NEW TREATMENT FOR GENETIC DISEASE CITED IN NEW ENGLAND JOURNAL
Scripps Clinic Physician is Member of Research Team

LA JOLLA, CALIF. Feb. 20, 1991 -- This week's New England Journal of Medicine reports the successful results of a 13-center international study of recombinant human interferon gamma for the treatment of chronic granulomatous disease (CGD), a genetic disorder affecting some 250 to 400 Americans.

One of the principal investigators was John T. Curnutte, M.D., of Scripps Clinic and Research Foundation, who has specialized in studying and treating CGD patients for 19 years.

Seen primarily in boys, but also in some girls, CGD usually becomes clinically apparent within the first two years of life. Prognosis has previously been poor, but with aggressive antibiotic treatment, some children are now living into their early twenties or thirties.

The one-year study reported in the Feb. 21 issue of the New England Journal found that injections of interferon gamma three times a week reduced the frequency and severity of serious infections, prolonged the interval between infections, and was an effective and well-tolerated therapy for CGD. Of the 128 patients in the study, 25 were seen at Scripps Clinic.

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"The disease is characterized by an inability to fight frequent, serious infections to vital organs such as the lungs, liver or kidneys," Curnutte explained. "Complications from the disease can lead to death."

CGD is usually diagnosed within the first two years of life when parents and physicians notice severe infections that are unusual in babies and children.

"These aren't children who are just cranky with an ear infection," Curnutte said. "We're talking about big time pneumonia or abscesses in the liver."

"I recall a baby girl from Alabama," he continued, "who, within the first few days of life in the newborn nursery, developed fungal pneumonia. In December, I saw a baby from Ohio who had developed pneumonia three different times within the first six weeks of life."

Chula Vista resident Rosa Garcia noticed something was wrong with her baby during his first year of life.

"Ramon always seemed to have a very high fever. I didn't even need to take his temperature; I could feel how hot his head was with my hand," she remembers.

When he was 18 months old, she took him to a series of doctors who couldn't diagnose the cause. One physician discovered that the child had a serious lung infection. Within a short time, the lung collapsed.

"A doctor told me he had cancer and they'd have to take out his lung," Garcia said. "Luckily I took him to other doctors and one diagnosed CGD."

Two years old by this time, Ramon was immediately put on antibiotic treatment, which saved his lung and helped him cope with other serious infections over the years.
In 1988, nine-year-old Ramon entered the Scripps Clinic portion of the interferon gamma studies and since then has been nearly infection-free, his mother says. He attends school and lives as any normal child, while continuing on his interferon gamma therapy.

"Ramon and the other 24 children we saw during the study came to Scripps Clinic for a week while we verified the diagnosis and taught them or their parents how to inject the drug," Curnutte said.

The interferon gamma needs to be injected in the thigh or arm three times a week, indefinitely. "We're not certain when or if the drug can be stopped without losing its beneficial effects," he added.

Now that the 13-center test of the drug has ended, Curnutte plans further studies of interferon gamma with an additional 25 to 30 patients.

"We'll follow them every six months to look at the long-term side effects, if any," he said. "We'll also study the mechanism of the drug's action. If we can discover how interferon gamma works, we may be able to identify additional diseases that will benefit."

Curnutte saw his first CGD patient in 1972 while he was a biochemistry major at Harvard University. Over the years, as he studied to become a doctor, he continued his research on the blood cells of CGD patients. As a physician, he specialized in pediatrics, and as a researcher, he was awarded an additional doctorate in biochemistry.

"By the time I was an intern at Massachusetts General Hospital in Boston, I had developed a reputation for work with CGD patients; doctors were sending their cases to me" he said.

Since 1979, he's seen close to 60 patients from throughout the
United States, with most of those at Scripps Clinic since 1986.

"CGD is a chronic condition, but two factors have led to longer lives for patients of the disease," he said. "Improved antibiotics have given us the ability to treat some very nasty infections, and within recent years more physicians have become aware of CGD so that children are getting antibiotic treatment sooner."

Interferon gamma, administered along with antibiotics, now appears to be the "best therapy for clinical improvement of CGD patients," he continued. "However, there's no reversal of the underlying defect."

At Scripps Clinic, Curnutte is a member of the Department of Molecular and Experimental Medicine and associate director of the General Clinical Research Center, one of 78 centers nationwide funded by the National Institutes of Health to provide experimental therapies.

In June, 1990, Curnutte was presented with the Outstanding Young Investigator Award from the International Congress on Inflammation for his research on chronic granulomatous disease.

Last December, the Food and Drug Administration approved the use of interferon gamma as a treatment for CGD, noting that the therapy "appears to boost the white cells' effectiveness."

A bioengineered form of immune-enhancing substance produced naturally in the body, interferon gamma is developed, produced and marketed by Genentech, Inc., San Francisco, using recombinant DNA technology.

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