THE ETIOLOGY AND THE EFFECTS OF MINOR GRADES OF ANAEMIA IN YOUNG CHILDREN

STUDIES AT A GROUP OF WAR-TIME DAY NURSERIES

BY

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Introduction. The etiological factors influencing the haemoglobin level of the community in this country and the effects of minor grades of anaemia are still incompletely known, and the present investigation represents an attempt to obtain data bearing on these subjects among children attending war-time day nurseries. Many of the inferences have, however, a wider application.

Clinical material. The 913 children examined attended one or other of eight war-time day nurseries in Islington in North London. Some, whose attendance was short, had one examination only; some had repeated haemoglobin estimations for over two years between August, 1942, and December, 1944. The capacity of the individual nurseries varied between 33 and 70 places, and the 8 nurseries could accommodate 441 children at any one time. As some children were always absent, and it was desired to keep the nurseries full, each matron was instructed to keep on her register 20 per cent. more children than the nursery had space for. The children's mothers were all wage-earners, nearly all full time, working in factories, shops, transport, etc. Breakfast, dinner and tea were provided for the children in the nurseries. These were at first open for twelve hours on six days a week: latterly the hours were reduced by closing on Saturday afternoons (Mackay, Dobbs and Bingham, 1945). During the time of the investigation the children received no iron treatment in the nurseries other than that set forth in the section below on the effect of iron therapy.

Large-scale evacuation of children from London during the flying bomb attack in the summer of 1944 resulted in an exodus from the nurseries, and continuity of treatment and of observation were prevented after May, 1944.

Technique. Estimates were made with a Haldane colour standard, the National Physical Laboratory B.S.I. correction being applied for colour tube and pipette, and a mean percentage correction for the

diluting tubes: the technique was the same as that previously used by the writers (Mackay, Dobbs and Bingham, 1945). All three observers used the same colour standard.

COLOUR TUBE CHANGES AND COLOUR MATCHING. All haemoglobin estimations were made by K.B., R.H.D. and H.M.M.M. Excepting for the changes, necessitated by R.H.D. leaving to join the R.A.M.C. in May, 1943, all observations at any one nursery were made by one observer. Colour tube 1 was in use by all three observers until January, 1943, when it was broken, and thereafter colour tube 2 was used for all observations until the end of the investigation in December, 1944. Colour tube 2 was throughout not as pink a standard as colour tube 1, but a comparison of mean values obtained with the two standards and with a third standard used in a test series (see table 1, section (a) and (b)) does not suggest that this influenced the readings. Differences in colour matching between the three observers were small. K.B. tended to match at a slightly lower level than H.M.M.M., both using colour tube 2, but the difference in a test in 1945 was less than 1 per cent. (table 4, section c). No direct comparison of mean values obtained by R.H.D. and the other two observers is available, but many comparisons of individual readings makes it certain that any difference in this case also was small. In order to determine whether both observers K.B. and H.M.M.M. might have changed their level of colour matching during the 2½ years the observation lasted, comparison with an independent standard was desirable, hence H.M.M.M.'s colour matching is compared with that of another observer, Dr. Lucy Wills. A comparison of H.M.M.M.'s mean values with colour tube 2 and L.W.'s mean value with a pinker standard first in 1943 (Macfarlane, 1945) and again in December, 1944, showed that L.W. tended to match at a slightly lower level than H.M.M.M. on both occasions, but the difference between the two observers in 1943 and in 1944 altered by less than 1 per cent., a difference which is not significant.

As will be shown later, changes observed in the mean haemoglobin level were not uniform at all

TABLE 1
THE COLOUR TUBE AND COLOUR MATCHINGS

Observer	Date	Colour tube	Group examined		Mean Haemoglobin	Comments
			Group	Number		
(a) Similarity of mean haemoglobin values obtained with colour standard 1 (broken in January, 1943) and colour standard 2 (in use from February, 1943, to December, 1944).						
H.M.M.M.	1943 January February	1 } 2 }	Nursery A	{ 33 39	86.9 89.1	{ Continuation between January and February of previous steady rise in haemoglobin.
K.B. and R.H.D.	1942 November and 1943 Jan. 1943 February	1 } 2 }	Nursery B and C	{ 52 58	79.6 79.8	{ Little change, as with previous estimations in these nurseries.
K.B., R.H.D. and H.M.M.M.	1942 November 1943 February and March	1 } 2 }	County council school	{ 67 73	91.4 91.1	{ Little change.
(b) Similarity of mean haemoglobin values obtained by H.M.M.M. with colour standard 2 and with colour standard 3 (colour standard 3 being pinker).						
H.M.M.M.	1943 October	2 } 3 }	Nursery E	{ 15 15	82.4 82.3	{ Estimates with both colour tubes on same children.
(c) Similarity of mean haemoglobin values obtained by H.M.M.M. and K.B., both using colour tube 2.						
H.M.M.M. K.B.	1945 May	2 } 2 }	Nursery B	{ 13 13	86.9 86.0	{ Estimates by both observers independently on same children.
(d) Similarity of mean haemoglobin values obtained by H.M.M.M. in 1943 and in 1944 with colour tube 2, using values obtained by L.W. as the standard of comparison.						
H.M.M.M. L.W.	1943 September	2 } 4 }	Med. Res. Council, colour matching test	{ 10 10	97.6 96.3	{ H.M.M.M.'s mean 1.3 per cent. higher than L.W.'s.
H.M.M.M. L.W.	1944 December	2 } 4 }	County council school	{ 157 162	91.3 89.2	{ H.M.M.M.'s mean 2.1 per cent. higher than L.W.'s, therefore change in difference since September, 1943, less than 1 per cent.

TABLE 2
MEAN HAEMOGLOBIN LEVEL BY AGE DURING DIFFERENT PERIODS
UNTREATED NURSERY CHILDREN IN 1942, 1943 AND 1944 AND WELFARE CENTRE CHILDREN IN 1941

Group	Date	6 months-1 year		1-2 years		2-3 years		3-4 years		4-5 years	
		No. obs.	Mean hb.	No. obs.	Mean hb.	No. obs.	Mean hb.	No. obs.	Mean hb.	No. obs.	Mean hb.
Welfare centres in or near London	1941	52	79.5 $\pm$ 1.2	49	79.4 $\pm$ 1.2	32	84.7 $\pm$ 1.4	21	89.0 $\pm$ 1.5	10	91.4
Nurseries A, B and C ..	1942 Aug.-Sept.	11	77.7	36	73.9 $\pm$ 1.4	45	79.7 $\pm$ 1.1	34	83.0 $\pm$ 1.1	25	85.5 $\pm$ 1.2
Difference: Nurseries in 1942 less welfare in 1941 ..			-1.8		-5.5 $\pm$ 1.8		-5.0 $\pm$ 1.8		-6.0 $\pm$ 1.9		-5.9
A, B, C, D, E, F and G ..	1943 Jan.-Dec.	59	80.1 $\pm$ 1.1	209	78.1 $\pm$ 2.3	209	78.4 $\pm$ 1.4	225	83.6 $\pm$ 1.2	132	86.2 $\pm$ 0.5
A, B, D, E, F, G and H ..	1944 Jan.-Dec.	77	79.7 $\pm$ 1.5	202	80.4 $\pm$ 0.6	204	84.2 $\pm$ 0.3	152	85.7 $\pm$ 0.5	115	86.0 $\pm$ 0.6
Difference: Nurseries in 1944 less nurseries in 1941 ..			+2.0		+6.5 $\pm$ 1.5		+4.5 $\pm$ 1.1		+2.7 $\pm$ 1.2		+0.5 $\pm$ 1.3
A, D, E, G and H ..	1944 July-Dec.	24	82.9 $\pm$ 1.4	76	84.6 $\pm$ 0.7	86	86.7 $\pm$ 0.6	54	87.7 $\pm$ 0.9	44	89.6 $\pm$ 0.7
B and F	1944 July-Dec.	12	72.8	18	76.1	23	78.1	3	83.9	8	77.0
A-H combined	1943 and 1944	136	79.9 $\pm$ 1.0	411	79.2 $\pm$ 1.2	413	81.3 $\pm$ 0.7	377	84.1 $\pm$ 0.8	247	86.1 $\pm$ 0.4

ages, and could not, therefore, be attributable to changes in colour matching. It is, therefore, legitimate to assume that no changes in mean haemoglobin values found at these nurseries during the 2½ years of the observation were due to a change in colour standard used or to changes in colour matching by the observers.

Changes in haemoglobin level of untreated children

(a) **Changes with age.** Between one and five years of age there was a continuous rise in mean haemoglobin level with age. This steady rise has been noted by various observers. Table 2 shows the mean haemoglobin levels at the nurseries during three different periods: (a) in August and September, 1942, i.e. at the beginning of the observations (nurseries A, B and C); (b) during the whole of 1943 (nurseries A to G inclusive), and (c) during the whole of 1944 (nurseries A to H inclusive, excepting nursery C where no examinations were made in 1944). Mean haemoglobin values for observations in all nurseries combined are also given for the years 1943 and 1944 together. These means include all observations on untreated children in all the nurseries where the investigations were made, excepting that where more than one observation had been made on any one child in a single three-month period, the average was used when calculating the mean of all observations.

In the nursery series of 1942 the youngest children aged six to twelve months, had a mean haemoglobin level within 2 per cent. of the corresponding age group at welfare centres where children were examined in 1941 (Wills et al., 1942), but the children of one year and upwards had a mean haemoglobin level lower by 5 to 6 per cent. than the welfare centre children of corresponding ages, and the differences at one, two and three years old were significant.

In the nursery series of 1943 and of 1944 the mean haemoglobin level was consistently higher after 12 months of age than the levels found in the nurseries in the summer of 1942, and the rise was most marked in the children between one and three years of age so that in 1944 the nursery children under three years of age, had mean haemoglobin levels closely similar to the welfare children of 1941. The mean rise between 1942 and 1944 in one-, two- and three-year-old children was statistically significant. It is of interest that the mean haemoglobin values at 6 to 12 months of age in the welfare centre group of 1941, and in the combined nursery groups of 1943 and 1944 respectively was remarkably constant, namely 79.5 to 80.1 per cent., and very little higher than the mean found by one of us (Mackay and Goodfellow, 1931) nearly 20 years ago in 1926-29 for infants in the East End of London, namely 76.5 per cent. (when the B.S.I. correction for the colour standard has been applied). Also the mean haemoglobin value in the nursery group at 4 years of age in 1942, 1943 and 1944 was almost constant: the improvement among nursery children during these years occurred in the intermediate age groups, that is in the one-, two- and three-year-olds.

In the latter part of 1944, the mean haemoglobin values at two nurseries (nurseries B and F) were considerably lower at all ages than those at the other five (nurseries A, D, E, G and H) and similar to the

values obtained at the three nurseries examined in 1942. The values for each age in these two groups are shown separately and demonstrate differences which may occur in nurseries under the same administrative control.

(b) **Changes with year and season.** Table 3 shows the mean haemoglobin level of all children examined at each nursery during the third and fourth quarters of 1942, and the first, second, third and fourth quarters of 1943 and 1944 respectively, together with the mean age in years of each group. As the mean age varies and the mean haemoglobin level changes considerably with age, a better comparison of the haemoglobin level at different dates is obtained by calculating the 'expected' haemoglobin level for each group from its age composition, deducting the observed mean, and so finding the difference from the expected mean. By this means the complicating factor of difference in age between the groups is eliminated from the comparison (table 4). The expected mean value for each of the groups has been calculated from the value for each age (shown in table 1) for untreated children at all the nurseries in 1943 and 1944. The differences from the expected mean for different groups are shown in table 4.

If we look at the changes in haemoglobin value (based on differences from the expected mean) at individual nurseries (table 5), we find that of four nurseries examined in the first quarter of 1943 the haemoglobin levels in three (nurseries B, C and D) rose 4.0 to 6.3 per cent. by the third quarter, and the rise at each nursery was statistically significant. The children in the fourth nursery (nursery A) had already by the first quarter of 1943 reached a level considerably higher than the rest, having shown a steady rise from the summer of 1942 onward. Of six nurseries examined in the first quarter of 1944 four (nurseries A, D, E and G) showed a rise of 1.0 to 3.9 per cent. by the third quarter, which was, on the whole, maintained in the fourth quarter, and the rise at three of these nurseries was statistically significant. The children in the two nurseries (nurseries B and F) where the haemoglobin level was lowest showed little change in haemoglobin level between the first and third quarter in 1944, but the number of estimations was small.

If we consider the changes in haemoglobin level (again based on difference from the expected mean) for children from all the nurseries, excepting nursery A, combined, we find that between the first or second quarters and the third quarter of 1943 there is a rise of about 5 per cent. (which is statistically significant), and between the second and third quarters of 1944 there is a corresponding but smaller rise of 2.25 per cent. (also statistically significant), whereas in the preceding winter period as well as in the intervening winter period the values vary only very slightly (tables 5 and 4).

The mean haemoglobin level in nursery A began at a higher level in 1943, but from the third quarter of 1943 onwards the values here showed the same trend as at the majority of nurseries.

Effect of iron, or iron combined with copper and proteolyzed liver, on the haemoglobin level.

The use of iron cooking utensils at some of the nurseries did not materially influence the iron intake, as the quantity of cooked fruit consumed was

TABLE 3
MEAN HAEMOGLOBIN BY YEAR AND SEASON
UNTREATED CHILDREN AT INDIVIDUAL NURSERIES

Nursery	1942						1943						1944																		
	Aug.-Sept.			Oct.-Dec.			Jan.-March			April-June			July-Sept.			Oct.-Dec.			Jan.-March			April-June			July-Sept.			Oct.-Dec.			
	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	No.	Mean hb. yrs.	Mean age yrs.	
A	60	80.7	2.8	62	84.6	3.0	58	87.8	2.7	58	84.3	2.7	58	84.5	2.6	53	85.7	2.6	44	83.9	2.9				37	85.2	2.7	48	87.9	2.4	
C	36	81.8	2.5	32	81.0	2.6	29	80.3	2.6				31	84.1	2.5																
D							49	76.3	2.7				53	81.8	2.6	32	81.6	2.6	32	83.1	2.6	18	83.2	2.8	18	87.5	2.7	31	86.2	2.5	
E													44	84.2	2.7	29	84.4	2.6	39	85.2	2.5	23	82.6	2.6	20	87.7	2.6	28	86.0	2.4	
G													55	83.4	2.5	55	84.1	2.6	44	83.5	2.6	39	82.9	2.4	18	84.4	2.6	32	86.4	2.6	
H																						47	83.4	2.6	19	84.6	2.6	33	87.3	2.8	
B	55	77.9	2.7	66	78.1	2.4	41	77.1	3.2		46	78.5	3.0	53	83.4	3.1	18	81.9	2.8	34	79.5	2.8	24	81.1	2.6	13	78.7	2.3	12	80.5	2.5
F													49	80.9	2.7	12	81.6	2.8	34	77.0	2.4	24	77.3	2.5	12	76.8	1.7	27	74.0	2.2	

TABLE 4
MEAN HAEMOGLOBIN LEVEL BY YEAR AND SEASON
DIFFERENCES FROM EXPECTED MEAN FOR AGE, UNTREATED CHILDREN
Expected mean calculated from the values for all nurseries (A-H) for 1943 and 1944, shown in Table 1, lowest line

Nursery	1942				1943				1944											
	Aug.-Sept.		Oct.-Dec.		Jan.-March		April-June		July-Sept.		Oct.-Dec.		Jan.-March		April-June		July-Sept.		Oct.-Dec.	
	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean	No.	Diff. from expected mean
A	60	-1.7±0.9	62	+2.0±0.6	58	+5.5±0.8	58	+2.4±0.8	58	+2.7±0.8	53	+3.7±0.8	44	+1.3±0.9			37	+3.4±0.8	48	+6.3±0.7
C	36	+0.03±1.3	32	-1.0±1.3	29	-1.6±0.9														
D					49	-5.8±1.1			31	+2.4±1.2	32	-0.5±1.2	32	+1.3±1.1	18	+1.1	18	+5.2	31	+4.5±0.8
E									53	-0.1±1.0	29	+2.4±1.3	39	+3.6±1.0	23	+0.6	20	+5.7	28	+4.3±1.0
G									44	+1.9±1.0	55	+1.5±0.9	44	+1.5±0.9	39	+1.3±1.2	18	+2.5	32	+4.5±1.2
H									55	+1.5±0.9					47	+1.5±0.9	19	+2.7	33	+5.0±1.1
B	55	-4.4±0.9	66	-3.4±0.8	41	-6.0±0.9	46	-4.3±1.0	53	+0.3±0.9	18	-0.8	34	-2.9±1.0	24	-1.3	13	-2.9	12	-0.9
F									49	-1.3±0.8	12	-0.7	34	-4.6±1.2	24	-4.5	12	-4.0	27	-7.0
C, D, E, G, H, B and F					119	-4.8±0.6	46	-4.3±1.0	285	+0.7±0.4	146	+1.0±0.6	183	-0.05±0.5	175	+0.1±0.5	100	+2.2±0.7	163	+2.3±0.6
C, D, E, G and H					78	-4.2±0.8			183	+1.3±0.5	116	+1.5±0.6	115	+2.1±0.6	127	+1.2±0.6	75	+4.0±0.7	124	+4.6±0.6
B and F					41	-6.0±0.9	46	-4.3±1.0	102	-0.5±0.6	30	-0.8±1.1	68	-3.8±0.8	48	-2.9±1.1	25	-3.4	39	-5.1±1.2

TABLE 5

RISES IN MEAN HAEMOGLOBIN LEVEL BETWEEN THE FIRST QUARTER AND THE THIRD OR FOURTH QUARTER IN 1943 AND IN 1944. UNTREATED CHILDREN. FIGURES BASED ON DIFFERENCES FROM THE EXPECTED MEAN, AS SHOWN IN TABLE 4.

Nursery	1943	1944	
	1st to 3rd quarter	1st to 3rd quarter	1st to 4th quarter
A	-2.8±1.1	+2.1±1.2	+5.0±1.1
C	+4.0±1.5	—	—
D	+5.7±1.5	+3.9	+3.2±1.3
E	—	+2.1	+0.7±1.4
G	—	+1.0	+3.0±1.5
B	+6.3±1.3	+0	+2.0
F	—	+0.6	-3.4
C, D, E, G, H, B and F	+5.5±0.7	+2.25±0.9	+2.35±0.8
C, D, E, G and H	+5.5±0.9	+1.9±0.9	+2.5±0.8
B and F	+5.5±1.1	+0.4	-1.3±1.4

small, and this is the foodstuff most likely to dissolve and take up iron from the vessel in which it is cooked. Iron therapy, by 'fortification' of National bread with iron, in quantities sufficient to provide about 14-20 mg. of extra iron daily was without effect on the haemoglobin level. Children not having breakfast in the nursery received about 14 mg., those having breakfast, dinner and tea received about 20 mg. daily by means of this fortification. Details of these investigations have already been published (Mackay, Dobbs and Bingham, 1945). As it seemed probable that the negative result with 'fortified' bread was due to the presence of phytic acid in the bread producing an insoluble iron compound, iron therapy in other forms was tested.

At each nursery where children were treated with iron, other children in the same nursery of similar age and, at the start, similar haemoglobin level, served as controls. The drugs were given to the children by the matron personally, or by the sister-in-charge. Of necessity, absence from the nursery entailed stopping the drug till the child's return. Iron therapy was given in different amounts and forms as follows:—

(a) Ferrous sulphate to provide about 20 mg. of iron daily was given in nursery H. This dose was comparable with the amount of iron previously provided by fortifying bread with ferrous carbonate. The mixture used was the mist. ferri pro infantibus of the National War Formulary: Ferrous sulphate $1\frac{1}{2}$ grains, dilute sulphuric acid $\frac{1}{4}$ minim, syrup 20 minims and chloroform water to 60 minims.

Sixty minims, the daily dose, contained 19.6 mg. Fe. This mixture was readily taken by the children.

(b) Ferrous sulphate to provide about 120 mg. of iron daily was given in nurseries B and E. This was given to provide a liberal therapeutic dose. The same mixture was used as above, and 3 fluid drachms were given twice daily.

(c) Ferrous ascorbate to provide about 23 mg. of iron daily was given in nursery G. Ferrous ascorbate under the proprietary name of Ferro 66 has been shown to be effective in the treatment of iron deficiency anaemia. The preparation used in the present investigation was supplied by the Glaxo Laboratories and was a colourless and palatable syrup, which was readily taken by the children. It contained in each cubic centimetre 13 mg. of ferrous iron and 85 mg. of ascorbic acid. Half a fluid drachm or about 1.8 c.c. was given daily.

(d) Ferrous sulphate and copper sulphate with about 5.5 g. of proteolyzed liver, providing in all say 22 mg. of iron and 1 mg. of copper daily, was given in nurseries D and F. Each child was given daily one fluid drachm of mist. ferri pro infantibus, to which had been added 3.5 mg. of copper sulphate ($\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$), and this dose of the mixture provided 19.6 mg. of iron and 0.87 mg. copper. Five and a half g. of the proteolyzed liver contained about 2.2 mg. of iron and 0.16 mg. of copper. The liver preparation was taken fairly well by the children but a few refused it on account of its taste.

The proteolyzed liver was prepared by the Evans Biological Institute. It was a dry, granular, hygroscopic powder, and one gramme was derived from

TABLE 6
EFFECT OF THERAPY ON THE HAEMOGLOBIN LEVEL
COMPARISON OF 'TREATED' CASES AND CONTROLS AT EACH NURSERY

Treatment ordered*	Nursery	Date	Haemoglobin			
			No. of obs.	Observed mean	Expected mean for age	Mean of observed minus expected values
20 mg. Fe, as ferrous sulphate, daily. Controls	H	Aug.-Dec. 1944	16 52	88.8 86.3	82.5 82.1	6.3 (a) 4.2 ± 0.89 (b)
						2.1 (not significant) 0.3 > P > 0.2
120 mg. Fe, as ferrous sulphate, daily. Controls	E	Nov. 1943-May 1944	54 91	86.2 84.3	81.9 81.9	4.3 ± 0.78 (a) 2.4 ± 0.69 (b)
						1.9 ± 1.04
120 mg. Fe, as ferrous sulphate, daily. Controls	B	Nov. 1943-June 1944	42 76	83.9 80.6	83.3 82.5	0.6 ± 0.76 (a) -1.9 ± 0.71 (b)
						2.5 ± 1.04
23 mg. Fe, as ferrous ascorbate, daily. Controls	G	Jan.-May 1944	50 83	86.2 83.2	82.7 81.8	3.5 ± 0.62 (a) 1.4 ± 0.76 (b)
						2.1 ± 0.98
20 mg. Fe, with 1 mg. Cu, and with liver digest, daily. Controls	D	Nov. 1943-May 1944	58 82	85.5 82.5	82.8 81.9	2.7 ± 0.82 (a) 0.6 ± 0.73 (b)
						2.1 ± 1.10
20 mg. Fe, with 1 mg. Cu, and with liver digest, daily. Controls	F	Nov. 1943-May 1944	41 70	84.8 77.9	83.1 81.8	1.7 ± 0.89 (a) -3.9 ± 0.91 (b)
						5.6 ± 1.27

* All children for whom treatment had been ordered are included in the 'treated' group, irrespective of the amount or duration of the treatment received—some are known to have had a few days treatment only, having been absent from the nursery on account of illness.

about 6 g. of raw liver. The liver was digested with papain, and the ultimate product contained both hydrolyzed protein and the anti-pernicious anaemia principle. It is believed by the makers, that, being a whole liver preparation it would also contain Whipple's 'secondary anaemia factor.' Riboflavin was found in a concentration of about 10 mg. per 100 g., but the quantity of other B vitamins present is not known. Pernicious anaemia patients treated with 7.75 to 28 g. (2 drachms to 1 ounce) of proteolyzed liver daily by mouth responded well (Davis et al., 1943).

A satisfactory comparison of treated cases and controls proved difficult on account of the high absentee rate and the changing population of the nurseries. To include only children having regular treatment, would have involved eliminating all those who had suffered from illnesses and so been absent, and a similar group would then have had to be eliminated from the controls, leaving excessively small numbers. Hence in table 6 every child has been included as a 'treated' case if one or more haemoglobin estimations had been made after iron treatment had been ordered, irrespective of the amount or duration of the treatment, or its interruption by absence from the nursery. The comparison in most of the nurseries is carried only to the end of May, 1944, on account of the large number of children then evacuated from London because of the flying bomb attacks.

Table 6 shows the observed mean of observations on all children who had been ordered iron in any form, compared with the observed mean of observations on children not ordered iron and attending during the same period. If two observations were made on one child in any one quarter an average figure for this child was taken for inclusion in the total. It is obvious that this does not in any way show the maximum effect obtainable with treatment, as children might be included in the iron group who had been long absent from the nursery and had, therefore, only had a few days iron treatment in all, or who had stopped iron during a recent illness and had just returned to the nursery. During times of epidemic, the inclusion of such children would be likely to mask entirely rises in haemoglobin shown by regular attenders. Nevertheless, in each nursery the mean value for treated children was higher than for the controls by 1.9 to 6.9 per cent. As the treated children tended to be slightly older than controls, the expected haemoglobin for the age has been calculated, again using for the calculation the mean values for untreated children obtained in 1943 and 1944. When using the 'expected mean' as a standard, the haemoglobin values for treated children are again, in each nursery, higher than those of the controls: the differences are shown in the last column in table 6. The differences are small: 1.9 to 2.5 per cent., except in one nursery (nursery F) where the controls had an unusually low mean, and here treatment showed more effect and the difference was 5.6 per cent. Even with the scales thus weighted against iron-treated cases, the differences in haemoglobin level between treated cases and controls are statistically significant at four out of the six nurseries (nurseries B, G, D and F). Moreover, the consistent superiority of the treated cases provides proof of the effect of iron on the haemoglobin level, this being the only addition common to all groups.

There is, unfortunately, no means of judging

whether one form of treatment was superior to another. The degree of rise in treated cases at any given nursery depended on the extent to which the mean haemoglobin of controls at that nursery was subnormal, and when the mean values of controls are arranged in sequence, it is found that the degree of rise in the treated cases also falls into a sequence. The only exception is nursery H, where numbers were too low to give a significant result. Thus the largest difference between controls and iron cases occurred at the nursery where the level of controls was the lowest of the whole group, i.e. only 77.9 per cent. (nursery F). At this nursery, copper sulphate and proteolyzed liver were given in addition to ferrous sulphate, but at the other nursery receiving all three drugs (nursery D), where the mean haemoglobin of controls was higher, the difference in haemoglobin level between treated and control cases was only 2.1 per cent., i.e. the same as at nursery G receiving ferrous ascorbate only, so that there is no evidence that the larger rise at nursery F was due to the copper and liver therapy.

As already stated, the degree of improvement in haemoglobin level which might be brought about by giving iron regularly—with or without copper and liver therapy—is not shown in table 6 since this includes every child for whom iron had been ordered, irrespective of the duration or amount of iron therapy. In table 7 cases are classified according to the length of time that had elapsed since the iron was first ordered, though again on account of the absentee rate, very few children had continuous iron therapy throughout this period and some had been absent for long periods. The table shows the mean of the individual changes in haemoglobin level since before treatment was ordered in the 'treated' group and in control cases available over a similar period. In the second month after treatment was ordered, treated cases showed a mean rise of 2.5, controls a mean rise of 0.2, hence the difference between treated cases and controls was 2.3. Similarly, the difference in the fourth month after treatment was 3.2, and the difference in the sixth month was 4.5. This comparison is open to the objection that there is an element of arbitrariness in determining what controls are to be used in the comparison and beginning at what dates, since both age and season must be taken into consideration. Care has, however, been taken to make the comparison as fair as possible, but because of the inherent element of selection further statistical data about this group have not been included.

Children receiving breakfast, dinner and tea in the nursery and giving iron medicated bread had their iron intake augmented to about the same extent as did the children at nurseries G, D and F. At each of these nurseries, iron given as a mixture produced a significant rise in haemoglobin level, whereas a similar amount of iron in the 85 per cent. extraction loaf was without effect, which supports the view that phytic acid in the flour interfered with the absorption of the added iron.

The effect of food changes on the haemoglobin level: untreated children

In May, 1943, as a result of teaching and instructions from the medical staff, the purchase of various foodstuffs for the nurseries were increased, and a definitely more liberal diet was provided. Exact figures of mean food intake cannot be given

TABLE 7

EFFECT OF THERAPY ON THE HAEMOGLOBIN LEVEL: MEAN CHANGES IN HAEMOGLOBIN LEVEL AT VARYING INTERVALS AFTER TREATMENT ORDERED

Group	Before treatment		Mean changes in hb. level since before treatment					
	No. of cases	Mean hb.	In 2nd month		In 4th month		In 6th month	
			No. of cases	Mean change	No. of cases	Mean change	No. of cases	Mean change
All 'treated' children*	129	82.7	103	+2.5	84	+2.8	63	+5.2
Controls	120	82.6	93	+0.2	60	-0.4	42	+0.7
Difference between 'treated' and controls				+2.3		+3.2		+4.5

* All available children for whom treatment had been ordered are included in the 'treated' group irrespective of the amount of treatment received, provided they attended at the appropriate dates.

TABLE 8

FOOD PURCHASES PER HEAD FOR 6 DAYS AT TWO NURSERIES, SHOWING THE MORE LIBERAL DIET SUPPLIED FROM JUNE, 1943

Nursery	Month: 1943	Meat: pence expended	Bacon: oz.	Fish: pence expended	Egg—dried: oz.	Cheese: oz.	Green-groceries: pence expended
A	Jan.	6.7	0.8	2.5	?	0.6	5.3
	Feb.	6.1	1.2	2.3	?	0.8	4.6
	March	6.7	0.7	2.6	?	0.6	5.2
	April	6.1	1.0	2.2	0.3	0.9	4.8
	May	4.9	0.8	1.9	0.5	0.9	4.6
	June	8.0	2.1	2.8	1.0	2.2	6.7
	July	9.4	1.7	1.7	1.0	1.7	10.0
	Aug.	8.5	1.6	1.7	0.9	1.7	9.2
B	Jan.	6.8	?	1.6	0.3	?	3.6
	Feb.	7.7	?	0	0.5	?	3.4
	March	7.0	?	0	0.5	?	3.3
	April	6.2	1.6	2.4	0.5	1.0	3.1
	May	5.2	1.4	2.3	0.7	0.9	3.2
	June	8.5	2.6	3.2	0.9	2.0	4.2
	July	9.4	3.0	2.1	1.6	1.8	6.3
	Aug.	8.1	2.0	2.8	1.0	1.6	5.5

because of variability in the nursery population, both children and staff, because allocation of individual items of food between adults and children varied, and because of incompleteness of certain records. Moreover, it must be remembered that the children slept at home, and the great majority had some food at home every morning and evening, as well as at week-ends, and the quality of this home feeding might vary with the financial status or hours of work of the mother. Nevertheless, tentative figures for food available per child in two nurseries (nurseries A and B), are shown in table 8. In drawing up this table one-third of the total of each of the items purchased has been deducted for staff meals, and the rest has been divided by the number of children actually attending the nursery,

exclusive of absentees. It is obvious that this allocation of one-third of the quantity purchased to staff, irrespective of whether there is a full attendance of children and absences among the staff, or whether as the result of an epidemic, the children attending are reduced by half, is inexact, though it is hoped it provides a rough indication of the food available to the children.

These two nurseries are chosen as representative, but in all the nurseries after May, 1943, there were increased supplies of meat, bacon, dried egg and cheese, and in some nurseries more fish and green-groceries were also available. As already shown, the haemoglobin level at three out of four nurseries (nurseries B, C and D) showed a rise of 4.0 to 5.7 per cent. (as indicated by the differences from the

expected means) about the time the diet was improved; and at the fourth (nursery A) the level had already risen. The rise in the three nurseries occurred at a time when a seasonal increase in haemoglobin level might be expected, but was greater than the rises in the corresponding period of 1944. In some nurseries the rise which occurred in the summer of 1943 was maintained: the largest rise was at nursery D, where there was an increase in mean haemoglobin level from 76.3 per cent. in the early spring of 1943 to 86.2 per cent. by the end of 1944, i.e. an increase of 10 per cent. It is clear, therefore, that this rise in the summer of 1943 was not a purely seasonal one to be followed by a drop at the end of the summer. We conclude, therefore, that the improvement in the diet in May, 1943, produced an increase in haemoglobin level over and above the rise which might have been expected at this season.

With the data available, it is impossible to compare satisfactorily the diet at one nursery with that at another. At the same time, if it be granted that the rise in haemoglobin level observed after May, 1943, was largely due to better diet, it seems likely that differences in diet accounted for some, at least, of the differences in haemoglobin level observed between the nurseries; for example the rise in haemoglobin level at nursery A in the winter of 1942-43 when the haemoglobin level at nurseries B and C remained almost unchanged. Nursery F, where the mean haemoglobin levels of untreated children were lower than at any other nursery, was in a notoriously poor district and the low haemoglobin level might well be the result, in part, of poorer homes. The fact that in the nurseries as a whole the children aged one and two years showed by 1944 a larger rise in haemoglobin level than did the older children, or the children aged six months to one year, was, we believe, the result of a greater improvement in the diet at this age. When the observations were begun, the smaller children received relatively little meat or bacon. The medical officers in charge stressed the importance of such food being also given to the younger children, and there is no doubt that, as a result, their share of these foods in 1944 as compared with 1942 increased considerably.

The particular dietetic factors which were deficient in the nursery diet at the beginning of the observation and which had been sufficiently augmented by the summer of 1943 to cause a rise in haemoglobin level, need consideration. More meat, bacon, cheese, dried eggs and greengroceries would increase the supply, among other things, of animal protein, vitamin B complex, vitamin C, and iron. Since the children received throughout concentrated orange juice and cod-liver oil compound, their supplies of vitamin C and of vitamins A and D were adequate from the beginning, and it can, therefore, be assumed that the rise in haemoglobin was not due to any increase in these three vitamins.

The fact that the provision of iron, as a drug, produced a rise in haemoglobin level, directs attention to the iron in the diet. The authors are indebted to R. A. McCance and E. M. Widdowson for estimations of the children's iron intake. Details of the collection of food have been given elsewhere (Mackay, Dobbs and Bingham, 1945). Only one estimation of iron intake is available for the period before the end of May, 1943, (i.e. before the diet was improved), and that was at nursery A

where the haemoglobin level had already risen. The mean daily iron intake (breakfast, dinner, and tea) for children aged two to three and a half years at nursery A, estimated for six days in May, 1943, was 3.9 mg. Three estimations are available for similar periods in nursery A and nursery B, after the improvement in the diet:—they were 4.1, 4.4 and 5.8 mg. daily respectively. No generally accepted figure exists for the iron requirements of young children, but the 'recommended daily allowance' for children aged one to three years in the report of the Committee on Food and Nutrition (1941) of the U.S.A. National Research Council is 7 mg. daily. This accords with the views of various independent investigators (Rose et al., 1930, Leichsenring and Flor, 1932, Daniels and Wright, 1934), though one writer (Porter, 1941) has put the requirement at about half this amount. The allowance advised for an infant of five months of age by Stearns and Stringer (1937), is over 6 mg. daily, and their work is supported by the findings of Oldham and Schlutz (1937). Hence the consensus of opinion indicates an allowance of not less than 6 mg. of iron daily for a two-year-old child. Judged by this standard, many of the untreated nursery children are likely to have been short of iron, even allowing for the fact that food consumed at home on weekdays would contain some iron to augment that derived from the nursery diet.

It is not possible to say whether after May, 1943, the haemoglobin level was influenced by the consumption of more animal protein—apart from the iron content of the foods—or by a larger intake of vitamins of the B complex. It is possible that higher protein intake and a more liberal diet may influence iron absorption by increasing hydrochloric acid secretion in the stomach, thus helping to remedy a conditioned iron deficiency (Hellström, 1937).

The effect of season on the haemoglobin level

As already pointed out (table 4), there was a rise in the mean haemoglobin level for all nurseries combined (excluding nursery A), in the summer of 1943 and again in the summer of 1944, the level in the intervening months remaining almost stationary, so that the mean value for the combined nurseries in the fourth quarter of 1944 was about 7 per cent. higher than in the first quarter of 1943. At nursery A, the mean haemoglobin level was already relatively high before the summer of 1943. A tendency for the haemoglobin of school children to rise in summer has already been noted. In municipal school children observed by us in 1942-43, the year's increment for age in haemoglobin occurred between March and July (Dobbs, Mackay and Bingham, 1944), and Davidson and his co-workers (1944) also noted a rise in the haemoglobin level of school children in Edinburgh after the winter. Hence the seasonal trend in this group of nursery children corresponds with these earlier observations. The most likely explanation of this seasonal trend, would seem to be that infections in the winter months tend to inhibit a rise, and when health improves the haemoglobin also improves.

The interrelation between infection and haemoglobin level

It has already been shown that the incidence of cross infection in the nurseries was high (Mackay,

Dobbs and Bingham, 1945). Over a six-month period from September, 1942, to March, 1943, the total days absent given as a percentage of the total possible attendances was 22.4 per cent. at nursery A and 27.7 per cent. at nursery B, or a total of approximately 25 per cent. at the two combined. It was clear from the records, that a large proportion of the absences in this period was due to illness of the child, though the mother's illness or the father's leave from the Forces accounted for the non-attendance of some children.

A similar calculation was made for absences for the five months from January to May, 1944, from nurseries D and E, and from nursery F, though for this period unfortunately no complete records exist of the cause of absences, and also in this period some absences were attributable to air raids. Any child ceasing to attend was included in the investigation only until his last attendance; thus a child evacuated from London on account of air raids, or absent owing to illness and not re-attending, ceased to count as a member of the group from the first day away.

Nursery F was in a specially poor district; many of its children looked in poor health and the haemoglobin level for untreated children was low (table 6). The standard of health in nurseries D and E, judged by the children's appearance, was better, and the mean haemoglobin level of untreated children was about 4.5 to 6 per cent. higher, as indicated by differences from the expected mean (table 6). However, the percentage of absences among untreated children was similar, namely 25.8 per cent. at nurseries D and E, and 25.4 per cent. at nursery F. (table 9). This result, combined with the appearance of the children, makes one doubt the validity of mean absence rates as an index of relative illness rates in different nurseries. In a previous paper, we have drawn conclusions from the absence rates as to the relative morbidity rates in nursery A and in nursery B. These conclusions were supported by a study of the relative incidence of infectious fevers, pneumonia, otorrhoea, etc. In the light of later experience, however, we do not think that the relative incidence of infections at two nurseries can be deduced from a comparison of absenteeism; though conclusions can fairly be based on a comparison of absentee rates in two groups at one nursery over the same period.

It is difficult to provide reliable figures to show the effect of illness on the mean haemoglobin level in these nurseries, since children with any acute illness were excluded, but ample evidence already exists to show that infections readily depress the haemoglobin level (Mackay and Goodfellow, 1931).

As regards the effect of haemoglobin level on incidence of illness, we obtained definite evidence. At nursery F, where the mean haemoglobin level of untreated children was lowest, treated children had during January to May, 1944, a haemoglobin level about 6 per cent. higher and an absentee rate 26 per cent. lower than the controls (table 9). This difference is statistically significant, the probability of its occurring by chance is less than 1 in 100. Tables 9 and 10 are based on absentee rates from January onwards because Christmas holidays of varying length upset the comparison during December. In each month from January to May, 1944 (table 10), the 'treated' children have a lower absentee rate, and in January, March and April,

when the absentee rate among controls is particularly high, the absentee rate among treated cases is significantly lower. We can, therefore, legitimately conclude that a difference of about 6 per cent. in haemoglobin percentage influenced resistance to infection sufficiently to prevent much illness, in spite of the close contacts inevitable in nursery life.

At the other nurseries the difference in haemoglobin level between treated cases and controls was much less than at nursery F. At nurseries D and E it was only 0.9 and 1.6 per cent., these figures being based on the difference from the expected mean between January and May, 1944, and the absentee rate of untreated cases and of controls differed only slightly, a difference of 4.3 per cent. in favour of the controls. As already stated, not only was the mean haemoglobin level of controls lower at nursery F than at nurseries D and E, but the appearance of the children suggested a distinctly lower standard of health. Yet the absentee rates of controls were similar. We presume that children continued to attend nursery F during minor illnesses for which they would probably have stayed at home had they been at one of the other two nurseries. Owing to the large amount of labour involved in obtaining the figures for this analysis, a similar comparison was not carried out at the other nurseries.

We have, therefore, obtained evidence that raising the haemoglobin level by about 6 per cent. by drug therapy increased resistance to infection, and reduced absenteeism by about a quarter. Though proteolyzed liver and copper were also given at the nursery where this result was obtained, similar treatment at nursery D, where the initial haemoglobin level was higher and where the rise in haemoglobin level with treatment was consequently slight, did not improve resistance to infection, as judged by the absentee rate. We, therefore, conclude that the lower absentee rate among the treated children at nursery F was the direct result of the improved haemoglobin level.

Discussion

The fact of greatest importance emerging from this investigation is that an increase in mean haemoglobin level of about 6 per cent., brought about by treatment, reduced the absentee rate by about a quarter, and this in spite of the probability that when infection is introduced into a nursery exposure to it is likely to be gross. The greatly diminished incidence of infection which can be brought about by raising the haemoglobin level with iron therapy (Mackay and Goodfellow, 1931) or with iron and copper (Usher et al., 1935) is established for infants. The incidence of illness was approximately halved among babies living in their own homes whose haemoglobin level by twelve months old had been raised to a figure about 10 per cent. higher than that of controls (Mackay and Goodfellow, 1931). The present investigation in children of pre-school age whose haemoglobin level was subnormal shows that a corresponding improvement in resistance to infection can be expected at this age also. There seems every reason to suppose that when a similar grade of anaemia of a type responsive to iron therapy exists

TABLE 9

HAEMOGLOBIN LEVELS AND ABSENTEE RATES OF CHILDREN ORDERED IRON AND OF CONTROLS AT THREE NURSERIES BETWEEN JANUARY AND MAY, 1944

Group	Nursery	Haemoglobin level: diff. from expected mean for age	Total possible attendances	Actual attendances	Absences as per- centage of possible attendances	Absences of 'iron cases' as percentage of absences of controls
Children ordered iron	F	+1.0 (a)	2349	1907	18.8 (a)	74.0
Controls ..	F	-5.5 (b)	3005	2243	25.4 (b)	$\lambda^2 = 31.959$ $P < 0.01$ (significant)
Difference (a-b) ..		+6.5			-6.6	
Children ordered iron	D and E	Nursery D Nursery E	4678	3422	26.9 (a)	104.3
Controls ..	D and E	+1.6 (a) +3.3 (a)	5738	4258	25.8 (b)	$\lambda^2 = 1.4301$
Difference (a-b) ..		+0.7 (b) +1.7 (b)			+1.1	$0.3 > P > 0.2$ (not significant)
		+0.9 +1.6				

TABLE 10

ABSENTEE RATES OF CHILDREN ORDERED IRON AND OF CONTROLS AT NURSERY F BETWEEN JANUARY AND MAY, 1944

Group	January			February			March			April			May		
	Total possible attendances	Actual attendances	Absences as per- centage of pos- sible at- tendances	Total possible attendances	Actual attendances	Absences as per- centage of pos- sible at- tendances	Total possible attendances	Actual attendances	Absences as per- centage of pos- sible at- tendances	Total possible attendances	Actual attendances	Absences as per- centage of pos- sible at- tendances	Total possible attendances	Actual attendances	Absences as per- centage of pos- sible at- tendances
Children ordered iron	488	381	21.9	521	438	15.9	478	386	19.2	414	337	18.6	448	365	18.5
Controls ..	507	341	32.8	535	446	16.6	635	451	29.1	581	407	29.9	747	598	19.9
Difference ..			-10.9			-0.7			-9.9			11.3			-1.4
Absences of 'iron cases' as percentage of absences of controls ..			66.8			95.8			66.0			62.2			93.0
			$\lambda^2 = 14.071$ $P < 0.01$ (significant difference)			$\lambda^2 = 0.0513$ $0.9 > P > 0.8$ (difference not significant)			$\lambda^2 = 13.325$ $P < 0.01$ (significant difference)			$\lambda^2 = 15.912$ $P < 0.01$ (significant difference)			$\lambda^2 = 0.276$ $0.7 > P > 0.5$ (difference not significant)

in older subjects, a similar—and reversible—fall in resistance to infection would result, though the difference is likely to be less than in the first years of life.

A seasonal rise in haemoglobin may well depend on whether or not the winter incidence of infection is high. In infants living in their own homes, one of us (Mackay, 1928) found no significant seasonal variation in haemoglobin, but in these nursery children, as in school children (Dobbs, Mackay and Bingham, 1944, Davidson et al., 1944) it seems that the winter incidence of infection does adversely affect haemoglobin level and that there is consequently a summer rise.

Two facts show, however, that the type of anaemia at these nurseries was largely nutritional in origin: (1) a general improvement in the diet produced a rise in haemoglobin; (2) the administration of iron, with or without copper and proteolyzed liver, also raised the haemoglobin level. It has been suggested that iron therapy may stimulate haemoglobin formation even in the absence of previous iron deficiency in the diet. But in these children iron therapy not only raised the haemoglobin level but also improved health by raising resistance to infection, which proves that the children were previously suffering in health from a deficiency of iron. Whether or not the deficiency was a conditioned deficiency, induced in part by other deficiencies in the diet or by diminished acid secretion in the stomach resulting from infection (Stewart, 1937) remains unknown. The iron intake in the diet was below optimum standards as judged by the few metabolic investigations which have been published, though the more liberal diet provided from May, 1943, onwards, certainly contained more food-iron than the earlier diet. The lack of effect of an iron supplement given in National bread emphasized that the adequacy of iron in the diet cannot be assessed simply from the iron intake, since its satisfactory utilization depends in part on whether the iron is present in a form in which it is easily absorbed.

The children received concentrated orange juice daily throughout the investigation; hence an ascorbic acid deficiency can be eliminated as a cause of the anaemia. It is probable that the nursery meals, at least from May, 1943, onwards, provided a diet at least as good, and possibly better, than many of the children would have received in their own homes. Moreover, the mothers could also purchase the children's rations for use at home, and rationed food was undoubtedly given to the children at home during weekends and some during the week also. The diet given produced between 1942 and 1944 a considerable improvement in the haemoglobin level of children aged one and two years, and a lesser improvement in the older children. This, we believe, corresponds with the fact that the younger children had previously received less than their share of meat, eggs, bacon, etc., in the nurseries, and once more emphasizes the importance of giving these foods from the age of

weaning at 5 to 7 months of age. Even so, anaemia in children under one year was little affected. It is disappointing and regrettable that the mean haemoglobin level between 6 and 12 months of age found among welfare centre children in 1941 and among nursery children in 1942, 1943 and 1944, respectively, was only about 78 to 80 per cent., as compared with 76.5 per cent. (B.S.I. correction for colour standard applied) for infants in the East End of London in 1926–29, for this anaemia is largely preventable by the simple means of giving iron. Since the degree of anaemia found in 1926–29 was associated with a serious lowering of resistance to infection, the importance of combating the anaemia of infants from an early age with iron therapy, and not by diet alone, is manifest, and we hold that iron should be supplied to all infants from two to twelve months of age. We hope that the Ministry of Food may yet include in its provision of dried milks one fortified with iron, as by this means regular iron therapy could be ensured for large numbers of infants.

Summary and Conclusions

An attempt has been made to determine some of the etiological factors influencing the haemoglobin level of children attending eight war-time day nurseries in Islington, a borough in North London. The investigation lasted nearly two and a half years, and over 900 children were examined.

There was a rise in mean haemoglobin level in the summer months both in 1943 and in 1944. The larger rise was in 1943, and was noted after the children's diet had been improved. We conclude that the better diet accentuated a seasonal rise, which would have occurred in any case as a result of fewer infections during the summer months; the winter infections having prevented any rise.

Even after improvement of the diet, the daily iron intake of two- and three-year-old children at nurseries A and B was of the order of 4 to 6 mg. daily, which suggests that the diet in the nurseries remained deficient in iron. This view is confirmed by the fact that administration of ferrous iron led to a small but statistically significant rise in mean haemoglobin level, varying between 1.9 and 5.6 per cent. for 'treated' children attending in each of the 6 nurseries (figures based on differences from the expected mean). In the sixth month after treatment was begun, the mean rise in haemoglobin level of 'treated' children at all nurseries was 5.2 per cent., that of controls was 0.7 per cent. for the same period. Iron therapy was necessarily irregular on account of the high absentee rate, and a greater effect might be expected from continuous treatment. Iron was supplied as ferrous sulphate and as ferrous ascorbate, and in some nurseries copper sulphate and proteolyzed liver were given in addition, but the conditions of the investigation prevented any final conclusion as to the relative merits of these forms of therapy. It has already been shown that when the iron was supplied by 'fortifying' the national loaf (85 per cent. extraction flour) with

ferrous carbonate the haemoglobin level was not affected, and it is, therefore, presumed that the iron given in bread was rendered insoluble by phytic acid.

The diet provided at the nurseries, augmented with more rationed food at home, was, we believe, better than most children receive at home, hence it is probable that many children of pre-school age living at home receive insufficient iron in their food. Since the morbidity rate was high, there is little doubt that infections depressed the mean haemoglobin level and retarded the full effect of iron therapy.

A 6 per cent. rise in haemoglobin level produced by iron therapy was accompanied by a reduction in the absentee rate of about 26 per cent. compared with that of a control group in the same nursery, i.e. the degree of anaemia present at this nursery was sufficient to lower resistance to infection; and resistance could be raised by giving iron. We conclude that the anaemia affecting the nursery children was largely a nutritional iron deficiency anaemia responding to iron therapy, that other factors in the diet, for example phytic acid, influenced iron absorption, and that the high incidence of infections was also a factor of importance in the aetiology of the anaemia. Similar grades of anaemia are known to be common in the child population of this country. It follows that widespread prophylaxis of anaemia in infants and young children by the means open to us is capable of providing a striking reduction in morbidity rates.

An investigation of this nature throws much extra work on nursery staffs and others collaborating in it. We are, therefore, extremely grateful for the continuous and generous help and support we have received, in spite of war-time difficulties, from the Deputy M.O.H. for Islington, Dr. K. M. Hirst, and from Matrons, Sisters and nursing staff in every nursery in which we worked. We are

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