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Office of Medical Information
The University of Texas Health Science Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235
214/688-3404

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CONTACT: Ann Harrell
OFFICE: 214/688-3404
HOME: 214/520-7509

****Children with cholesterol problem seek treatment in Dallas

DALLAS -- The General Clinical Research Center at The University of Texas Health Science Center at Dallas -- a federally funded "mini-hospital" where pioneering studies in human research are the norm -- is usually a quiet place. However, for the last couple of months its sober halls have rung with the clatter of little feet and the sounds of children's laughter.

For the first time, the Dallas GCRC -- one of 22 National Institutes of Health-sponsored top research units around the country -- has had four children at once as its special guests. They are there because they have a rare genetic disease that causes heart attacks in children or adolescents because of cholesterol buildup in the arteries.

In 1986 the GCRC at the Dallas health science center became known around the world because of the survival of Stormie Jones, a six-year-old girl who is the only survivor of a tandem liver and heart transplant. Stormie, who had been receiving medical care here, returned to the unit for complete metabolic workups over a six-week period following her historic surgery in Pittsburgh by Dr. Thomas Starzl. Again last summer Stormie returned to the GCRC for a complete going-over to determine how her ongoing treatment was progressing under the care of Dr. David Bilheimer, UTHSCD professor of internal medicine, and his associates.

Because Stormie is doing so well, says Dr. Ricardo Uauy, associate professor of pediatrics, she had only a two-week stay in which to play hostess and role model to the three younger patients. Joining Stormie in August were Georgina Elkhoury, 5, a pretty preschooler of Syrian descent who lives with her parents in Venezuela, and Ricardo and Joanna Garcia, 9 and 5 respectively, from San Antonio. The new patients have been sent to the GCRC for diagnosis and treatment for the same condition that Stormie suffers from. It's called homozygous familial hypercholesterolemia, or FH, a rare genetic condition in which the person inherits abnormal genes from both parents.

In the early 1970s Drs. Joseph Goldstein and Michael Brown first unraveled the complicated genetics and biochemistry of this disease, which led to their being awarded the Nobel Prize for Medicine in 1985. Since that time Drs. Bilheimer and Scott Grundy, director of the Center for Human Nutrition at UTHSCD, have been working to further understand and treat the disease. This year the cholesterol researchers have been joined by Uauy, a pediatric nutrition specialist.

Like Stormie, the new patients have no, or almost no, receptors that recognize a form of cholesterol known as low density lipoprotein (LDL) and remove it from the bloodstream. The receptors take the LDL cholesterol into the cells, where it is used in the manufacture of cell wall membranes, hormones and other needed body products.

With no receptors, Stormie's body had no way to remove cholesterol from her blood until she had a liver transplant. Work at UTHSCD by Dr. John Dietschy, professor of internal medicine, had shown that the liver, which is vital in the removal of cholesterol takes up 70 percent or more of LDL cholesterol from the bloodstream. Thus it was felt a liver transplant was necessary to Stormie's life.

Following the transplant, the UT researchers began using a combination of colestipol and Mevinolin, drugs that have proven effective in lowering the cholesterol level in patients with heterozygous FH by stimulating the single normal gene to make more receptors. While final results are not in on the use of these drugs with the homozygous type of FH, Stormie seems to be doing well.

Uauy says that the health science center is being increasingly recognized as a referral center for patients with homozygous hypercholesterolemia. So far all the new patients who have come in for long stays at once are Spanish-speaking. As a native of Chile, Uauy's language skills as well as his medical skills are needed.

(more)

Georgina, who was born in New Orleans because her mother had been referred to a high risk-pregnancy unit there, is picking up English at a fast pace. Before eight-year-old Stormie left the unit to get ready to go back to school, the two were inseparable. Not only did the older child help Georgina with her English, but she comforted her after painful procedures that sometimes must be endured as a part of the research regimen and encouraged her to eat all her metabolically balanced diet.

Uauy is very excited about working with Georgina, who was referred to the GCRC by her New Orleans physicians. Because her mother was familiar with two adolescent heart deaths in her family, she quickly recognized Georgina's xanthomas (wart-like deposits of cholesterol on top of the skin). Georgina, he says, is the first patient the GCRC researchers have had the opportunity to work with who has not already suffered heart damage. Therefore, he believes that the little girl may have an excellent chance of avoiding a transplant in the future if her LDL cholesterol levels can be maintained low enough.

Avoiding transplant surgery for her children is one of the major motivations of Yolanda Garcia, mother of Joanna and Ricardo. "I hope that some other treatment will be able to work so they will not have to have a transplant," she says. Again, xanthomas that didn't go away but kept getting bigger alerted the mother that something was wrong. She took her children to a barrio clinic where the doctor referred them to a dermatologist. A biopsy of the "wart" revealed that it was a cholesterol deposit, and the Garcias were referred to the Dallas GCRC, one of the few places in the country doing this kind of research.

Currently the researchers are working with plasmapheresis as well as experimental drugs in treating the children. The goal of each of these kinds of treatment is to remove as much cholesterol as possible from the blood. The idea of plasmapheresis as a treatment for hypercholesterolemia is to separate the red cells from the plasma outside the body, discarding the patient's plasma and replacing it with a non-cholesterol-containing protein solution. Next, the patient's red cells and the cholesterol-free protein solutions are introduced back into the patient's body.

Uauy says that the new treatment on the horizon is LDL-pheresis. This new treatment, which is being used on a limited basis in Germany and in Japan, where it was developed, is currently awaiting FDA approval in the United States. In LDL-pheresis, the red blood cells and plasma are separated outside of the body, as they are in plasmapheresis. However, in LDL-pheresis the plasma is then passed through a column containing dextran sulfate or antibodies to the protein in LDL. These compounds act as a binder or magnet that attracts and holds the "bad" LDL. The bound LDL is selectively removed from the plasma while other lipoproteins, such as the "good" high density lipoproteins (HDL), are maintained. The patient's cleansed plasma and red blood cells are returned to the patient. Uauy says that the development of these procedures was made possible because of the major cholesterol research done at UTHSCD and a few other outstanding centers.

Another area of cholesterol research that Uauy and his associates want to pursue is the occurrence of hyperlipidemia with no apparent genetic cause. Uauy, whose pediatric background includes neonatology as well as nutrition, an interest that he developed at MIT, is also studying cholesterol regulation in normal infants during the first year of life as affected by the fat composition of the diet.

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Distribution: AA,AB,AC,AF,AG,AH,AI,AK,AM,SC,SL

NOTE: The University of Texas Health Science Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and the School of Allied Health Sciences.