UT SOUTHWESTERN MEDICAL CENTER NEWS

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UT Southwestern researchers investigate predictors for sickle-cell-anemia complications

DALLAS – Feb. 29, 2008 – Researchers at UT Southwestern Medical Center have determined that the level, or saturation, of oxygen in blood could be used to identify children with sickle cell anemia who are at an increased risk of stroke.

In a related study, they have also found that a published method used to predict severe complications of the disease may not be adequate.

"Stroke is a serious but increasingly preventable complication of sickle cell disease," said Dr. Charles Quinn, assistant professor of pediatrics at UT Southwestern and lead author of a study appearing in February's *British Journal of Haematology*. "Several factors have been identified that increase risk for stroke, but better screening tools are still needed."

Hemoglobin is an oxygen-transport protein in red blood cells. People with sickle cell disease, including an estimated 100,000 Americans, have a genetic error affecting their hemoglobin. The defect turns normally soft, round blood cells into inflexible, sickle-shaped cells. The altered shape causes blockages in blood vessels and prevents body tissues from receiving oxygen.

The researchers reviewed the cases of 412 children who are part of the Dallas Newborn Cohort, the world's largest group of patients with sickle cell disease who were initially diagnosed by newborn screening. All patients reviewed were born after Jan. 1, 1990, a date chosen because patient data was available electronically.

Oxygen saturation in the children's blood was tracked over time, and the records of those who suffered a stroke were compared to those who did not. The children who had lower levels of oxygen in their blood were more likely to develop stroke, the researchers found.

"A decline in oxygen saturation over time seems to further increase the risk of stroke," said Dr. Quinn. "Oxygen saturation is easily measured, potentially modifiable and might be used to identify children with sickle cell disease who are at greater risk of having a stroke."

Another study by Dr. Quinn and his colleagues appeared in the January issue of the journal *Blood*. That study examined how effectively a model developed by the Cooperative Study of Sickle Cell Disease (CSSCD) predicted severe disease in the newborn cohort.

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Because sickle cell disease can affect children in many different ways, it is difficult to identify young children who are at high risk of adverse outcomes before irreversible organ damage occurs. Such outcomes include death, stroke, frequent pain or recurrent acute chest syndrome. The CSSCD criteria, which evaluates patients based on factors such as occurrences of dactylitis – a type of painful swelling of the hands and feet – in the first year of life, steady-state hemoglobin concentration in the second year of life, and steady-state leukocyte count in the second year of life, was created in hopes that a predictive model would allow early, tailored therapy to prevent adverse outcomes.

"We found the CSSCD model was not better than random prediction when applied to the Dallas Newborn Cohort," said Dr. Quinn, the *Blood* study's lead author. "Most subjects who experienced adverse events were predicted to be at low risk for adverse events, and no subject who was predicted to be at high risk actually experienced an adverse outcome. We concluded that the model was not clinically useful, at least not in the Dallas cohort."

Dr. Quinn said the findings suggest the CSSCD model should not be used as the sole criterion to initiate early, high-risk intervention and that a robust early prediction model is still needed.

In 2002 UT Southwestern and UT Dallas received a multimillion-dollar five-year grant from the National Institutes of Health that established the Southwestern Comprehensive Sickle Cell Center at UT Southwestern. The first of its kind in the Southwest, the center is directed by Dr. George Buchanan, professor of pediatrics and senior author of the study in *Blood*. The center is one of 10 chosen to form the first national clinical trials network for the disease. The principal clinical site for the UT Southwestern component of the network is located at Children's Medical Center Dallas.

UT Southwestern medical student James Sargent contributed to the *British Journal of Haematology* study. Dr. Zora Rogers, associate professor of pediatrics; Nancy Lee, UT Southwestern medical student; Elizabeth Shull, a research nurse at Children's; and Naveed Ahmad, a statistician at Children's; contributed to the study in *Blood*.

Both studies were supported by grants from the NIH.

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