

Biomedicine

Diane D. Edwards reports from Washington, D.C., at the National Kidney Foundation's Science Writers Briefing

Blunting cyclosporine's kidney toxicity

Hailed as a breakthrough in organ transplantation, the drug cyclosporine suppresses the immune system, reducing the chances of transplant rejection. More recently, scientists have been testing the drug as a treatment of suspected autoimmune diseases, such as type 1 diabetes (SN: 11/7/87, p.292). But cyclosporine is toxic to the kidneys and frequently causes high blood pressure. Now, William M. Bennett of Oregon Health Sciences University in Portland reports on his research and that of others aimed at minimizing the drug's toxicity.

At the front line of this effort, says Bennett, is the development of more sensitive techniques for monitoring levels of the drug. The most promising of these, he says, are monoclonal antibodies that affix to the drug in the patient's blood. But even when such a test is available, researchers will continue to walk the narrow line between cyclosporine doses that are effective and those that are toxic. According to Bennett, those doses are likely the same—suggesting that it may be beneficial to directly block cyclosporine's constriction of blood vessels supplying the kidneys rather than to rely on dose adjustment alone. Scientists suspect this vessel constriction is the basis for the observed kidney toxicity.

Some researchers are testing drugs that specifically inhibit the synthesis of thromboxanes, substances made by the body that cause vessels to constrict. Two preliminary clinical trials of such drugs have just begun, says Bennett. In addition, blood-pressure-lowering drugs called calcium channel blockers dilate these blood vessels—but they also raise the level of cyclosporine in the blood. Although Bennett says the use of such drugs along with cyclosporine appears promising if cyclosporine levels are precisely monitored, he and his co-workers have been looking at the "vehicle" solution in which the water-insoluble cyclosporine is dissolved before use.

Alcohol and olive oil are two standard vehicles used by physicians, but Bennett and colleague Vickie Kelley at Brigham and Women's Hospital in Boston think that omega-3 fatty acids found in some fish oils may offer a two-fold advantage. Fish oils have attracted attention recently for their potential lowering of heart disease risk (SN: 11/28/87, p.342). Bennett says they apparently reduce thromboxane synthesis and the clumping of blood-clotting cells called platelets. And Kelley has evidence that dietary fish oils also suppress the immune system. Their animal studies show that dissolving cyclosporine in fish oil "markedly reduces" kidney toxicity, and that even giving fish oil supplements separately decreases side effects, Bennett says. He doesn't advocate that fish oil now be taken with cyclosporine, but does expect a two-year clinical trial currently underway to reveal whether administration of fish oil will lead to lower effective doses of cyclosporine and less kidney toxicity.

Creating a new wave in neobladders

Stapling together replacement bladders from loops of the bowel could replace urine-collecting bags and catheters now attached to the outside of the body in patients who have lost their original bladders. Surgeons at Johns Hopkins Hospital in Baltimore report success in creating an internal, so-called neobladder from bowel segments that is then connected to urine-carrying tubes, allowing patients to urinate normally. Fray Marshall of Johns Hopkins calls the technique a "significant change" in restoring quality of life to patients after surgery for bladder cancer, which will cause an estimated 46,000 new cases this year in the United States. He and his co-workers have performed the experimental operation on 17 patients thus far, reducing the time needed for the procedure from 14 hours to 8 hours. He cautions that many patients, particularly the elderly, may not be candidates for the procedure.

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Earth Sciences

When winds blow, does the earth quake?

Unusual air pressure patterns off the coast of California may trigger some of the numerous moderate-size earthquakes in this state, according to a controversial report by a meteorologist who has been studying West Coast weather for several decades. If true, this finding may help seismologists predict months in advance the likelihood of earthquakes during certain atmospheric conditions.

As evidence for the pressure-earthquake connection, Jerome Namias of the Scripps Institution of Oceanography in La Jolla, Calif., has found that California earthquakes are often preceded months in advance by persistent patterns of air pressure several hundred miles off the coast. Although he first noted this association more than 30 years ago, Namias now has reported on the subject, in the April *GEOPHYSICAL RESEARCH LETTERS*. In the past, seismologists have rejected outright the idea of any relationship, says Namias, and this criticism had kept him from raising the idea. While most earthquake experts remain highly skeptical, some have recently become more receptive to the possibility that patterns of air pressure may have some effect, he says.

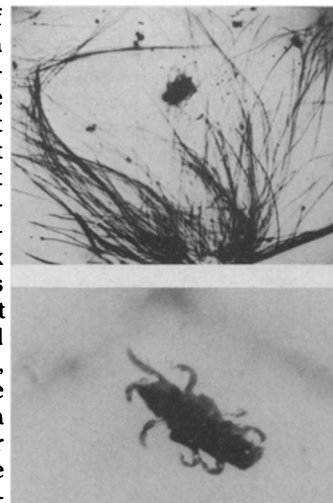
Namias' paper reports on two series of southern California quakes—in July 1986 and October 1987. For a month to six weeks before the seismic activity, large, recurring patterns of high pressure developed off the coast. These pressure systems were much stronger than normal, says Namias. "In my experience, and judging from the large values and gradients, it seems unlikely that this correspondence is due to chance," he says.

Seismologists have long contended that air pressure has no effect on faults. And although he has faith in the association, Namias lacks a theory to explain how pressure patterns might indirectly trigger the release of stress built up along faults. He speculates, however, that pressure systems may generate winds or changes in sea level that could indirectly set off quakes.

Strands that stand the test of time

In a candy bar or bowl of soup, the appearance of a piece of hair can be particularly unpleasant. But George Poinar Jr., an entomologist at the University of California at Berkeley, is thrilled by the tuft of animal hair he found encased in amber from the Dominican Republic. Dating back nearly 40 million years, this hair—probably from a rodent—is the oldest evidence of land mammals in the Caribbean, and may help prove that the West Indies have supported a diverse animal population for tens of millions of years, he says. As a bonus, four flea-sized parasites also were preserved by the amber, which is a fossilized form of tree resin.

Previous evidence for land mammals in this region went back only 100,000 years, and scientists have traditionally thought that most animals reached the islands only recently by swimming, flying or floating on debris. This new find, however, supports a rival theory that the West Indies were long ago attached to either North or South America, where animals roamed. Then the islands separated through plate tectonics and drifted to their present positions, carrying along an assortment of creatures isolated from the continent.



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