Growth in Children with Thalassaemia Major and Effect of Two Different Transfusion Regimens

C. G. D. BROOK, E. N. THOMPSON,* W. C. MARSHALL, and R. H. WHITEHOUSE

From The Hospital for Sick Children, Great Ormond Street, and Institute of Child Health, University of London

The belief that children with thalassaemia major are small is common, but few detailed studies have been recorded. Johnston and Krogman (1964) claimed that growth and skeletal maturity were retarded; however, the majority of patients were seen only once. Wolman (1964), as a result of a cross-sectional study, concluded that children treated with high-level transfusion seemed in better health and grew more normally than those transfused at lower levels. He postulated that chronic hypoxia was more significant than iron overload in limiting growth in these patients. Johnston, Hertzog, and Malina (1966) in a longitudinal study confirmed that growth and skeletal maturity were delayed after the age of 4 years, and found that the pubertal growth spurt did not occur. They showed that high-level transfusion did not affect any of these parameters.

This study reports rates of growth in 28 Cypriot children with thalassaemia major, who were under regular supervision for periods ranging from 2 to 12 years. In 20 of them comparison was made to determine whether high-level transfusion altered the growth pattern in the individual concerned.

Material and Methods

The 12 boys and 16 girls attended the out-patient department at least once a month, when height and weight were measured and Hb estimated. Before 1966, transfusions were given when the Hb level had fallen to 4·6 g./100 ml. (low level); since then transfusions have been given at Hb levels of 8·8-9·4 g./100 ml. (high level), attempting to raise the Hb to 14·5 g./100 ml.

Height was plotted on the standard charts for British children (Tanner, Whitehouse, and Takaishi, 1966) and the average centile position read off by eye from the curve for the years before and the two years after institution of high-level transfusion. Height velocities were calculated from the observed measurements at two years and one year before high-level transfusion had

started and one year and two years after. The velocity of each of the two years before and of the two years after was recorded as a fraction of the expected (i.e. 50th centile) height velocity for the chronological age, and the average for the two periods was calculated in each case.

Skeletal maturity was assessed by examination of the hand and wrist x-ray immediately before the high-level transfusion regimen and two years later. The bone age was calculated by the Tanner-Whitehouse method (Tanner, Whitehouse, and Healy, 1962) and is expressed as a fraction of the chronological age.

Results

The serial growth data are shown in Tables I and II and Fig. 1-4.

As can be seen from the Tables and from the composite growth charts the children have grown normally. Only 3 out of 28 are beneath the 10th centile. Growth velocity and bone age are also within the normal range. However, in all three cases old enough for the pubertal growth spurt to be expected, it appears to be delayed (Fig. 1 and 2). Clinical examination confirms that puberty is delayed, and this is reflected in the skeletal maturity scores of the older children (Fig. 3 and 4).

Table I shows the growth data on 20 children on two different transfusion regimens. Though there was a marked difference in the average haemoglobins at the time of transfusion in the two periods studied, high-level transfusion has made no significant difference to the parameters of growth studied in the group as a whole. However, expected velocity figures are difficult to apply to the three oldest children with delayed puberty, and statistical examination of the height velocities of the remaining 17 children shows a significant ($p = <0.01$) decrease during the two years of high-level transfusion.

Discussion

In this series prepubertal growth was observed to be normal, and the 'fall-off' in growth after

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* Present address: Department of Child Health, Welsh National School of Medicine, Cardiff.

TABLE I

Growth Data and Pretransfusion Hb Levels of 20 Children with Thalassaemia Major on Two Transfusion Regimens*

Case No.	Year of Birth	Splenectomy	Years of Follow-up	Mean Height Centile		Velocity Expressed as Fraction of Expected Velocity for Age		Bone Age Expressed as Fraction of Chronological Age		Average Hb at Transfusion (g./100 ml.)	
				Pre '66	Post '66	Pre '66	Post '66	1966	1968	Pre '66	Post '66
Boys											
1	1952		12	25	3†	0.59	0.82	0.99	0.90	6.4	9.0
2	1957	1959	9	75	70	1.10	0.65	1.38	1.22	6.1	9.5
3	1957	1959	6	75	90	1.47	1.24	—	1.22	5.3	9.8
4	1957		7	75	75	1.17	0.92	—	1.14	4.6	9.0
5	1958		5	1	1	0.83	0.73	—	0.91	5.5	8.1
6	1958		8	20	10	0.78	0.78	—	1.00	4.0	8.7
7	1959	1961	7	45	30	1.07	0.65	1.23	1.19	5.9	8.4
8	1959		7	75	80	1.18	1.13	1.25	1.31	5.3	8.1
9	1960	1963	6	25	30	0.82	1.20	1.10	1.08	5.9	8.9
10	1962		5	50	60	1.18	1.06	0.80	1.12	5.2	9.2
11	1962		6	65	65	1.10	0.99	1.48	1.36	5.6	9.6
Girls											
13	1954	1956	12	80	25†	0.60	0.72	—	0.91	5.9	9.8
14	1955	1958	9	25	7†	0.64	0.48	0.91	0.82	5.3	9.5
15	1957		10	85	75	0.93	0.81	1.11	1.01	6.2	8.7
16	1957	1959	7	90	60	0.93	0.98	1.13	1.01	6.7	8.9
17	1961		5	45	45	0.95	0.86	0.79	0.97	5.6	9.9
18	1962	1964	4	45	45	1.38	1.05	1.42	1.31	5.5	8.7
19	1962	1964	4	50	65	1.18	1.35	1.04	1.22	6.9	9.9
20	1963		3	55	55	1.12	0.97	1.09	1.26	5.9	8.1
21	1963		3	25	30	1.37	1.10	0.71	0.99	6.2	8.9
	Mean		6.75	51.55	46.05	1.02	0.92	1.095	1.097	5.70	9.03
	S E			5.69	6.17	0.057	0.05	0.06	0.036	0.15	0.13

* Before 1966 transfusion given when Hb had fallen to 4–6 g./100 ml; after 1966 when Hb had fallen to 8.8–9.4 g./100 ml.

† Delayed puberty.

the age of 4 years recorded by Johnston *et al.* (1966) was not seen. Skeletal maturation was also normal in the prepubertal children. We have confirmed, in 2 girls and 1 boy, that adolescent growth spurt and puberty are delayed when

compared to British standards. Unfortunately no comparable standards in growth to puberty are available for these children, all of whom are Cypriot. However, the fact that the growth rates in these patients are comparable with the British standards

TABLE II

Growth Data of 8 Children with Thalassaemia Major

Case No.	Year of Birth	Years of Follow-up	Mean Height Centile	Velocity Average for 1966–68
Boys				
12	1961	3	60	0.84
Girls				
22	1960	5	10	0.79
23	1960	4	1	0.88
24	1961	3	40	1.08
25	1963	2	25	0.82
26	1964	2	50	1.06
27	1965	2	50	0.85
28	1966	2	50	0.92
Mean		2.9	36	0.90

FIG. 1.—Composite growth chart for 12 boys with thalassaemia major.

suggests that the pubertal delay may be significant in relation to their disease rather than a feature of Cypriot children in general.

The finding that high-level transfusion depresses prepubertal growth velocity must be taken as a drawback to this regimen. Though the parents consider that the children are subjectively better with high-level transfusion, this has to be balanced against the adverse effects on growth.

We consider, therefore, that as far as growth is concerned transfusions should be given in order to maintain well-being, and Hb should be maintained at not less than 6.6 g./100 ml.

Summary

Longitudinal data on height, growth, and skeletal maturation on 28 children with thalassaemia major

FIG. 2.—Composite growth chart for 16 girls with thalassaemia major.

are reported. Prepubertal growth and skeletal maturity were within normal limits, but in 3 children where puberty would have been expected, it appeared to be delayed.

In 20 children, in whom a comparison of height velocity before and after a high-level transfusion regimen was possible, the latter was associated with a significant depression of prepubertal growth. So far as growth is concerned, high-level transfusion is of no advantage and may be deleterious.

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REFERENCES

- Johnston, F. E., Hertzog, K. P., and Malina, R. M. (1966). Longitudinal growth in thalassaemia major. *Amer. J. Dis. Child.*, **112**, 396.
 —, and Krogman, W. M. (1964). Patterns of growth in children with thalassaemia major. *Ann. N.Y. Acad. Sci.*, **119**, 667.
 Tanner, J. M., Whitehouse, R. H., and Healy, M. J. R. (1962). *A New System for Estimating Skeletal Maturity from the Hand*

FIG. 3.—Skeletal maturity scores for 11 boys with thalassaemia major.

FIG. 4.—Skeletal maturity scores for 9 girls with thalassaemia major.

and Wrist, with Standards Derived from a Study of 2,600 Healthy British Children. Centre Internationale de l'Enfance, Paris.

—, —, and Takaishi, M. (1966). Standards from birth to maturity for height, weight, height velocity, and weight velocity: British children, 1965. Parts I and II. *Arch. Dis. Childh.*, **41**, 454 and 613.

Wolman, I. J. (1964). Transfusion therapy in Cooley's anemia: growth and health as related to long-range hemoglobin levels. *Ann. N.Y. Acad. Sci.*, **119**, 736.

Correspondence to Dr. C. G. D. Brook, Institute of Child Health, 30 Guilford Street, London, W.C.1.