

after a jejunoileal shunt, however, unlike that with most dietary regimens, is usually both substantial and sustained, so that the effect of weight reduction on blood pressure is more apparent.

I thank Professor J R A Mitchell for constructive criticism of this paper, Miss Jayne Patrick for typing the manuscript, and the department of clinical chemistry for the biochemical estimations.

References

- ¹ Kannel, W B, Schwartz, M J, and McNamara, P M, *Diseases of the Chest*, 1969, **56**, 43.
- ² Kannel, W B, *et al*, *Annals of Internal Medicine*, 1971, **74**, 1.
- ³ Pelkonen, R, *et al*, *British Medical Journal*, 1977, **2**, 1185.
- ⁴ Kannel, W B, *et al*, *Circulation*, 1967, **35**, 734.
- ⁵ Keys, A, *et al*, *Annals of Internal Medicine*, 1972, **77**, 15.
- ⁶ Report of a Joint Working Party of the Royal College of Physicians of London and the British Cardiac Society, *Journal of the Royal College of Physicians*, 1976, **10**, 32.
- ⁷ Boe, J, Humerfelt, S, and Wedervang, F, *Acta Medica Scandinavica*, 1957, **157**, suppl No 321, p 215.
- ⁸ Stamler, J, *et al*, *Circulation*, 1962, **26**, 672.
- ⁹ Ostrander, L E, and Lamphiear, D E, *Circulation*, 1976, **53**, 152.
- ¹⁰ Montoye, H J, Epstein, F H, and Kjelsberg, M O, *American Journal of Clinical Nutrition*, 1966, **18**, 397.
- ¹¹ Rappaport, F, and Eichhorn, F, *Clinica Chimica Acta*, 1960, **5**, 161.
- ¹² Lartillot, S, and Vogel, C, *Feuillets de Biologie*, 1970, **11**, No 53, 39.
- ¹³ Bruusgaard, A, *et al*, *Scandinavian Journal of Gastroenterology*, 1976, **11**, 833.
- ¹⁴ Slack, J, *et al*, *British Medical Journal*, 1977, **2**, 353.
- ¹⁵ Leelarthaeapin, B, *et al*, *Lancet*, 1974, **2**, 1217.
- ¹⁶ Ashley, F W, and Kannel, W B, *Journal of Chronic Diseases*, 1974, **27**, 103.
- ¹⁷ Kannel, W B, *et al*, *Annals of Internal Medicine*, 1967, **67**, 48.
- ¹⁸ Weinsier, R L, *et al*, *American Journal of Medicine*, 1976, **61**, 815.
- ¹⁹ Mann, G V, *New England Journal of Medicine*, 1974, **291**, 178.
- ²⁰ Dahl, L K, *American Journal of Clinical Nutrition*, 1972, **25**, 231.
- ²¹ Keys, A, Henschel, A, and Taylor, H L, *American Journal of Physiology*, 1947, **150**, 153.
- ²² Fletcher, A P, *Quarterly Journal of Medicine*, 1954, **23**, 331.

(Accepted 4 April 1978)

Early deaths in Jamaican children with sickle cell disease

D W ROGERS, JENNIFER M CLARKE, LENA CUPIDORE, ANGELA M RAMLAL, B R SPARKE, G R SERJEANT

British Medical Journal, 1978, **1**, 1515-1516

Summary and conclusions

In Jamaican children with homozygous sickle cell (SS) disease diagnosed at birth two-year survival was 87%, compared with 95% in children with sickle cell-haemoglobin C (SC) disease, and 99% in normal controls. Death among those with SS disease occurred most often between the ages of 6 and 12 months. Principal causes were acute splenic sequestration and pneumococcal infection.

Neonatal diagnosis of haemoglobinopathies must be followed by close observation if mortality is to be reduced by early diagnosis and treatment of these complications.

Introduction

Mortality from homozygous sickle cell disease shows considerable geographical variation. In some African populations with a high prevalence of sickle cell trait the rarity of sickle cell (SS) disease in adults can be explained only by high childhood mortality among homozygotes.^{1,2} In the Belgian Congo (now Zaire) the Lambotte-Legrands³ followed 300 children diagnosed at a mean age of 1 year 5 months and reported that 120 (40%) died before the age of 2.

Higher living standards and improved health care may contribute to the improved survival of homozygotes in North America, but early mortality remains high: Porter and Thurman⁴

reported a 16% mortality in the first year of life among 64 infants diagnosed before the age of 1. Actual mortality rates may exceed this, since infants die before SS disease is suspected.⁵

Survival of patients with SS disease to adult life is common in the West Indies, but childhood mortality has not been estimated. A cord blood screening programme, started in Jamaica four years ago, has attempted to identify all newborn cases of SS disease in a maternity hospital with about 14 000 deliveries a year. Follow-up of these infants has made it possible to calculate a survival curve and to monitor the causes of death.

Methods

Since July 1973 cord blood samples from Victoria Jubilee Hospital, the main government maternity hospital serving Kingston, have been screened by haemoglobin electrophoresis.⁶ The diagnosis of SS disease was based on the presence of only haemoglobins (Hb) S, F, and A₂ on electrophoresis on both cellulose acetate and agar gel, an Hb A₂ level below 3.2% at 1 year to exclude sickle cell-β⁰-thalassaemia,⁷ and family studies whenever possible. A probable case of sickle cell hereditary persistence of Hb F (Hb F level of 39.3% at 1 year; greater than 2 SD above the mean for children with SS disease) was excluded from the study although confirmatory family studies were not possible. The diagnosis of sickle cell-haemoglobin C (SC) disease was based on two major haemoglobin bands in the position of Hb S and Hb C on electrophoresis on cellulose acetate and agar gel.

From July 1973 to January 1976 32 000 cord blood samples, representing samples from 92% of all deliveries, were screened, and 109 cases of SS disease and 67 cases of SC disease were detected.

These patients together with 230 age- and sex-matched controls with normal (AA) haemoglobin born in the same hospital were followed prospectively in a special clinic at the University Hospital of the West Indies. Defaulting patients were visited at home when possible. The surviving children were aged from 2 years to 4 years and 6 months on 15 January 1978, the date on which the analysis was based. Survival curves were calculated by the method of Berkson and Gage as described by Armitage.⁸ The method assumes the same mortality in defaulters as in those successfully followed up. Significance levels were calculated from the log rank test.⁹

Necropsies were performed when possible but otherwise the cause of death was deduced from the clinical history and available records. A detailed pathological report of the necropsies is in preparation.

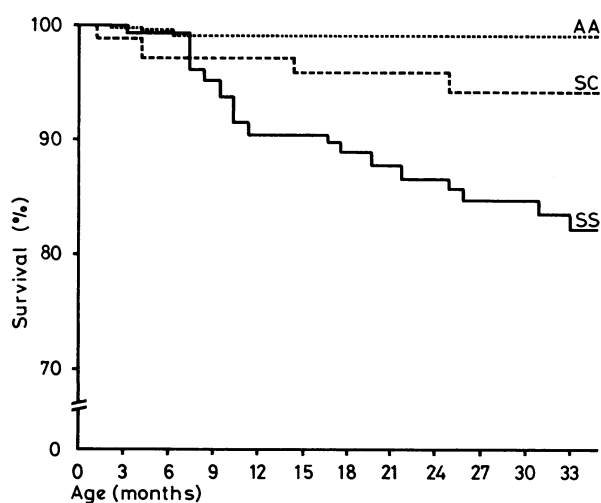
MRC Laboratories (Jamaica) and Department of Pathology, University of the West Indies, Kingston 7, Jamaica

D W ROGERS, MRCP, DCH, member of scientific staff
 JENNIFER M CLARKE, MRCP, DCH, member of scientific staff
 LENA CUPIDORE, SRN, SCM, member of scientific staff
 ANGELA M RAMLAL, DM, DCH, member of scientific staff
 B R SPARKE, MB, DCP, lecturer in pathology
 G R SERJEANT, MD, FRCP, director of MRC Laboratories

Results

During the study 53 (9 SS; 5 SC; 39 AA) of the initial 406 children were lost to follow-up by emigration, removal to remote areas of Jamaica, or default. The percentages of the initial children in each genotype lost to follow up were 4%, 1%, and 13% at one year and 6%, 6%, and 16% at two years for SS, SC, and AA genotypes respectively.

Eighteen children with SS disease, four with SC disease, and three normal controls died. Survival curves for the three genotypes are shown in the figure. Mortality was similar in the different genotypes during the first six months but rose significantly ($P < 0.001$) between 6 months and 1 year in SS disease, half the deaths in children with the SS genotype (9/18) occurring during this period. Overall mortality among children with SC disease was higher than in controls ($P < 0.05$). Infant mortality rates (deaths in the first year per 1000 live births) calculated from the survival curve were 95 for SS disease, 30 for SC disease, and 13 for AA controls, compared with an overall infant mortality rate in Jamaica of 26 in 1975. No deaths have yet been observed after the age of 3.



Survival in Jamaican children with genotypes AA, SC, and SS diagnosed at birth.

Cause of death in the 25 patients who died according to age and genotype

Case No	Age in months	Cause of death	Bacteriological findings
<i>SS genotype</i>			
1	3	Gastroenteritis*	No cultures taken
2	7	Gastroenteritis	<i>D pneumoniae</i> (middle ear), pathogenic <i>Escherichia coli</i> (rectum)
3	7	ASS, pneumonia	<i>D pneumoniae</i> (blood)
4	7	ASS, pneumonia	<i>D pneumoniae</i> (bronchi)
5	8	Cot death*	No cultures taken
6	9	ASS	<i>D pneumoniae</i> (middle ear)
7	9	Gastroenteritis*	No cultures taken
8	10	Pneumonia*	No cultures taken
9	10	ASS	No significant growth
10	11	Cardiac failure (?ASS, ?septicaemia)	No cultures taken
11	16	Meningitis	<i>D pneumoniae</i> (middle ear), <i>Salmonella typhimurium</i> (middle ear)
12	17	ASS	No significant growth
13	19	Uncertain*	No cultures taken
14	21	ASS	<i>D pneumoniae</i> (blood)
15	24	Uncertain* Pneumonia, malnutrition	No cultures taken
16	25	?Meningitis*	No significant growth
17	30	Gastroenteritis, ASS	No significant growth
18	32		
<i>SC genotype</i>			
19	1	Cot death*	No cultures taken
20	4	Gastroenteritis*	No cultures taken
21	14	Gastroenteritis	No significant growth
22	24	Gastroenteritis	No cultures taken
<i>AA genotype</i>			
23	2	Congenital heart disease*	No cultures taken
24	3	Gastroenteritis*	No cultures taken
25	6	Gastroenteritis*	No cultures taken

*Clinical diagnosis, no necropsy performed. ASS = Acute splenic sequestration.

The causes of death are summarised in the table. Acute splenic sequestration¹⁰ was diagnosed from sudden splenic enlargement, acute anaemia, and circulatory failure; necropsy findings were an enlarged congested spleen with hypercellular marrow and pallor of the other organs, sometimes with peripheral oedema or pleural effusions. Acute splenic sequestration was the commonest cause of death, occurring in seven of the 11 patients for which necropsy results were available.

Blood cultures when reported were performed before or immediately after death, and further bacteriological specimens were taken at necropsy. Infection with *Diplococcus pneumoniae* was found in six of the 11 cases for which bacteriology results were available, and in four of these cases acute splenic sequestration had also occurred.

Discussion

The 13% mortality in the first two years found in Jamaican children diagnosed at birth as having SS disease is similar to estimates based on North American experience.^{4,5} In the first six months mortality in children with SS and SC disease followed the pattern seen in Jamaican children with AA genotype, with gastroenteritis as the principal cause of death. In the second six months nearly 10% of children with SS disease died mainly with acute splenic sequestration or pneumococcal infection. Further deaths from these causes occurred in children with SS disease in the second and third years. Deaths from these causes were not observed in controls or children with SC disease.

Isolation of the pneumococcus in four cases of acute splenic sequestration suggests that infection with this organism may play a part in the aetiology of this poorly understood condition. Acute splenic sequestration and pneumococcal septicaemia were both extremely acute in onset, an apparently well child becoming moribund within hours, and this rapid progression may have contributed to the continuing high mortality despite close follow-up. In an attempt to achieve earlier diagnosis mothers were instructed to watch for signs of breathlessness, listlessness, or pallor in the child; to check for enlargement of the spleen if easily palpable; and to seek medical attention early if the child's condition gave any cause for concern. Episodes of acute splenic sequestration and of septicaemia were successfully treated on this basis, by emergency blood transfusion and parenteral penicillin respectively. Penicillin is now given to all patients with acute splenic sequestration because of the risk of underlying pneumococcal septicaemia.

As the principal causes of the high mortality among children with SS disease can be treated by prompt medical intervention, this high mortality rate might be reduced by intensive follow-up and careful maternal education. Penicillin prophylaxis and immunisation with pneumococcal vaccine also require assessment, and a trial of these is planned.

We gratefully acknowledge the help of the departments of child health and microbiology, University of the West Indies, and thank the staff of the Medical Research Council Laboratories and Victoria Jubilee Hospital for their co-operation in the study.

References

- Lehmann, H, and Raper, A B, *British Medical Journal*, 1956, **2**, 333.
- Jacob, G F, *British Medical Journal*, 1957, **1**, 738.
- Lambotte-Legrand, J, and Lambotte-Legrand, C, *Annales de la Société Belge de Médecine Tropicale*, 1955, **35**, 53.
- Porter, F S, and Thurman, W G, *American Journal of Diseases of Children*, 1963, **106**, 35.
- Powars, D R, *Seminars in Hematology*, 1975, **12**, 267.
- Serjeant, B E, et al, *Clinical Chemistry*, 1974, **20**, 666.
- Serjeant, B E, Mason, K P, and Serjeant, G R, *British Journal of Haematology*. In press.
- Armitage, P, *Statistical Methods in Medical Research*. Oxford, Blackwell Scientific Publications, 1974.
- Peto, R, et al, *British Journal of Cancer*, 1977, **35**, 1.
- Seeler, R A, and Schwiaki, M Z, *Clinical Pediatrics*, 1972, **11**, 701.

(Accepted 6 April 1978)