'Rotten egg' drug controls rare disease in children

A diagnosis of the rare genetic disease cystinosis used to be a death sentence for a baby or toddler. Now a drug offers much hope.

Clinical trials show the drug cysteamine preserves kidney function in children suffering from cystinosis.

The tests were performed by Jess G. Thoene, M.D., a University of Michigan professor of pediatrics and communicable diseases, and 10 other physicians and scientists. Their research was published in The New England Journal of Medicine.

Cysteamine is "very unpleasant," said Thoene. "It stinks like rotten eggs and has to be taken in liquid form four times a day. Some of the kids just couldn't drink it. Some threw it up."

For the children who could tolerate the drug, it brought results. "We found that the children on cysteamine did not lose kidney function," he said. The best results came when children were started on the drug by their first birthday."

CYSTINOSIS is a rare disease, affecting an average of one child in every 100,000 live births. Thoene, who is also an assistant professor of biological chemistry at U-M Medical School, estimates that 200 children in North America have the disease.

Cystine is one of 20 amino acids present in food and in everyone's body. Persons who have cystinosis, carried by a recessive gene, lack the ability to transport cystine within their cells.

Parents begin to sense something is wrong with their child at the age of about six months, when the baby has a constantly wet diaper and an unquenchable thirst.

Eventually, these children accumulate so much cystine in their cells — up to 100 times the normal amount — that their growth is stunted. The amino acid begins to crystallize in their bone marrow, corneas and kidneys.

In the past, children with the disease died of kidney failure by the age of 10. The only known treatments before cysteamine were long-term dialysis or kidney transplants. Neither technique, however, could help the body get rid of the excess cystine.

"THIS PROJECT has taken a long time, but it's been very exciting — the most rewarding work of my career," said Thoene, who began to research cysteamine with skin cells in 1975 and to do clinical trials in 1978.

Thoene became interested in cystinosis in 1975 while he was conducting research with Jerry A. Schneider, M.D., of the University of California, San Diego. Schneider is one of the co-investigators for the New England Journal article.

Schneider was exploring ways of ridding the tissues of cystine. Thoene began to experiment with the aminothiol compound, cysteamine, on cell cultures of skin cells. The results were positive not only in the cultures but in a young patient who was facing a kidney transplant.

Thoene and Schneider applied to the Food and Drug Administration for emergency Investigational New Drug status for cysteamine. Their application was accepted.

They and other researchers began clinical trials, using the facilities of the clinical research centers at their respective institutions. Of the 93 children who were in the study, 19 eventually dropped out because they couldn't tolerate cysteamine.

MAKING THE drug more palatable by masking its taste and smell is a long-term project which Thoene hopes a drug company will undertake. But he has discovered that it is difficult to interest drug companies in manufacturing drugs for rare diseases, no matter how effective the cure.

"It is frustrating that business decisions take precedence over saving lives," he said, crediting two parties whose help was crucial in continuing the drug trails of cysteamine.

U.S. Rep. Henry Waxman, D-Los Angeles, sponsored the Orphan Drug Act, legislation passed by Congress in 1983 which uses tax incentives to make the business climate more favorable for production of orphan drugs, an expression used to describe drugs for rare diseases. The Generic Pharmaceutical Industry Association Institute for Orphan Drugs gave the researchers a grant to purchase enough cysteamine to finish the clinical trails. But that supply is running out, and a new source of the drug is needed.

THE LONG-TERM impact of cysteamine on cystinosis patients isn't known yet. "Our oldest subject is nine years old, so we don't know what the next decade will bring for them," said Thoene.

Cystinosis is like diabetes — no cure is known. But at least now there is a drug that can help manage the disease.