

High blood pressure, anemia put children with sickle cell disease at risk for silent strokes

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A team of researchers from the Johns Hopkins Children's Center, Vanderbilt University and elsewhere have demonstrated that high blood pressure and anemia together put children with sickle cell disease (SCD) at serious danger for symptomless or so-called "silent" strokes, although either condition alone also signaled high risk.

The results are part of an ongoing NIH-funded international multicenter trial, believed to be the largest study of its kind to date in [children](#) with SCD. A report on the findings is published online Nov. 17 in the journal *Blood*.

In the study, brain MRI scans revealed that nearly a third (31 percent) of 814 children, ages 5 to 15, had suffered [silent strokes](#). None of them had a history of stroke or seizures, and none showed overt stroke signs at the time of the study.

Extremely rare in children overall, stroke is a common neurologic complication in children with sickle cell disease, a genetic disorder marked by the "sickling" or bending of red blood cells that store and distribute oxygen in the body. The misshapen blood cells cause anemia and also clog tiny blood vessels, causing pain, tissue damage and stroke. A stroke can occur when a blood vessel in the brain bursts or leaks ([hemorrhagic stroke](#)) or be caused by [oxygen deprivation](#) ([ischemic stroke](#)), the predominant kind of brain injury in children with SCD.

Overt strokes lead to sudden dramatic symptoms, including excruciating headaches, one-sided paralysis of the face or body and loss of speech or vision. Silent strokes, by contrast, cause none of these overt symptoms but they do cause subclinical brain damage, can lead to learning disabilities and put children who have them at risk for overt strokes and repeat episodes of silent strokes, the investigators said.

The new findings underscore the need to identify early signs of anemia and high [blood pressure](#) because they are modifiable risk factors, the researchers say. The findings also may pave the way for new therapeutic targets for SCD.

"Silent strokes are typically seen in older adults and these findings give us additional insight into why they tend to occur so often in children with sickle cell disease," said senior study investigator James Casella, M.D., director of hematology at Hopkins Children's.

To analyze the interplay between silent stroke and blood pressure and anemia, researchers looked at children's medical histories, neurological exams and levels of hemoglobin, the oxygen carrier of [red blood cells](#). Anemia — defined by low levels of hemoglobin — and high blood pressure drove up the risk separately and incrementally, but the combination of the two carried the highest risk. Children with the highest systolic blood pressure (above 113) and the lowest hemoglobin (below 7.6 g/deciliter) had a nearly four-fold risk of silent strokes compared with children with the highest hemoglobin and the lowest blood pressure.

As blood pressure went up and hemoglobin down, the researchers found, so did the risk of stroke. Incremental changes in hemoglobin and blood pressure corresponded to changes in risk. Children who had the lowest hemoglobin had more than twice the risk of silent stroke, compared with children with the highest hemoglobin levels. Children with the highest

systolic blood pressure had 1.7 times the risk of silent stroke, compared with children with the lowest blood pressure. The risk was particularly high in a tiny subset of children — those diagnosed with hypertension, or persistently elevated blood pressure. In this group, 83 percent (five of six) had suffered silent strokes.

The exact cascade of metabolic events leading to a silent stroke remains unknown, but researchers believe anemia is the key.

All children with SCD are anemic, resulting in lower oxygen in the blood. To cope with this chronic anemia, children and adults with SCD develop a compensatory mechanism in which the brain vessels dilate to improve blood flow and allow more oxygen. In this context, the investigators suspect, even moderate blood pressure elevations can exact further toll on the brain vessels and — when exacerbated by anemia — lead to stroke.

"Our findings underscore the importance of correcting anemia, at least partially, and may thus lay the groundwork for primary prevention of silent stroke," says principal investigator Michael DeBaun, M.D., of Vanderbilt University, the lead author on the current report.

SCD affects nearly 100,000 Americans.

Provided by Johns Hopkins Medical Institutions

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