tors failed to demonstrate that what they saw was not just a spontaneous variation in heart rhythms.

Freis and his associates recently did obtain such 24-hour electrocardiograms in patients who had arrhythmias and who were taking diuretics. These researchers then gave the patients potassium supplements and again took 24-hour continuous electrocardiograms. They saw no significant effect of the potassium on the arrhythmias.

Since the evidence that dangerous potassium deficiencies result from diuretic therapy is so inconclusive and since it is quite possible that potassium supplements themselves may be hazardous to some patients, Kassirer says, "I think the treatment with potassium supplements may be just as bad as or even worse than potassium deficiency."

Although the MRFIT analysts say they have no proof of potassium deficiencies in the trial participants, they suspect drug toxicity in the hypertensive men taking diuretics because those men did not reduce their death rate from heart disease as expected. Potassium deficiency, they believe, is a starting place to look for toxicities. But Freis points out that blood pressure lowering has not been shown to lower the risk of death from heart disease in patients with mild hypertension—like the MRFIT men. Those studies purporting to show a lower heart disease death rate were, he says, of "questionable design."

Another explanation of the MRFIT results, and one that has not yet been rejected by the study analysts, is that the high death rate among the subgroup of hypertensives is a statistical quirk. The trials are designed to be analyzed as a whole, not to be carved up into small subpopulations. Frequently, when analysts look at such subgroups, they find that some, by chance, do worse than expected and others, by chance, do better.

What concerns Freis and the New England Medical Center researchers is that with the publicity over the MRFIT results, the dogmas that potassium supplements are necessary and that treatment of even mild hypertension prevents heart attacks will become more firmly entrenched. As a result, patients may needlessly take potassium supplements and patients whose hypertension is too mild to justify the risks of treatment may start on a lifetime of taking antihypertension drugs.—GINA KOLATA

Additional Reading

1. "Our national obsession with potassium," J. T. Harrington, J. M. Isner, J. P. Kassirer, *Am. J. Med.* **73**, 155 (1982).
2. "Should mild hypertension be treated?," E. D. Freis, *N. Engl. J. Med.* **307** (No. 5), 306 (1982).

Predicting Susceptibility to Epileptic Seizures

An increased concentration of the enzyme β-glucuronidase in the blood is associated with susceptibility to grand mal epileptic seizures, according to a report by Ranbir Varma and Rajendra Varma of Warren State Hospital in Warren, Pennsylvania, at the recent American Chemical Society (ACS) meeting.* It is not clear whether high concentrations of the enzyme are a secondary effect or help cause the seizures, but the observation could provide a new way to monitor therapy of epileptics.

Using blood samples obtained for other purposes, the Varmas measured β-glucuronidase levels in 30 patients who had a history of epilepsy and in whom grand mal seizures were observed by the hospital staff. The samples were obtained as much as 5 weeks before a seizure and as long as 9 weeks after. The samples showed enzyme concentrations of 182 to 400 units per 10 milliliters of serum, compared to 56 to 146 units in healthy individuals. Enzyme levels were not increased in medicated epileptics who had not had a seizure within the prior year or in patients with other types of mental disorders. Enzyme concentrations were also elevated in patients with retinal degradation associated with diabetes, with liver injuries, and with cancer, but those conditions were readily distinguishable. The observations were independent of age or sex.

β-Glucuronidase degrades glycosaminoglycans, which are polyanionic mucopolysaccharides that form part of the structure of neurons (nerve cells). They bind positively charged biogenic amines and cationic electrolytes that are important in the electrical discharge or firing of neurons. Previous studies by several investigators have shown that an abnormal excretion of glycosaminoglycans in urine from epileptic patients and that application of β-glucuronidase directly to the surface of the brain induces an excess firing of neurons that mimics an epileptic seizure. The concentration of glycosaminoglycans in the blood of the Varmas's subjects was, however, found to be normal.

*184th National Meeting, 12 to 17 September, Kansas City, Missouri.

Potential New Drugs for Duodenal Ulcers

A potential new approach to the therapy of duodenal ulcers was described by Sandor Szabo of Harvard Medical School. Szabo and John L. Neumeyer of Northeastern University have found that dopamine agonists (chemicals that compete for the same binding sites as dopamine and thereby stimulate its activity) can both retard the formation of duodenal ulcers in rats and speed their healing. Duodenal ulcers are four to ten times more common than gastric ulcers; Szabo estimates that 8 to 10 percent of the population will develop ulcers at least once in their lives.

Szabo and Neumeyer's results stem from the search for chemicals that will induce duodenal ulcers in laboratory animals. In the early 1970's, Szabo and Hans Selye of the University of Montreal found that propionitrile and cysteamine specifically induce duodenal ulcers in rats. Further study showed that the ulcerogenic activity of these and subsequently discovered chemicals derives from a two-carbon (ethyl) group bearing methyl, cyano, sulfhydryl, or amino moieties on one or both ends of the carbon chain. Such groups are a common feature of histamine, gastrin, ibuprofen, aspirin, indomethacin, and phenylbutazone, all of which are known to stimulate excess acid secretion or to exert other undesired gastrointestinal effects. Such a group is also present in dopamine.

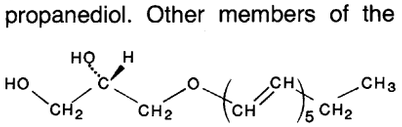
It has previously been observed that patients with untreated Parkinson's disease, which is associated with excess production of dopamine, have a high rate of ulcer disease, while schizophrenics (who may have an excess of L-dopa) are virtually immune to the disease. The Boston investigators thus studied several dopamine agonists, including bromocriptine, lergotrile, L-dopa, and apomorphine and its derivatives, and found that the best of these were about 10 to 20 times more potent than ergot alkaloids in preventing chemically induced duodenal ulcers in rats; these same compounds were about 200 times more potent than cimetidine, the most widely used therapeutic agent for ulcers.

0036-8075/82/1022-0362$01.00/0

In contrast, dopamine antagonists such as haloperidol and pimozide aggravated the formation of ulcers. The agonists also significantly speeded the healing of established ulcers. Szabo says that "several of these compounds are now close to the clinical stage of testing," but he concedes that it may be necessary to find agonists that don't affect other dopamine systems before the approach can be really effective.

Potent Mutagen from Human Feces Identified

A potent mutagen that may be associated with colon cancer in humans has been isolated and characterized by a team from Virginia Polytechnic Institute and State University. David G. I. Kingston reported at the ACS meeting that the unusual compound, isolated from human feces, is (*S*)-3-(1,3,5,7 - dodecapentaenyloxy) - 1,2 - propanediol. Other members of the



team were Tracey D. Wilkins, Roger L. Van Tassell, and Nobuhiro Hirai.

The presence of a mutagen in human feces was first noted in 1977 by W. Robert Bruce of the Ludwig Institute for Cancer Research in Toronto. The mutagen is produced by at least five species of intestinal bacteria from an as yet unknown precursor. Its mutagenic strength in the Ames assay, Kingston says, is comparable to that of several of the most potent known carcinogens.

The evidence associating the mutagen with colon cancer is still tenuous, but is highly suggestive. About 3 percent of North Americans develop colon cancer, Kingston says, and about 3 percent of individuals that the group has tested have high levels of the mutagen in their feces. High levels of bile acids in the intestines have been associated with colon cancer, and the Virginia group has shown that incubation with bile acids increases bacterial production of the mutagen. Similarly, high levels of fiber in the diet are thought to decrease the risk of colon cancer, and the group has found that fiber decreases production of the mutagen.

Wilkins and colleagues in South Africa have shown that levels of the mutagen are significantly higher in a population (of white South Africans) which has a high risk of colon cancer than they are in another population (of black South Africans) which has a low risk. The only potentially discordant evidence, so far, is the observation that individuals with polyps in their colons—who have been shown to have an above-normal risk of colon cancer—do not have high levels of the mutagen. The group is now attempting to synthesize the unstable compound to have enough for further studies.

A New Type of Rechargeable Battery

A new type of rechargeable battery with an unusually long service life was announced at the ACS meeting by Rodney F. Moody and Glenn R. Schaer of the Battelle Columbus Laboratories. The new battery, which has so far been produced only in laboratory versions, weighs less and produces more energy per weight of lead than conventional lead-acid batteries.

The new battery uses lead dioxide and copper electrodes immersed in an electrolyte of fluoboric, perchloric, or fluosilicic acids and the metal salts of the acids. A battery is fabricated by immersing an inert electrode core into the electrolyte and applying a potential. Lead dioxide plates out on the positive electrode, while copper plates out on the negative. As the battery is discharged, the electrodes dissolve into the electrolyte; recharging reforms them.

In a conventional lead-acid battery, insoluble products such as lead sulfate are produced during discharge. As these products build up on the electrodes and in the electrolyte, they can short out the cells and make the battery prematurely unusable. In the new battery, however, no insoluble products or insulating films are formed, resulting in an efficient use of the active materials and a long life. In fact, says Moody, the operating efficiency is very close to 100 percent, whereas conventional batteries operate at only 50 to 70 percent efficiency.

Partially offsetting this advantage, however, is the battery's output of only slightly more than 1 volt per cell—about half that of a conventional battery. But, says Moody, the new battery contains just the right amount of lead theoretically required for electrical generation, whereas a conventional battery contains twice as much. This gives the new battery a distinct weight advantage. Moody predicts that the battery could find wide use as a storage medium for electrical utilities, for bulk energy storage in solar power systems, and in electric cars.

Clearing Pesticides from the Body

A new approach to the removal of halogenated pesticides and other chemicals from animals and, perhaps, humans, was reported at the ACS meeting by Karl K. Rozman of the University of Kansas Medical Center. The treatment involves administration of aliphatic hydrocarbons such as mineral oil and hexadecane, which are poorly absorbed in the gut.

The conventional treatment for removal of halogenated compounds, developed in 1978 by Philip S. Guzelian of the Medical College of Virginia, involves administration of cholestyramine, which binds to halogenated chemicals in the intestine and promotes their excretion. Pesticides stored in body fat then migrate to the intestine by passive diffusion to maintain a balance between stored and mobile chemicals. Rozman and Tibor Rozman of the Gesellschaft für Strahlen und Umweltforschung mbH of Munich have demonstrated that this diffusion can be stimulated as much as 13-fold in rats and rhesus monkeys by feeding the animals small amounts of the aliphatic hydrocarbons. The treatment would thus be complementary to use of cholestyramine.

G. Stanley Smith of New Mexico State University also reported that he and Karl Rozman were able to speed the elimination of labeled hexachlorophene from sheep and mirex from goats by feeding the animals aliphatic hydrocarbons at a rate of 5 percent in the diet. Fecal excretion of the halogenated materials was increased threefold in the sheep and twofold in lactating goats without increasing the concentration of the chemicals in blood or milk.

Thomas H. Maugh II