New multiple sclerosis drug clears hurdle

Multiple sclerosis (MS) begins as a tragic case of mistaken identity.

In this autoimmune disease, white blood cells, the body's roving guardians against infection, view the fatty sheath surrounding nerve fibers as a threat. The cells promptly begin to digest bits of the nerves' insulating coating. Like frayed wires, the damaged nerves short-circuit, blocking communication between brain and muscles.

Fascinated with such processes, Ruth Arnon, Michael Sela, and Dvora Teitelbaum at the Weizmann Institute of Science in Rehovot, Israel, set out 27 years ago to create synthetic molecules capable of provoking an immune response. They ended up developing an entirely new way of treating MS—and perhaps other autoimmune diseases as well.

The pivotal step involved making a replica of a protein from the sheath of human nerve cells. This protein triggers an MS-like response when injected into guinea pigs, and the researchers had hoped that their replica would do the same. Instead, they found, it appears to act as a decoy, diverting the immune onslaught from nerve tissue.

"It is a new approach to the treatment of autoimmune diseases," Sela asserts. Although it will not prevent the disease, he says he thinks of the new treatment as "a synthetic 'vaccine' against MS."

The research achieved a practical milestone on Sept. 19. A Food and Drug Administration advisory committee recommended that the agency approve one of the group's decoys, copolymer 1, as a treatment for MS. The FDA typically follows its advisory committees' advice.

If approved, copolymer 1 would be the third drug in 3 years okayed for the treatment of MS, an incurable disease known for intermittent and progressively more severe episodes of pain and paralysis.

Until recently, all doctors could do to slow the steady slide into paraplegia was prescribe steroids. They hoped that the anti-inflammatory drugs would hamper the immune system, forcing it to leave the nerves alone. That solution rarely worked for long.

The two other new remedies for MS are Avonex and Betaseron, genetically engineered versions of the immune modulator interferon. Both cause unpleasant, flulike side effects.

Copolymer 1, which patients must inject daily, appears to be free of major side effects other than a temporary inflammation at the injection site and a fleeting tightness in the chest. Like the interferons, copolymer 1 cuts the number of MS episodes by about one-third.

"Two well-controlled, double-blind studies indicate that the drug reduces the rate of relapses of MS," says Sid Gilman, chairman of the FDA advisory committee and a neurologist at the University of Michigan Medical Center in Ann Arbor.

Made of a combination of four amino acids, copolymer 1 was developed for clinical use by Israeli chemical giant Teva Pharmaceutical Industries. The company trade-named the new drug Copaxone and designed the larger of the two trials that demonstrated its effectiveness.

This study, carried out at 11 medical centers in the United States, involved approximately 250 patients. Half of them received the drug; the other half were given a placebo.

Completed in 1994, the study found that people taking copolymer 1 for 35 months had 32 percent fewer relapses than those taking the placebo. People in the drug treatment group were also more likely to improve or retain the nerve function they had when entering the study, whereas those taking the placebo tended to get worse, says Teva Vice-President Carole Ben-Maimon, who presented the company's case to the FDA committee. An earlier study of just 50 patients yielded similar results, she says.

After the committee's vote, Ben-Maimon expressed delight that the members were convinced by the firm's evidence. "We're happy for patients as well as ourselves." —*S. Sternberg*

'Clean' water may infect swimmers

People who go into water downstream from sewage treatment plants can develop gut-wrenching gastroenteritis from exposure to germs carried by feces. Now, a study also links sewage-derived wastes to flulike diseases and to ear problems in swimmers.

A swimmer's risk of developing either respiratory disease accompanied by fever or an ear infection rose in lockstep with increasing evidence of fecal contamination in seawater—even though the measured contamination never exceeded government limits.

"This demonstrates that even 'clean' beaches produce significant health effects," concludes David Kay of the University of Leeds in England, an author of the new report.

His team recruited 1,216 adults to visit one of four coastal beaches in England. Upon arriving, half of the volunteers learned they were to enjoy themselves without entering the water, while the rest had to spend some 10 minutes frolicking in the frigid waves, submerging themselves at least three times. Kay's team then took samples of the water where each swimmer had been playing.

Globally, most water quality limits or guidelines are based on counts of fecal coliform bacteria. The Leeds team tested their samples for these bacteria along with four others. Such gastrointestinal microbes, all considered harmless, serve as markers of fecal contamination, which includes other microbes, including viruses.

In the September AMERICAN JOURNAL OF PUBLIC HEALTH, Kay and his colleagues now report finding that respiratory disease in the swimmers was associated with their exposure to fecal streptococcus, a type of noncoliform bacterium.

This is the first study to link fecal strep with an infection other than gastroenteritis, observes Alfred P. Dufour of the Environmental Protection Agency in Cincinnati. Moreover, he says, the researchers identified the threshold contamination necessary to trigger those infections. For the flulike disease, that turned out to be 60 streptococci per 10 milliliters of water. For gastroenteritis, the threshold was even lower.

In an earlier analysis by Kay's team, fecal strep also outperformed fecal coliform bacteria as a gauge of gastroenteritis risk (SN: 10/15/94, p. 255). It now appears that if just one bacterial species is to be monitored, fecal strep would be the most useful one, says Jay M. Fleisher, a public health researcher at the State University of New York Health Science Center at Brooklyn and a coauthor of the studies.

In fact, Dufour notes, EPA published recommendations a decade ago arguing that, for regulatory purposes, fecal strep—also known as enterococci—are the best indicator of fecal contamination. To date, however, state regulators have all but ignored the recommendation.

In the new British study, ear infections correlated with the fecal coliform measurements but not with fecal strep. Fleisher interprets the data as arguing that a single marker of fecal contamination, whether coliform or strep bacteria, offers too little water quality information to protect public health.

"I agree that more than one indicator organism is needed to establish marine standards for recreational water quality," says Joan B. Rose, a water pollution microbiologist at the University of South Florida in St. Petersburg. Better yet, she argues, health officials should monitor for the actual pathogens that cause disease.

Says Fleisher, "We're trying, and it looks more and more like they are going to be viral agents." —*J. Raloff*