Chemistry

Janet Raloff reports from Chicago at the American Chemical Society's 190th national meeting

Clues to the kidney stone mystery

Every year an estimated 300,000 Americans develop kidney stones. According to John Pahira, director of the Center for Kidney Stone Disease at Georgetown University in Washington, D.C., 70 to 75 percent of these cases will involve calcium-oxalate stones. What causes them, why 60 to 80 percent of their victims are male and why this disease rarely affects children have remained mysteries. Now researchers at the University of Chicago think they've uncovered at least a partial answer to the question of what causes the stones.

Kidney stones grow in much the same way rock candy does. A tiny calcium-oxalate crystal, formed in the kidney from a chemical reaction between excreted calcium and oxalic acid (a component of such foods as spinach, rhubarb, celery and nuts), serves as the seed crystal around which a stone can develop in a high-sugar urine. Four years ago the Chicago researchers identified a mechanism that appears to keep the seed crystals formed by normal persons from growing into large stones: a glycoprotein in their urine coats the microscopic seed crystals, preventing further deposition of calcium-oxalate layers.

Early this year the Chicago researchers identified what makes chronic stone formers different. In normal individuals, explains chemist Yasushi Nakagawa, an enzyme transforms a precursor molecule produced by the kidney into the stone-inhibiting glycoprotein. But in calcium-oxalate-stone-forming individuals, the enzyme responsible for making gamma-carboxy-glutamic acid either malfunctions or is present in insufficient quantities, Nakagawa says, because some of the "inhibitor" present in their urine will lack this apparently crucial amino acid. While inhibitor lacking this amino acid will cover the seed crystal, it does not block crystal growth.

The researchers have developed an immunological assay to detect what proportion of the stone-inhibiting glycoprotein in a person's urine is functional. Those earmarked as prone to stone formation by the assay can make dietary changes to slow the rate of any incubating stone's growth. But the ultimate goal of this work, says Nakagawa, is to find ways to restore the ability to make functional crystal-growth inhibitors and to understand what partially shuts down the production of gamma-carboxy-glutamic acid in the kidneys.

Possible new assay for cancer

A biochemist at the University of Tennessee's Center for the Health Sciences in Memphis is developing a pair of general cancer screening tests based on the presence of a biological marker that he has identified in the blood sera of humans and animals. Edsel T. Bucovaz says that this "B-protein" marker apparently "is produced by the body in response to rapid, abnormal cell growth." As such it is far from a foolproof diagnostic test, he cautions, since production of the protein might be stimulated by benign tumors or by the third trimester of pregnancy. However, as a rough-cut screening test during physicals, it might offer an early warning of asymptomatic cancer, he says. But Bucovaz sees its most important value as a periodic screen in patients who have undergone cancer therapy.

In tests involving 2,500 cancer patients, he says his group detected 87 percent. For controls, they tested urine from 3,500 noncancerous hospital patients aged 30 to 65 and from several hundred younger, healthy adults. False positive findings among these groups ranged from 5 to 10 percent.

Bucovaz says he's leaving follow-up efficacy testing — needed to win Food and Drug Administration approval — to any commercial developers of the test. A qualitative test that takes only minutes to analyze might be performed in a physician's office for less than $5, Bucovaz says. Positive findings could be confirmed using a slightly more expensive and complicated laboratory-analyzed quantitative assay.

Technology

Stormy weather at crystal surfaces

Atoms on the surfaces of microscopic gold crystals appear to be in constant motion. Not only do they hop from site to site, but they also continually shuttle between a crystal's orderly columns and clouds of atoms hovering near certain surfaces. These recent observations result from the combination of a high-resolution electron microscope and a video-recording system that magnifies gold crystals about 20 million times and, on an atomic scale, tracks their growth as it happens.

"The motion of atomic columns and the existence of atom clouds revealed here may have important consequences for crystal growth, surface science and catalysis studies," say David J. Smith of Arizona State University in Tempe and his colleagues at the University of Lund in Sweden. Their report appears in the Sept. 5 NATURE.

The researchers use a powerful electron beam to bombard 55-atom clusters of gold scattered across a carbon film. These tiny crystals turn out to be unstable, and some crystals begin to grow at the expense of others. A TV monitor allows the scientists to watch the rapid changes in crystal shape and orientation.

It's like watching living atoms, says Smith. "You can sit and look at one small particle for 10 minutes," he says. "You may get 29 different shapes in 30 seconds, and then it will sit still for a while, and then it goes on. We also see different effects according to how big the particles are." In addition, the ever-changing cloud shapes seem to show the pathways that atoms follow out of or into the lattice columns. In some instances, parts of a cloud look like miniature tornadoes directed toward particular crystal columns.

"It may well be that column hopping and changes of cloud shape are an indication of how atoms locate the most favorable lattice position during crystal growth," the researchers say. Using the same equipment, it should also be possible to monitor the way in which a variety of atoms interact with a metal surface. This is an important question in the study of how catalysts work.

One concern about the research is that the motion observed may be due to the effect of the electron beam rather than a characteristic of crystal behavior. "We're on a fact-finding mission," says Smith. "How general is the phenomenon that we have observed?" So far, the researchers have seen similar although not identical behavior at platinum crystal surfaces.

Into the chemistry of the heart

In the last few years, advances in nuclear magnetic resonance spectroscopy have allowed medical researchers to gather much information about the molecular chemistry that takes place inside living cells (SN: 10/15/83, p. 250). Recently, attention has focused on the isotope phosphorus-31, which occurs naturally in the human body and has a permanent magnetic moment that interacts with an external magnetic field. By detecting the faint signals from these nuclei, researchers can track high-energy phosphate metabolism. These measurements provide valuable diagnostic information about various human muscular and brain disorders without the use of ionizing radiation like X-rays and without cutting open a body or inserting probes. Now, similar measurements have been recorded for a living human heart.

Using a new technique called depth-resolved surface coil spectroscopy, Paul A. Bottomley of the General Electric Research and Development Center in Schenectady, N.Y., obtained phosphorus spectra from the heart of a volunteer. These spectra showed the relative amounts of inorganic phosphorus and the metabolites phosphocreatine and adenosine triphosphate — normally present in minute quantities and very difficult to detect. Changes in the ratios of these substances, which are involved in the transfer of energy in living cells, often mirror the effects of heart disease. Bottomley's report appears in the Aug. 23 SCIENCE.

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