THE MANAGEMENT OF BETA-THALASSAEMIA IN AN URBAN DISTRICT HOSPITAL

P.C.W. LYN
H.C. TEH
R.F. MULVEY

SUMMARY

This paper is based on the beta-thalassaemia programme at the Duchess of Kent Hospital, Sandakan, Sabah. It seeks to show that a hypertransfusion regimen which improves the quality of life of children with thalassaemia major can be practised in district and general hospitals if there is an organised blood recruitment programme, at least at departmental level. Such a programme reduces the demand on the hardpressed hospitals' blood banks. Frequent and regular transfusions can be given with minimal interference with the school and family life of affected children and reduces immeasurably the social, emotional and financial strain on the affected families.

There is also an urgent need to define the magnitude of the problem of beta-thalassaemia through population studies so that genetic counselling can be given and adequate resources can be allocated to improve the quality of life of affected patients.

P.C.W. Lyn, MA (Oxon) BM BCH, MRCP (UK)
H.C. Teh, MBBS
R.F. Mulvey, BA BSW (Melbourne)
Depts. of Medicine & Social Work
Duchess of Kent Hospital
Sandakan, Sabah

INTRODUCTION

Homozygous beta-thalassaemia (thalassaemia major) is a hereditary anaemia, often presenting during infancy or early childhood. The defect lies in the absence or grossly reduced production of beta-globin chains in haemoglobin synthesis. The incidence of the heterozygous form of the disease in South-East Asia has been variously estimated to be between 3 to 5%;[1,2] the prevalence of the homozygous form in Malaysia which has a multiethnic population is unknown although the disease is commonly encountered in hospitals throughout the country.

The management of children with beta-thalassaemia major (TM) is based on frequent and repeated blood transfusions. It is now generally accepted that the maintenance of haemoglobin level above 10g/dl greatly improves the growth and well-being of affected children and minimizes bone expansion and deformity by suppressing endogenous erthyropoeisis.[3,4,5] Implementation of this 'hypertransfusion' regimen however makes heavy demands on the hospital's blood bank and in the absence of an organised blood recruitment service at district hospital level, management of TM children often becomes reduced to irregular transfusion on an 'ad hoc' basis. This unfortunate state of affairs may also exist at the general hospital level.

The thalassaemia programme at the Duchess of Kent Hospital in Sandakan, Sabah, was started

two-and-a-half years ago in an attempt to address this problem. The hospital serves as a referral centre for a mixed urban population of around 74,000 and an additional large rural population of 78,000 (Fig. 1). Here, in the absence of a hospital blood transfusion service, a small scale department-based blood recruitment programme ensures adequate blood supply for all children with thalassaemia seen.

PATIENTS AND METHODS

Between January 1982 and June 1984, all children with suspected TM were screened by haemoglobin electrophoresis after exclusion of other causes (Fig. 2). These children usually presented with anaemia with or without hepato-splenomegaly. Blood samples were sent to

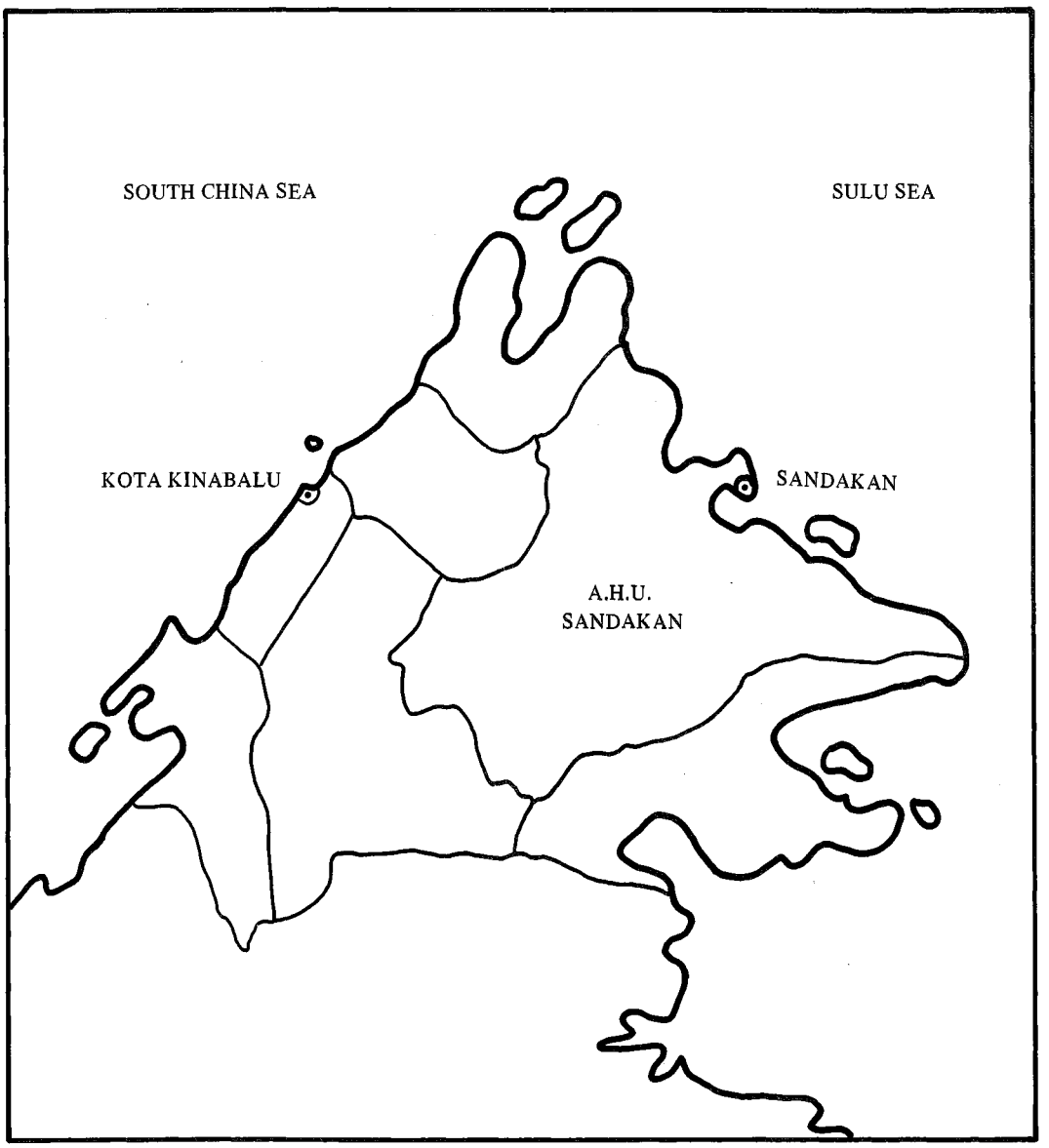

Fig. 1 The Area-Health Unit of Sandakan.

the referral centre (Queen Elizabeth Hospital, Kota Kinabalu) for peripheral blood film examination, and cellulose acetate haemoglobin electrophoresis prior to transfusion. Patients who had been previously diagnosed as TM before the establishment of the thalassaemia programme were also rechecked by haemoglobin electrophoresis before entering the programme. In all cases, parental blood film examination and haemoglobin electrophoresis were done to help confirm diagnosis and family studies were done where possible to trace other possibly affected family members. A total of 25 patients between the ages of five months and 12 years were found to have homozygous thalassaemia (major or intermedia) and were followed up in the beta-thalassaemia transfusion programme.

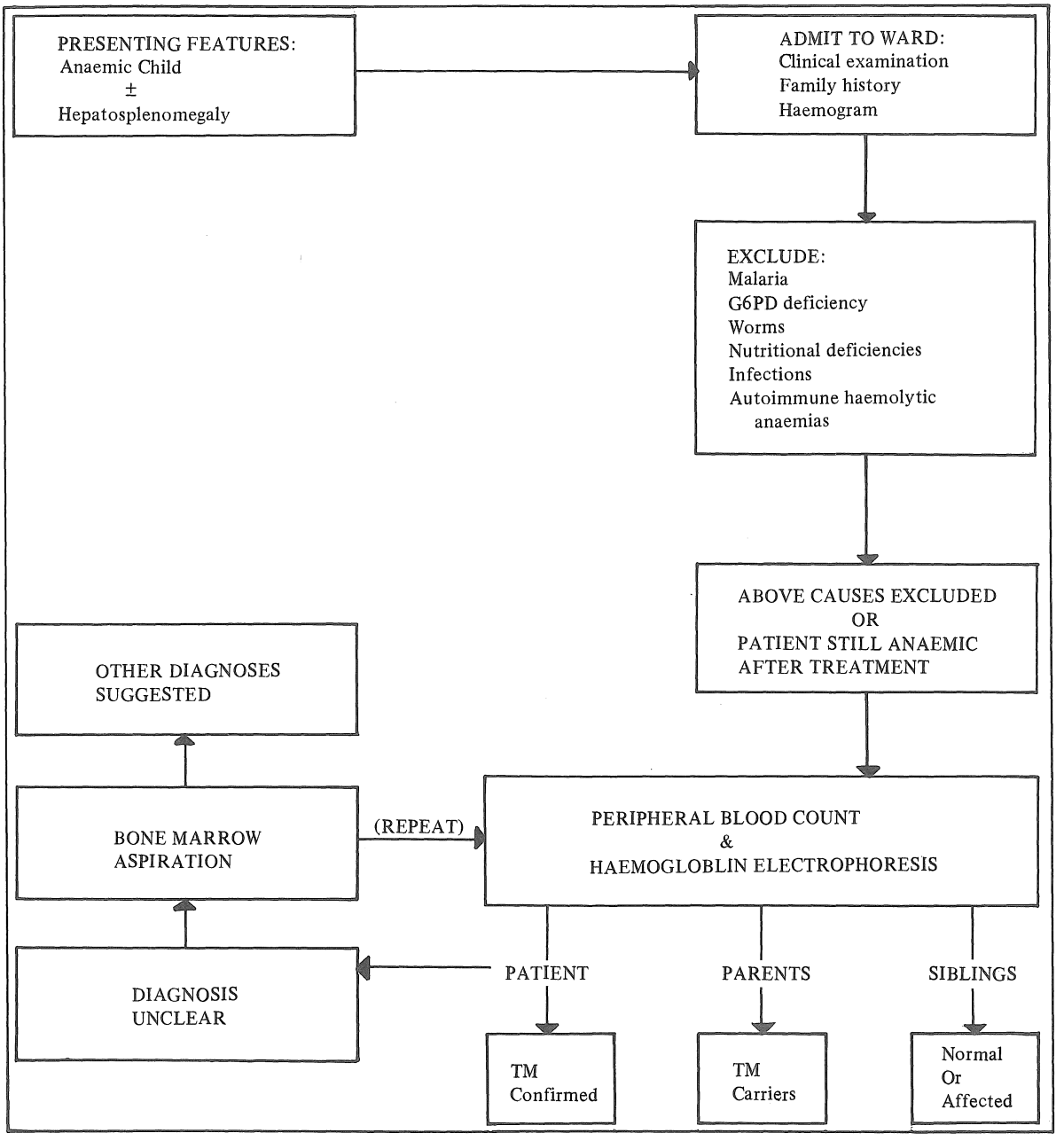

Fig. 2 **Flow Chart of diagnosis of thalassaemia major.**

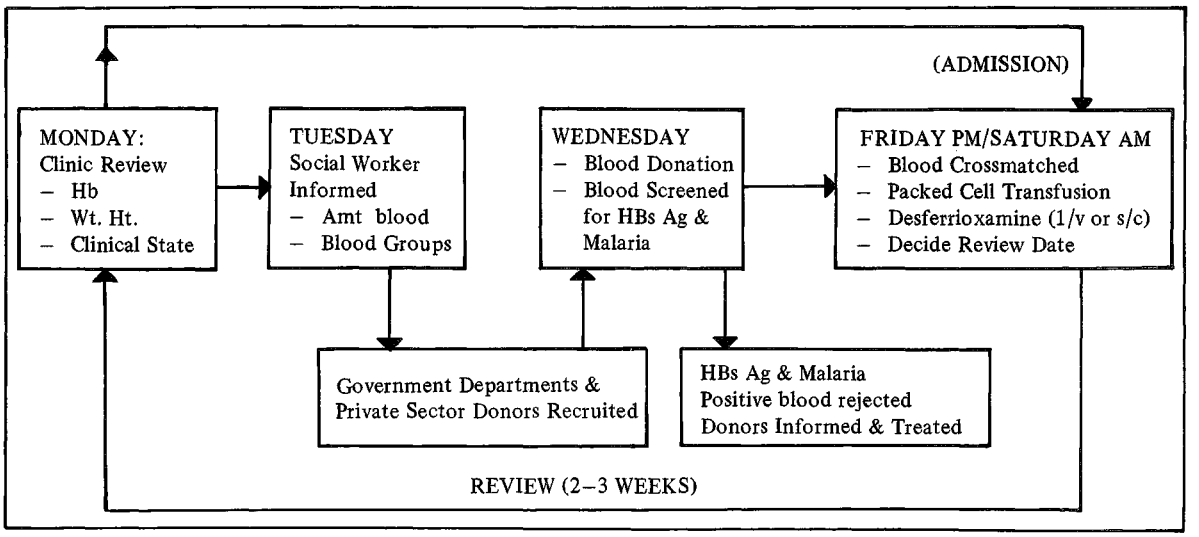

Fig. 3 Flow Chart on the follow-up management of thalassaemia children.

The programme consists of regular fortnightly to three-weekly clinic attendances. At each visit (on a Monday), the haemoglobin, height, weight and clinical state of the child are checked. Arrangements are made for the admission of the child for blood transfusions later in the week (Friday or Saturday) if the haemoglobin level is below 11g/dl. The approximate total amount of blood required for the weekend admissions is estimated at the Monday clinic and the information passed on to the social work department.

The latter then liases with the heads of government departments or private companies and arranges for a specific number of healthy employees to donate blood on a voluntary basis during mid-week. The flow chart (Fig. 3) illustrates the usual sequence of events from the time the patient is seen in clinic until his admission for blood transfusions.

RESULTS

Patients and their families

A total of 25 patients are presently in the thalassaemia programme. Nine (36%) of these were diagnosed before the start of the programme in January 1982, the remaining 16 (64%) entered between January 1982 and June 1984. The male to female ratio was approximately equal (13:12). The ages of presentation ranged between five months and 12 years with a mean age of 2.5 years.

Of the 25 patients, 23 (92%) lived in the urban and suburban areas within easy access of the hospital, the remaining two (8%) lived in the rural interior. The largest racial groups were the Kadazans and Sungei people, who formed 32% and 28% of our clinic, respectively (Table I).

21 families were able to cooperate in a questionnaire interview to determine income bracket and other relevant information relating to their children's illness. Most of the families were from the lower income group (social class III or below) (Table II). Financial burden relating to the possible need to purchase blood was the single major cause of worry amongst the parents (Table III).

All parents stated that the health of their children had improved with the thalassaemia programme; nearly all agreed that their child's appetite and physical activity had also improved. Of the 21 children, nine were of schooling age. Of these, eight attended school, one received home tuition through a longstanding arrangement predating the thalassaemia clinic. School attendance improved in 89% of those attending school (Table IV).

Regular hospital admissions for transfusions were, on the whole, well tolerated – over 70% of the

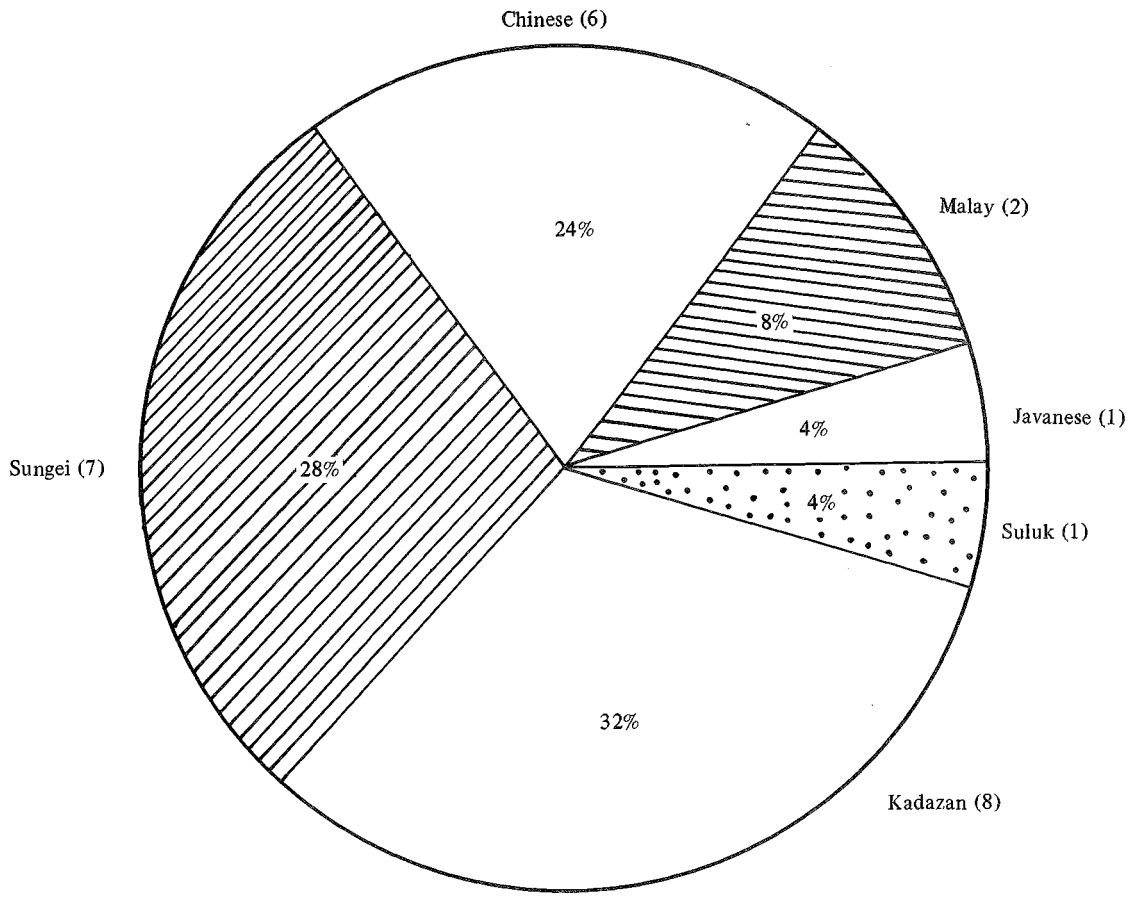

TABLE 1
RACIAL COMPOSITION OF THE PATIENTS IN THE THALASSAEMIA PROGRAMME
(No. of parents in parenthesis)

TABLE II
FAMILY INCOME BRACKET OF THALASSAEMIA PATIENTS

Social class	Monthly income bracket (M$)	No.	(%)
I	> $2000	3	(14)
II	$1000 – 2000	4	(18)
III	$501 – 999	6	(29)
IV	$280 – 500	6	(29)
V	< $280	2	(10)
	Total	21	(100)

TABLE III
MAIN WORRIES OF PARENTS ON DISCOVERING THAT THEIR CHILD HAD THALASSAEMIA MAJOR

	No.	(%)
Financial burden from finding blood donors	15	(71)
Travelling difficulties	1	(5)
Knowledge of patient's shoft life-expectancy	1	(5)
Poor health of child	3	(14)
Others	1	(5)
Total	21	(100)

TABLE IV
IMPACT ON PATIENT'S LIFE AFTER JOINING
THE THALASSAEMIA PROGRAMME

Patient	Improvement No.	(%)	Same condition No.	(%)	Worse condition No.	(%)
Health	21	(100)	–	–	–	–
Appetite	20	(95)	1	(5)	–	–
Physical activity	20	(95)	1	(5)	–	–
School attendance*	7	(89)	1	(19)	–	–
Willingness for regular hospital transfusions	15	(71)	5	(24)	1	(5)

*Total no. attending school = 8.

children come in readily (Table IV). Overall, 20 (95%) of the patients expressed satisfaction with the functioning of the thalassaemia programme; the only exception being an understandable case of distance – the family lived more than a hundred miles from hospital.

Blood donation and transfusion programme

Taking the six months period from January and June 1984, a total of 192 pints of blood were donated. Of these, 172 pints (89.5%) were donated by government employees and 20 pints (10.5%) by individuals or private sector employees (Table V). The average amount of blood donated per week was 7.4 pints. The mean frequency of transfusion over the same period was approximately once every four weeks per patient. This means that of the 25 children, an average of six were admitted each weekend for transfusion. The average amount of blood transfused per weekend was 5.6 pints. Donation therefore exceeded use by approximately 1.8 pints per week. This excess is accounted for by HBs Ag positive or malaria positive blood which were rejected.

DISCUSSION

The aims of the thalassaemia programme are two-fold. Firstly, it is the improvement of the quality of life of the affected children with minimal interference in their schooling and home life. This improvement on the hypertransfusion regime is seen at several levels. The children continue to be active both at school and at home. In fact, overall health improved in all the children, and nearly all have an improved level of physical activity and appetite (Table IV). Parental satisfaction was profound. Also anthrophometric and clinical indices (to be presented in a later paper) indicate improved or normal growth in most cases. Clinics and hospital admissions (for transfusions) are organised so as not to clash with school hours. The patients attend the Monday clinics in the morning if their school hours are in the afternoon and *vice versa*. Similarly, weekend admissions for blood transfusions are organised so that those who attend school are admitted on Saturdays. Non-school attenders come in on Fridays.

Parents are encouraged to ensure that their children do not miss school. The children are not discouraged from normal sporting or physical activities at school or at home. On the hyper-transfusion regimen, most of these children are hardly recognised as 'abnormal' as they do not develop the marked morphological features of thalassaemia and therefore integrate easily with their peers.

Secondly, the programme undoubtedly reduces the emotional and social stress to the family. Responses of the parents and family to the

thalassaemia child can often include worry, sadness, anxiety, shock, guilt and depression.[6] As a consequence of the child's improved state of well-being, these stresses are minimized and family stability is more likely to be ensured.

In addition, the programme reduces the financial strain which in a recent survey was shown to be the biggest cause of stress among parents of beta-thalassaemia children.[6] This was also confirmed in our survey of parents of the TM children (Table III). It has already been noted that the majority of children come from the poorer social strata (Table II). It is therefore obvious that unless a regular blood donation system is organised by the medical department, the parents are not in a position to organise donations or purchase blood privately for their children. Even in a close-knit extended family situation, the potentially large numbers of family donors available will be rapidly exhausted by the high frequency of blood transfusion for one affected child. The burden of finding regular blood donors is an extremely heavy one for any single family and should therefore be carried out by the hospital or medical unit.

Following diagnosis, the parents are told about the disease and its hereditary basis. Genetic counselling is given where possible. Ocasionally, however, strong social customs and traditions override genetic consideration. Other forms of practical support may also be necessary. Parents who have difficulty in taking time off from work to accompany their children to hospital are given explanatory letters for their superiors or department heads. In nearly every case, cooperation from superiors and department heads have been readily obtained.

To ensure maximum viability of each transfusion only fresh blood is used. All blood transfused are less than three days old (Fig. 3) and are fully cross-matched with the sera of the recipient. The exclusion of Hepatitis-B surface antigen and malaria positive blood is important. Hepatitis-B carriers significant morbidity in patients already with chronic liver problems from iron overload. Haemolysis from malaria in an already anaemic patient may be rapidly fatal.

It needs to be stressed here that the programme is aimed primarily at improving the quality of life and not necessarily the life span of thalassaemia children. For reasons of cost and logistics we have not found it possible to address adequately the problem of iron overload – the single most common cause of early death.[7] The iron chelator, desferrioxamine is an expensive drug and all except two of the families cannot afford it or the subcutaneous infusion pump for home use.

All children, however, receive an overnight subcutaneous or intravenous infusion of desferrioxamine (0.5 to 1g) following each blood transfusion. Intensive intravenous and subcutaneous infusions have been shown to be more effective than the intramuscular route in achieving iron excretion[8,9] but the infrequent infusions of desferrioxamine in our case (once every three to four weeks) are probably inadequate to achieve negative iron balance. The question, however, of whether daily subcutaneous desferrioxamine significantly prolongs survival is presently a subject of extensive clinical trials. All our thalassaemia children are in addition given daily low dose ascorbic acid (50–200mg) and folic acid (5–10mg). Correcting the deficiency of ascorbic acid associated with iron overload is known to increase urinary iron excretion during desferrioxamine infusion still further[10] although high dose ascorbic acid has been implicated as being detrimental to cardiac function in thalassaemia patients.[11] High dose ascorbic acid supplement is not used in our patients.

The Area Health Unit of Sandakan covers a largely rural area of some 10,000 square miles (Fig. 1). The patients recruited to our clinic however live mainly in the urban and sub-urban areas which implies that our thalassaemia management programme falls short of offering any significant services to the population living in the rural interior. This is largely due to the poor accessibility of the hospital to the rural population. There may be, however, a significant and perhaps even larger population of thalassaemia patients in the interior. This is because the Kadazans and Sungei people who already form the largest racial sub-groups of our existing clinic are the two major races in the

TABLE V
SOURCES OF BLOOD DONATED
(JANUARY – JUNE 1984)

Donors	No. of donation units	(%)
Government departments	147	(76)
Armed Forces	21	(11)
Colleges/schools	4	(2)
Private companies	6	(3)
Individuals	14	(8)
Total	192	(100)

rural interior of Sandakan. A population survey is urgently needed to define the magnitude of the thalassaemia problem in Sabah and indeed in Malaysia so that early genetic counselling can be given where possible and adequate steps taken to improve the quality of care of thalassaemia patients.

Our data on blood donors (Table V) indicate that blood donation from the private sector and from individuals is lagging far behind that of the government sector and armed forces. Obviously this is a responsibility that cannot be borne by one sector of the public alone and increased public education is desperately needed to redress this imbalance. There is little doubt that the shortage of blood for thalassaemia patients represents only the tip of the proverbial iceberg in an ever present supply-and-demand problem in hospitals throughout the country. We have shown that a department-based blood recruitment programme circumvents this problem and feel that the institution of similar programmes could benefit thalassaemia patients in district and general hospitals.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the help of Assistant Nurse Josie Kwan of the thalassaemia clinic, Lucy Smail of the social work department, Sister H.F. Ling and the nursing staff of the children's ward, without whom this programme would not have seen the light of day. Thanks are also due to Nancy Lyn who typed the manuscript and to Dr. Mechiel K.C. Chan, Director of Medical Services, Sabah for permission to publish this article.

We also wish to acknowledge our debt to Dr A.K. Ghosh (MD) under whom this programme first began.

REFERENCES

1 Kendall A G. Thalassaemias. *Med Int* 1983;26:1169-1173.

2 Todd D, Kan S P. Anaemia in pregnancy in Hong Kong. *J Obst & Gynae* 1962;72:738-744.

3 Piomelli S, Karpatkin M H, Arzanian M, *et al.* Hypertransfusion regimen in patients with Cooley's anaemia. *Ann N Y Acad Sci* 1974;232:186-192.

4 Modell B. Total management of thalassaemia major. *Arch Dis Child* 1977;52:489-500.

5 Weiner M, Karpatkin M H, Hart D, *et al.* Cooley's anaemia: High transfusion regimen and chelation therapy, results and perspective. *J Paed* 1978;92:653-658.

6 US Dept. of Health Education & Welfare. *Assessment of Cooley's anaemia – research and treatment.* NIH Publication 1980;80/1653:51-60.

7 Engle M A. Cardiac involvement in Cooley's anaemia. *Ann N Y Acad Sci* 1964;119:694-702.

8 Anonymous. Intensive iron chelation therapy in thalassaemia: *Br Med J* 1978;282:782-783.

9 Propper R, Cooper B, Rufo R R, *et al.* Continuous subcutaneous administration of desferrioxamine for iron overload. *New Eng J Med* 1977;297:418-423.

10 O'Brien R T. Ascorbic acid enhancement of desferrioxamine induced urinary iron excretion in thalassaemia major. *Ann N Y Acad Sci* 1974;232:221-225.

11 Nienhuis A W, Bez Jr E J, Propper R, *et al.* Thalassaemia major: molecular & clinical aspects. *Ann Int Med* 1979; 91:883-897.

12 Mieli Vergani G, Vergani G, White Y, *et al.* Hepatitis B virus infections in thalassaemia major treated in London and Athens. *Br Med J* 1984;288:1804.