Cyclosporin therapy heals colon ulcers

A pilot study suggests a potent immunosuppressive drug can help people with severe ulcerative colitis, an inflammatory disease of the colon. If further research confirms the finding, the drug may save some colitis patients from surgery to remove part of the large intestine.

Simon Lichtiger and Daniel H. Present of the Mount Sinai Medical Center in New York City report that colitis symptoms improved in six of 11 patients treated with cyclosporin, a drug well known in the field of transplantation for its ability to prevent organ rejection.

"Considering the fact that all of these patients would have lost their colon in surgery, we believe a 55 percent response rate is a significant breakthrough in the treatment of ulcerative colitis," Lichtiger said at this week's Digestive Disease Week meeting in Washington, D.C. The meeting was sponsored by the American Gastroenterological Association and three other medical subspecialty groups.

Researchers suspect ulcerative colitis results from the immune system's misguided attack on a person's own colon cells. Immunosuppressants are prescribed to curb such attacks.

Lichtiger and Present studied hospitalized patients with severe colitis who did not respond to conventional treatments such as steroid drugs. All 11 were surgery candidates but opted for the experimental cyclosporin treatment in a last-ditch attempt to save their colons. The researchers gave these patients intravenous cyclosporin for one to two weeks. Those who responded to the initial dose were sent home and given steroids and oral cyclosporin for six months.

At the end of the six-month period, the researchers found that five of the six patients who had responded to the drug were in complete remission — they felt better, had stopped taking steroids and cyclosporin and showed no signs of the raw ulcers that had peppered the linings of their colons. The sixth patient had improved but still needed steroid therapy to control colitis symptoms, the researchers report.

Many questions about the experimental therapy remain, including a concern that cyclosporin causes kidney damage. So far, Lichtiger and Present say they haven't seen evidence of such damage, as measured by blood levels of waste products. But a larger study they are planning in conjunction with researchers at the University of Chicago and the University of California, Los Angeles, should provide a better idea of the drug's efficacy and safety in ulcerative colitis. Researchers expect to begin enrolling patients in that study this August. — *K.A. Fackelmann*

Brighter than the lights of big cities

Frederick Rich/Geophysics Laboratory, Hanscom Air Force Base

Lights from Chicago and Miami pale in comparison with the auroral glow over North America during the March 13, 1989 geomagnetic storm. This white-light image from the F9 satellite of the Defense Meteorological Satellite Program captured the aurora a few hours after its peak. The largest auroral event since 1972, these normally northern lights brightened the night sky even over Texas when they reached maximum strength. The aurora developed a few days after an extraordinarily large solar storm spewed a mass of energetic particles toward Earth (SN: 4/8/89, p.212). The planet's geomagnetic field directed the particles to the higher latitudes, where they penetrated the atmosphere and energized oxygen and nitrogen, which released energy by glowing.

'Magic angle' reveals zeolite reactions

Strange things happen in a zeolite. A labyrinth of molecule-wide corridors zigzags through this crystal, and within such narrow confines, chemical reactions become skewed. Chemists have learned to harness zeolites' reaction-altering properties to synthesize compounds, but they have yet to determine how the reactants yield the products.

Using a technique called magic-angle-spinning nuclear magnetic resonance, researchers at the University of Cambridge in England have solved some of the mystery lurking in these crooked corridors. In the May 18 NATURE, Jacek Klinowski and Michael Anderson describe the first clear look into a zeolite reaction.

Zeolites' networks alter chemical reactions through a process of "shape selection": The cramped quarters prevent some bulky molecules from getting in and others from getting out. The zeolite studied by the Cambridge group, ZSM-5, exerts its shape-selecting influence in a way that's especially useful for making gasoline. In a reaction converting methanol to gasoline, ZSM-5 favors products with high octane ratings. This zeolite-catalyzed reaction provides one-third of all gasoline produced in oil-scarce New Zealand, notes George Kerr of Lawrenceville, N.J., a retired chemist with the Mobil Oil Corp.

Scientists didn't understand the mechanism of the widely used reaction until Anderson and Klinowski unveiled it with a powerful technique — a variation on nuclear magnetic resonance (NMR) spectroscopy. In NMR, atoms of sample molecules exposed to a specific radio frequency give off identifying signals as the strength of an external magnetic field changes. Each atom's "fingerprint" is largely determined by the types of atoms nearby. For instance, a carbon atom at the end of a carbon chain will create a signature different from that of a carbon atom situated between two other carbons in a ring.

NMR generally doesn't work in zeolites and other solids because of various obscuring effects that arise when solid molecules hold a fixed orientation with respect to an applied magnetic field. For each atomic bond, the obscuring effects are minimized when the bond sits at what chemists call a "magic angle" of 54.44° in relation to the magnetic field. That's where the magic angle spinning comes in. By spinning a zeolite sample around an axis pointing at the magic angle from the magnetic field, Klinowski says, he can cancel out enough of the damaging effects to get a clear signature for each molecule.

With this method, the researchers discerned 29 different players in the gasoline-making reaction. The distribution of compounds they observed within the zeolite was very different from the combination of products appearing at the end of the reaction. For the first time, Klinowski and Anderson detected carbon monoxide as an important reaction intermediate. They also found some compounds that got stuck in the zeolite passages, including several isomers of tetramethylbenzenes — chemicals as bulky as their name.

Kerr suggests the Cambridge study will lead to better zeolite-mediated reactions. Chemists today are challenged with a wide choice of zeolites to use for each given reaction. "If you know the mechanism," Kerr says, "you might be able to make better choices between the many zeolites available." — *F. Flam*