Antidepressant Helps Obsessive-Compulsives

Preliminary results of a multicenter study of clomipramine, an antidepressant drug not approved for use in the United States, indicate it substantially improves the condition of many people with obsessive-compulsive disorder.

The Food and Drug Administration (FDA) is now considering making the drug available in "serious or life-threatening situations," says psychiatrist Joseph DeVeaugh-Geiss of Ciba-Geigy Pharmaceutical in Summit, N.Y., director of the 21-center clinical trial. He reported on the new study last week at the American Psychiatric Association's annual meeting in Montreal.

Ciba-Geigy manufactures clomipramine under the brand name Anafranil and has sold it for 20 years in Europe, Canada and elsewhere. If the drug's promise holds up in the multicenter study, the company will ask for full FDA approval.

There is no standard treatment for obsessive-compulsive patients, but in recent years small studies in the United States have reported clomipramine's effectiveness with the disorder (SN: 4/20/85, p.245). Clomipramine blocks the action of serotonin, a chemical messenger in the brain. The mounting data prompted Ciga-Geigy to undertake more extensive trials required for an FDA approval. Previously, the company saw no reason to gain approval for an antidepressant drug with no apparent superiority to others already available.

Obsessive-compulsive disorder is considered an "anxiety disorder" by psychiatrists, although depression often accompanies it. Obsessions are recurrent ideas and impulses experienced as senseless or repugnant; compulsions are bizarre rituals suggested by obsessive thoughts and aimed at preventing harm to oneself or others.

For example, a woman may spend six hours a day repeatedly washing herself, pursued by the fear that she might pass on a deadly disease to anyone she touches. Or a man might stop cooking and continually check electrical appliances for fear of causing a fire.

Nearly 5 million people in the United States suffer from this disorder, which often begins during childhood or adolescence. Many victims are ashamed of their behavior and attempt to keep it secret, rarely seeking treatment.

In the Ciba-Geigy trials, 578 adult obsessive-compulsives — many of whom had gone seven years or more before seeking help — received either clomipramine or a placebo for 10 weeks. The patients were divided into those with and without mild depression.

According to physician ratings, obsessive-compulsive symptoms were reduced by about 40 percent in both clomipramine groups, compared with a 5 percent reduction in the placebo groups. Clomipramine patients rated themselves as significantly more improved than placebo patients.

Clomipramine is not without side-effects, and DeVeaugh-Geiss notes that 10 percent of the patients dropped out of the clinical trial. Adverse reactions include nausea, dry mouth, dizziness, tremor and a reduction in sex drive. But most patients, he says, felt that alleviation of their obsessive-compulsive symptoms clearly outweighed any side-effects.

Effective clomipramine treatment often extends over a year or more, says psychiatrist Michele A.T. Pato of the National Institute of Mental Health in Bethesda, Md. She and her colleagues report that 16 of 18 obsessive-compulsive patients who responded well to clomipramine over an average of 11 months of treatment became significantly worse after receiving a placebo for seven weeks. A gradual decrease in the clomipramine dose might result in fewer symptoms returning, she notes.

But evidence suggests the first treatment for obsessive-compulsives should be behavior therapy, contends psychologist Edna Foa of the Medical College of Pennsylvania in Philadelphia. This approach includes supervised exposure to objects and situations that provoke anxiety, prevention of compulsive rituals and discussions with a therapist about irrational fears.

After three weeks of behavior therapy — a total of 15 sessions, each about two hours long — 16 of 21 obsessive-compulsive patients showed substantial improvement lasting at least three months, Foa reported at the psychiatric meeting. "Clomipramine may be helpful with those who do not respond to behavior therapy," she explains. It may also lessen the anxiety of many obsessive-compulsives who are afraid to undergo behavior therapy, thus allowing them to participate in the intensive psychological treatment.

Investigators have not yet examined the effectiveness of combining behavior therapy with clomipramine. — *B. Bower*

Bowel-brain link may be key to diseases

Researchers delving into the chemistry of the bowel have discovered a specific chemical link between the nervous system and the immune system. The discovery may lead to new treatments for such painful bowel diseases as ulcerative colitis and other inflammatory conditions.

The discovery has to do with the action of a neurotransmitter called substance P. The peripheral neurons that release substance P are thought to send pain signals to the brain and to help regulate the immune response in damaged tissues. The scientists, from the University of California at Los Angeles, the Harvard Medical School in Boston and the Veterans Administration Wadsworth Medical Center in Los Angeles, found that people with chronic inflammatory bowel diseases have high numbers of receptors for substance P in their intestinal tissue.

The scientists suggest the receptors cause disease when they short-circuit the normal response to intestinal distress. For example, the condition might start when a harmful bacterium or virus in the intestinal tract interacts with a sensory neuron. The neuron, in turn, lets the body know something is wrong by both sending pain signals to the brain and releasing substance P into the tissues to mobilize the immune response. But in people with too many substance P receptors, the immune system seems to overreact, causing enough inflammation to trigger the sensory neurons to send more pain signals and release more substance P. "Something else may start the inflammation, but then it takes off on its own and gets caught in a loop," explains Patrick Mantyh of UCLA and Wadsworth.

The researchers, who report their results in the May PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol.85, No.9), found up to 2,000 times the normal density of substance P receptors and an irregular distribution of the receptors. "Normally, substance P receptors are just expressed on muscle tissue in the intestine," says Mantyh. "In tissue from chronically inflamed bowels, we found the receptors on blood vessels and immune cells, too."

The researchers are now trying to find a molecule that would block the substance P receptor and thereby interrupt the inflammatory cycle. Mantyh believes asthma and arthritis may also be caused by excess substance P receptors in the lungs and joints, and suggests that a receptor-blocking molecule might be used to treat those diseases.

— *C. Vaughan*