THMs: A sobering drinking problem

Scientists long have eyed with suspicion the common use of chlorine to kill bacteria in public drinking water. Since 1974, researchers have believed that chlorine reacts with natural substances in drinking water to form compounds called trihalomethanes (THM's)—one of which, chloroform, causes cancer in laboratory animals. Now, evidence from studies under review by members of the U.S. Council on Environmental Quality seems to establish a firm link between heavily chlorinated water and human cancer.

The studies are case-control analyses of thousands of cancer deaths in North Carolina, Illinois, Wisconsin and Louisiana, says CEQ member Robert Harris. Persons who had died of lower gastrointestinal cancer were matched in age, sex and other variables with individuals who had died of other causes. When researchers traced the sources of drinking water for persons in both the cancer and control groups, they discovered that a significantly higher proportion of cancer victims had drunk from chlorinated water supplies. Harris says these studies strongly support EPA's attempt to regulate the level of THM's in public drinking water.

The EPA regulation, promulgated in November of 1979, establishes a maximum contaminant level (MCL) of 0.10 milligrams per liter of water, or 100 parts per billion, for total THM's. The first stage of this regulation, to begin this month, calls for monitoring community water systems serving 75,000 or more persons for THM's content. Monitoring of community water systems serving 10,000 to 75,000 persons must begin within two years, and, if all goes as planned by the EPA, the MCL will go into effect within three years in all communities with more than 10,000 persons.

But the American Water Works Association—a nonprofit group with membership open to "anyone with an interest in water supply"—is challenging EPA's plan. AWWA representatives have asked the D.C. Circuit Court of Appeals to review what it terms "serious scientific, technical and procedural issues arising from EPA's development and promulgation of the regulation." Harris says AWWA is "far behind in its understanding of water supply and public health effects." Both sides have filed briefs in the lawsuit.

Meanwhile, researchers are investigating ways to lower the level of THM's in drinking water. One method is to use activated carbon filters before adding chlorine to remove the organic materials that react with the disinfectant. Another method is to use disinfectants that will not cause the formation of THM's — chlorine dioxide, ozone, chloramines and bromine chloride, for example.

Chlorine dioxide, which has been commonly used as a water disinfectant in Europe for about 25 years, now is being tested for use in U.S. drinking water supplies. Researchers, however, are concerned with the health effects of chronic chlorine dioxide ingestion: The oral intake of this disinfectant by laboratory animals has been associated with certain blood abnormalities. But preliminary results of studies conducted on humans appear to be more encouraging. Joseph R. Bianchine of Ohio State University in Columbus reported at the recent meeting of the American Society for Pharmacology and Experimental Therapeutics in Rochester, Minn., that chlorine dioxide in amounts commonly used for water disinfection appeared to be safe in both short- and long-term (12 week period) studies involving human volunteers. Still, says Bianchine, the effects on the general population of drinking water containing chlorine dioxide for more than 12 weeks have yet to be considered. □

More mammoth meat

Despite the chilly relationship between the United States and Soviet Union on many fronts, cooperation continues in the mammoth arena. Morris Goodman of Wayne State University, who has analyzed tiny samples of the baby mammoth called Dima (SN: 5/10/80, p. 301), will receive from Soviet scientists 25 grams more of frozen tissue from that mammoth and 2 kilograms of air-dried material from less well-preserved mammoths discovered more recently in Siberia. Goodman says this is the first time his laboratory will have enough material to make "a decent search" for mammoth DNA. Goodman believes that increased activity in northern Siberia and increased interest in mammoth investigation make it likely that more and better-preserved mammoths will become available in the future. □

Geneticist leaves post

The researcher who jumped forward in genetic engineering by performing the first known gene-splicing experiments on humans has stepped down as chief of the division of hematology and oncology at the University of California at Los Angeles. At the request of the chairman of the department of medicine at UCLA, Martin J. Cline gave up his position as division chief until the controversy surrounding his experiments is resolved (SN: 10/18/80, p. 245). He maintains his faculty position. In July, Cline tried in Israel and in Italy to introduce healthy genes into the defective blood-forming cells of two women with beta-thalessemia. Later that same month, a UCLA committee denied him permission to perform similar experiments on campus until further animal tests had been conducted. □

Brain cancer deaths possibly job-linked

Calling them the "largest single series of presumably occupationally related brain cancers" in medical history, federal health investigators reported last week that 18 brain cancer deaths among workers at a Union Carbide petrochemical plant in Texas City, Tex., apparently were job-related.

The report, presented at a New York Academy of Sciences meeting on brain tumors and the chemical industry, is part of a continuing two-year study initiated by Union Carbide and carried out by scientists at the Occupational Health and Safety Administration and the National Institute of Occupational Safety and Health. The researchers did not elaborate on actual causes of the cancers, but noted that the deaths, which occurred between 1956 and 1980, were four to five times as many as those expected for the Texas county. A spokeswoman for Union Carbide said, however, "We have no reason to believe there is any correlation between these tumors and occupational exposures. ... Nor does the report make any specific connection" between jobs and the disease, pointing out that the workers had different jobs in separate parts of the plant. □

Enkephalins: Link to brain disease?

During the past decade a group of brain proteins, loosely dubbed the endorphins, have been found to produce an astonishing variety of both positive and negative psychological-behavioral effects in humans and animals. The effects range from pleasure, improved concentration and symptomatic relief from mental retardation, depression, schizophrenia, senility and pain to violence, irritability and migraine headaches (SN: 9/2/78, p. 164; 11/25/78, p. 364). And now two of the endorphins (the enkephalins) may produce still another psychological-behavioral effect—human brain disease—according to a report in the Oct. 16 NEW ENGLAND JOURNAL OF MEDICINE by Niels Jacob Brandt of the University of Copenhagen and his colleagues. "Such a profound role for the enkephalins in regulating brain function has never before been proposed," says Solomon H. Snyder of Johns Hopkins School of Medicine in Baltimore and a leading brain protein-opiate researcher in an accompanying editorial.

The report of Brandt and his colleagues is based on only one case history, but it is an unusual one—a child who apparently was normal until eight months of age when he started having attacks characterized by drowsiness, lethargy, perspiration, loss of muscle coordination, drooping eyelids,

unconsciousness and lack of breathing. The child became increasingly clumsy, suffered mental deterioration and died before his second birthday.

While the child was alive, Brandt and colleagues worked hard to diagnose the disease and to treat it. What struck them most was that the symptoms mimicked those of acute morphine poisoning. Thus they suggested that the disease might be caused, at least in part, by an excess of enkephalins — the two endorphins that seem to be the brain's own natural morphine or pain-killing molecules. The researchers took samples of spinal fluid from the child and found an excess of endorphins (most likely enkephalins) — about 100 times greater than that found in healthy children of the same age. Then the researchers gave the child naloxone, which is known to counter the effects of both morphine and the enkephalins, in hopes that it would help. The first three times the naloxone had no effect; the fourth time it did. Within several minutes after naloxone injection, the child emerged from his coma and embraced his mother. Unfortunately, further naloxone injections didn't help. Nonetheless, the fact that naloxone had produced at least some improvement in the child is further evidence that an excess of enkephalins could in some way be involved in the disease. Another sign that this might be the case was the child's unusual resistance to pain.

After death, autopsy provided still more evidence linking the disease with an excess of enkephalins. Tissue from the child's cortical and subcortical brain areas was found to contain enkephalin levels 100 or more times greater than those of control children. In contrast, levels of beta-endorphin (another endorphin) were barely detectable in the victim's cortical and subcortical brain areas and did not differ in levels from those of control children. Thus, excessive enkephalin levels probably caused, or at least contributed to, the child's disease, Brandt and colleagues conclude. And in his editorial, Snyder agrees: "Presumably, the patient's gross brain-stem degeneration had elicited clinical manifestations, including coma, through release of excess enkephalin. Such a profound role for the enkephalins in regulating brain function has never before been proposed. The extraordinary changes in brain levels of enkephalin, however, would fit such dramatic conclusions."

Snyder points out, though, that weaknesses in the study techniques Brandt and his colleagues used might have erroneously led to the above results. And Brandt and his colleagues admit that they are not sure if excessive enkephalin levels were the initial cause of the child's disease or a secondary one, because the child's brain gave evidence not only of elevated enkephalin levels but of a genetic disease called Leigh's syndrome. □

Alligator rhythm without a pineal

Alligators move out of the water in the morning and back into the water at night. They breed in the spring and become less active in the fall. Such daily and seasonal rhythms are sustained even though alligators have no pineal gland, the organ generally thought to regulate temperature, activity and reproductive rhythms through its cyclical production of the hormone melatonin (SN: 10/11/80, p. 229).

Experiments with alligators are difficult because their large size makes them hard to manage, says Jan J. Roth of the National Institute of Mental Health. He and colleagues, however, succeeded in sampling the blood every three hours of five alligators at the St. Augustine (Fla.) Alligator Farm. They found a constant low level of melatonin, similar to that of animals whose pineal glands have been surgically removed. This melatonin may come from a gland in the corner of the eye, the retina or intestinal cells. But Roth says it probably does not regulate the daily cycles of alligator life.

Alligators are the modern representatives of the subclass of reptiles to which dinosaurs belong, and fossil skulls indicate that most dinosaurs, like alligators, had no pineal gland. Roth and colleagues suggest in the Oct. 31 SCIENCE that the dinosaurs evolved during a period of less dramatic seasonal change. In a continually warm climate, less precise timing of daily and seasonal activities may be sufficient, Roth explains. But with the glaciers of the Ice Age, animals again needed to be keenly sensitive to differences in seasonal conditions, and only a few animals lacking pineal glands survived to modern times. Today alligators inhabit only warm climates, as do anteaters, armadillos, sloths and manatees, the other extant animals lacking pineal glands. □

The effects of stress at the cellular level

Stress during pregnancy can affect one's offspring, some animal studies and clinical observations have suggested. Among the possible results are cleft palate, harelip, aberrant sexual behavior, irritability, hyperactivity and feeding problems. Now stress during gestation has been found to exert an even more serious effect, according to a study reported in the Oct. 31 SCIENCE by G. Miller Jonakait, Martha C. Bohn and Ira B. Black of Cornell University Medical College in New York City. Their work with rats suggests that stress can alter the way embryonic nerve cells express their genetic potential. "That is a change at a very fundamental level," Black told SCIENCE NEWS.

Jonakait and her colleagues stressed pregnant rats pharmacologically with reserpine, an antipsychotic drug that, when given to pregnant animals in the past, has resulted in neurological or behavioral abnormalities in their offspring. But this time the researchers were attempting to see what effect reserpine had, if any, on a select population of developing central nerves in fetal rats. They found that reserpine extends the period during which the cells normally express the neurotransmitter noradrenaline. Thus reserpine was found to be capable of altering the phenotypic expression of developing embryonic cells (that is, of altering the expression of their genetic potential). Presumably stressors besides reserpine could produce still other effects of this nature, the researchers believe. For this reason, along with the connection already made between prenatal stress and birth defects, they counsel pregnant women to avoid stress as much as possible during pregnancy.

The researchers next attempted to determine how reserpine exerted its effect on embryonic nerve expression. Because reserpine is known to increase blood levels of glucocorticoids, they suspected that these adrenal steroid hormones might be a link between reserpine and the alteration of embryonic nerve expression. They found that this was the case. For instance, when they implanted glucocorticoids in pregnant rats, the hormones produced the same effect on the developing nerves as did reserpine: The nerves expressed noradrenaline beyond their usual time. And when a glucocorticoid inhibitor was injected into pregnant rats, reserpine did not extend the production of noradrenaline in the embryonic nerve cells. This is "the first time that maternal glucocorticoids have been found to directly affect phenotypic expression of neurons in the fetus," Jonakait explains. Still other maternal hormones besides the glucocorticoids may mediate other stressful effects on fetal nerve expression, she, Bohn and Black contend. In other words, they may have just uncovered the tip of an iceberg as far as the ability of stress to alter embryo phenotypic expression goes and as far as the intermediary role that hormones may play in such alterations is concerned. □