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Improving survival for children with sickle cell disease: newborn screening is only the first step

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In this issue of *Paediatrics and International Child Health*, Sabarensé and colleagues report on the newborn screening (NBS) for sickle cell disease (SCD) in Minas Gerais, Brazil.¹ In their cohort of 2591 infants diagnosed with SCD over a 14-year period, they demonstrate an improved but still increased under-5 mortality rate of 7.4%. These data demonstrate the importance and benefits of NBS, but also highlight the need for ongoing sickle cell education programmes for families and health professionals to improve overall sickle cell awareness and care in the community.

SCD is a common and life-threatening inherited haemoglobin disorder which affects over 400,000 infants each year.² Without early identification by NBS and early access to preventive care such as penicillin prophylaxis and pneumococcal vaccination, many infants will die of undiagnosed acute anaemia, pneumococcal sepsis or severe malaria.³ Owing to the protective effect of fetal haemoglobin, infants with SCD are largely protected from clinical symptoms and the life-threatening complications of the disease in the first 6 months of life. However, in the first 6–12 months, fetal haemoglobin levels decrease rapidly and sickle haemoglobin begins to predominate and the clinical manifestations of SCD begin to appear (haemolytic anaemia, dactylitis, acute splenic sequestration crisis). SCD is an excellent disease to identify by NBS because this 6-month window allows for timely identification and retrieval of affected infants, provision of sickle cell education to families and the initiation of important preventive care. Most conditions included in NBS programmes are those for which early identification and initiation of appropriate therapy can be curative, such as congenital hypothyroidism and phenylketonuria (PKU). In contrast, early diagnosis by NBS for SCD reduces early morbidity and mortality, but there is no simple curative treatment for SCD. The optimal management of infants diagnosed by NBS should include a comprehensive care programme with access to medications such as penicillin and hydroxyurea and important vaccinations (*Streptococcus pneumoniae*, *Haemophilus influenzae* type B), safe and available blood transfusion services, and access to screening tests such as transcranial Doppler (TCD) ultrasonography to identify young children at risk of stroke. In addition to the availability of these medications and services, it

is critical to have appropriately trained healthcare personnel, not only in the sickle cell clinic, but also in the emergency department and in the community. General awareness of SCD in the community also needs to be strengthened so that families can become more alert to the signs and symptoms of SCD and the importance of knowing their own carrier status when making reproductive decisions.

In the United States and Europe, in the context of universal or targeted NBS and comprehensive sickle cell care programmes, death of a child with SCD is a rare event with survival to adulthood demonstrated to be as high as 95–99%.^{4,5} The well described Jamaican SCD programme has also demonstrated the benefits that NBS and close follow-up can have upon morbidity and mortality in a lower resource setting.^{6,7} In Brazil, NBS and comprehensive sickle cell care has improved the survival of infants born with SCD, but mortality remains high.^{1,8} These outcomes are all in stark contrast to sub-Saharan Africa where NBS and comprehensive care are largely unavailable, and 50–90% of infants with SCD are likely to die before the age of 5 years of age.³ Because their ministries of health increasingly recognise that SCD is an important public health problem, many African countries are only recently beginning to develop national sickle cell strategies, including pilot NBS programmes.^{9–13} As NBS and comprehensive sickle cell strategies are developed, it will be important for African countries to learn lessons from the sickle cell programme developed in Brazil during the last 15 years.

The Brazilian strategy for the screening and care of infants and children with SCD should serve as a model for developing or limited-resource countries as they design their own sickle cell strategies. The Brazilian health system, including the care of children with sickle cell disease, aims to decentralize the management of these children and to promote close participation by community health centres.¹⁴ The National Newborn Haemoglobinopathy Screening Programme, established by the Brazilian Ministry of Health in 2001, has resulted in reduced early mortality and improved quality of life for infants born with SCD.¹⁵ Specialized sickle cell centres have been developed across the country, including the one in Minas Gerais described in this issue (Hemominas) and another large center in Rio de Janeiro (HEMORIO).^{1,15} The specialized care at these large centres, including the use of hydroxyurea and the introduction of TCD screening, has resulted in significant improvements in morbidity and mortality.^{16,17} However, as has been demonstrated in the sickle cell population of Minas Gerais, this is still not enough.^{1,8} The recognition of SCD as a major public health problem is the first step, and the introduction of a systemic NBS programme is a logical starting point, but any NBS programme must be associated with a careful and systematic sickle cell strategy. This strategy should include a plan for who will care for identified infants. Will penicillin be easily available and affordable? Will the children have access to hydroxyurea and blood transfusion services? Are families adequately educated about SCD and do they know when to seek emergency medical care? When they do seek emergency care, will the healthcare providers in their community know how to appropriately evaluate and treat the acute and life-threatening complications of SCD? True comprehensive care of children with SCD requires a multi-disciplinary team and a reasonable and locally feasible solution to each of the above questions must be addressed as a national strategy is developed. Even a well organized health system with a focused commitment to SCD, such as the one in Brazil, struggles with continued early mortality for

children with SCD. The report in this issue and others are important to highlight the need for continued action to fight the largely unaddressed global burden of SCD, not only in Brazil, but also in the well resourced countries of North America and Europe and in the low-resource countries of sub-Saharan Africa.

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