Chapter 31

Newborn Screening for Sickle Cell Disease: Socio-Ethical Implications

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Introduction

Newborn screening is now integrated into routine neonatal practice in many parts of the world, and the overall ethical acceptability of newborn screening programmes is well recognised.[1] Although the procedure corresponds in essence to genetic screening, it is seldom referred to as such and is often categorised as a public health disease prevention programme aimed at early detection and treatment of asymptomatic newborns affected by specific treatable disorders. Accordingly, the overall ethical issues that have been dealt with extensively in the context of medical genetics, such as the principle of autonomy and the requirement for informed decision-making, have been considered less significant with regard to publicly mandated newborn screening, because these newborn public health programmes are believed to be implemented in the paediatric interests of children and therefore override the need for an explicit or written informed consent.[2] The WHO considers that newborn screening should be mandatory if early diagnosis and treatment will benefit the newborn.[3]

As scientific and genetic technologies advance, classical newborn screening programmes aimed at detecting only preventable diseases are now being revisited and expanded. In some countries, they are being redesigned to include new disorders which are not in total compliance with the long-established WHO criteria of conditions suitable for screening.[4] Using the same blood sample collected to screen

1 Kerruish, N.J. and, Robertson, S.P., 'Newborn Screening: New Developments, New Dilemmas', (2005) 31 *J. Med. Ethics*, 393-8.

2 Laberge, C., Kharaboyan, L. and Avard, D., 'Newborn Screening, Banking, and Consent',

(2004) 2(3) *GenEdit*, available at: http://www.humgen.umontreal.ca/int/GE/en/2004-3.pdf.

3 World Health Organization (WHO), *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services*, Geneva, December 15 and 16, 1997, available at: http://whqlibdoc.who.int/hq/1998/WHO_HGN_GL_ETH_98.1.pdf (accessed 11/08/04).

4 Wilson, J. and Jungner, G., *Principles and Practice of Screening for Disease*, Geneva, World Health Organization (Public Health Paper), 1968.

for classical disorders like phenylketonuria (PKU) and congenital hypothyroidism, laboratories are now able to examine DNA and test newborn bloodspots for conditions which are still not treatable, to identify a genetic predisposition not manifested until adulthood, to indicate genetic susceptibility to common multifactorial diseases and, finally, to reveal incidental results such as carrier status for both treatable diseases and untreatable conditions.

There are many disorders currently being considered for inclusion in newborn screening programmes, such as inborn errors of metabolism,[5] cystic fibrosis,[6] muscular dystrophy,[7] and Type I diabetes.[8] Here we will focus on one illustrative example: newborn screening for sickle cell diseases (SCD). Sickle cell disease is an example of a genetic condition that is considered a global health problem. Increasingly, industrialised countries are integrating sickle cell disease into their newborn screening programmes.[9] Screening for SCD can occur during the prenatal or neonatal period. In this chapter we will focus on neonatal screening.

Although sickle cell disease can be treated through early detection and supportive therapies, neonatal screening for sickle cell disease is controversial and raises new challenges. Screening programmes provide clinical advantages, but there is also the risk of harm. In particular, there are three socio-ethical issues we would like to explore. First, as a result of neonatal screening and without having requested the information, we can identify carriers of the sickle cell trait at a time when concern about carrier status may not be a priority. Second, there are a number of approaches to neonatal screening for SCD. For example, infants can be screened on a selective basis (only high-risk infants) or by using a universal approach (all newborns). The issue of whether a programme screening for SCD should be universal or selective raises concerns about equity, the risk of discrimination and cost. Third, given the trend to promote community engagement, and the mounting pressure from advocacy groups to expand newborn screening programs, a decision to introduce newborn screening for SCD must proceed with careful consideration of the relevant ethical and social issues. This chapter does not discuss SCD newborn screening as part of the overall newborn screening programme or whether it should be integrated with the current neonatal screening programmes.

In the first part of this chapter, we will examine the rationale for sickle cell screening, including background, prevalence, and program description. This will be

5 Seymour, C.A., Thomason, M.J., Chalmers, R.A., *et al*., 'Newborn Screening for Inborn Errors of Metabolism: A Systematic Review', (1997) I *Health Technology Assessment*.

6 Wald, N.J. and Morris, J.K., 'Neonatal Screening for Cystic Fibrosis', (1998) 316 *B.M.J*., 404-405.

7 Parsons, E.P., Bradley, D.M. and Clarke, A.J., 'Newborn Screening for Duchenne Muscular Dystrophy', (2003) 88 *Arch. Dis. Child*, 91-92.

8 Bennett, J.S., Baughcum, A.E., Carmichael, S.K., She, J.X. and Schatz, D.A., 'Maternal Anxiety Associated with Newborn Genetic Screening for Type 1 Diabetes', (2004) 27 *Diabetes Care*, 392-7.

9 Weatherall, D.J. and Clegg, J.B., 'Inherited Haemoglobin Disorders: An Increasing Global Health Problem', (2001) 79 *Bulletin of the World Health Organization*, 704-12.

followed by a discussion of ethical and social issues, such as the identification of carriers, the constraints of using selective or universal approach for such programmes, and the pressures exerted on decision-makers by advocacy groups.

The Rationale for Neonatal Screening of Sickle Cell Disease

Background

Sickle cell disease (SCD) consists of a group of life-threatening, genetically inherited disorders, characterised by large amounts of abnormal haemoglobin in the red blood cells. Most infants with SCD are healthy at birth and become symptomatic later, in infancy or childhood. Affected infants generally present clinically during infancy or early childhood with painful swelling of the hands and feet (dactylitis), pneumococcal sepsis or meningitis, severe anaemia and acute spleen enlargement, acute chest syndrome, pallor, jaundice, or splenomegaly.[10] The long-term consequences of SCD include chronic organ damage, such as degeneration of the kidneys, bones and joints, and chronic pain and disability, which compromise quality of life. These persons live under the possibility of early sudden death related to the disease[11] and the lifespan varies between 42 years for males and 46 years for females.[12]

With the exception of bone marrow or stem cell transplantation, only available for a limited number of patients with compatible donors, there is currently no definitive cure for SCD.[13] Nevertheless, improvements in the medical care of children with SCD have increased their life expectancy and studies have shown that prognosis for patients has improved considerably through early diagnosis and treatment such as the early use of prophylactic penicillin and ongoing effective management of infections in children with the condition.[14]

Prevalence

The disease mostly affects people whose ancestors are from Africa but is also prevalent in people of Mediterranean, Caribbean, South and Central American,

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10 American Academy of Pediatrics (AAP), 'Health Supervision for Children with Sickle Cell Disease – Policy Statement', (2002) 109(3) *Pediatrics*, 526-35.

11 Thomas, V.J. and Taylor, L.M., 'The psychosocial experience of people with sickle cell disease and its impact on quality of life: Qualitative findings from focus groups', (2002) 7 *British Journal of Health Psychology*, 345-63.

12 Quinn, C.T., Rogers, Z.R., Buchanan, G.R., 'Survival of children with sickle cell disease', (2004) 103(11) *Blood*, 4023-7; Platt, O.S., Brambilla, D.J., Rosse, W.F., Milner, P.F., Castro, O., Steinberg, M.H., *et al.*, 'Mortality in sickle cell disease: Life expectancy and risk factors for early death', (1994) 330 *New England Journal of Medicine*, 1639-43.

13 Weatherall, Clegg, *loc cit*.

14 Ballas, S.K., 'Sickle Cell Disease: Clinical Management', (1998) 11 *Clinical Haematology*, 185-214.

Middle Eastern and Indian ancestry.[15] The population at risk of SCD in Canada is unknown, and there are no available statistics to show whether there has been an increase in sickle cell disease in Canada over recent years as a result of increased migration.[16] Estimates indicate that, in the United Kingdom, the prevalence of sickle cell disease and other haemoglobinopathies (genetically inherited disorders of haemoglobin) amongst newborns is now higher (1:2380) than cystic fibrosis (1:2500),[17] a disease that is predominantly prevalent in Caucasian populations[18] and that has received much more attention than SCD.[19]

Types of Screening Programmes

Newborn screening aims to identify affected infants and begin preventive treatment before disease manifestation. Outside of Canada (e.g. in the US, the UK and France), newborn screening for sickle cell disease has generally been accepted as an effective intervention. However, an important drawback is the lack of consistent policies for SCD screening.[20] For example, Wertz reported that in the United States, where programmes for sickle cell anaemia screening exist, differences exist among primary care physicians in the commitment to, and acceptability of, screening of all newborns, with 71 percent of paediatricians, 46 percent of obstetricians, and 40 percent of family practitioners agreeing that at risk groups should be screened.[21]

Neonatal screening programmes can be offered universally or selectively. Universal screening is generally considered a routine public health intervention offered to the entire newborn population or to all pregnant women. In fact, universal neonatal screening for SCD has been implemented in most of the United States[22] and in all of England as of April 2005.[23] In contrast to universal screening, selective or targeted screening concentrates on subpopulations with the aim of identifying high-risk infants and, indirectly, of identifying high-risk parents to offer them the opportunity of screening in future pregnancies.

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15 American Academy of Pediatrics, *supra* note 10.

16 D. Soulières, hematologist, personal communication.

17 Streetly, A., *Policy Decision for Implementing Neonatal Screening for Sickle Cell Disease*, NHS Sickle & Thalassaemia Screening Programme, 2002.

18 Parsons, Bradley, *supra cit.*, note 7.

19 Kmietowicz, Z., 'Screening for Sickle Cell Disease and Thalassaemia Saving Lives', (2004) 329 *B.M.J.*, 69.

20 Streetly, A., 'A National Screening Policy for Sickle Cell Disease and Thalassaemia Major for the United Kingdom', (2000) 320 *B.M.J.*, 1353-4.

21 Wertz, D., 'Ethical Issues in Pediatric Genetics', (1998) 6 *Health Law Journal*, 3-42.

22 National Newborn Screening and Genetics Resource Center (NNSGRC), *U.S. National Screening Status Report*, Austin, July 5, 2004, http://genes-r-us.uthscsa.edu/nbsdisorders.pdf (accessed on 03/08/04).

23 NHS Sickle Cell and Thalassaemia Screening Programme, *Policy for Newborn Screening*, London, July 2004, http://www-phm.umds.ac.uk/haemscreening/Documents/NewbornScreeningPolicy.pdf (accessed on 04/08/04).

The decision whether to adopt a universal or selective strategy rests with public health authorities and involves complex arguments about the risk of discrimination, equity, and cost-effectiveness.[24] Although deciding on a screening approach is not an easy task, long-standing principles have been established to guide policy-makers in their decision-making.

Perhaps the most cited source of screening criteria are the 1968 Wilson and Jungner principles of early disease detection.[25] Essentially, they prescribe that conditions that are screened for should present an important health problem (i.e. be relatively prevalent); that an acceptable treatment be available to treat the screened condition; that facilities for diagnosis and treatment be widely available; that the cost (including diagnosing and treating patients) be economically balanced in relation to possible expenditure on medical care as a whole; and that diagnosed patients benefit from timely follow-up services.

A condition that complies with the above criteria is suitable for universal newborn screening. Although there is no definitive cure for SCD, it does fit the 1968 criteria: increased survival and health development of children with the condition is largely attributed to neonatal screening with prompt prophylactic penicillin treatment and to the effective management of infections.[26],[27],[28] Because of this, the establishment of a newborn screening programme for sickle cell disease has been described as justifiable and unquestionable.[29] Accordingly, since the publication of the NIH consensus statement on mandatory newborn screening for haemoglobinopathies in 1987,[30] 48 American states as well as the District of Columbia have implemented universal newborn screening programmes for SCD.[31] Moreover, as of April 2005, all babies in England are being screened for SCD as part of the centralized newborn programme, which screens for phenylketonuria (PKU) and congenital hypothyroidism.

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24 Aspinall, P.J., Dyson, S.M. and Anionwu, E., 'The Feasibility of Using Ethnicity as a Primary Tool for Antenatal Selective Screening for Sickle Cell Disorders: Pointers from Research Evidence', (2003) 56 *Social Science & Medicine*, 285-97.

25 Wilson, Jungner, *supra cit.*, note 4.

26 Zeuner, D., Ades, A.E., Karnon, J., Brown, J., Dezateux, C. and Aninowu, E.N., 'Antenatal and Neonatal Haemoglobinopathy Screening in the UK: Review and Economic Analysis', (1999) 3(11) *Health Technology Asessment.*

27 Davis, S.C., Cronin, E., Gill, M., Greengross, P., Hickman, M. and Normand, C. 'Screening for Sickle Cell and Thalassaemia: A Systematic Review with Supplementary Research', (2000) 4(3) *Health Technology Assessment*.

28 NIH Consensus Development Program, *Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies: National Institutes of Health Consensus Development Conference Statement*, April 6-8, 1987, http://consensus.nih.gov/cons/061/061_statement.htm (accessed on 14/09/04).

29 Streetly, *supra cit.*, note 20.

30 Consensus Conference, 'Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies', (1987) 258 *J.A.M.A.*, 1205-9.

31 National Newborn Screening and Genetics Resource Center, *supra cit*., note 22.

In instances where the disease is not prevalent in all regions or in all spheres of the population, authorities might opt for a targeted approach instead of a universal screening programme. For example, France has chosen to offer SCD screening to all high-risk infants[32] by adopting a targeted screening approach in metropolitan areas, where infants are offered sickle cell screening if they fall under one of the 5 criteria defined by the Association Française pour le Dépistage et la Prévention des Handicaps de l'Enfant.[33] The 5 criteria are as follows: 1) if one of the two parents is originally from a country where the incidence of SCD is significant; 2) if one of the parents is from one of the above countries and the other is from Asia; 3) if the mother is at risk and the father is not known; 4) if a parent suffers from a haemoglobin disorder or is aware of any family history in this regard; and 5) if there is any doubt with regard to the 4 previous points. A concern with this approach is that some infants belonging to high-risk groups may be difficult to identify.[34] Following the introduction of the SCD screening programme there is evidence that early sudden death for children born with SCD is rare. However, follow-up studies of the long-term impact on reducing morbidity and mortality are lacking.[35]

Due to global migration, it is estimated that immigrants from visible minorities account for 11.2 percent of the Canadian population.[36] The greatest concentration of visible minorities is in large urban areas, with nearly 42 percent living in Toronto, 18 percent in Vancouver and 13 percent in Montreal.[37] Within the province of Quebec, Montreal is home to 92 percent of the black population (from areas like the Caribbean, French Antilles and northern Africa) as well as immigrants from Arab/West Asian countries.[38] Therefore, a high concentration of SCD carriers or patients is likely in major Canadian cities. However, in the absence of a screening programme of neonates for SCD, in Montreal and elsewhere, small selective programmes, initiated only by individual clinicians, currently operate in Montreal.[39] In Toronto, a presentation to 'The Commission on the Future of Health Care in Canada' draws

32 Briard, M.L., 'Le dépistage néonatal de la drépanocytose en métropole', (2000) 39 *La Dépêche*.

33 Association française pour le Dépistage et la Prévention des Handicaps de l'Enfant, *Guide pratiques pour les professionnels de santé – Le dépistage néonatal*, March 2001.

34 Cronin, E.K., Normand, C., Henthorn, J.S., Hickman, M. and Davies, S.C., 'Costing model for neonatal screening and diagnosis of haemoglobinopathies', (1998) 79 *Arch. Dis. Child. Fetal Neonatal Ed.*, F161-7.

35 Farriaux, J.-P., 'Le dépistage néonatal de la drépanocytose' (2003) *Ann Biol Clin*, 61: 376-8.

36 Compiled from the 2001 Statistics Canada Census website.

37 Statistics Canada, '1996 Census: Ethnic Origin, Visible Minorities', *The Daily Tuesday*, February 17, 1998: http://www.statcan.ca/Daily/English/980217/d980217.htm (accessed 01/08/05).

38 *Id.*

39 Edgar Delvin, personal communication.

attention to the need for guidelines, education, and training regarding sickle cell disease.[40]

Socio-ethical Concerns Related to Screening for SCD in Newborn Screening Programmes

Classical newborn screening usually occurs in the absence of explicit written parental consent.[41] However, for every one affected child, haemoglobin electrophoresis also identifies around 50 carriers[42] who require follow-up because their parents may be at risk and therefore in need of genetic counselling. While withholding carrier information from parents is unacceptable, no consent to knowledge of carrier status is obtained prior to screening. If consent was required, some believe that parental refusal could jeopardise the overall preventive goals of newborn screening.[43] Policymakers must face the difficult issue of carrier information when deciding whether or not to include the disease in universal newborn screening panels. A second dilemma decision-makers face is determining the type of screening programme most appropriate for a certain population given the constraints of costs and the selective profiling on the basis of ethnicity. A final issue that will be discussed pertains to the pressures exerted by patient advocacy groups to include new diseases in the universal newborn screening programme.

The Identification of Carriers and Incidental Results

Perhaps the most critical issue related to the implementation of a universal SCD screening program is that, in addition to finding affected newborns, disease screening also identifies carriers.[44] Detection of the sickle cell trait in newborns can

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40 Sickle Cell Parents' Support Group (prepared by Anne C.D. Clarke), 'Presentation to the Commission on the Future of Health Care in Canada: The Care and Treatment of Canada's Multi-Racial Population', 28 May 2002.

41 Avard, D. and Knoppers, B.M., 'Screening and Children Policy Issues for the New Millenium', (2001) 2(3) *ISUMA*, 46-57.

42 Council of Regional Networks for Genetics Services (CORN), 'US Newborn Screening System Guidelines II: Follow-up of Children, Diagnosis, Management, and Evaluation', (2000) 137(4) *J. Pediatrics*, S1.

43 Stewart, R., Oliver, S., 'What is known about communication with parents about newborn bloodspot screening?', UK Newborn Screening Programme Centre, London: http://www.newbornscreening-bloodspot.org.uk

44 Screening for sickle cell syndromes is unique because both homozygotes and heterozygotes may be detected during screening. Indeed approximately 50 infants who are carriers of haemoglobin variants are identified for every one individual who is detected with sickle cell disease. See Council of Regional Networks for Genetic Services, *Guidelines for Follow-up of Carriers of Hemoglobin Variants Detected by Newborn Screening*, Texas, September 10, 1995: http://www.gemdatabase.org/gemdatabase/docs/HemGuide.pdf (date accessed: August 6, 2004).

offer opportunities for extended family testing and genetic counselling to parents for future reproductive choices: if an infant is a carrier, one or both parents are carriers. This information is useful to parents if they do not know their carrier status.

However, identifying carriers raises a number of ethical dilemmas for the family. First, while identification of carriers may be beneficial for the parents, birth is generally considered a poor time for communicating carrier screening information. Moreover, this information is of minimal benefit to the child; indeed, it may not be useful until the child reaches adolescence or reproductive age. There is no certainty that the genetic information will reach the child in an understandable form and at the appropriate time for the benefits to accrue: i.e. during adolescence or adulthood.[45] Additional disadvantages of knowing carrier status include alteration of self-esteem,[46] impact on a family's perception of the child,[47] lack of choice to be tested,[48] increased anxiety,[49] blaming oneself for the condition and possible discrimination against the child in education, insurance and employment.[50]

Past experiences have demonstrated that, in the absence of proper public education and parental counselling, confusion about the significance of carrying the common sickle cell trait (about 1 in 12 African Americans are carriers[51]) and the rare sickle cell anaemia (with a frequency of 1 in 600) has led to discrimination and stigmatisation.[52] Consequently, with the establishment of a newborn SCD program, the detection of carriers (both parents and children) should be accompanied by adequate counselling. Furthermore, the information provided during the screening programme and follow-up should specifically describe the characteristics of carrier screening.

While identification of carrier status has no implication whatsoever for the health or the medical care of the newborn, it increases parents' knowledge of haemoglobin variants so that they will not confuse benign states with the disease. It can also help identify and counsel couples with the sickle cell trait who are at risk of having other children with sickle cell disease. However, providing information to parents

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45 McCabe, L.L. and McCabe, E.R.B., 'Genetic Screening: Carriers and Affected Individuals', (2004) 5 *Annual Reviews Genomics Human Genetics*, 57-69.

46 Working Party of the Clinical Genetics Society (A. Clarke, Chairman), 'The Genetic Testing of Children', (1994) 31 *J. Med Genet*., 785-97.

47 American Society of Human Genetics, American College of Medical Genetics (ASHG/ACMG), 'Points to consider: Ethical, Legal and Psychological Implications of Genetic Testing in Children and Adolescents', (1995) 57 *Am. J. Hum. Gen*., 1233-41.

48 Wertz, D.C., Fanos, J.H. and Reilly, P.R., 'Genetic Testing for Children and Adolescents. Who Decides?', (1994) 272 *J.A.M.A*., 875-81.

49 Working Party of the Clinical Genetics Society, *supra cit.*, note 46.

50 Working Party of the Clinical Genetics Society, *supra cit.*, note 46; American society of Human Genetics, American College of Medical Genetics, *supra cit.*, note 47.

51 From the American Sickle Cell Association website: http://www.ascaa.org/comm.htm.

52 Farriaux, J.P. and Dhondt, J.-L. (eds), *New Horizons in Neonatal Screening*, Excerpta Medica, Amsterdam, 1994; Knoppers, B.M. and Laberge, C.M. (eds), *Genetic Screening: From Newborns to DNA Typing*, Excerpta Medica, Amsterdam, 1990.

for decision-making is secondary to the primary reason for neonatal screening.[53] In short, where screening can detect a treatable disease and at the same time reveal carrier status, the recommendations are that parents be advised of this possibility before the test and that results be given to the parents, in combination with any necessary counselling.[54]

Informing, educating and counselling families of carriers identified by newborn screening are major challenges from a logistical perspective; adequate funding is needed for comprehensive educational programme care. As mentioned earlier, a universal newborn screening programme would potentially identify thousands of carriers who require primary health care workers to provide counselling.[55] There are few studies that report on the way health services are organised for children with SCD or for carriers of the SC trait.[56] In fact, very little is known about who informs parents about SC screening, whether information is provided before or after screening, what expertise the health providers have, or what type of information is provided and in what form. We also do not know what happens to carriers of the SC trait: are parents are informed? Are they offered counselling? Are parents and other family members offered screening to determine if they are carriers? Who ensures that the child is told upon reaching adolescence?

The long-term use of carrier status information impacts on consent issues. Many official policies concerning carrier status strongly advise against notifying the child, particularly because of the relative absence of programmes to support counselling.[57] Not only does this mean that the child has been tested without his or her consent, but he or she is also effectively denied relevant reproductive information.

Certain questions must be answered before implementing universal screening programmes capable of detecting carriers. For instance, should screening be conducted without prior consent, seeing as it can yield genetic information which some parents would prefer not knowing? How and under what circumstances should information about the sickle cell trait be conveyed to parents? Is it ethically justifiable not to inform parents if their child is a carrier of the sickle cell trait? Is it ethically acceptable to screen newborns when adequate education and counselling cannot be provided? If SCD screening is implemented, how will it affect newborn screening for treatable conditions?

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53 Council of Regional Networks for Genetic Services, *supra* note 44.

54 British Medical Association, *Human Genetics Choice and Responsibility*, London, Oxford University Press, 1998, at p. 100.

55 World Health Organisation (WHO), *Control of Hereditary Disease – Report of a WHO Scientific Group*, Geneva, 1996.

56 See Goldbloom, R.B., 'Screening for Hemoglobinopathies in Canada', in Canadian Task Force on the Periodic Health Examination, *Canadian Guide to Clinical Preventive Health Care*, Ottawa, Health Canada, 1994; Yorke, D., Mitchell, J., *et al*., 'Newborn screening for sickle cell and other hemoglobinopathies: a Canadian pilot study', (1992) 15(4) *Clin. Invest. Med*., 376-83.

57 Lane, P.A., 'Issues Regarding Identification of Hemoglobinopathy Carriers by Neonatal Screening', (1998) 15 *Genetic Drift* (Newsletter).

If SCD screening is conducted, parents will need to be given information about various subjects: for example, the significance of results and their right to accept or decline SCD screening or notification should they prefer not knowing about carrier status.

The Constraints of Using Ethnicity as a Primary Tool for Selective Screening

Race and geographical origin constitute a significant factor in the incidence of SCD. The disease mostly affects people whose ancestors are from Africa, India, the Mediterranean, the Caribbean, South and Central America and Middle Eastern countries. However, in multicultural, melting-pot societies, it may become difficult to determine individuals' ethnicity or origin simply by looking at their skin colour. While resource-based arguments suggest that a targeted approach (selecting certain infants on the basis of race and ethnicity) for SCD screening is most efficient, the consensus view, based on practical experience in the UK,[58] and the US experience in the state of Georgia,[59] is that universal screening of all newborns for SCD is preferable. Programmes that screen in only specific high-risk segments of a population tend to miss individuals who are inaccurately registered. Because the benefits of screening for SCD are so compelling, leaving the selection based on ethnic and racial groups to the discretion of individual physicians or health care facilities has been abandoned in the United States[60] and in the United Kingdom.[61] Indeed, since SCD occurs among a wide range of ethnic and racial groups, efforts at targeting specific high-risk groups for newborn screening inevitably miss some affected infants because of difficulties in properly assigning race or ethnic origin during the prenatal period or in the newborn nursery.[62] Professional assessment of the mother's race is often wrong.[63]

Definition of the screened population is a controversial topic in haemoglobinopathy screening. Guidelines and reviews of screening programmes have been published by various agencies around the world. Some have recommended universal screening for all newborns, while others have suggested that screening strategies, whether universal or selective, should depend on the proportion of high-risk individuals in a community.[64] One of the problems with targeted screening lies in the difficulty of identifying and selecting individuals. For instance, investigators in Georgia, US, compared the number of black newborns screened for haemoglobinopathies

58 Sassi, F., Archard, L. and Le Grand, J., 'Equity vs efficiency: A Dilemma for the NHS', (2001) 323 *B.M.J.*, 762-3; Panepinto, J.A., Magid, D., Rewers, M..J. and Lane, P.A., 'Universal Versus Targeted Screening of Infants for Sickle Cell Disease: A Cost-Effectiveness Analysis', (2000) 136 *J. Pediatrics*, 201-8.

59 Harris, M.S. and Eckman, J.R., 'Georgia's Experience with Newborn Screening: 1981-1985', (1989) 83(suppl.) *Pediatrics*, 858-60.

60 NIH Consensus Development Program, *supra cit.*, note 28.

61 NHS Sickle Cell and Thalassaemia Screening Programme, *supra cit.*, note 23.

62 Goldbloom, *supra cit*., note 56.

63 Wertz, *supra cit*., note 21.

64 Goldbloom, *supra cit.*, note 56.

between 1981 and 1985 with black birth figures for the same period, and estimated that approximately 20 percent of black newborns were not screened.[65] Results of a study of universal screening in multiethnic California also indicated that an approach of targeting certain groups in that state would have missed at least 10 percent of those whose sickle cell disease was actually diagnosed at birth.[66] Indeed, the US experience suggests that adequate targeting strategies are difficult to define and the criteria used to identify ethnic origin in relation to risk of sickle carrier status are likely to vary between and within countries, thus making the generalisability of such analyses difficult to interpret.[67]

Critics of the targeted approach have also raised the issue of the cost of determining race and ethnicity in the newborn nursery.[68] Another criticism is that a selective approach could be seen as discriminatory.[69] Before implementing a newborn screening programme for SCD, policy-makers will need to consider whether universal screening in a given area constitutes a rational policy.

Political Pressure by Advocacy Groups

Newborn screening for PKU, developed in the 1960s, originated with the work of Robert Guthrie, a highly motivated parent who had a son with mental retardation and a niece with PKU.[70] He helped organise parents to lobby their governments to establish newborn screening programmes. Similarly, parents today continue to press for screening programmes.[71]

Partnership and public consultation have become important tools in policy development because they increase legitimacy and improve transparency in the policy development process. A review of the literature on public consultation and involvement shows that public involvement in policy development is no longer limited

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65 Harris, Eckman, *supra cit*., note 59.

66 Shafer, F.E., Lorey, F., Cunningham, G.C., Klumpp, C., Vichinsky, E. and Lubin, B., 'Newborn Screening for Sickle Cell Disease: 4 Years of Experience from California's Newborn Screening Program', (1996) 18(1) *J. Pediatr. Hematol. Oncol*., 36-41.

67 Lees, C.M., Davies, S. and Dezateux, C., 'Neonatal Screening for Sickle Cell Disease (Cochrane Review)', in *The Cochrane Library*, Issue 3, Chichester, UK, John Wiley & Sons, 2004.

68 Lane, J.R. and Eckman, P.A., 'Cost-effectiveness of Neonatal Screening for Sickle Cell Disease', (1992) 120(1) *J. Pediatrics*, 162-3; Cronin, Normand, Henthorn, Hickman, Davies, *supra cit*., note 34.

69 Sassi, Archard, LeGrand, *supra cit.*, note 58.

70 McCabe and McCabe, *supra cit.*, note 45.

71 Guthrie, P., 'Pressure Mounts to Expand Screening of US Newborns', (2005) 173(1) *J.A.M.C*., 22; See March of Dimes: https://www.marchofdimes.com ; See also Genetics Interest Group: http://www.gig.org.uk ; Eggertson, L., 'Canada Lags on Newborn Screening', (2005) 173 *C.M.A.J*., 23; Gillot, J., 'Childhood Testing for Carrier Status: the Perspective of the Genetic Interest Group', in Clarke, A. (ed.), *The Genetic Testing Children*, Oxford, Bios Scientific Publishers, 1998, at p. 97.

to the reactions to particular services or products.[72] As early as 1986, the Ottawa Charter[73] emphasised the importance of public health and promotion and greater consultation with the public. The belief is that the result of involving communities of users, the public, and the health professionals will be greater harmonisation and successful implementation of an initiative or programme. The partnership of parents and health professionals will encourage the dissemination of balanced information.[74] These steps need encouragement, and many drawbacks to effective implementation exist: there are wide gaps in knowledge, language barriers, cultural differences, and economic issues, and there are also time constraints.[75]

What is known about the views and experience of families and health professionals? For example, the public needs to understand the difference between carrier status and clinical diagnosis.[76] There is insufficient information about family values and expectations with regard to SCD screening. It is important to consult high-risk populations to understand if identified infants are being enrolled in a programme for treatment and care, if certain types of services or programs are deemed necessary to prevent the birth of children with the disease, and if there is a need for community education, couples counselling, and/or carrier screening to all high-risk populations of childbearing age.

Research on other screening programmes suggests that the perspectives of health professionals differ from those of parents. According to a survey by Wertz on topics relevant to the genetics of paediatrics, the views of parents and primary care physicians differ significantly. Increasingly, parents do not accept a paternalistic approach but rather believe that nothing should be withheld from them.[77]

Furthermore, there is an inadequate number of certified counsellors to respond to the need for support.[78] While medical care personnel are increasingly exposed to genetics, difficulties in the interpretation of DNA reports raise important educational challenges. There are also concerns about resources available to establish newborn follow-up and trait counselling programs. For example, in the USA,[79] counselling to

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72 Butler, A., *Consumer Participation in Australian Primary Care: A Literature Review*, Australia, National Resource Centre for Consumer Participation in Health, 2002.

73 1st International Conference on Health Promotion, *Ottawa Charter*, Ottawa, November 1986.

74 National Health and Medical Research Council and Consumers' Health Forum of Australia, *Statement on Consumer and Community Participation in Health and Medical Research*, Australia, 2001.

75 Hamlett, P.A., 'Technology Theory and Deliberative Democracy', (2003) 28(1) *Science Technology and Human Values*, 112-140.

76 McCabe and McCabe, *supra cit*., note 45.

77 Wertz, *supra cit.*, note 21.

78 Task Force on Life and the Law, 'Genetic Testing and Screening in the Age of Genomic Medicine', New York, November 2000, http://www.health.state.ny.us/nysdoh/taskfce/screening.htm.

79 Day, S.W., Brunson, G.E. and Wang, W.C., 'Successful newborn sickle cell trait counselling program using health department nurses', (1997) 23 *Pediatric Nurse*, 557-61.

families with infants with a trait is either very limited in scope or non-existent and with little follow-up facilities. Follow-up of SCD is often fragmented and acceptance of counselling is low.[80]

Finally, in the care of carrier status, there is uncertainty about how best to inform parents about the diagnosis of the sickle cell trait in the newborn.[81] The possible benefits for the child are educational and useful only when the child is older. However, it is unclear whether informing parents is beneficial to the child and how best to inform parents. Hence, focusing more on the needs, wants, and opinions of parents is key to facilitating participation and to helping with the presentation of information materials.

Conclusion

Neonatal screening for SCD allows early diagnosis and therefore early treatment and education. However, such a screening programme must take into consideration a number of socio-ethical concerns.

We presented three main socio-ethical concerns with respect to SCD neonatal screening. First, the need to address the difficulties raised by revealing carrier status; second, whether neonatal screening should be selective or universal; and third, the need to address the role of consumer groups if screening is to reach its promise of predictive and preventive aspects.

Neonatal screening can detect most high-risk infants, but what should be communicated about carrier status? Ultimately, the identification of carriers calls for a re-examination of classical newborn screening consent procedures. How to do this without affecting or harming the newborn screening programme for immediately treatable conditions is the central issue. Deciding to screen for SCD and identifying carriers raise wider questions regarding parents' rights to refuse newborn screening for sickle cell diseases. Consequently, newborn screening for SCD cannot be carried out in the same manner as screening for treatable conditions occurs today because of the ethical issues related to carrier identification in the former. Informed consent with a clear understanding of the potential social and psychological harms is a key ethical issue. Considering the possible 'harm' of SCD consent process on classical screening programs, should SCD be universal or selective?

There is a difference of opinion about whether SCD screening should be selective or universal, and there is even less consensus on whether or how ethnicity or race should be used in selective screening programmes for sickle cell disorders. Experts debate whether it should be decided on the basis of proportion of the population from ethnic minorities, whether it is cost-effective without the risk of reduced

80 Kladny, B., Gettig, E.A. and Krishnamurti, L., 'Systematic follow-up and case management of the abnormal newborn screen can improve acceptance of genetic counselling for sickle cell or other hemoglobinopathy traits', (2005) 7 *Genetics in Medicine*, 139-42.

81 P.T. Rowley, 'Parental Receptivity to Neonatal Sickle Trait Identification/, (1989) *Pediatrics*, 891-3.

effectiveness, and whether there is risk of discrimination. The best way to address this dilemma is to improve available data on cases of SCD, carrier rates, and by using standardised instruments for collecting ethnicity data.[82] Neonatal programs have the ability to identify newborns with SCD and identify carriers of the SC trait. Estimates indicate that about half of all infants in the UK who are carriers have mothers who are carriers.[83] Some say that it is more economical to ask women about their ethnic origin and offer screening only to those with genetic backgrounds in areas where the disorder is highly prevalent. Others suggest that such policies miss a significant number of affected cases because the screening criteria might be inadequate and inconsistently applied.

Finally, how can we best involve the parents? Obviously, there is a need for appropriate information and counselling prior to screening and for appropriate resources as well for adequate follow-up services. This should be combined with educational programmes and resources. Public interest in sickle cell disease has prevailed since Robert Guthrie's initiative in the 1960s. The involvement of ethno cultural groups and their representatives in assessing the risks and benefits of neonatal screening for sickle cell is needed. Generally, recommendations regarding such a programme are derived from professionals or bioethicists and the voice of parents – consumers – is rarely heard at the discussion table.[84] The drive towards more equal partnerships in decision-making in health programmes implies the need to promote and initiate dialogue with parents on a range of these socio-ethical issues.

Despite the socio-ethical quandaries of carrier identification, targeted versus universal approaches, and, in part, because of the experience of pressure from parents, newborn screening programmes for sickle cell disease have been introduced in numerous countries. Based on lessons from the past, it is important that genetic counsellors in sickle cell screening programmes discuss the confidentiality of results and the potential for genetic discrimination by life and medical insurance companies with families, to ensure that they understand the significance of carrier identification. It is also vital that policy-makers provide proper public education so that discriminatory practices do not take place.

Perhaps a novel way to change the contours of the debate would be to take the best interests of the child approach. Where, when, and how can those interests be ensured? Though many answers to our research questions are still lacking and the social constraints of resources or failures such as discrimination are important political and systemic issues, to answer the SCD questions, the rights and interests of the child should be paramount.

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82 Hickman, M., Modell, B., Greengross, P., Chapman, C., Layton, M., Falconer, S. and Davies, S.C., 'Mapping the Prevalence of Sickle Cell and Beta Thalassaemia in England: Estimating and Validating Ethnic-specific Rates', (1999) 104 *Br. J. Haematol*., 860-7.

83 NHS Sickle Cell and Thalassaemia Screening Programme, *supra cit*., note 23.

84 Wertz, D.C. and Gregg, R., 'Genetics services in a social, ethical and policy context: a collaboration between consumers and providers', (2000) 26 *Journal of Medical Ethics*, 261-5.

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