New Misgivings About Low Magnesium

The average American consumes only about 40 percent of the recommended daily allowance of magnesium, according to data collected by the U.S. government. While this dietary deficiency produces no overt symptoms, it probably is not benign either, researchers reported last week in St. Louis at the 22nd annual Conference on Trace Substances in Environmental Health. Their data and analyses link low-magnesium diets to diabetes, high blood pressure, pregnancy problems and cardiovascular disease, including arrhythmias and high blood pressure.

The data, derived largely from animal studies, paint a consistent and troubling picture, says Mildred S. Seelig, executive director of the American College of Nutrition in Scarsdale, N.Y. The studies suggest many people face serious consequences — including death — from preventable magnesium deficiency, she says, and contributing to the problem is that this deficiency "is likely to be silent until it is severe."

Among the more provocative data unveiled last week were findings from a trio of animal studies by the husband-wife team of Burton and Bella Altura. The two physiologists at the State University of New York Health Sciences Center in Brooklyn reported that:

• High blood pressure can be prevented in rats that have been treated to initiate salt-induced hypertension. All it takes is spiking the rats' drinking water with four to eight times their recommended daily allowance of magnesium.

• Most of the ill-effects of pulmonary hypertension (elevated blood pressure only in the lungs), in this case chemically induced in rats, can be prevented by supplementing a rat's drinking water with similar amounts of magnesium. Untreated rats suffer a tripling of lung blood pressure, a doubling or tripling of right-heart size and a three- to seven-fold thickening in arterial walls, along with reductions in the diameter of the vessels' interior.

• Among young rabbits, blood lipid levels and the formation of artery-clogging fatty deposits depend in part on dietary magnesium. Animals were fed diets with normal or high (1 or 2 percent) cholesterol levels. The diets were also deficient, sufficient or highly supplemented with magnesium. When compared with rabbits getting just 40 percent of their magnesium requirement, those eating normal cholesterol and getting five or more times the recommended daily allowance of magnesium showed 30 to 40 percent reductions in blood levels of cholesterol and other lipids. Similarly, among rabbits on a high-cholesterol diet,

those getting the megadose of magnesium experienced a 50 to 65 percent decline in their quite elevated blood lipid levels, compared with those in the low-magnesium group. But most important, Burton Altura says, is that the rabbits on the high-cholesterol/low-magnesium diet experienced 80 to 90 percent more atherosclerosis than those on the high-cholesterol/high-magnesium diets. Rabbits on a magnesium-sufficient diet developed changes somewhere between those of rabbits fed high or low levels.

Commenting on this last study, directed by his wife, Altura says, "I know of no one [else] who has been able to lower cholesterol and triglyceride levels in a normal, healthy animal" — one that had previously experienced no serious blood lipid elevations. These studies, he says, point not only toward a new magnesium-lipid connection, but also to serious effects at levels characteristic of the U.S. population.

At the same conference, Kenneth Weaver, an obstetrical researcher at East Tennessee State College of Medicine in Johnson City, described his studies with sheep and humans indicating that magnesium deficiencies during pregnancy can result not only in migraines and pregnancy-associated high blood pressure, but also in low-birthweight babies, miscarriages and stillbirths. Conversely, magnesium supplements can dramatically reduce the incidence of these events, animal and human studies by Weaver and others show.

Weaver's data indicate a magnesium deficiency can set up spasms in blood vessels. "Then blood platelets become a problem," he says. "They can actually plug up some of the small [blood] vessels" in the placenta and in the mother's body.

Adding to the problem is the ability of phosphates to bind magnesium in the bowel and prevent its absorption, his studies show. A 12-ounce can of carbonated soft drink might contain 30 milligrams of phosphate, he says, and could "take out an equivalent quantity" of dietary magnesium.

Seelig believes 80 to 90 percent of the U.S. population may be notably magnesium deficient. At particular risk of "severe" deficiency, she says, are alcoholics and persons taking medications that interfere with magnesium absorption or increase its excretion — including diuretics, digitalis and other heart drugs, as well as some antibiotics and anticancer drugs. In addition, she says, studies by herself and others have shown that "stress, whether psychological or physical, increases magnesium requirements."

What's the solution? While green, leafy vegetables, seafoods and whole-grain cereals are rich sources of magnesium, Weaver says, it's often hard to get enough of the metal through the diet. That's why some, like Weaver, suggest taking supplements. "If I were to name just one thing I'd supplement everybody with," he says, "it would probably be magnesium."

— J. Raloff

Speaking to an understanding SPHINX

Until now, the award for best performance by a computer able to understand spoken words has gone to systems trained to recognize a particular individual's voice. The SPHINX system, recently developed by graduate student Kai-Fu Lee of Carnegie-Mellon University (CMU) in Pittsburgh, matches that level of performance — but with a significant difference. It responds to just about any voice. Users don't have to endure the lengthy preliminary process of providing speech samples to ensure the computer can understand their words. Lee describes SPHINX as the world's first "accurate, large-vocabulary, speaker-independent" speech recognition system.

Researchers have long felt that speaker-independent systems can't work as well as speaker-dependent ones, says CMU's D. Raj Reddy, who more than a decade ago pioneered the HEARSAY speech program. "For the first time, we seem to have at least one [speaker-inde-

pendent] system doing about the same as or better than a speaker-dependent system."

"Lee's achievement is definitely noteworthy," says James R. Baker of Dragon Systems, Inc., in Newton, Mass., a company specializing in speech-processing technology. "There's no question he has singlehandedly produced a state-of-the-art speech recognition system."

Computer-based speech recognition is already well established. Systems that recognize single words or simple phrases from a limited vocabulary are used in factory settings for controlling machinery, checking inventory, entering data and inspecting parts on an assembly line. In some hospitals, to keep their hands free for working with critically ill patients, nurses wear microphones so that they can describe their actions and observations to a computer that logs the information and keeps the necessary records. Lee's system, with a 997-word

vocabulary, is designed so Pentagon planners, simply by asking the appropriate questions, can speedily search for and find specific information stored in a database.

In the SPHINX system, sound waves captured by a microphone are first converted into strings of digits. Further processing reduces the number of digits necessary to represent the information contained in a waveform so that a single number characterizes 10 milliseconds of speech. Doing the signal processing in three different ways produces three such numbers for each speech segment. The system is programmed to look for patterns among these sets of numbers, and in a short time, it produces its best guess as to what the spoken words were.

The SPHINX system's superior performance can be attributed largely to a sophisticated computer program combining a powerful mathematical technique, known as hidden Markov modeling, with carefully formulated principles derived from human knowledge about speech, Reddy says. Furthermore, by analyzing large collections of speech samples from many different people, SPHINX can automatically fine-tune its capabilities.

"The [learning] technique we're using happens to be fairly sensitive to the amount of training," says Lee. "The more you train it, the better it gets." About 10 hours of training on 4,200 sentences spoken by different people is enough to let almost anyone thereafter use the system with good results.

Lee's achievement raises the intriguing question of whether the techniques he used would also enhance the performance of speaker-dependent systems. "We may find that if other people use all of the new techniques that Kai-Fu Lee introduced in his system, speaker-dependent systems might do better too," says Reddy. That possibility has yet to be tested.

Another possibility is a system that combines the best qualities of a speaker-independent system like SPHINX with the learning capabilities of a speaker-dependent system. Such a hybrid system would have a considerable store of knowledge about the human voice and the capacity for automatically adapting to a new speaker. After only a brief period training the system, the user would be ready to use it.

"A generalized model will never match your voice as well as a model derived from your own voice," says Janet M. Baker, Dragon Systems president. "As soon as you get specific information about a given speaker's voice, you want to make use of that. That's how you'll get the best performance."

Lee himself has studied the effect of adding procedures to SPHINX allowing the system to tailor its operation to a particular speaker. However, he found that with his methods the improvement in performance was disappointingly small. He attributes the small gain to the fact that the speaker-independent version of SPHINX is already quite accurate.

Lee wants to improve his SPHINX system so that it can handle a larger vocabulary and more complex relationships among words. So far, the system has dealt with only simple grammars. He's also considering alternative ways of adding human knowledge about words and sounds to his system.

"At this point, it's clear that one can get speech recognition at a respectable level of performance without requiring any training for individual speakers, and that's very encouraging," says Reddy. "The challenge is to get human-like performance. We're still an order of magnitude away from that." — *I. Peterson*

Study shows AIDS virus may be hiding out

A sensitive new genetics test has uncovered traces of AIDS-virus DNA in the few infected people who first tested positive for AIDS antibody in their blood on standard tests and later tested negative, scientists announced this week. In some of these cases, the scientists were unable to detect even that trace of the virus in later runs with the new test, and they question whether this means the virus has gone deeply into hiding or disappeared completely.

Most standard AIDS tests reveal exposure to the virus, known as HIV, by finding antibodies to it rather than by finding the virus itself. A year ago a research team announced that out of 1,000 homosexual men studied, four who initially showed antibodies to the virus slowly lost those antibodies. This process, called seroreversion, usually occurs only in the last stages of the disease, when the immune system becomes too enfeebled to mount any antibody response to the virus. However, these four men had no symptoms of the disease. The most likely explanations were that the men had managed to conquer the invading virus, or that the virus had entered a latent phase and become undetectable with available blood-screening tests.

The new research provides preliminary evidence that the virus may be going into latency and not provoking an immune response, rather than disappearing altogether in these men, reports a group of medical researchers in the June issue of the ANNALS OF INTERNAL MEDICINE. A test using a newly developed technique called polymerase chain reaction (PCR), which allows scientists to search directly for very small amounts of DNA, led to the discovery of bits of AIDS-virus DNA embedded in the men's own DNA, say the scientists. The team includes researchers from the Johns Hopkins School of Hygeine and Public Health in Baltimore, the National Institutes of Health in Bethesda, Md., Northwestern University in Chicago, the University of California at Los Angeles, the University of Pittsburgh and Cetus Corp. in Emeryville, Calif.

In two of the four cases, the men later lost even the small amounts of HIV DNA detectable with PCR tests. The reason for this disappearance is unclear, and it may be that the viral DNA is present in too low a concentration for even the new test to find, or the virus could be hiding in the brain or spleen, the scientists report. In the latter case the virus might be acting somewhat like the herpes virus, which lives in the nerve cells where the immune system cannot attack it, and occasionally breaks out and multiplies, says Johns Hopkins researcher Homayoon Farzadegan, one of the paper's coauthors. Only a long-term follow-up study can determine whether these men will start producing HIV antibodies again and come down with the disease, the researchers say.

One implication of the report is that HIV-infected blood donors who have seroreverted might endanger the blood supply, because blood screening currently depends on the presence of HIV antibodies. The risk to the U.S. blood supply as a result of seroreversion is extremely small because loss of HIV antibodies in the early stages of infection is so rare, the report's authors say. Only 0.4 percent of the HIV-positive men in this study seroreverted, points out coauthor B. Frank Polk of Johns Hopkins, and although such people may be infected with the virus, they may not be able to pass on the infection. "The virus is present in the men in extremely low quantities and is found only in the genetic material of their infected cells," he says.

In an editorial accompanying the article, Thomas Zuck of the University of Cincinnati Medical Center asserts there is little additional risk to the blood supply because high-risk donors usually exempt themselves from giving blood, and because any HIV-infected donors who do slip through the HIV screening will probably fail the hepatitis test. At one medical center, researchers found a 38 percent correlation between HIV infection and hepatitis B infection, Zuck writes. However, he notes, there are always risks associated with blood transfusions, even though the blood supply is safer now than at any time since AIDS emerged. "It is essential that the public understand the futility of pursuing a policy of a zero-risk blood supply," he says. Farzadegan says there is already a small risk to the blood supply because someone could donate shortly after infection and before antibodies appear. Seroreversion poses less risk than this, he says. — *C. Vaughan*