Racial differences in red cell indices

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SUMMARY A high prevalence of iron deficiency was found in apparently healthy Asian immigrant children in Harrow. After excluding children with overtly abnormal red cell indices, Asian and European children had identical haemoglobin values, but Asian children had much lower mean cell volume and mean corpuscular haemoglobin values and higher red blood cell values.

The criteria that define children as normal for inclusion in haematological reference ranges are critical. Viteri *et al* excluded all children with hookworm in a central American population, and also those with low serum concentrations of iron, folate, and vitamin B₁₂, although the authors did not state how their criteria for normal serum concentrations were derived.¹ Other workers included data from all children attending infant welfare clinics,² or kindergartens,³ or used longitudinal data on healthy full term infants.⁴ We analysed data from supposedly normal children attending child welfare clinics and schools. The data were subdivided and analysed according to age and race.

Subjects and methods

The subjects were normal healthy children attending infant welfare clinics and schools in the Harrow area between May 1980 and June 1981. They were aged between 6 months and 6 years of age: children with known haematological disorders (one child with thalassaemia trait) and those taking haematinics (two children taking oral iron preparations) were excluded from the study. Blood was already being taken, with informed parental consent, for a study on pertussis antibodies (to be published elsewhere). When sufficient blood had been obtained by venepuncture 0.3–0.5 ml was placed in a paediatric sequestrene tube and agitated gently. Specimens were analysed on a model S Coulter counter within six hours of venesection.

Initially, if particular results were evidently abnormal (haemoglobin < 10.0 g/dl or mean cell volume < 70 fl, or both) the child was traced and blood taken

for serum iron concentration, total iron binding capacity (TIBC), and haemoglobin electrophoresis. At a later stage of the study an attempt was made to trace all statistically defined abnormal children (outliers) to perform the same studies, but this was not always possible.

Beta thalassaemia trait was diagnosed when HbA₂ concentrations were greater than 3.5% or when those of HbF were greater than 2.0%, or both, in the presence of microcytosis and a near normal haemoglobin value. Iron deficiency was diagnosed on the basis of a serum iron concentration below 12 µmol/l (67 µg/100 ml) and iron binding capacity above 75 µmol/l (4/8.1 µg/100 ml) (our laboratory normal range).

A few children with one or more haematological values well outside the other values—that is, statistical outliers—were excluded from analysis in the 95% reference ranges. The method used for development of the reference ranges was as described previously for serum immunoglobulin values in childhood.^{5,6} Briefly, the data were transformed so that the ensuing data values were reasonably normally distributed at all ages. The transformation for which the subsequent values were closest to a normal distribution was found using Shapiro and Wilk's W test.⁷ A polynomial regression model was fitted to the transformed data and another polynomial regression model was fitted to the standard deviations of the residuals from the previous regression. For this purpose the age range was subdivided into eight. The reference range was calculated as follows:

$$f_1(\text{age}) \pm (\text{SD } (1.96)) f_2(\text{age})$$

f_1 and f_2 are the fitted functions of age derived by the two polynomial regression models. The goodness of fit of the models was carefully assessed.

Results

Data were available from 251 children, 189 of whom were of European and 62 of whom were of Asian extraction. Fifteen children with extreme results were excluded from the derivation of reference ranges (Table). Of these 15 children, seven (six Asian, one European) had iron deficiency, three (two Asian, one European) had β thalassaemia trait, and five (four Asian, one European) could not be traced. Thus all statistical outliers who could be traced were abnormal. The incidence of confirmed iron deficiency based on our criteria was, therefore, six in 62 or 9.6/1000 Asian children compared with one in 189 or 5.3/1000 European children ($p < 0.001$, Fisher's exact test).

After the outliers' results had been excluded haematological data were analysed as previously described⁵ and examined for variability with age, sex, and race. No difference between sexes was found for any variable.

Haemoglobin

There was a weak but significant age effect ($p = 0.025$) corresponding to an increase in haemoglobin concentration of 0.06 g/dl per year. Fig. 1 shows the results. The mean haemoglobin concentration can be calculated as $(12.11 + 0.00562A)$ g/dl where A = age in months, and the standard deviation (SD) is 0.76 g/dl. There was no significant difference between the mean haemoglobin for European children and Asian children: mean haemoglobin values were 12.30 (0.80) g/dl and 12.39 (0.82) g/dl, respectively ($t = 1.57$, $p = 0.1$).

Red blood cell count

There was a significant difference between the mean red blood count for European children ($4.69 (0.32) \times 10^{12}/l$) and Asian children ($5.00 (0.36) \times 10^{12}/l$); $t = 5.87$, $p < 0.0001$. The 95% reference ranges were

Fig. 1 Reference range for haemoglobin (Hb) for European and Asian children. $\circ$ = Normal children; * = Iron deficient; $\times$ = β -thalassaemia trait; + = Outlier lost to follow up; Mean $\pm$ 2 standard deviations is shown.

(4.05 to $5.33 \times 10^{12}/l$) for European children and (4.36 to $5.64 \times 10^{12}/l$) for Asian children. There was no significant age effect ($p = 0.8$).

Packed cell volume

Packed cell volume did not change with age. Analysing European and Asian children together, the mean packed cell volume was 37.52 (2.26)%. When considered separately the mean packed cell volume for Europeans was 37.37 (2.23)% and for Asians 38.01 (2.34)%; $t = 1.92$, $p = 0.06$. The 95% reference range for Europeans and Asians combined at any age from 6 months to 6 years was 33.09–41.95%.

Table Characteristics of children with abnormal haematological values

Age (year)	Sex	Race	Red blood cells ($\times 10^{12}/l$)	Haemoglobin (g/dl)	Packed cell volume (%)	Mean cell volume (fl)	Mean corpuscular haemoglobin (pg)
2y 0m	M	Asian	5.70	10.3	35.9	63	18.1
2y 0m	F	Asian	5.19	10.4	35.8	69	20.0
2y 7m	M	Asian	5.40	10.1	35.6	66	18.7
2y 1m	F	Asian	5.74	9.8	36.2	63	17.1
1y 8m	F	Asian	4.56	7.2	26.0	57	15.7
0y 7m	F	Asian	4.99	10.3	32.9	66	20.6
5y 7m	M	European	4.64	9.0	28.8	62	19.4
3y 0m	F	Asian	5.89	10.3	35.9	61	17.4
4y 4m	F	European	5.41	9.8	33.5	62	18.1
2y 7m	M	Asian	6.42	10.8	34.8	54	16.8
1y 4m	F	Asian	5.22	9.8	34.9	67	18.3
1y 3m	M	Asian	5.85	10.9	37.0	63	18.6
1y 4m	M	Asian	5.09	9.9	34.1	67	19.4
3y 5m	M	Asian	4.87	10.4	33.1	68	21.4
1y 2m	F	European	6.24	12.2	41.1	66	19.5

ND = Not done

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Mean corpuscular volume

Mean corpuscular volume increased significantly with age. It also differed significantly by race: the mean corpuscular volume for Asian children of 76.02 (3.26)fl was far lower than that for European children, 79.70 (3.14)fl ($t = 7.16$ $p < 0.0001$). Separate equations were, therefore, derived for the mean corpuscular volume for Asian and European children using a common regression slope for the two groups: Asian children, mean corpuscular volume = $(75.11 + 0.033A)$ fl; European children, mean corpuscular volume = $(78.66 + 0.033A)$ fl; Asian and European children, standard deviation = 3.10 fl ($A =$ age in months). Figs. 2 and 3 show the reference ranges.

Fig. 2 Reference range for mean corpuscular volume for Asian children. $\circ$ = Normal children; * = Iron deficient; $\times$ = β -thalassaemia trait; + = Outlier lost to follow up; Mean $\pm$ 2 standard deviations is shown.

Fig. 3 Reference range for mean corpuscular volume for European children. $\circ$ = Normal children; * = Iron deficient; $\times$ = β -thalassaemia trait; + = Outlier lost to follow up; Mean $\pm$ 2 standard deviations is shown.

Mean corpuscular haemoglobin

Mean corpuscular haemoglobin, like mean corpuscular volume, increased with age and also showed a significant difference between European and Asian children (mean corpuscular haemoglobin = 26.10 (1.29) and 24.87 (1.59) pg, respectively; $t = 5.65$, $p < 0.0001$). The models derived, analysing separately for race, were as follows:

Asian children, mean corpuscular haemoglobin = $(24.42 + 0.015A)$ pg; European children, mean corpuscular haemoglobin = $(25.62 + 0.015A)$ pg; Asian and European children, standard deviation = 1.32 pg ($A =$ age in months). Figs. 4 and 5 show the reference ranges.

Mean corpuscular haemoglobin concentration (g/dl)	Serum iron concentrations (μ mol/l)	Total iron binding capacity (μ mol/l)	Haemoglobin electrophoresis	Diagnosis
28.7	5	114	Normal	Iron deficient
29.1	8	90	Normal	
28.4	6	96	Normal	
27.1	4	99	Normal	
27.6	10	93	Normal	
31.3	5	88	Normal	β -thalassaemia trait
31.3	3	74	Normal	
28.7	24	42	A ₂ 4.6% F 1.9%	
29.2	14	35	A ₂ 5.9% F 2.4%	
31.0	34	60	A ₂ 5.5% F 2.6%	
28.0	ND	ND	ND	Lost to follow up
29.5	ND	ND	ND	
29.0	ND	ND	ND	
31.4	ND	ND	ND	
29.6	ND	ND	ND

Fig. 4 Reference range for mean corpuscular haemoglobin for Asian children. $\circ$ = Normal children; * = Iron deficient; $\times$ = β -thalassaemia trait; + = Outlier lost to follow up; Mean $\pm$ 2 standard deviations is shown.

Mean corpuscular haemoglobin concentration

There was no apparent age effect, either in mean values or variability, of mean corpuscular haemoglobin concentration, so the best model was mean corpuscular haemoglobin concentration of 32.77 (1.09) g/dl, 95% reference range, 30.63–34.91 g/dl. There was no difference between mean corpuscular haemoglobin concentration for Europeans and Asians

Fig. 5 Reference range for mean corpuscular haemoglobin for European children. $\circ$ = Normal children; * = Iron deficient; $\times$ = β -thalassaemia trait; + = Outlier lost to follow up; Mean $\pm$ 2 standard deviations is shown.

(mean (SD), = 32.77 (0.96) g/dl and 32.81 (1.51) g/dl, respectively; t = 0.16, p = 0.8).

Discussion

A high rate of overt iron deficiency in Asian immigrant children has been recognised for some time and is related to early weaning⁸ and weaning on to diets deficient in iron.^{9,10} This may partly be related to social class as iron deficiency and iron deficiency anaemia are considerably more prevalent in low income families.^{11,12} Not only did we find that six of the 62 Asian children studied had abnormal red cell indices and low serum iron concentrations, but four of the five children with abnormal red cell indices who were lost to follow up were also Asian. Thus in this small survey at least 9.7% of Asian children were frankly iron deficient, and 3.4% had β -thalassaemia trait. The Asian children in Harrow tend, however, to come from families of higher socioeconomic class than those in Wolverhampton,⁸ Blackburn,⁹ and Tower Hamlets,¹⁰ and the prevalence of iron deficiency in Asian children in Harrow is thus surprisingly high. Unfortunately, we did not obtain a dietary history on the children studied.

Haemoglobin values increased with age, but there was virtually no difference between the mean haemoglobin concentrations of European and Asian children at any given age. Packed cell volume and mean corpuscular haemoglobin concentration were also very similar in European and Asian children. Even allowing for age, however, mean cell volume and mean corpuscular haemoglobin were significantly lower in Asian children than in Europeans at the $p < 0.0001$ level, and red blood cells significantly higher, suggesting an effect that was certainly not arbitrary. There would seem to be two possible explanations for these racial differences. The first is that there was a high prevalence of mild subclinical iron deficiency in the Asian children, causing an effect on the most sensitive red cell indices, red blood cells, mean cell volume, and mean corpuscular haemoglobin, but not on overall measurements of haemoglobin. A second possibility is that there was some inherent difference in the morphology of the red cell between Asian and European children. We did not routinely measure serum iron concentrations or any other variable of iron balance and are unable to say if either of these suggestions is valid. The high prevalence of overt iron deficiency in a middle class Asian immigrant population, however, particularly evident in children between 18 and 36 months old (Table), suggests that the diet of many Asian immigrant children, regardless of social class, may be deficient in iron. Further studies are necessary to clarify this issue.

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Surgical Pathology of Bone Marrow. Core Biopsy Diagnosis. Major Problems in Pathology. Vol 17. B Wittels. (Pp 162; £35.50.) WB Saunders. 1985.

The interpretation of bone marrow pathology continues to present difficulties both for pathologists and haematologists, who for different reasons tend to feel inadequate for the task. This book aims to provide the kind of guidance which both require. Emphasis has been placed on key issues; comprehensiveness has not been attempted, although the scope is quite wide ranging. Histopathologists, in particular, will appreciate the option for standard histological methods. Specialised techniques such as plastic embedding and ultrastructure are thought to be too laborious, too restrictive, and, with some notable exceptions, unnecessary for general purposes. The sections on myeloproliferative disorders and metastatic tumours are probably the best. The approach to lymphoid disorders is less avant garde; little mention is made, for example, of T cell neoplasia. A few eyebrows will be raised by the assertions that histiocytosis X is neoplastic and that the so called malignant histiocytosis complicating acute leukaemia is benign and reactive. Nevertheless, pathologists and haematologists will unquestionably benefit from reading this stimulating, if at times rather controversial, monograph.

FD LEE

Some new titles

The receipt of books is acknowledged, and this listing must be regarded as sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits.

A Practical Approach to Infectious Diseases. Ed RE Reese, RG Doublas. (Pp 798; soft cover £30.65.) Churchill Livingstone. 1985. ISBN 0 316 73712 7.

Transformation Assay of Established Cell Lines; Mechanisms and Application. IARC Scientific Publications no 67. Ed T Kakunaga, H Yamasaki. (Pp 225; £20.) Oxford University Press. 1986.

Growth factors in biology and medicine. Ciba Foundation Symposium 116. (Pp 283; £27.95) Pitman. 1985. ISBN 0 272 79818 5.

Biochemistry of Macrophages. Ciba Foundation Symposium 118. (Pp 256; £27.95.) Pitman. 1985. ISBN 0 272 79832 3.

Prenatal and Perinatal Infections; report on a WHO meeting. EURO reports and studies no 93. (Pp 147; Sw fr 12.) World Health Organisation. 1985. ISBN 92 890 1259 5.

Modern Cell Biology. Vol 4. Series ed Birgit H Satir. Modern Cell Biology Series. (Pp 240; £28.) Alan R Liss Inc. 1985. ISBN 0-8451-3303-9.

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Correction

The formula on page 105 of the January issue should read:

$f_1(\text{age}) \pm 1.96 f_2(\text{age})$ and not $f_1(\text{age})$ (SD 1.96) $f_2(\text{age})$