

IRON-RESISTANT ANAEMIA AND LATENT RICKETS IN SCHOOLCHILDREN

BY

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The clinical association of rickets and anaemia has often been described and frequently denied.

Of thirty children, aged between one and four years, with active rickets examined by Findlay (1909), only nine were anaemic, and he concluded that the anaemia was due to secondary complications of the rickets. Hess (1929) states that anaemia is usually found in advanced rickets, but is not characteristic. Parsons (1934) says that anaemia is in no sense a symptom of rickets, although a degree of nutritional anaemia is not unusual, because a diet which is defective in one factor is likely to be defective in others. McDonough and Borgen (1937) studied thirty children, aged between six months and three years, with active rickets. Of the nineteen uncomplicated cases, six had haemoglobin values below 60 per cent., whilst only three had values above 80 per cent. Of the eleven complicated cases, six had haemoglobin values below 60 per cent. (two being below 40 per cent.), whilst none had values above 80 per cent. The ' complications ' were poor diet, cleft palate, upper respiratory infections, otitis media and suppurative adenitis. Since these authors regard only values below 60 per cent. haemoglobin as indicating anaemia, they conclude that the anaemia seen in rickets is due rather to secondary infection or lack of other nutritional factors than to lack of vitamin D. If 80 per cent. be taken as the minimal normal haemoglobin value for the young child, their figures show only three rachitic children with normal values.

It appears that rachitic children are often, but not always, anaemic. It has not been possible to find any description of anaemia in late rickets or in latent rickets. The work to be described here shows that existence of iron-resistant anaemia in school-children, associated with latent or chemical rickets, and the therapeutic results seem to indicate a close connexion between the anaemia and the rickets.

Source of cases

The cases were sent by the medical officer of the Hoxton and Star Cross L.C.C. Nutrition Clinics. Cases reach these clinics from five sources : (1) school medical officers ; (2) care committees, who deal with poor families ;

(3) minor ailments clinics ; (4) sun-ray clinics ; (5) direct requests by parents. Of a hundred and thirty-one children seen at these two nutrition clinics between 1936 and the middle of 1938, fifty-two had haemoglobin between 80 and 85 per cent., whilst a further twenty-three had haemoglobin below 80 per cent. All children in whom the anaemia failed to respond to iron in doses of ferrous sulphate 3 grains t.d.s. or Blaud's capsules 15 grains t.d.s., as well as a few untreated anaemic children, were referred to the Royal Free Hospital. Eighteen children in all were examined. Their ages ranged from five and a half to twelve years. The investigations were done between January and September, 1938, but the majority were in the first quarter of the year.

Method

A full history was taken from each parent, with special reference to whether signs of rickets were or had been present. Each child was subjected to a complete physical examination, and the wrists and fore-arms were x-rayed for evidence of rickets. Blood was removed by venupuncture, part into an oxalate mixture. The oxalated blood was used for the estimation of inorganic phosphorus, haemoglobin, total red cell count and mean corpuscular volume. The serum was used for the estimation of the serum calcium. The haemoglobin was estimated by Haldane's method, the inorganic phosphorus by Briggs' modification (1922) of the Bell-Doisy method and the serum calcium by the Clark-Collip modification (1925) of the Kramer-Tisdall method. Any child with a haemoglobin percentage below 85 per cent. was regarded as definitely anaemic, and any child with a calcium-phosphorus product below 40 as suffering from latent rickets.

To ensure that the anaemia was truly iron-resistant, each child was treated with ferrous sulphate 5 grains b.d. for four weeks. Each was then given four 50,000 international unit tablets of vitamin D concentrate (200,000 units of vitamin D in all), and the dose repeated after one fortnight. After one month on vitamin D only, ferrous sulphate, 5 grains b.d., was added, and thus for the last four weeks of treatment each child received 100,000 units of vitamin D and 70 grains of ferrous sulphate per week. Clinical and blood examinations were done throughout at fortnightly intervals.

So massive a dosage with vitamin D was adopted for two reasons. The first was that this 'vitamin Stoss' therapy has been highly recommended by Harnapp (1936a, b) and Braulke (1937) in cases in which rapid improvement in rickets is required. Braulke gave single doses of 600,000 I.U. of vitamin D with satisfactory results and no ill-effects in fifty children. The second reason was that the swallowing of the tablets could be personally supervised in these out-patient children and thus failures due to their not having been taken at home were avoided. None of the children showed any ill-effects from these massive doses. The maximum dose in any child was 800,000 I.U. over a period of eight weeks.

Results

Initial findings.—Table 1 gives a summary of the initial findings in the eighteen children. The lowest haemoglobin reading was 71 per cent. and the highest 85 per cent. The colour indices varied between 0.84 and 0.97. The mean corpuscular volumes varied between 78 and 98 cubic μ . The serum calcium values varied between 9.11 and 11.00 mgm. per 100 c.c. (normal range 9 to 11 mgm. per 100 c.c.). With the exception of cases 6, 8, 9 and 10, the inorganic phosphorus values varied between 2.16 and 3.88 mgm. per 100 c.c., the mean being 3.15 mgm. per 100 c.c. (normal range in children between five and twelve years : 4.0—5.5 mgm. per 100 c.c.). Cases 6, 8, 9 and 10 had phosphorus values within normal limits. The cases with low phosphorus values had correspondingly low calcium-phosphorus products (Ca \times P).

TABLE I
INITIAL FINDINGS

CASE NO.	SEX	AGE IN YEARS	DURATION OF PREVIOUS IRON TREATMENT	HÆMOGLOBIN PER CENT. (HALDANE)	RED BLOOD CELLS (MILLIONS PER C.MM.)	COLOUR INDEX	MEAN CORPUSCULAR VOLUME IN CU. μ .	Ca (MGM. PER 100 CC. SERUM)	P (MGM. PER 100 C.C. BLOOD)	Ca X P
1	F	9	2 months	77	4.05	0.96	95	9.41	3.34	31.5
2	F	8½	4 months	77	4.19	0.92	—	9.11	3.81	34.4
3	F	9	1 year	83	4.44	0.94	79	10.37	3.15	32.7
4	F	10	—	85	4.59	0.93	78	9.38	3.10	30.1
5	F	8	—	74	3.96	0.93	98	10.37	2.78	29.0
6	F	5	2 years	76	4.07	0.93	84	9.26	4.46	41.3
7	F	12½	15 months	80	4.35	0.90	89	9.80	3.33	32.6
8	M	5½	—	80	4.77	0.84	—	10.32	4.26	45.5
9	M	7	—	74	3.86	0.96	—	10.56	4.37	46.1
10	M	11	—	80	4.32	0.90	—	9.26	4.63	43.0
11	M	12	5 months	86	4.47	0.93	88	9.72	2.16	21.0
12	F	6	6 months	75	4.00	0.90	92	10.15	2.76	28.0
13	M	9	6 months	76	4.10	0.90	93	10.50	2.90	30.5
14	F	6	1½ years	83	4.75	0.89	85	9.22	3.60	33.2
15	M	6	3 months	71	4.42	0.81	86	10.48	2.08	21.8
16	M	6	2 months	83	3.65	0.93	94	10.40	3.73	38.8
17	F	8½	1 year	76	3.90	0.97	97	10.37	3.88	40.3
18	M	8	4 months	85	4.43	0.96	—	11.00	3.50	38.0

Cases 1, 4, 8, 15 and 17 showed clinical evidence suggestive of old rickets (slight bossing of the skull, slight enlargement of the epiphyses, or rickety rosaries). In none of them was there anything suggestive of florid rickets. On x-ray cases 16 and 17 showed irregularity of the radial and ulnar epiphyseal lines, suggestive of rickets. Cases 1 and 18 showed clinical chorea without cardiac involvement. Cases 3 and 4 and cases 7 and 18 were sisters, cases 9 and 10 were brothers, and cases 12 and 13 were siblings. Case 5 was a high-grade mental defective. Cases 4, 5, 8, 9 and 10 had received no previous iron therapy.

Of the four children with normal phosphorus values, three were not seen

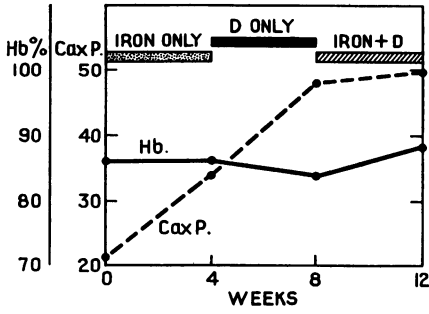


FIG. 1.—Case 11.

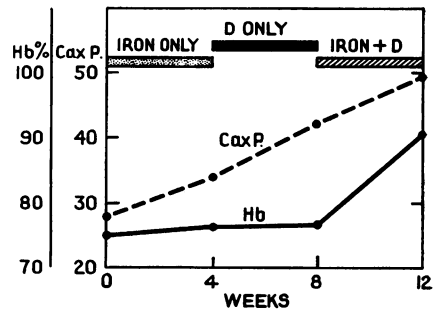


FIG. 2.—Case 12.

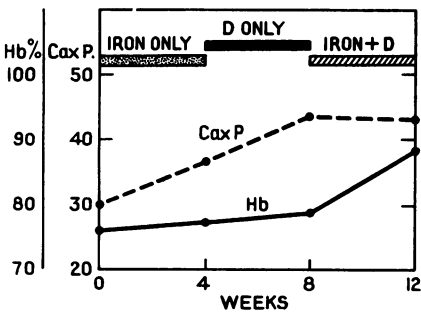


FIG. 3.—Case 13.

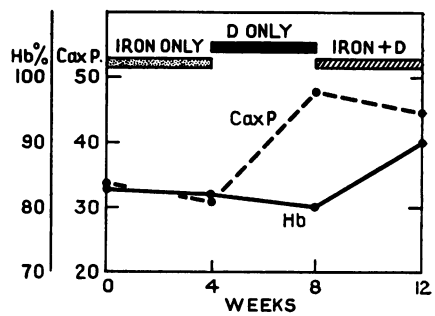


FIG. 4.—Case 14.

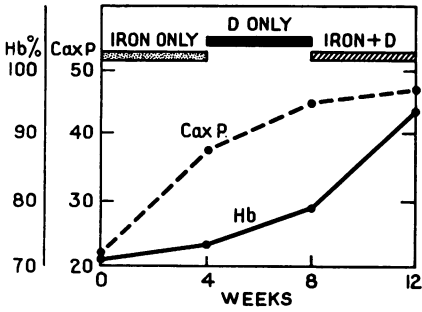


FIG. 5.—Case 15.

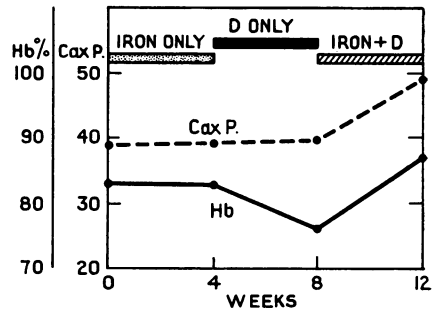


FIG. 6.—Case 16.

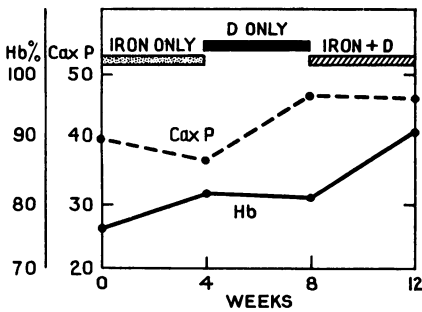


FIG. 7.—Case 17.

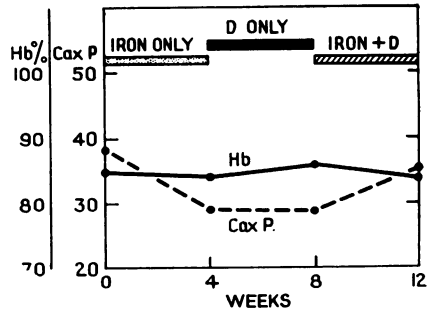


FIG. 8.—Case 18 (Chorea).

again. The fourth, case 8, responded rapidly to iron. Only one of the four, case 6, had received previous iron therapy. Excluding these four and the two children with chorea, cases 1 and 18, the remaining twelve children present a definite clinical picture of orthochromic, normocytic or hypochromic microcytic anaemia associated with a low inorganic blood phosphorus, without gross physical signs of rickets. In all but two, this anaemia had been adequately treated with iron, and had failed to respond.

Results of treatment.—Owing to non-attendance, only eight children (cases 11–18) could be subjected to the full scheme of treatment. The results of this treatment are shown in table 2 and fig. 1–8. Two children showed slight increases in haemoglobin on either iron or vitamin D alone (cases 15 and 17). The remainder showed no significant increase. In every child except case 18, vitamin D restored the blood phosphorus to normal. Further, in every child except case 18, a combination of iron and vitamin D restored the haemoglobin to normal. Excluding case 18, the mean haemoglobin reading after iron alone and vitamin D alone was 79 per cent. After a combination of iron and vitamin D, the mean was 89 per cent. Case 18 was suffering from chorea, and, in spite of a rise in blood phosphorus, her haemoglobin was unaffected by treatment.

TABLE 2
RESULTS OF TREATMENT

CASE NO.	INITIAL FIGURES			AFTER IRON ALONE			AFTER VITAMIN D ALONE			AFTER IRON + VITAMIN D		
	HAEMOGLOBIN	P MGM. PER CENT.	Ca X P	HAEMOGLOBIN	P MGM. PER CENT.	Ca X P	HAEMOGLOBIN	P MGM. PER CENT.	Ca X P	HAEMOGLOBIN	P MGM. PER CENT.	Ca X P
11	86	2.16	21.0	86	4.01	34.0	84	4.71	48.0	88	4.76	49.8
12	75	2.76	28.0	76	3.01	33.4	76	4.26	41.8	90	4.86	48.6
13	76	2.90	30.5	77	3.29	36.5	79	4.59	43.9	88	4.34	43.0
14	83	3.60	33.2	82	2.95	31.5	80	4.76	47.6	90	4.47	44.7
15	71	2.08	21.8	74	3.51	37.7	79	4.50	44.7	94	4.47	46.9
16	83	3.73	38.8	83	3.73	38.8	76	4.27	39.5	87	4.40	48.5
17	76	3.88	40.3	82	3.87	36.3	81	4.42	46.7	91	3.91	46.0
18	85	3.50	38.0	84	2.62	29.1	86	2.98	29.1	84	4.05	35.1

Conclusions

From the results it is justifiable to state that a mild iron-resistant hypo- or orthochromic anaemia associated with latent low-phosphorus rickets, is to be found among school-children. The low blood phosphorus is rapidly corrected by massive doses of vitamin D, but the anaemia is relieved only by a combination of iron and vitamin D. It appears that adequate supplies of vitamin D are essential in these children if iron is to be properly utilized for blood formation.

Summary

1. In twelve children, aged between six and twelve and a half years, an iron-resistant hypo- or orthochromic anaemia was found, associated with a low inorganic blood phosphorus, but with no definite clinical signs of rickets.

2. Vitamin D, given in two single doses of 200,000 international units at fortnightly intervals, restored the blood phosphorus values to normal in one month, but had no effect on the haemoglobin values.

3. A combination of similar doses of vitamin D and ferrous sulphate, 5 grains b.d., raised the mean haemoglobin readings from 79 per cent. to 89 per cent. in one month.

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