still associated after the effects of heart rate had been taken into account.

We cannot explain our finding satisfactorily, but through the investigation of children we have been able to exclude explanations which have relevance only to adults. If our findings are not simply an artefact of the examination procedure, then they suggest that in the more developed countries the relations seen in adults between four risk factors for CHD—blood pressure, adiposity, blood sugar, and serum cholesterol—are already evident in childhood.

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Growth, behaviour, and educational achievement of Jamaican children with sickle-cell trait

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Summary

A longitudinal study of the mental and physical development of 200 children with normal haemoglobin and 21 with the sickle-cell trait was carried out in a small rural community in Jamaica. At about 2 and 10 years of age heights and weights showed no significant differences. At about 10 years of age classroom behaviour, sociability, and educational achievement were similar. The results suggest that the sickle-cell trait does not affect growth and mental development.

Introduction

In homozygous sickle-cell disease some 80-97% of the total haemoglobin is sickle haemoglobin (Hb S), and these high levels are associated with well recognised pathophysiological sequelae. Heterozygous sickle-cell trait, however, is characterised by about 20-50% Hb S and is essentially benign, though in this disease generalised or localised anoxia may occasionally produce conditions such as splenic infarction¹ or haematuria.² Vascular occlusive episodes have also been attributed to the sickle-cell trait but the causal role of Hb S has not been confirmed.³

A report from the USA⁴ suggested that some aspects of the physical and mental development of children with the sickle-cell

trait may be impaired. In view of the far-reaching implications we have compared the growth, behaviour, and educational achievement of Jamaican children with the trait and with normal haemoglobin.

Subjects and methods

All the children had been included in early childhood studies of growth and development in Lawrence Tavern, a rural area of Jamaica.^{5 6} The geographically defined district is about 30 sq km and has a total population of 8000, mainly of African origin. The predominant occupation is subsistence farming, and the people are, in general, poor, although few are destitute. The pattern of disease is like that of a temperate rather than tropical country. Parasitic infections such as malaria, schistosomiasis, and filariasis are absent, although intestinal helminthiasis is common. Mortality rates in the first two years of life are high but subsequently fall to about the same as in the United Kingdom.

In 1974, 247 children aged 9-11½ years who were still living in the area were available for further investigations. A test of reading, spelling, and arithmetic (the Wide Range Achievement Test)⁷ was given to each child individually. The children, with the exception of four who were not enrolled at any school, were pupils at nine local schools. Teachers and fieldworkers completed questionnaires, from which indices of classroom behaviour and sociability were derived. School attendance was obtained for the previous two terms from school registers. Medical histories were taken and clinical examinations performed if deemed necessary. Socioeconomic status, based on housing, furnishing, income, and employment, was assessed on a four-point scale after a home visit by a field worker. Family structure, which may also influence educational achievement and behaviour, was recorded. Heights and weights at about 2 years of age were obtained from the children's records and were measured again in 1974. Each measurement was expressed as a standard score, which is the number of standard deviations by which the measurement differs from the mean of a reference population of the same age and sex.⁸

In 1975 venous blood was obtained from 231 (94%) of the 247 children and examined by haemoglobin electrophoresis on cellulose acetate and agar gel. The presence of Hb S was confirmed by metabisulphite sickle tests. The study was "double blind," since genotypes were determined by staff unaware of the results of other assessments.

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Results

Electrophoresis showed normal haemoglobin in 200 children (genotype AA) and the sickle-cell trait in 21 (genotype AS), subsequent analysis being confined to these two groups. The genotypes of the other 10 children were AC (6), SC (1), and rarer variants (3).

The health of the children was, in general, good. Twenty-four had had admissions to hospital, mainly for trauma (six), minor surgery (six), and infections (four). No differences were apparent in the prevalence or pattern of hospital admissions between children with the AA and AS genotypes. Four children, all with AA genotype, had chronic incapacities (severe mental retardation, epilepsy, Hirsch-

sprung's disease, and congenital leg deformity). Mean haemoglobin levels measured in 1975 showed no significant difference with sex or genotype, the mean level in children with the AA genotype being $12.1 \pm \text{SD } 0.9 \text{ g/dl}$ and in those with the AS genotype $12.3 \pm 0.7 \text{ g/dl}$.

Table I shows that the AS and AA children were alike in age, ethnic origin, socioeconomic status, school attendance, and family structure, as assessed by the proportion living with both parents. The standard scores for height and weight at 2 and 10 years (table II) and assessments of educational achievement, school behaviour, and sociability (table III) showed no consistent trends or significant differences between the two groups.

TABLE I—Comparison of various factors that may influence growth, achievement, or behaviour among children with AA and AS genotypes

Factor	Boys		Girls		Both sexes	
	AA (n = 111)	AS (n = 7)	AA (n = 89)	AS (n = 14)	AA (n = 200)	AS (n = 21)
Mean age in years/months (range)	10/7 (9/0-11/6)	NS 10/9 (9/8-11/3)	10/9 (8/11-11/6)	NS 10/7 (9/1-11/6)	10/8 (8/11-11/6)	NS 10/8 (9/1-11/6)
Ethnic origin (No of children):						
Black or mainly Black	104	6	83	13	187	19
About half Black, half White	6	1	3	1	9	2
Indian, mainly Indian, or half Black, half Indian	1	0	3	0	4	0
Socioeconomic status (% of children):		NT		NT		NT
A (higher)	5	0	4	7	5	5
B	39	29	40	57	40	48
C	33	57	34	29	34	38
D (lower)	23	14	21	7	22	10
Living with both parents (% of children)	50	NT 57	57	NS 71	53	NS 67
School attendance (mean % (SD) of possible attendances)	62 (23)	NS 55 (38)	68 (20)	NS 68 (22)	*	*

*Boys and girls not combined owing to overall differences between sexes.

NS = No significant difference (*t* test, χ^2 test, or Fisher's exact test).

NT = Not tested owing to small numbers.

TABLE II—Height and weight (standard scores*) at about 2 and 10 years of age of children with AA and AS genotypes

Growth measure	Boys		Girls		Both sexes	
	AA	AS	AA	AS	AA	AS
Mean height scores (SD)						
At 2 years	-0.11 (0.97)	-0.03 (0.73)	-0.27 (1.13)	-0.10 (0.89)	-0.18 (1.04)	-0.08 (0.82)
No of children	111	7	88	14	199	21
At 10 years	+0.25 (0.97)	+0.46 (0.73)	+0.34 (1.00)	+0.41 (0.80)	+0.29 (0.99)	+0.43 (0.76)
No of children	111	7	89	14	200	21
Mean weight scores (SD)						
At 2 years	-0.01 (1.01)	-0.04 (1.21)	-0.07 (0.94)	-0.05 (0.88)	-0.03 (0.97)	-0.05 (0.97)
No of children	111	7	88	14	199	21
At 10 years	+0.01 (1.03)	-0.24 (1.13)	0.00 (0.99)	-0.06 (0.60)	+0.01 (1.01)	-0.12 (0.79)
No of children	111	7	89	14	200	21

*A standard score of 1.0 represents about 3.3 cm and 1.3 kg at 2 years and 6.9 cm and 4.7 kg at 10 years.

No significant differences were found between children with AA and AS genotypes (*t* test).

TABLE III—Indices of educational achievement, school behaviour, and sociability in children with AA and AS genotypes

Index	Boys		Girls		Both sexes	
	AA	AS	AA	AS	AA	AS
Mean grade of educational achievement (SD)	2.52 (1.27)	3.17 (2.36)	3.94 (1.36)	3.39 (1.38)	*	*
No of children	110	7	89	14		
School behaviour (% of children):		NS		NS		
Best quartile (for own sex)	22	80	25	28	23	43
Intermediate quartiles	53	3	53	34	53	24
Worst quartile	25	17	23	39	24	32
No of children	109	6	88	14	197	20
Sociability (% of children):		NT		NT		NS
Best quartile (for own sex)	25	25	24	29	25	28
Intermediate quartiles	50	58	50	52	50	54
Worst quartile	25	17	26	19	26	18
No of children	109	6	88	14	197	20

*Boys and girls not combined owing to overall differences between sexes.

NS = No significant difference (*t* test or χ^2 test).

NT = Not tested owing to small numbers.

Discussion

Growth, behaviour, and educational achievement are influenced by many factors, and, although we found that the AA and AS children were alike in some of these, we cannot be certain that they were alike in all. Every child, however, had lived since early childhood in a small community in which living standards, child rearing practices, and educational opportunities varied within narrow ranges, and there were unlikely to be major differences in the backgrounds of the two groups.

The absence of differences in growth and achievement between children with the two genotypes conflicts with some of the results of the study in the USA,⁴ in which significantly lower weights and poorer performances in psychological-intellectual tests were found in 19 AS compared with 241 AA children aged 10-16 years. No evidence was presented in that report, however, to show that the two groups were matched for socioeconomic or other factors that might have influenced the measurements. Furthermore, the selection of patients from twin studies may complicate assessment of the results. Perinatal hypoxia is more likely to occur in twins, and, although levels of Hb S are low in the sickle-cell trait at birth, the possible role of severe hypoxia precipitating sickling cannot be entirely excluded.

Both studies were limited by small numbers, and carefully controlled investigations of larger groups of children are needed. Meanwhile, the available evidence does not warrant the conclusion that the sickle-cell trait affects physical and mental development.

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Comparison of intra-amniotic prostaglandin F_{2α} and hypertonic saline for induction of second-trimester abortion

International multicentre study by the Task Force on the Use of Prostaglandins for the Regulation of Fertility of the World Health Organisation's Expanded Programme on Research, Development, and Research Training in Human Reproduction

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Summary

The efficacy and safety of intra-amniotic prostaglandin (PG) F_{2α} (25 mg repeated in six hours) and hypertonic saline (200 ml 20% NaCl) were compared in an international multicentre randomised study organised by the World Health Organisation's prostaglandin task force.

Clinical co-ordinators of the study were: M Bygdeman (Karolinska Hospital, Stockholm, RTC*); M P Embrey (John Radcliffe Hospital, Oxford); P Gillett (Montreal General Hospital, Montreal, CRC†); R Wilson (Human Reproduction Unit, World Health Organisation, 1211 Geneva); and N Wiqvist (Karolinska Hospital, Stockholm, RTC).

Participating centres were: Edmonton University Hospital, Edmonton, Canada, CRC (Dr D Reid); Halifax University Hospital, Halifax, Canada, CRC (Dr C Tupper); Notre Dame Hospital, Montreal, CRC (Dr L Fortier); Jewish General Hospital, Montreal, CRC (Dr M M Gelfand); Montreal General Hospital, Montreal, CRC (Dr P Gillett); Saskatoon University Hospital, Saskatoon, CRC (Dr T B MacLachlan); Toronto General Hospital, Toronto, CRC (Dr J Gare); Toronto Western Hospital, Toronto, CRC (Dr W Paul); Vancouver General Hospital, Vancouver, CRC (Dr N Lee); Winnipeg General Hospital, Winnipeg, CRC (Dr A T Coopland); Institute for Research in Reproductive Biology, KEM Hospital, Bombay, CRC (Professor Purandare); Post Graduate Institute of Medical Education and Research, Chandigarh, India, CRC (Professor Devi); All India Institute of Medical Sciences, New Delhi, RTC (Professor Hingorani); Women's Hospital University of Southern California, Los Angeles, CRC (Dr Ballard); All Union Institute of Obstetrics and Gynaecology, Moscow, RTC (Professor Persianinov); Ginekolosko-Akuserska Klinika, Belgrade (Professor Husar); and Ginekolosko-Akuserska Bolnica, Belgrade (Dr Rajkavac).

*RTC = Collaborative centre for research and training in human reproduction.

†CRC = Collaborative centre for clinical research on human reproduction.

Both hypertonic saline and PGF_{2α} were found to be effective in terminating second-trimester pregnancy. The main advantage of PGF_{2α}, however, was its greater efficacy, with significantly higher success rates in the first 48 hours. Out of 717 women given PGF_{2α} 614 (85.6%) aborted within 48 hours; by 24 hours 439 (61.2%) had aborted, and by 36 hours 574 (80.1%) had aborted. Out of 796 women given hypertonic saline 641 (80.5%) aborted within 48 hours; however, by 24 and 36 hours, respectively, only 161 (20.2%) and 462 (58%) had aborted.

Although PGF_{2α} was associated with a somewhat higher frequency of minor side effects than hypertonic saline, notably vomiting and diarrhoea, these were within acceptable limits. Only 59 women (8.2%) in the prostaglandin group had more than four episodes of vomiting and 11 (1.5%) more than four episodes of diarrhoea. Other side effects occurred only occasionally. No difference was found between the two groups in the frequency of incomplete abortion or excessive bleeding.

Introduction

Early studies of the intra-amniotic administration of prostaglandin (PG) F_{2α} showed that doses of 5-25 mg often needed to be repeated to induce therapeutic abortion.¹⁻⁸ When an initial dose of 25 mg was repeated in 24 hours (if abortion was not imminent) a success rate of about 95% was achieved within 48 hours with an induction-abortion interval of about 30 hours.^{4 9-11} When the second injection was given after six hours the success rate was as high or higher and the induction-abortion interval fell to about 20 hours.^{10 11}

Since the half life of PGF_{2α} (25-40 mg injected) in amniotic fluid is 13-18 hours,¹¹⁻¹³ its concentration may fall too low for