction of nervous tissue, adding that he is unaware of the evidence Heffez cites of such nerve damage in humans.

The Hopkins scientists are trying to see whether they can prevent the damage by surgically intervening in a second procedure to cover the exposed spinal cord after one day's exposure to amniotic fluid. So far, they have successfully closed the wounds of two such rats, which appeared normal at birth. Two control pups, whose wounds were not closed, showed severe neurological deficits, Heffez says.

"If [the Hopkins researchers] are right, then it's an important finding because it indicates that [myelomeningocele] is a progressive disease [and so] we should be doing something to interrupt [its progression] while the fetus is still in the uterus," McLone says. What will turn out to be the best "interruption" remains unclear. To minimize or prevent spina bifida's symptoms, Heffez suggests, physicians may someday modify human amniotic fluid, induce premature delivery – if problems associated with premature birth can be overcome – or even perform fetal surgery. *– I. Wickelgren*

Chlorination: Residues cloud water safety

Roughly 200 million U.S. residents drink water disinfected with chlorine. Decades of research have demonstrated chlorination's benefits in limiting outbreaks of typhoid fever and other acute diseases from microbial contaminants. However, four groups of federal researchers report that these benefits may come at the expense of a small added risk of chronic disease – most likely heart disease or cancer.

Each team stresses that the disinfecting benefits of chlorination still appear to far outweigh any potential side effects. But validation of their preliminary findings could prompt calls for stricter limits on soil runoff and industrial releases of chlorinated pollutants into water, says Ellen K. Silbergeld of the Environmental Defense Fund in Washington, D.C.

In 1985, a study of Wisconsin farmers by Elaine Zeighami and her co-workers at Oak Ridge (Tenn.) National Laboratory suggested that "hard" water, characterized by high levels of calcium and magnesium, reduces mortality from heart attacks and stroke. Reasoning that hard water's minerals might affect blood pressure or how the body uses lipids – primarily cholesterol and the lipoproteins that shuttle it around the body – Zeighami recently returned to survey blood factors in 1,520 residents of 46 Wisconsin towns.

The only correlation she found was between water chlorination and serum cholesterol, especially in women. After adjusting for age and other possible confounding factors, Zeighami found mean cholesterol levels about 4 percent higher (248 milligrams per deciliter) in women who drank municipally chlorinated water than in women drinking unchlorinated well water. As a rule of thumb, cardiovascular researchers estimate that each 1 percent increase in serum cholesterol elevates heart attack risk by roughly 2 percent.

In men from homes with chlorinated tapwater, Zeighami observed a statistically significant 1 percent cholesterol increase, to 236 mg/dl. In women and men, chlorinated drinking water was also linked to comparable increases in low-density lipoproteins – the so-called "bad" lipoproteins that carry cholesterol into the bloodstream – but without any changes in the "good" high-density lipoproteins that remove cholesterol from blood. Zeighami reported her findings in Cincinnati this week at a conference sponsored by the University of Missouri System.

At the same meeting, J. Peter Bercz and his colleagues at EPA's Health Effects Research Lab (HERL) in Cincinnati described similar small "abnormalities" in the lipid metabolism of mice drinking highly chlorinated water (15 parts per million) and eating diets with a fat content comparable to that in most Americans' diets. With dietary fat factored out, their lipids – "subtly but noticeably shifted from the high-density to the low-density lipoproteins" – offer the first "unimpeachable" evidence that chlorinated drinking water can change the way the vertebrate body handles cholesterol and lipids, Bercz told SCIENCE NEWS.

Two other HERL teams report data on mutagens that form in drinking water when chlorine interacts with humic material – soil products formed by plant decay. One of these is a chlorinated furanone known as MX. Trace quantities of MX have shown up in every chlorinated drinking water source where researchers have looked for it, and it appears to be the single largest contributor of mutagenic activity in those waters as measured by the Ames bacterial assay, according to EPA chemist H. Paul Ringhand. Scientists use mutagenicity – the ability to cause genetic mutation – as a rough gauge of potential carcinogenicity.

DCA, another mutagen found in chlorinated water, is known to cause liver cancers. F. Bernard Daniel and his coworkers report new data showing that DCA is a peroxisome proliferator. Such chemicals, often capable of exerting powerful effects on cholesterol metabolism, have been shown to trigger uncommon liver cancers (SN: 2/25/89, p.119). HERL researchers are now trying to determine whether the trace levels of DCA and MX in chlorinated water pose human hazards. *– J. Raloff*