

## Mobilizing partnerships to impact sickle cell disease in Africa

*Report from a Roundtable Discussion held in parallel with the 2018 World Health Assembly May 22<sup>nd</sup>, Geneva, Switzerland*

### Summary

Sickle cell disease (SCD) is a neglected health problem in sub-Saharan Africa (SSA) where more than half of affected individuals die before their 5th birthday due to preventable complications.<sup>1</sup> In response, a “Sickle-cell anemia” resolution (WHA59.20) was passed at the 59th World Health Assembly in 2006, urging Member States and the WHO Director-General to promote and support actions to address SCD.<sup>2</sup> That was followed in 2010 with adoption by the WHO Regional Office for Africa of “Sickle-cell disease: a strategy for the WHO African Region” (AFR/RC60/8), which offered a comprehensive situation analysis and roadmap for implementing priority interventions.<sup>3</sup>

However, despite these and other major policy achievements, as well as increasing documentation of the substantial disease burden and poor outcomes, the problem of SCD in SSA remains virtually non-existent on the global agenda. While there have been clear areas of investment and action, little progress has been made overall in translating the gains made in high-income countries to resource-limited settings.

This year, in parallel with the 71st World Health Assembly, a half-day roundtable discussion was held in Geneva to discuss ways forward for public-academic-private partnerships to positively impact the health of people living with SCD in Africa.

The gathering involved representatives from national governments, academic institutions, professional associations, philanthropic organizations, a donor agency, and industry. Africa-based clinicians, researchers, and advocates joined from Democratic Republic of Congo, Ghana, Kenya, Nigeria, Tanzania, and Uganda. Additional participants joined from Canada, France, Kuwait, Switzerland, United Kingdom, and the United States. The meeting was chaired by the President of the Sickle Cell Foundation of Ghana, Professor Kwaku Ohene-Frempong, and the Head of Corporate Responsibility at Novartis, Dr. Patrice Matchaba. Opening remarks were delivered by Dr. Leon Tshilolo from the Centre de Formation et d'Appui Sanitaire (CEPA)/ Centre Hospitalier Monkole in DRC. The event was sponsored by Novartis.

The roundtable dialogue was structured in three parts: review of the current status of SCD in Africa; analyses of country-level successes and barriers in tackling the disease; and exploration of potential ways forward in pursuit of sustained advances that will improve and extend the life of individuals with SCD in SSA. Each of the countries represented at the roundtable demonstrated achievements in research, policy, and programming that will help to pave the way for informed action (Box 1). At the same time, there are many outstanding questions (Box 2) that will need to be addressed to achieve sustained improvements for the health of patients with SCD in SSA over the next decade.

### Box 1: Priorities to improve outcomes for individuals with SCD in SSA.

- Pursue government-led efforts to sustain and scale-up evidence-based activities including newborn screening, disease management guidelines, penicillin prophylaxis, immunization, and patient education.
- Call on WHO to promote and support efforts to address SCD, including implementation of the recommendations of the 2006 World Health Assembly “Sickle-cell anemia” resolution.
- Integrate SCD management services into community-based healthcare programs.
- Unite and empower patient groups to help promote self-advocacy and reduce stigma and misconceptions about SCD.
- Identify ways to raise the profile of SCD as a global health priority and influence engagement by international technical organizations, aid agencies, and other stakeholders.
- Address data gaps with targeted research that will directly inform actions to improve patient outcomes.
- Urge national governments to commit to ensuring medicines and treatment are available and affordable for patients with SCD.

### Box 2: Outstanding questions to inform effective research, policy, and patient care.

- What factors will most influence prioritization of SCD on the agendas of national governments in countries in SSA where it is highly prevalent?
- How can SCD services be efficiently integrated into existing health systems?
- What is the entry point for effective and sustained SCD programming at the community level?
- Can universal newborn screening programs be implemented within public systems in SSA?
- In the future will point-of-care newborn screening for SCD be feasible in terms of scale, cost, and public health coordination?
- How can the cost-effectiveness of newborn screening and primary care for individuals with SCD be demonstrated in SSA?
- What are the population health and clinical management research priorities?
- How can traditional misconceptions about SCD be addressed to improve patients’ quality of life and reduce barriers to care?
- How can the ongoing and planned activities by current stakeholders be leveraged to engage new partners to this space?

### Status of sickle cell disease in sub-Saharan Africa

Sickle cell disease is known as the first “molecular disease” (the term was coined in 1949 in relation to SCD) and is a prototypical genetic condition in that a single nucleotide mutation (replacement of adenine with thymine in the beta-globin gene [HBB: c.20A>T] changing codon GAG to GTG on chromosome 11), and leading to substitution of valine for glutamic acid (p.Glu>Val) as the 6<sup>th</sup> amino acid of beta globin, is the root cause of its clinical manifestations.<sup>4</sup> It is a lifelong disease only curable through hematopoietic stem cell transplantation or gene therapy (under clinical trials).

Approximately 80% of individuals with SCD globally live in SSA, where the sickle mutation is thought to have emerged 7,000 years ago.<sup>5</sup> More than 400,000 babies are born with the common types of SCD each year, most in SSA, with the highest numbers in Nigeria and DRC (85,000 and 40,000, respectively).<sup>6</sup> Although data are limited, SCD is thought to account for 5-16% of under-5 mortality in SSA (WHO Report, 2006), and an estimated 75% of patients die before age 5 (range 50-90%). A confounding factor is that SCD is widely under-diagnosed in SSA. The mortality risk appears to be higher in rural areas compared with urban settings.



The burden of SCD, a chronic, life-threatening disease with multiple complications and high demand for medical services, is made worse in low resourced countries with limited healthcare services.

Clinical phenotypes in children under age 5 with SCD in SSA include hand-foot syndrome (dactylitis) and other SCD-related pain episodes, acute anemia, splenic sequestration, overwhelming bacterial sepsis, acute chest syndrome, stroke, and bone infections. A persistent large spleen (hypersplenism) with lower hemoglobin levels is common in children with SCD in SSA, and may be due to persistent malarial parasitemia.

Basic management approaches for patients with SCD include penicillin prophylaxis beginning in infancy, anti-inflammatory and opioid therapy to address pain, maintenance hydroxyurea therapy when indicated, and chronic blood transfusions for patients with or at risk for major complications. Access to these resources in Africa is limited by availability and affordability. Perhaps the most important gap in in SSA is absence of national newborn screening programs and, thus, systematic delivery of preventative care and effective management of complications beginning in early life. No country in Africa has a national newborn screening program while newborn screening routinely takes place in Belgium, Brazil, France, Netherlands, the United Kingdom, and the United States—countries that have much lower rates of babies born with SCD (for example, countries such as France and the United Kingdom each have approximately 400 new cases annually).

Gaps exist in education for both health workers and the public. Health workers will require enhanced training to provide preventative care and to capably manage the numerous medical complications of SCD. For the public, negative misconceptions about the disease remain highly prevalent in some regions (e.g., that SCD is caused by “witchcraft”). These traditional misconceptions need to be addressed so that having SCD is not a shameful experience and patients can be empowered to advocate for themselves and can safely access skilled care when necessary.

The WHO-endorsed policy statements remain highly relevant, and it was noted that if even half of those actions had been implemented up until now, the status of patients with SCD in SSA would be much improved.

### **Country-level successes and barriers**

In Ghana, programs to combat SCD were started in the late 1960s, and the development of a comprehensive medical center to care for patients with SCD was established in the 1970s at Korle Bu Hospital in Accra, the country’s capital. Newborn screening was initiated in the 1990s as a pilot project through a research grant from the US National Institutes of Health through Children’s Hospital of Philadelphia (Ohene-Frempong, P.I.) in collaboration with the Ministry of Health, Noguchi Memorial Institute for Medical Research (Noguchi), University of Ghana, and the Ghana Health Service.<sup>7</sup> The newborn screening program in Ghana was originally conceived to be scaled up in to a national public health program. The Ministry of Health formally inaugurated a National Newborn Screening Programme for SCD in 2010, appointed the Sickle Cell Foundation of Ghana as the Programme Managers, and established Noguchi as the National Newborn Screening Laboratory. However, only 4% of babies born in Ghana each year are currently tested, thereby detecting only a fraction of the 15,000 babies that are estimated to be born with SCD annually. A 5-year (2011-2016) plan was developed with health authorities, with the aim to conduct newborn screening nationally, but for various reasons that has not yet materialized.

Additional efforts ongoing in Ghana are aimed at training nurses and health educators to provide counseling for families affected by SCD, as well as work to improve knowledge about SCD at the community level to help reduce stigmatization. Since 1995, Novartis has engaged in public-private partnerships to help address SCD in Ghana by providing support for international symposia, development of standard treatment guidelines, and development of a mobile app to increase efficiency in data collection and management for newborn screening.

In DRC, a pilot study for newborn screening led to the design of a national program for SCD, but that has so far been limited due to budget constraints. Collaborators from several

countries in Central and East Africa created the Sickle Cell Disease Research Network in Central Africa (REDAC) as a platform to harmonize efforts of scientists and physicians across Central Africa; currently, 12 countries are involved. Centers in DRC (along with Angola, Kenya, and Angola) participated in the REACH (Realizing Effectiveness Across Continents with Hydroxyurea) study to investigate use of hydroxyurea in this context.<sup>8</sup>

In 2014-2015, researchers in Uganda conducted a prevalence study of SCD involving nearly 100,000 HIV-exposed infants across ten regions and 112 districts.<sup>9</sup> The prevalence of SCD and sickle cell trait was as high as 1.5% and 24%, respectively, in some districts. Subsequently, the Uganda Ministry of Health implemented newborn screening in high burden districts, developed standard guidelines for SCD, and established specialized treatment centers.

Nigeria was one of first countries to devise country-specific guidelines for SCD. While these have not yet been widely disseminated, stakeholders are now looking to leverage the Sickle Cell Support Society of Nigeria (SCSSN), a large network of SCD treatment centers, to help distribute guidelines. The SCSSN routinely conducts trainings for health workers and is currently working to incorporate a SCD curriculum into government training programs. The government has invested in equipment and infrastructure for newborn screening and stakeholders are seeking to design a national screening program that would be linked with evidence-based best practices for community-based care of individuals with SCD. Physician-researchers in Nigeria have been exploring various point-of-care testing approaches that could be used by frontline health workers. Two products (Sickle SCAN and HemoTypeSC) have been found technically feasible for clinical use.<sup>10</sup> It was noted that capacity exists in Nigeria for clinical trials of new drug candidates, and indeed the first successful allogeneic hematopoietic stem cell transplant for SCD in Africa took place in Nigeria in 2011 where a transplant center has been established.<sup>11</sup>

In Tanzania, the SCD carrier rate is estimated at 16-21%, and up to 11,000 new babies are born with SCD each year. There have been important recent policy achievements in Tanzania. In 2016, for the first time, SCD was featured in Tanzania's national Non-Communicable Disease Action Plan (2016-2020) as a disease of public health importance. A two year "Newborn screening for SCD" pilot project (funded by DfID) provided a foundation for future newborn screening scale-up, and the MoH has now received a draft newborn screening policy. In 2017, The Tanzania Ministry of Health established a formal SCD Task Force that successfully advocated for inclusion of hydroxyurea in Tanzania's essential drug list and development of draft management guidelines for SCD. Prof. Julie Makani in Tanzania is the Principal Investigator for the NIH-funded Sickle Pan-African Research Consortium (SPARCO), a multi-year program to build and strengthen capacity for SCD-related research and patient care in Africa (SPARCO also includes partners in Ghana, and Nigeria). Another accomplishment in Tanzania has been the involvement of patient groups in advocacy-focused activities.

With respect to barriers to SCD policies and services at the country level, several common themes emerged. Most importantly, national government support for SCD in SSA was reported to be variable. Support from WHO for SCD activities was generally felt to be lacking. WHO was viewed by the group to be an authoritative body that could help to mobilize national governments to implement programs for SCD. In the past, WHO had developed initiatives in hemoglobinopathies through its Human Genetics Program, however, they have been inactive for some time.

Locating children that test positive in newborn screening programs was highlighted by many participants to be a major operational challenge in SSA. In one program it was reported that only 50% of children that screened positive could be traced. Another difficulty encountered with newborn screening is the price of reagents for laboratory testing. The cost of reagents for sites in SSA was reported to be double that in high-income countries. This financial challenge will need to be addressed to help ensure sustainability of newborn screening programs in SSA over the long-term.

A summary of these and other successes and barriers discussed are presented in the Table.

**Table: Successes and barriers for SCD-focused actions in sub-Saharan Africa**

|                  | <b>Patient awareness &amp; advocacy</b>                                | <b>Screening and diagnosis</b>                                  | <b>Treatment and prevention of complications</b>                                    | <b>Government ownership and policies</b>   | <b>Funding</b>  |
|------------------|--|---|---|--|---|
| <b>Successes</b> | National SCD networks established in multiple countries                | Newborn screening programs implemented in multiple countries    | Research completed and ongoing to study efficacy and safety of hydroxyurea          | Several governments have been mobilized by prevalence data to implement evidence-based interventions | Support given from European Union and some Foundations                      |
|                  | REDAC regional SCD network established in Central Africa               | Research conducted on point-of-care testing methods             | Trainings for health workers and the public established in multiple countries       | Guidelines and Task Force developed in some countries  | Screening programs increased access to pneumonia vaccination                |
|                  | Lessons learned from Thalassemia advocacy efforts                      |   | Lessons learned from Brazil's integrated newborn screening and patient care program | Equipment and infrastructure for SCD-related services acquired or planned                            |   |
| <b>Barriers</b>  | Lack of sustained advocacy, particularly involving patients themselves | No national screening in any country in Africa                  | Absence of specialized SCD centers outside of major cities                          | Low sustained engagement   | Lack of global funding mechanism  |
|                  | Stigma associated with carrier status and disease                      | Challenges in tracing diagnosed patients                        | Limited knowledge and education among providers                                     | Lack of dedicated budget   | Lack of cost-effectiveness studies provide evidence for SCD control efforts |
|                  | Low trust in the healthcare system                                     | Newborn screening rarely conducted at community level           | Affordability of medicines (e.g., cost of hydroxyurea)                              | Data gaps to inform priority activities  |   |
|                  | Low levels of health literacy  | Costs of newborn screening services, equipment, and consumables | Focus on treatment services and not on preventative and public health               | Lack of end-to-end coordination  |   |
|                  |  |   |   | Lack of WHO and other international support  |   |



## Ways forward to achieve sustained impact

The roundtable participants advocated for the following approaches to achieve long-term gains in population health for SCD patients in SSA.

### 1. *Seek government ownership and greater involvement by WHO.*

Government involvement and promotion of activities by WHO was felt to be instrumental to achieving scale and sustainability for SCD programs in SSA. New programs must be integrated with established systems of care. While public-academic-private partnerships have important roles to play, ultimately national governments must be fully invested and provide oversight in order for programs to be maximally impactful.

### 2. *Prioritize the identification of individuals with SCD and tightly link diagnosis with comprehensive SCD patient care services.*

The optimal period to diagnose individuals with SCD is in early infancy so that penicillin prophylaxis can be initiated by 3 months of age and so families can be educated to provide vigilant care at home. Systematic diagnostic approaches can be achieved by screening at the time of birth or by testing at immunization visits. Just as essential as diagnosing patients is to enroll them in a comprehensive SCD management program. Brazil was highlighted as a country that has efficient universal newborn screening linked with comprehensive primary, secondary, and tertiary services for children with SCD. Lessons learned from Brazil and other regions could be leveraged to help design similar programs in SSA. It was noted that there are other metabolic problems in Africa besides SCD that also often go undiagnosed (e.g., congenital hypothyroidism). Newborn screening for SCD in SSA could therefore help to pave the way to newborn screening for other conditions, as well.

### 3. *Integrate SCD services into community-based care programs.*

There was wide consensus that SCD care must be brought to community settings, including in rural areas, since it is not feasible to conduct all diagnostic and treatment activities at small numbers of referral medical centers. If practical point-of-care diagnostic modalities for use in the community are not currently available, then it was suggested that greater investment is urgently needed for their development. It was acknowledged that health systems at the community level may not at this time be sufficiently robust to deliver comprehensive care for SCD patients and will need to be strengthened accordingly. A natural first step may be to clearly define what needs to be done for SCD patients at the primary level. This line of thinking was supported by a donor representative who remarked that vertical approaches for specific diseases are increasingly difficult to fund and so an integrated model for SCD services should be pursued wherever possible.

### 4. *Empower patients to advocate for themselves.*

Patient-led advocacy groups have already been established in multiple countries with notable successes. It was observed that these groups are strong but somewhat fragmented, which may hamper their impact, and there remains to be opportunities to empower SCD patients to advocate for themselves. Several roundtable participants are currently working to establish an international Federation for SCD that would incorporate a patient-driven organizational structure as a key component. Lessons from patient organizations in other disciplines (e.g., thalassemia) suggest that such groups can have a powerful voice that leads to action.

### 5. *Carefully consider how the problem of SCD should be framed in the context of global burdens of disease.*

There was discussion about how best to position SCD as a global health issue. This question was felt to have important implications for public health policy relating to SCD that might influence engagement of additional stakeholders in the global health ecosystem (e.g., public research funders, bilateral aid agencies, United Nations organizations, donors, etc). Dialogue specifically touched on whether SCD should be characterized in the group of non-communicable diseases (NCDs). Some viewed it as a double-edged sword with advantages



(e.g., NCDs are currently receiving major global attention) and disadvantages (e.g., the NCD field is crowded; SCD has unique status as a purely genetic disease). Dr. John Gyapong from Ghana shared his experience in addressing lymphatic filariasis for many decades and noted that the inclusion of that disease in the group of WHO-defined “Neglected Tropical Diseases” helped to mobilize resources that had not been previously available.

6. *Fill data gaps with research that will directly inform improved patient outcomes*

Many data gaps exist that prevent informed interventions to improve health for people with SCD at both population and individual levels. Also, it was noted at the workshop that a common approach to beginning new health programs, including for SCD in SSA, is to start with a small-scale “pilot project” with the intention that it will lead to broader implementation, guidelines, or policies. It was remarked that, unfortunately, too often implementation efforts end after the pilot experience without larger gains (e.g., national level programming) ever being realized.

## **Annex: List of participants**

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