A series of scientific studies in this country and abroad is stirring new concern among some scientists over the safety of aspartame, the immensely popular sugar substitute marketed as NutraSweet. But a spokesman for the company cited the same studies as evidence that the product is safe.

An estimated 4,000 tons of the sweetener, some 200 times sweeter than sugar, is consumed every year, and sales are estimated now at more than $1 billion annually and increasing rapidly.

Earlier this month, at a scientific conference that was closed to the press, researchers reported that heavy aspartame use appears to increase migraine headaches and seizures in susceptible individuals, cause changes in electroencephalogram (EEG) readings and may even be related to birth defects and retardation.

However, Dr. Frank Kotsonis, head of research for the NutraSweet Co., said he found the studies either seriously flawed or used to support unwarranted conclusions.

And Dr. Bennett A. Shaywitz, chief of pediatric neurology at Yale University, said he found the ambience at the conference "similar to past meetings on the usefulness of the Feingold diet as a cure for hyperactive children. There was a fanaticism there that made me very uncomfortable."

Shaywitz is conducting a study of aspartame in seizure-prone children between the ages of 5 and 12 but so far has been unable to demonstrate any adverse effects from the sweetener.

G.D. Searle, which manufactures aspartame, and the NutraSweet Co., which markets it, have maintained that the substance's 1981 Food and Drug Administration approval came with more safety studies than any product in history.

Some researchers believe, however, that because the tests were looking for acute deleterious effects, they missed the more subtle effects that may occur over a long period of time.

Dr. Paul Spiers, a clinical neuropsychologist of the Behavioral Neurology Unit and the Harvard Medical School's Comprehensive Epilepsy Center at Beth Israel Hospital in Boston, presented at the meeting some preliminary evidence that use of aspartame over a period of time might affect intellectual functioning in normal users.

In an interview, Spiers said that the findings had been something of an accident. He had been planning to study the effects of aspartame on individuals who reported that they had suffered seizures after ingesting aspartame. However, he was first ethically bound to run the tests on normal control subjects to confirm their safety.

"For that reason," he said, "we went out and selected people specifically who had a history of using NutraSweet
products and were not aware of it having any adverse effects on them. We picked people who had normal neurological histories, no history of psychiatric illness and no physical problem -- nothing, in fact, that would suggest that we would expect to have any problems."

The group was given aspartame capsules up to the FDA's maximum allowable limit -- 50 grams per kilogram of weight -- three times a day for 12 days. Unexpectedly, the researchers began to find "cognitive deficits" in some of the neuropsychological tests then done on the group.

Among the tests was a sophisticated computer test called "Think Fast," which requires comparisons, copying and recall of patterns of blocks and sequences of letters. Spiers described it as "quite demanding and self-paced, becoming increasingly difficult. Normally when a test like this is repeated, subjects tend to improve in their performance as they learn how the test is done." Nevertheless, the subjects on aspartame failed to improve and "some of them frankly showed a reverse pattern where their performance got worse."

Although he was admittedly dealing with only a few subjects and checking performances on only a small number of the tests that were administered, Spiers believes the findings are important. A second group of volunteers who were given a placebo instead of aspartame showed none of the problems manifested by the aspartame group. The computer test and others measured functioning of the brain's frontal lobe, Spiers said, "simulating what the brain does in everyday life."

"We are wondering whether in fact this substance may be capable of having a subtle effect on cognitive functioning that people may not necessarily be aware of. Think of the implications, for example, on an average college student who starts consuming a liter of this stuff during examination period, and it may in fact be interfering with his concentration and attention skills."

Said Spiers, "This kind of neuropsychological cognitive examination has never been used to investigate the effects of new drugs of any kind. Now, we have food additives that are more like drugs than foods, that are introduced into the dietary chain but have direct effects on the brain's neurotransmitter system. But because the chemical industry is 20 years ahead of the regulators, thus far no one has attempted to apply more sophisticated methods of testing brain functions to these problems."

NutraSweet's principal ingredient is an amino acid called phenylalanine (PHE), which is found, along with other amino acids, in protein. There is a genetic disorder called phenylketonuria (PKU) in which the ability to normally process the amino acid is impaired. Without careful dietary restriction of protein, PKU babies may suffer severe, irreversible mental retardation. All products containing NutraSweet must warn against its use where PKU exists.

Now, however, specialists and researchers believe that there may be many more people who carry the gene for PKU but show no symptoms who, however, may be unable to deal with the extra load of PHE that comes from using products containing NutraSweet.

Dr. Reuben Matalon, a geneticist and pediatrician at the University of Illinois, warned those at the conference that perhaps millions of PKU carriers are at risk of varying reactions to aspartame, as are the fetuses of pregnant carriers. Another major study presented at the conference suggested that the use of aspartame could increase the frequency of migraine headaches fourfold. However, both Kotsonis and Shaywitz said they believed the study was poorly conducted. They cited another study done at Duke University, now awaiting publication, that found no link between migraines and NutraSweet.

Dr. Richard J. Wurtman, neurophysiologist at the Massachusetts Institute of Technology and one of the organizers of the conference, called for more studies of the 3,400 people who have complained of reactions to NutraSweet.

"Except for the migraine study, which is preliminary, at this point we cannot say aspartame is responsible for all those anecdotes. Still, given the basic science findings and the anecdotes," Wurtman said, "the index of suspicion is
Said Spiers: "I think it is in everyone's interest to do good research on this. It may turn out that it is just a labeling issue, that the warning needs to be broader. People still smoke, but they smoke knowing the consequences. The difference here is that people have not understood the consequences."

"How many people even know that the FDA has attached a limit to aspartame consumption?" asked James Wagoner, legislative aide to Sen. Howard Metzenbaum (D-Ohio). Metzenbaum has introduced legislation requiring that labeling include information about how much NutraSweet is contained in a serving of a given product. The FDA's limit of 50 grams per kilogram of body weight translates to about four liters of a diet drink for an adult but only to about three cans for a child who weighs about 30 pounds.

"Americans," Wagoner said at the conference, "drink over 20 billion cans of diet soft drinks" a year. And that doesn't count the gum, pudding, breakfast cereal, chewable vitamins, toothpaste, juices, frozen pops -- all sweetened with NutraSweet."

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