PERSPECTIVE

Thinking beyond survival

Quality of life has become a vital consideration for children with sickle-cell disease in high-income countries, says **Michael R. DeBaun**.

Children born with sickle-cell disease in high-income countries are now expected to live to adulthood, an improvement in life expectancy that is a major medical advance. In just 19 years, from 1983 to 2002, the mortality rate for sickle-cell disease in children younger than four years old living in the United States dropped[1] by 68%. Adults with the disease can now plan to live until their fifth decade. Yet this transformation from lethal disease to chronic condition has led to new challenges. Children with sickle-cell disease now face long-term health problems, such as stroke and incurable organ damage, and their care is complicated by issues in the home that are unrelated to the condition, such as poverty and parental mental health.

Now that children are living longer, their parents' priorities have shifted from simple survival to long-term, quality-of-life concerns — especially because sickle cell is accompanied by a high risk of brain injury, something that can affect a child's performance in the classroom as well as future employment opportunities. Brain injury occurs when a child has a stroke, which may be the greatest fear held by young people with the disorder and their parents. Because of the tendency for sickled red blood cells to stick together and block blood vessels, blood clots in the brain are a very real risk for children with the condition. These can take the form of overt strokes, which cause familiar, outward symptoms such as paralysis, or of 'silent strokes', which are more specific to people with sickle cell and do not have immediate, obvious effects but can significantly affect behaviour and IQ. Before the end of the Stroke Prevention Trial in Sickle Cell Anemia (STOP)[2] in 1998, approximately 11% of children with sickle-cell disease in high-income countries developed a stroke. The STOP results showed that regular blood transfusions reduce the relative risk of overt stroke by up to 92%. Since this was implemented, overt stroke occurs in just 1% of these children. But preventing strokes using regular blood transfusions comes at a cost: red blood cells contain a lot of iron, and increasing a person's blood volume with transfusions leads to excessive iron stores that eventually require removal through monthly, lifelong chelation therapy.

Unfortunately, although blood-transfusion therapy has proved helpful in preventing overt strokes, there is still no known strategy for preventing silent strokes (although transfusions are effective at preventing further strokes[3]). Today, silent strokes occur in at least 30% of under-14s who have sickle-cell disease. Silent strokes are associated with loss of cognition, which can affect education and employment, and lead to increased risk of further overt and silent strokes.

In addition to its potential effect on the brain, sickle-cell disease can pose serious risks to other vital organs. In the kidneys, it can trigger a condition known as glomerular hyperfiltration disease, which can lead to kidney failure. In the lungs, the disease can cause a life-threatening condition referred to as acute chest syndrome, which causes difficulty in breathing, chest pain and decreased oxygen delivery. Other affected organs include the eyes, causing retinopathy, which leads to blindness, and the heart, in which cardiovascular disease initiated by sickle-cell disease can cause premature death when compared to those without the condition.

REGULAR BLOOD TRANSFUSIONS REDUCE THE RISK OF OVERT STROKE BY UP TO 92%.

ROUTINE VISITS

Such complications result in a lifelong schedule of annual visits to an array of specialists to ensure appropriate disease management, in addition to regular health check-ups. Over a year, a typical ten-year-old with sickle-cell disease who lives in a high-income country will have a visit schedule that includes: a type of ultrasound scan to their head called a transcranial Doppler to determine risk of overt stroke; three or four visits for surveillance of toxicity associated with the only approved sickle-cell medication, hydroxyurea (we recommend hydroxyurea therapy to all our patients with sickle-cell anaemia who are over five years old); annual influenza immunization delivered by the primary care provider; a dental visit as part of routine oral hygiene; an annual ophthalmology visit; and, if the child has a history of wheezing, monitoring for obstructive lung disease.

Such a demanding medical schedule is rarely met by even the most diligent, stay-at-home parent. In reality, the majority of children with sickle-cell disease in the United States come from families in which parents live hand-to-mouth, which has a considerable impact on the biology of the disease. We illustrated this in a recent study, in which we found that a silent stroke was associated with a 5-point drop in IQ, and that having a non-college educated head of household was associated with a 6-point drop[4]. And every extra $1,000 of family income was associated with a 0.33-point increase. Any rigorous approach that evaluates the impact of silent strokes on IQ must also evaluate non-biological factors such as the home environment.

The roadmap for how to decrease childhood mortality from sickle-cell disease has been well established in high-income countries. Our current task is determining how to improve quality of life and decrease associated diseases while incorporating the context of a child's home environment, where poverty and other factors are likely to affect the disease. Both biological and non-biological risk factors must be considered collectively if we expect to not only extend the lives of children born with sickle-cell disease, but also improve their quality of life. ■

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