PERSPECTIVE

We need a global solution

The disparity in outcomes for children with sickle-cell disease in developed and developing countries is an injustice, says **Isaac Odame**.

It has been more than a century since sickle-cell disease was first described in the medical literature, and half a century since its genetic basis was understood at the molecular level. Medical management remains largely suboptimal, however, particularly in low-income countries where the burden of disease is heaviest.

From its origins in sub-Saharan Africa, the Arabian peninsula and the Indian subcontinent, the sickle-cell variant of the haemoglobin gene has spread through the rest of the world. Using geostatistical models, epidemiologists estimate that more than 300,000 babies with two copies of the sickle haemoglobin gene are born every year[1]. This is probably an underestimate, but it provides the best current approximation of populations afflicted with the disease. More than three-quarters of those affected are born in Africa, with half the global burden shouldered by just three countries: Nigeria, India and the Democratic Republic of Congo.

In high-income countries, which house less than 10% of the global burden, early mortality has been significantly reduced over the past few decades, with more than 90% of people with sickle cell surviving beyond 20 years of age. This can be attributed to widespread implementation of a range of interventions, including newborn screening, penicillin prophylaxis (because sickle cell increases susceptibility to pneumococcal infection), pneumococcal vaccination and parental education. By contrast, the World Health Organization (WHO) estimates mortality of those younger than five to be more than 50% in low-income countries, and has estimated that sickle cell accounts for up to 9% of all deaths in children under five in sub-Saharan Africa. Causes of mortality in these patients include malaria-associated severe anaemia, pneumococcal and other bacterial infections. In addition, the disease is associated with significant health challenges including recurrent debilitating pain, chronic anaemia and stroke.

HALF THE GLOBAL BURDEN IS SHOULDERED BY THREE COUNTRIES: NIGERIA, INDIA AND THE DEMOCRATIC REPUBLIC OF CONGO.

LIMITED RESOURCES

In low-income countries, limited resources for diagnosis and treatment, combined with a dearth of government strategies to combat the disease, have led to a paucity of care. This is only compounded by the lack of public understanding of sickle-cell disease, which perpetuates social stigma and myths about disease causation and results in few people seeking appropriate treatment. In 2010, the WHO Regional Office for Africa commissioned a strategy document that spelled out guidelines for actionable steps to combat sickle-cell disease, but these are yet to be translated into government action.

Part of the United Nations' Millennium Development Goals — a decade-long initiative to help the world's poorest citizens — aims to reduce mortality rates among children under five by two-thirds by 2015. Although most countries in Africa have yet to achieve this objective, the initiative has resulted in visible improvements in areas such as nutrition, immunization, management of diarrhoea, malaria control and antibiotic coverage — interventions that are reducing mortality in children under five and causing an epidemiologic transition whereby some children with sickle-cell disease who would have died undiagnosed in early life now survive and need continuing care[2]. So the burden of sickle-cell disease will continue to rise, placing an increasing strain on limited health-care resources. We must find affordable, evidence-based solutions that can be integrated into existing health-care systems to ensure their sustainability.

To address sickle-cell disease in low-income countries requires a number of feasible steps. First, the diagnostic barrier needs to be broken. Current laboratory methodologies are too costly to enable equitable and timely diagnosis. Low-cost, rapid, point-of-care diagnostic tools, which are currently being developed, are needed to facilitate early detection. Second, simple, life-saving interventions should be integrated into primary-care delivery systems[3]. The Gavi vaccine alliance, a public–private global partnership committed to improving access to immunization, has embarked on an initiative to expand primary pneumococcal vaccination that will be beneficial to children with sickle-cell disease in poor countries. Widespread introduction of hydroxyurea — a relatively affordable, disease-modifying drug — would help to improve quality of life and prolong survival. Clinical trials to determine the safety, dosing and effectiveness of hydroxyurea therapy in low-income countries have begun in Africa and are scheduled to end in 2016. If successful, the implementation and distribution could be scaled up using the same methods that proved effective for improving access to antiretroviral therapy for HIV-positive individuals. Research has already shown which interventions are effective. Now, emphasis must shift to implementation so that we can determine how to make them work for every child and adult.

We need public-awareness campaigns to combat stigma and misunderstandings about sickle-cell disease, and to provide opportunities for genetic counselling and initiatives that promote disease avoidance. Many effective interventions are affordable and within grasp if there is a will to act, and civil society and advocacy organizations in these low-income countries should be emboldened to lobby their governments to place sickle-cell disease high on their agenda. Finally, broad public–private partnerships are critical to finding and implementing sustainable solutions that reduce the global burden of the disease. Only then can we hope to bring an end to this century-long injustice. ■

Isaac Odame *is medical director of the Global Sickle Cell Disease Network and professor of Paediatrics at the Hospital for Sick Children and University of Toronto, Canada.*
e-mail isaac.odame@sickkids.ca

1. Piel, F.B. *et al. The Lancet* **381,** 142–151 (2013).
2. Weatherall, D. *et al. Blood* **105,** 921–923 (2005).
3. Aygun, B. & Odame, I. *Pediatr. Blood Cancer* **59,** 386–390 (2012).