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Sickle-cell anaemia

Report by the Secretariat

PREVALENCE OF SICKLE-CELL ANAEMIA

1. Sickle-cell anaemia is a common genetic condition due to a haemoglobin disorder – inheritance of mutant haemoglobin genes from both parents. Such disorders, mainly thalassaemias and sickle-cell anaemia, are globally widespread. About 5% of the world's population carries genes responsible for haemoglobinopathies and each year about 300 000 infants are born with major haemoglobin disorders – in more than 200 000 cases sickle-cell anaemia in Africa.

2. Sickle-cell anaemia is particularly common among people whose ancestors come from sub-Saharan Africa, India, Saudi Arabia and Mediterranean countries, and migration raised the frequency of the gene in the American continent. In some areas of sub-Saharan Africa, up to 2% of all children are born with the condition. In broad terms, the prevalence of the sickle-cell trait (healthy carriers who have inherited the mutant gene from only one parent) ranges between 10% and 40% across equatorial Africa and decreases to between 1% and 2% on the north African coast and <1% in South Africa. This distribution reflects the fact that sickle-cell trait confers a survival advantage against malaria and that selection pressure due to malaria has resulted in high frequencies of the mutant gene especially in areas of high malarial transmission. In west African countries such as Ghana and Nigeria, the frequency of the trait is 15% to 30% whereas in Uganda it shows marked tribal variations, reaching 45% among the Baamba tribe in the west of the country.

3. Frequencies of the carrier state determine the prevalence of sickle-cell anaemia at birth, which may thus be estimated and predicted. For example, in Nigeria, by far the most populous country in the subregion with about 120 million inhabitants, 24% of the population are carriers of the mutant gene and the prevalence of sickle-cell anaemia is about 20 per 1000 births. This means that in Nigeria alone, more than 100 000 children are born annually with sickle-cell anaemia.

4. The sickle-cell gene has become common in Africa because the sickle-cell trait confers some resistance to falciparum malaria during a critical period of early childhood, favouring survival of the host and subsequent transmission of the abnormal haemoglobin gene. Although a single abnormal gene may protect against malaria, inheritance of two abnormal genes leads to sickle-cell anaemia and confers no such protection, and malaria is a major cause of ill-health and death in children with sickle-cell anaemia. There is increasing evidence that malaria not only influences outcome but also changes the manifestations of sickle-cell anaemia in Africa.

5. The public health implications of sickle-cell anaemia are obvious as it causes either death or disability. Its impact on human health may therefore be assessed against the yardsticks of infant and

under-five mortality. As not all deaths occur in the first year of life, the most valid measure is under-five deaths. Although an increasing proportion of affected children now survive past five years of age, they have a chronic disease and remain at risk of premature death. When health impact is measured by under-five mortality, sickle-cell anaemia contributes the equivalent of 5% of under-five deaths on the African continent, more than 9% of such deaths in west Africa, and up to 16% of under-five deaths in individual west African countries.

6. In the United States of America median survival was estimated in 1994 to be 42 years for men and 48 years for women, whereas comparable figures for Jamaica published in 2001 suggested 53 years for men and 58.5 years for women. In Jamaica, the greatest mortality occurs between 6 and 12 months old when 10% of patients die despite considerable experience in the diagnosis and therapy of the condition and absence of malaria. There are, however, no firm data on the survival of patients with sickle-cell anaemia on the African continent. In sub-Saharan Africa mortality will be much higher, and in some areas estimates derived from the age structure of populations attending clinics suggest that half of those with sickle-cell anaemia have died by the age of five years usually from infections including malaria and pneumococcal sepsis, and from the anaemia itself.

CLINICAL FEATURES

7. Sickle-cell anaemia covers a wide spectrum of illness. Most affected people have chronic anaemia with a haemoglobin concentration of around 8 g/dl. The main problems arise from the tendency of the red blood cells to become sickle-shaped and block capillaries at low oxygen tension. In children, sickle-shaped red blood cells often become trapped in the spleen, leading to a serious risk of death before the age of seven years from a sudden profound anaemia associated with rapid splenic enlargement or because lack of splenic function permits an overwhelming infection. Between 6 and 18 months of age affected children most often present with painful swelling of the hands and/or feet (hand-foot syndrome). Survivors may also suffer recurrent and unpredictable severe painful crises, as well as “acute chest syndrome” (pneumonia or pulmonary infarction), bone or joint necrosis, priapism or renal failure. For most patients the incidence of complications can be reduced by simple protective measures such as prophylactic administration of penicillin in childhood, avoiding excessive heat or cold and dehydration, and contact as early as possible with a specialist centre. These precautions are most effective if susceptible infants are identified at birth. Some patients have such severe problems that they need regular blood transfusion and iron-chelation therapy. This situation together with the changing manifestations of sickle-cell anaemia in Africa (see paragraph 4 above) create an urgent need to develop models of care appropriate to the management of the disease in sub-Saharan Africa.

MANAGEMENT

8. In most countries where sickle-cell anaemia is a major public health concern, its management has remained inadequate, national control programmes do not exist, the basic facilities to manage the patients are usually absent, systematic screening is not a common practice and the diagnosis is usually made when a patient presents with a severe complication. Simple, cheap and very cost-effective procedures such as the use of penicillin to prevent infections are not available to most patients in many countries.

9. The most important challenge is, thus, to improve the prospects for the patients with sickle-cell anaemia in developing countries. The main aspect of comprehensive care for patients is early intervention for preventable problems with pain medication, antibiotics, nutrition, folic acid

supplementation and high fluid intake. Treatment with hydroxyurea has reduced many of the major complications. There is evidence that the neonatal screening for sickle-cell anaemia, when linked to timely diagnostic testing, parental education and comprehensive care, markedly reduces morbidity and mortality from the disease in infancy and early childhood. Even well-organized holistic care including expert counselling and access to needed care, irrespective of patients' ability to pay, can significantly reduce illness and deaths and improve the quality of lives of people living with sickle-cell anaemia in developing countries, Nigeria being a case in point.

10. Over the past 10 years, progress has been made in several respects: long-term treatment with hydroxyurea has decreased the rate of painful crises and thus improved the quality of life of patients with sickle-cell anaemia; imaging studies help in the prompt management of life-threatening complications, such as stroke and the chest syndrome; bone marrow transplantation, although not free of risk and not available for all patients, can cure sickle-cell anaemia; regular blood-transfusion programmes associated with iron chelation can prevent complications; gene therapy has been carried out successfully in animal models, but has yet to be tested in clinical trials in human subjects. Consequently, it is possible to provide a better quality of life, and, in some cases, a definitive cure for patients with sickle-cell anaemia. However, these advances, which are mainly applicable in high-resource countries, have unfortunately widened the gap in terms quality of life between patients in developed countries and those in developing countries, and that gap can be reduced only through a general improvement in health services.

PREVENTION

11. Sickle-cell anaemia can be prevented. Couples at risk of having affected children can be identified by inexpensive and reliable blood tests; chorionic villus sampling from nine weeks of pregnancy can be performed for prenatal diagnosis. Adoption of such measures goes hand-in-hand with pertinent health education. However, prenatal diagnosis can raise ethical questions which differ from one culture to another. Experience has clearly shown that genetic counselling coupled with the offer of prenatal diagnosis can lead to a large-scale reduction in births of affected children. The risk of having affected children can be detected before marriage or pregnancy; however, to do so requires a carrier-screening programme. There is extensive experience with such programmes in low- and high-income countries. For example, in the case of thalassaemia prevention, unmarried people in Montreal (Canada) and the Maldives are offered screening, premarital screening is national policy in Cyprus and the Islamic Republic of Iran, and pre-reproductive screening is emphasized in Greece and Italy. These approaches should be practiced in conformity with the three core principles of medical genetics: the autonomy of the individual or the couple; their right to adequate and complete information; and the highest standards of confidentiality.

12. The manifestations of sickle-cell anaemia are more unpredictable and variable than those of thalassaemias. Many affected individuals, however, have a good quality of life, and in some parts of the world (Bahrain, India, eastern Saudi Arabia) additional genetic factors reduce the severity of the disorder. Neonatal diagnosis allows provision of simple protective measures, including information for the parents, prophylaxis with penicillin and antimalarial treatment, all giving a better quality of life for the affected children. Neonatal diagnosis is useful only when there is appropriate counselling for the parents and adequate primary care for those affected.

13. The availability of diagnosis and treatment inevitably leads to a cumulative increase in numbers needing care, as patients live longer. The other usual consequence is an increase in annual cost per patient, which can have serious implications on countries, especially those with limited resources.

14. In view of the scale of the public health problem, a comprehensive approach to prevention and management of sickle-cell anaemia is urgently needed. At present, a large proportion of the African population receives no attention or care for this disease. As with all chronic disorders, improved management creates a cumulative demand for more services. Surveillance and education must be delivered at the community level through the primary health care system so as to increase public awareness of the problem and lengthen the survival of affected individuals.

RECOMMENDED ACTIVITIES

15. The model of a national control programme developed in high-resource countries is obviously not appropriate for most low-resource settings. Nevertheless, sickle-cell disorders should be covered by health-service planning in all countries where they are common. All components of prevention and treatment should be considered together, existing initiatives should be supported, and services should be introduced gradually starting with areas where this is most feasible. Systematic gathering of information on the most cost-effective approaches for prevention and treatment should be promoted. Therefore, essential areas of work should cover prevention and counselling, early detection and treatment, surveillance and research, and community education and partnership.

16. In areas where sickle-cell anaemia is common, dedicated centres are required in order to ensure adequate services for prevention and treatment. Ideally, the disease should be identified at birth as part of a screening programme or neonatal diagnosis and affected individuals urged to attend a centre periodically for evaluation. A close working relationship between the primary-care provider and the centre is essential for appropriate care. Staff in the centre should facilitate the formulation of effective national programmes that are integrated into the national health services, draw up guidelines and educational materials, and initiate and cooperate with national parent patient associations. Regional working groups of experts on the management of sickle-cell disorders are urgently required to cooperate with and coordinate the activity of such centres. There is enough evidence showing that even in countries with limited resources, relatively simple measures, such as counselling patients and parents (including education about preventive health and nutrition), prompt treatment of illness, free provision of vitamin supplements and malarial prophylaxis, can significantly reduce the incidence of illness and number of premature deaths from sickle-cell anaemia.

17. Activities for management of patients with sickle-cell anaemia should be based at the primary health-care level, with emphasis on programmes that use simple, affordable technology and reach a large proportion of the community. Examples include: public education, detection of genetic risks in the community by recording family history and on every contact of the patient with the health system paying due attention to that history, health and genetic counselling, and immunization against infections. The personnel involved in medical care will most likely be primary health-care practitioners with task-oriented basic training in sickle-cell anaemia. In order to accomplish these activities, primary health-care providers should have adequate links with secondary and tertiary levels of care for consultation.

18. Research and surveillance are important for planning and evaluating appropriate interventions. There is a need to study the natural history of sickle-cell anaemia in order to document the effects of malaria on clinical manifestations and gain knowledge that will be essential for the development of appropriate models of health care. A stepwise approach to surveillance and monitoring of sickle-cell anaemia and its risk factors is required in order to collect data for better decision-making and technical collaboration with countries, especially those with limited resources. A comprehensive surveillance

system also provides data on the effect of prevention, treatment and care that are essential for priority setting especially in low-resource countries.

19. In resolution WHA57.13, the Health Assembly urged Member States to mobilize resources for action on genomics and world health, and in May 2005 the Executive Board took note of the Secretariat's report on control of genetic diseases.¹ Subsequently, the Assembly of the African Union at its Fifth Ordinary Session (Sirte, Libyan Arab Jamahiriya, 4-5 July 2005) supported the inclusion of sickle-cell anaemia in the list of public health priorities.² In recent years, several nongovernmental organizations have emerged in Africa, such as the international *Fédération des associations de lutte contre le drépanocytose en Afrique*, which brings together many bodies including the Federation of Sickle Cell Clubs of Nigeria. National associations exist in Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Congo, Ghana, Guinea, Mali, Niger, Nigeria, Senegal and Togo. Further partnerships at national, regional and global levels and high-level advocacy are needed to ensure that governments of affected countries and international aid agencies are fully aware of the extent of the problem and pay attention to sickle-cell anaemia.

ACTION BY THE EXECUTIVE BOARD

20. The Executive Board is invited to note the report and to provide guidance.

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¹ Document EB116/2005/REC/1, summary record of the first and second meetings.

² Assembly/AU/Dec.81 (V).