



April 19, 2005

HEALTH

# New Hope for Treating Down Syndrome

## Early-Stage Research Suggests Alzheimer's Drugs Alleviate Some Symptoms

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April 19, 2005; Page D1

For the families of individuals with Down syndrome, one of the most frustrating aspects of the condition is the impaired ability to communicate and express oneself. But now, doctors and researchers believe they have discovered ways to improve some of these symptoms.

The work still is in the early stages, but small clinical trials involving both children and adults have shown that a number of drugs and compounds used to treat Alzheimer's disease appear to improve the communication, language and attention abilities of individuals with Down syndrome.

At centers including Duke University in North Carolina and the University of California in Irvine, researchers found that those taking the Alzheimer's drugs Aricept and Exelon often were able to express themselves more easily, using more complex sentences and new vocabulary. A larger trial with Exelon is expected to begin this year. There also are two trials under way testing whether high doses of vitamin E and a supplement cocktail including vitamins E and C can improve memory and cognitive function in people with Down syndrome.

### NEW APPROACHES

See where the research stands on drugs for Down syndrome.

The research grew out of work done in the field of Alzheimer's disease, after researchers discovered similarities in the two conditions. Many individuals with Down syndrome eventually will develop Alzheimer's disease after the age of 40, according to Down syndrome researchers. In both conditions, people don't produce enough of a chemical called acetylcholine in the brain, which results in learning and memory problems. Thus, the theory goes, treatments that work on Alzheimer's may also be beneficial with Down syndrome.

The improvements seen in the lives of people with Down syndrome offer new hope that, contrary to what doctors once believed, the genetic condition isn't intractable. The ultimate goal of researchers is to intervene early in the lives of those with Down syndrome, improving their ability to learn and communicate at an age when their brains are rapidly developing. That raises the prospect of eventually increasing the IQs of people with Down syndrome.

"Even a moderate shift of 10 to 20 points more in IQ would bring a lot of kids into the low normal or normal IQ range," said Albert Costa, a Down syndrome researcher at the University of Denver and the father of a child with Down syndrome.

The findings are preliminary, and researchers acknowledge that they have limitations. In most of the completed trials, the participants know they are receiving a drug, raising the possibility that the power of suggestion is partly responsible for the

gains. All the treatments have potential side effects, including gastro-intestinal upset and vomiting, which are of particular concern for younger people with Down syndrome, who can have difficulty swallowing. And the prescription drugs can be expensive, running from \$150 to \$300 a month. Many families have been paying out-of-pocket to continue the drugs after trial, since insurers often are unwilling to cover drugs for uses not approved by the Food and Drug Administration.



Chris Graythen/ Getty Images

**Carolyn Pic** with her mother **Jane Pic Adams** and stepfather **William Adams**.

Down syndrome is the most common chromosomal abnormality, occurring in one of every 800 to 1,000 births. More than 350,000 people in the U.S. are affected by it. Individuals with Down syndrome have varying degrees of mental retardation, which is defined as an IQ of about 70 or below, as well as memory, language and attention problems. People with Down syndrome also are at higher risk of other medical conditions, such as congenital heart defects, leukemia and digestive problems.

Medical advances have increased the life expectancy of people with Down syndrome, with many now living to age 55 and beyond, compared with an average of only 25 in 1983, according to the National Down Syndrome Society. Now the push is on to improve the quality of life.

The use of drugs such as Aricept, from Eisai Inc. and Pfizer Inc., and Exelon, from Novartis Pharmaceuticals Corp. to treat problems associated with Down syndrome opens up a potential new market for a class of drugs that has suffered some setbacks. The drugs haven't been shown to cure Alzheimer's, but rather to slow the progression of the disease, and the benefits appear to be transitory. One study just published online by the New England Journal of Medicine, testing Aricept in mild cognitive impairment (a possible precursor to Alzheimer's), found that the benefits were present only during the first year of the drug's use. Pharmaceutical companies say Alzheimer's still is their key market, although the potential for expanded use is gaining attention in the industry.

A growing body of literature suggests these drugs may work on other developmental disabilities, such as autism. Aricept, Exelon and a third Alzheimer's drug, Reminyl from Ortho-McNeil, a subsidiary of Johnson & Johnson, also have been tested in autistic individuals. Earlier this year, however, in a trial with patients with mild cognitive impairment 13 elderly patients taking Reminyl died.

Jane Pic Adams heard about an Aricept trial through her work as a columnist on disability issues for a New Orleans newspaper, and enrolled her daughter, Carolyn Pic, who is now 34 years old, in a study at Tulane University. She said her daughter found it hard to express herself and had trouble using sentences of more than four words. During the trial, she said friends, family and instructors all noticed gains in Carolyn's communication skills. "The gains have been small," concedes Ms. Pic Adams, who lives in Metairie, La., "but they are big for us."

That Pfizer-sponsored trial, involving 123 adults at multiple locations, didn't meet its primary goal. But Priya S. Kishnani, co-director of the Down syndrome clinic at Duke University, says there were "trends toward improvement" in communication and memory among many individuals that merit further study. A spokeswoman for Pfizer said, "We plan to share these important preliminary study results with the FDA."

In another study of Aricept published by Duke in 2003 involving six young adults, ages 20 to 41, with Down syndrome, the findings showed improvements in language. But it was a small, open study, where the participants knew they were getting drug. A study at Duke of Aricept given to seven children, ages eight to 13, showed improvements in expressive language, according to the results published last year.

Duke also recently completed a pilot trial of the Novartis drug Exelon, involving 11 adolescents age 10 to 17. They show improvements in language and memory, according to an abstract. Final results of the trial, which was paid for by Novartis, are still being studied. Peter Powchik, head of the neuroscience therapeutic area for U.S. clinical development and medical affairs at Novartis, said the company has agreed to provide the Duke researchers with Exelon for a larger, 36-week trial that may open this year if outside funding can be obtained. That study will have a placebo arm as a control.

In the trials on vitamins, the supplements are being given to adults with Down syndrome, some -- or, in the case of the supplement-cocktail trial, all -- of whom have dementia. One concern for researchers: Some studies have shown that high doses of vitamin E may pose serious health risk.



Tony Maddox

### Blair Williamson

One of the difficulties in evaluating any of these trials' results has been that benefits aren't easy to detect and measure on tests. Blair Williamson, 25, has been taking Aricept since last year. His mother says her son, an actor, is able to say lines in scripts that previously were too difficult for him. Mr. Williamson's doctor, the University of California's Dr. Lott, said the young man's improvements in test scores were very small and not the kind that can be "attributed directly to the medication." Still, for now, Mr. Williamson is being allowed to stay on it.

Many families say it is difficult to get insurance coverage. Mary Ann Dawedei whose 14-year-old son, Eli Lewis, participated in the Exelon trial last year, noticed improvements in his language. He described water as "Caribbean blue, and when he got angry at his older brother, called him "a lummoX," words he had never used before. Their insurer refused to pay the estimated \$300 a month to continue the drug after the trial, and his parents couldn't pay for it. Eli stopped taking the drug in September, and his mother has noticed that "he has retreated into his contented, less-aware self," she said. The language gains she noted haven't remained.

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