

ANÆMIA in INFANCY: ITS PREVALENCE AND PREVENTION.

By

HELEN M. M. MACKAY, M.D., M.R.C.P.

Physician to the Queen's Hospital for Children, London ;
Late British Medical Association Research Scholar.

The remarkable prevalence and the ill-effects of anæmia among London infants have been demonstrated by the following investigation, which also indicates a simple and efficacious method of prophylaxis.

Fairly large groups of artificially fed infant out-patients were observed for varying periods extending from October, 1925 to December, 1927. These infants were usually subnormal in health, but were not suffering from acute illnesses, and, after the first few weeks of attendance, compared not unfavourably with those at many London welfare centres. They were divided into the following groups:—(1) artificially fed infants without special treatment; (2) breast-fed infants; (3) those given light therapy; and (4) those given iron. Records were kept of the clinical history of each infant and of the hæmoglobin level of the blood.

Professor Major Greenwood, F.R.S., and Miss E. M. Newbold, M.Sc., kindly examined statistically many of the results, and the author is greatly indebted to them for this help. The results given in the appendix have been worked out or checked by them at the National Institute for Medical Research.

THE NORMAL PERCENTAGE OF HÆMOGLOBIN IN INFANCY.

A digression is here necessary to indicate a preliminary difficulty in determining the incidence of anæmia in infancy, namely the lack of any fixed standard of comparison. Authorities differ widely as to the normal hæmoglobin percentage in the blood of infants.

Aschenheim, for example, has placed the lower limit of normal as low as 55 per cent., Finkelstein¹ at 65 per cent., and Holt² states that 75 per cent. is "about the average in healthy children." Hutchison³ says that the hæmoglobin falls from 100 per cent. at 2 weeks to its minimum value of 70 per cent. at 6 months, thereafter remaining stationary until 2 years of age. C. S. Williamson's figures⁴ have been widely quoted. In 1916 he determined by the spectrophotometric method the average grams of hæmoglobin per 100 c.cm. of blood for groups of healthy infants. Each of his figures is the average for 30 to 34 cases, and, exclusive of the first two weeks of life, they are as follows:— $\frac{1}{2}$ to 2 months 18.42 gm. (say 133 per cent. by Haldane's clinical standard); 3 to 5 months, 13.66 gm. (say 99 per cent.); 6 to 11 months 13.70 gm. (say 99 per cent.); 12 months, 12.53 gm. (say 91 per cent.); and 2 years, 12.57 gm. (say 91 per cent.). The figures in brackets are calculated by taking the Haldane hæmoglobino-meter 100 per cent. standard as representing an oxygen-combining power of 18.5 per cent. or 13.8 gm. of hæmoglobin per cent. Williamson's figure for adults aged 21 to 25 years is 16.02 gm., say 116 per cent. by the clinical standard. Haden⁵, using Van Slyke's blood-gas apparatus, found that for blood containing five million red cells per cm. the oxygen combining

power was 20.9 c.cm., which is equivalent to 15.6 gm. of hæmoglobin per 100 c.cm. His cases were adults. On the other hand, Stitt⁶ states that in the adult the normal is usually given as 13 to 14 gm., per 100 c.cm. (say 94 per cent. to 101 per cent.), and that from 5 to 6 months until 12 to 15 years the normal is 11 gm. per 100 c.cm. (say 80 per cent.).

These statements sufficiently indicate the uncertainties of the subject. No figures appear available showing the level at each month of age in infancy, although it is hoped that the present investigation may in some measure have remedied this deficiency.

CLINICAL MATERIAL INVESTIGATED.

The total number of infants furnishing the material of this paper is 541, and the number of hæmoglobin estimations is 2,561. The most important group is that studied from 1925 to 1927 at the Queen's Hospital for Children and at a neighbouring clinic in Bethnal Green to which infant welfare medical officers sent children for consultation or light treatment. These numbered 434, of whom 333 were out-patients at the hospital and 101 at the clinic. Excluding 89 cases who had only one hæmoglobin estimation each, the average number of estimations per child was 6.2, performed at monthly intervals. The remaining 107 infants are included for comparison and fall into the following groups:— 53 unselected infants attending the Infant Welfare Department of the General Lying-In Hospital, Lambeth, in 1926; 21 out-patients at the Infants' Hospital, Westminster, examined in 1923; and 33 infants observed in a Vienna institution in 1921 and 1922. All statements, however, must be taken as referring to the 434 infants first mentioned unless the others are specifically included.

Economic status of the families. Both the Queen's Hospital for Children and the Bethnal Green clinic are situated in a poor and overcrowded district in the East end of London. Of 111 unselected, consecutive cases attending the Out-Patient Department of the Hospital in June, 1927, only 34 per cent. of the parents had a family income of over £3 per week, and 23 per cent. were receiving relief from the Guardians, or free milk from the borough, or both. At the General Lying-In Hospital the economic status was rather better. Of the infants examined in 1926, the parents of 18 per cent. were receiving relief or free milk, and this, in spite of possible differences in the scale of relief, probably represents a definite superiority in the average financial status of these mothers.

Age. The age of infants when first included varied from 3 weeks to 18 months, and none were over two years old at the end of their period of observation.

Physical condition. This was generally subnormal when first seen. The great majority were under normal weight, as judged for instance, by Griffith's standard weight curve⁷ for healthy breast-fed infants. The artificially fed infants examined at the Queen's Hospital and the neighbouring clinic in 1925 to 1926 averaged 80 per cent. of normal weight at the beginning, and 87 per cent. at the end, of their period of observation (Table F.). After the first few attendances, the infants were of the type usually found at welfare centres. No children with acute illnesses were included, but those who subsequently developed such illnesses were not necessarily excluded, but were, so far as possible, followed up. The majority of infants were brought up on account

of errors in feeding, either quantitative or qualitative; others attended with constipation, bronchitis, sore throat or other minor maladies, and a few were convalescent from some more severe illness.

Attendance. In some of the tables given later a certain number of infants who attended only once are included, but with the great majority the periods of attendance varied from 1 to 12 months, and some longer. Attendance was, on the whole, fairly regular, although its frequency varied greatly. Thus during a period of food adjustment an infant might be seen twice or three times in the week, but when progressing satisfactorily the mother was asked to come at weekly, fortnightly or monthly intervals. At each visit, the child was weighed and was seen by the author, full notes being kept of its condition and progress. Infants ordered light treatment were expected to attend three days weekly in the Light Department^s. General advice on hygiene and management was the same for all groups and was given by the writer.

Diet. In an investigation on anæmia the character of the diet is of importance. Two main dietetic groups were studied.

(1). *Artificially fed infants.* For these children the diet was wholly or chiefly artificial from the early months, though some cases received partial breast feeding until well on in infancy. To infants under eight months of age a fairly high percentage of the total caloric needs was given in milk with the idea of minimizing the risk of unsuspected deficiencies in any of the less well understood food constituents. Full cream dried milk (a roller-process milk), was used and cane sugar added. Usually between 70 and 85 per cent. of the total calories were supplied as dried milk, though this might occasionally sink to 60 per cent. for short periods. Thus the amount of milk given before mixed feeding was begun varied with the age and size of the child up to a maximum of about 2-lbs. of dried milk in the week, say, the equivalent of about $1\frac{3}{4}$ pints of fluid milk daily. Generally speaking, an infant of about 10 lb. consumed at least 1 lb. of dried milk weekly, the equivalent of nearly 1 pint of fluid milk daily. The amount of sugar varied from 6 to 9 drachms (90 to 135 calories), in the 24 hours. Young infants received a higher percentage of sugar than older ones.

All infants were ordered one or more teaspoonsful of orange or tomato juice daily, as well as cod-liver oil throughout the winter months.

It is well recognised that prolonged exclusive milk feeding may cause anæmia. In this investigation, however, mixed feeding was begun younger than is frequently advised. Between 8 and 9 months of age the daily consumption of milk was reduced to about 1 to $1\frac{1}{4}$ pints, and other foodstuffs were added to the diet, including eggs, three or more weekly, gravy, soup, fish, vegetables and a daily ration of fruit. At 12 months meat on three to six days in the week was ordered. On the whole, advice regarding diet appeared to be fairly satisfactorily carried out; that is, the kind of food advised was given.

(2) *Breast-fed infants.* The other main dietetic group consisted of children entirely breast-fed until 7 months of age or later. Many of these were given cod-liver oil and orange juice. The feeding advised from 8 months onwards was the same as for artificially fed infants.

The infants at the General Lying-In Hospital were fed on similar lines, but the diet of those at the Infants' Hospital and in Vienna was different and will be considered later.

HÆMOGLOBIN ESTIMATIONS.

The total number of hæmoglobin estimations on which this paper is based is 2,561, all done by Haldane's⁹ method. Haldane's standard tube is so calibrated that 100 per cent. represents an oxygen-combining power of 18.5 c.cm. or 13 grm. of hæmoglobin per 100 c.cm. All the estimations at the Queen's Hospital for Children and the Bethnal Green clinic were made by one observer, Miss Lörel Goodfellow, and numbered 2,228. The blood was taken in the forenoon from a prick in the heel, precautions being taken first to warm the foot. Whenever possible, the estimations were repeated for each child at monthly intervals. When the colour of the tubes was being matched, the previous reading was, as a rule, unknown. The estimations at the General Lying-In Hospital were also made by Miss Goodfellow, and those at the Infants' Hospital and in Vienna by the author using the same method. From observations made in Vienna, the author is of opinion that even when precautions are taken to warm the part, the average hæmoglobin estimation obtained by pricking an infant's heel is distinctly lower than that obtained by pricking the ear. This is presumably due to a difference in the capillary circulation, but as all estimations in this series were made from the heel, this factor need not be considered further.

THE EFFECT OF THE MERCURY VAPOUR QUARTZ LAMP ON THE HÆMOGLOBIN LEVEL OF ARTIFICIALLY FED INFANTS.

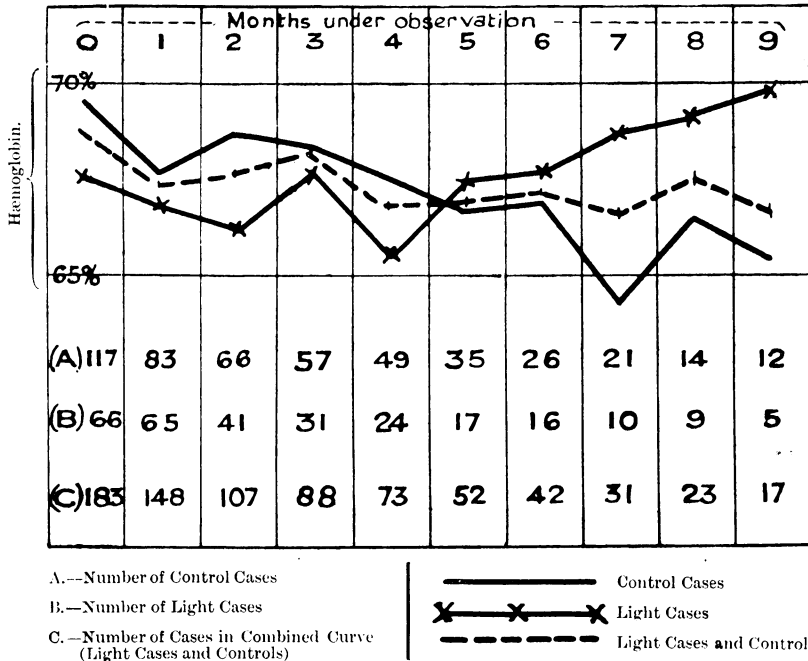
The first comparison was made between a control group of artificially fed infants and a similar group treated with the mercury vapour quartz lamp, the form of lamp most commonly used in this country for the treatment of infants. These two groups were followed up for thirteen months, from October 1925 to October 1926 inclusive. The general progress and the average hæmoglobin percentage of the blood of the two groups were compared, but in this paper only the latter will be considered as it has already been shown⁸ that there was little difference in rate of weight increase or in the number of intercurrent illnesses in the two groups, and that such differences as there were, were not all in favour of either the one or other group. Full details of treatment are given in the previous paper.

The control cases whose blood was examined numbered 218, and the cases given light treatment 66. Only those receiving a minimum of five light treatments per 4 weeks have been included. A few cases are included first in one group and then in the other. In each month a certain number ceased to attend and others were included, so that comparatively few cases could be followed up for the whole thirteen months.

The variations in the hæmoglobin level can most easily be studied in charts whenever the number of observations is sufficient to give a satisfactory average. Under each chart will be found figures indicating the number of observations upon which each average is based. For the present we are concerned with a comparison between light cases and their controls, and the significance of the curves obtained will be discussed later.

Cases classified according to time under treatment. Chart I illustrates the effect of duration of treatment, both in the control cases and in those given light treatment, and shows no appreciable difference between the two. They started within 2 per cent. of one another and after six months' observation were still within 2 per cent. of each other. After six months the number of cases remaining under observation is not sufficient for a fair comparison. Since, however, a greater contrast might be obtained by comparing the two groups in winter (November to May), when the exposure to sunlight was at a minimum, this was done and the results plotted on Chart II. The two curves follow each other remarkably closely. Some cases ceased to attend each month and the total numbers are comparatively small, so that an effort was made to

CHART I.
LIGHT TREATMENT: HÆMOGLOBIN LEVEL AT VARIOUS PERIODS UNDER OBSERVATION.



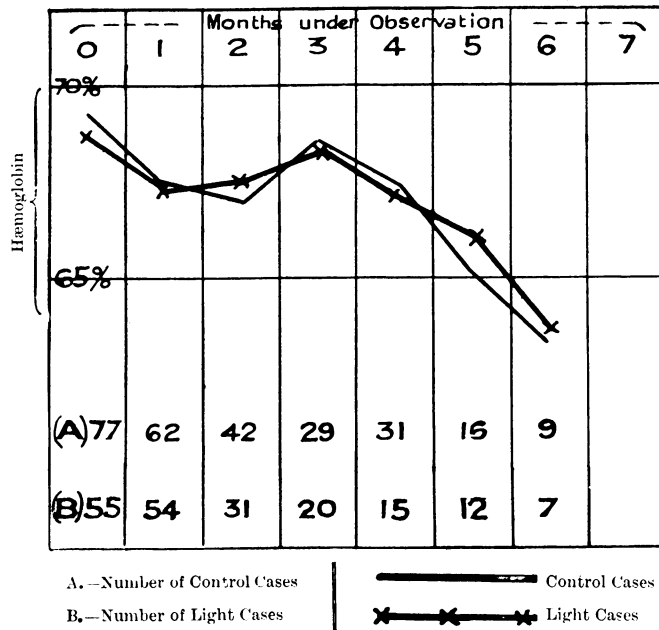
eliminate a possible source of error in comparison by averaging for each month the loss or gain in hæmoglobin instead of the whole numbers, as shown in Chart III. For the first three months the curves again run together and only diverge when the number of observations is small, again showing no appreciable difference between the light and non-light groups.

Cases classified by age. The same groups of cases are classified by age in Chart IV, showing that a similar curve exists in both groups, and that up to thirteen months of age the averages differ only very slightly. After this the numbers are too small to allow of any conclusions being drawn.

Cases classified by season. Neither curve (Chart V.) is smooth, but there is no evidence of the superiority of one group over the other.

Individual cases receiving light treatment. A study of individual case-sheets bore out the same conclusions and furnished no evidence that treatment with the mercury vapour quartz lamp, as here given, was either a prophylactic or a curative agent in anæmia. The average hæmoglobin percentage of the nine most anæmic cases of the light series was 50 per cent. at the beginning of observation. During light treatment (1 to 7 months), four dropped slightly and five rose slightly. The most anæmic were given other treatment after one or two months.

CHART II.
LIGHT TREATMENT: HÆMOGLOBIN LEVEL (WINTER) AT VARYING PERIODS UNDER OBSERVATION.



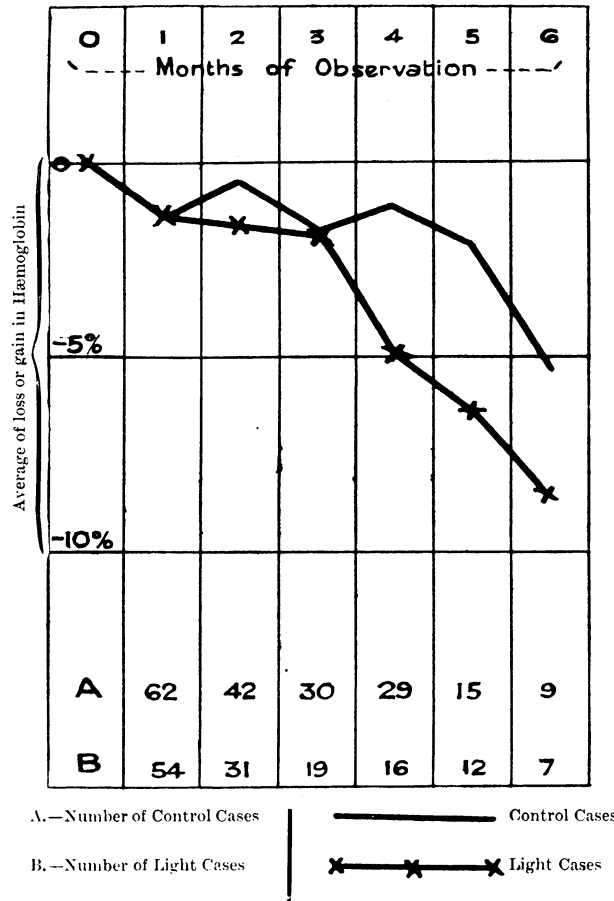
THE EFFECT OF THE CARBON-ARC LAMP ON THE HÆMOGLOBIN LEVEL OF ARTIFICIALLY FED INFANTS.

The cases treated with the long-flame carbon-arc lamp numbered only eleven and could, therefore, furnish no conclusive evidence of its effect. In individual cases, however, this treatment did not prevent a large drop in the hæmoglobin percentage, either in the first two months of life or after four to six months of age. In eight cases the final hæmoglobin estimation was lower than the first, and in three it was higher. Treatment was given two or three days weekly at a distance of about one yard, and the maximum exposure was half-an-hour. Barenberg and Lewis¹⁰ working with in-patients (9 irradiated cases and 10 controls), considered there was an initial stimulant effect followed by a depressant effect. The present investigation provided no evidence of these two phases.

THE HÆMOGLOBIN PERCENTAGE IN THE BLOOD OF ARTIFICIALLY FED INFANTS :
LIGHT AND NON-LIGHT CASES COMBINED.

Since it has been shown^a that there is no evidence that treatment with the mercury vapour quartz lamp altered in any way either the hæmoglobin level of the blood, or the weight curve, or diminished the liability to infection, it is legitimate to combine these two groups of artificially fed infants in order

CHART III.
ALTERATIONS IN HÆMOGLOBIN LEVEL IN WINTER AT VARYING PERIODS
UNDER OBSERVATION.



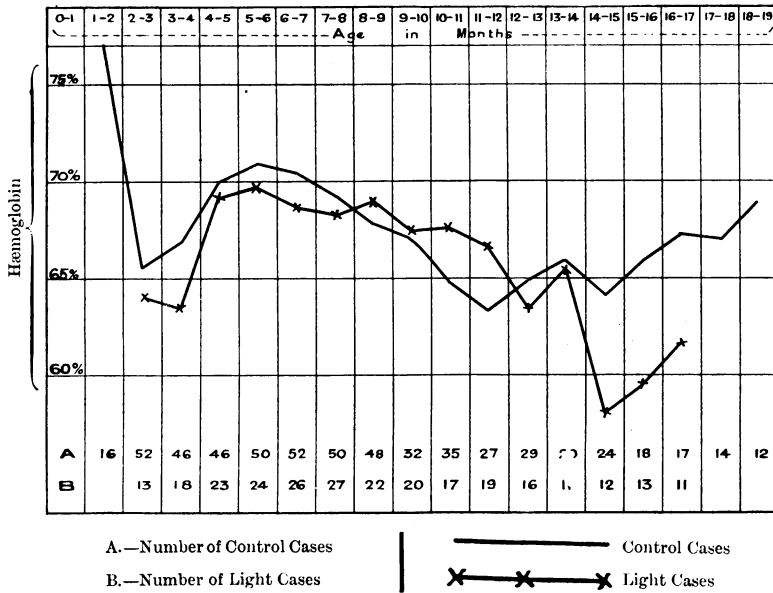
to obtain a larger control series for purposes of comparison. Charts I, V and VI show the hæmoglobin curves obtained by combining the light and non-light cases of 1925-26.

Effect of duration of attendance. The great majority of infants improved in general health while under observation, as would be expected. This was evident from their appearance and was supported by the fact that whereas at the beginning of observation they averaged about 80 per cent. of normal weight,

at the end they attained an average of about 87 per cent., Griffith's curve⁷ for healthy breast-fed infants being taken as the standard. This improvement in general health was, no doubt, due to many factors such as : better adjustment of diet, better general hygiene and management (*e.g.*, more out-door life), and the clearing up of any temporary ailment, such as an attack of bronchitis. An associated improvement in the percentage of hæmoglobin in the blood might have been expected, but on the whole this failed to appear. Chart I shows a slight drop in hæmoglobin during the time under observation. Of course in individual cases such an increase did occur, but it was more than balanced by the fall in others.

Effect of age. This is of special interest, and, so far as the author is aware, a curve showing the hæmoglobin level at each month for the first year of life

CHART IV.
HÆMOGLOBIN LEVEL AT DIFFERENT AGES.



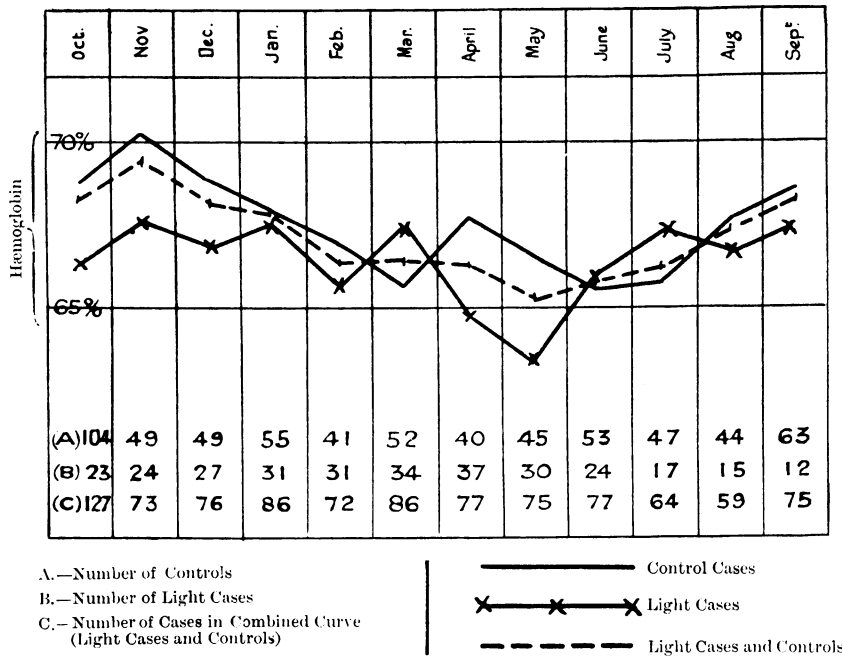
has not previously been published (see Chart VI). A figure for the new-born was not obtained, but it is well known that this is high, over 110 per cent at least. The drop of the first few weeks of life continues sharply down to about 65 per cent. at two months of age, thereafter there is a rise to about 70 per cent. at five months, followed by a steady fall until about twelve months of age when the average hæmoglobin percentage is under 65 per cent.

At every age infants dropped out of the series and fresh cases were included and it became desirable, therefore, to eliminate this possible source of error. Chart VII, which shows the average of the loss or gain of each child in hæmoglobin percentage at each month of age is, therefore, very probably a truer representation of the facts than Chart VI. The shape of the curve up to 12 months is the same ; from 12 to 18 months numbers are small, but the curve

shows the hæmoglobin level until 17 months remaining about the same as at 12 months. This type of curve with the double drop, the first from birth to two months and again after six months, is repeated so often that it cannot be the result of chance. Whether these figures reveal the presence of widespread anæmia depends on what the normal hæmoglobin level may be at each month of age and will be discussed later.

Effect of birth weight. The curves obtained by grouping the infants so far as possible according to their birth weight (Chart VIII) are suggestive though not conclusive, partly because of the uncertainty attaching to the mother's statement of birth-weight and also because the numbers are extremely small. The curves indicate, however, that *both* the initial fall in hæmoglobin and

CHART V.
HÆMOGLOBIN LEVEL AT DIFFERENT SEASONS.



the fall after the age of six months depend in part on the weight at birth. The smaller the infant at birth, the greater the fall. It is, of course, well known that premature babies nearly all become anæmic. It does not, however, appear to be known that they, as well as full-time children, show a double drop in hæmoglobin, with a rise till about five or six months old after the initial fall. The effect of birth weight is indicated in Table A.

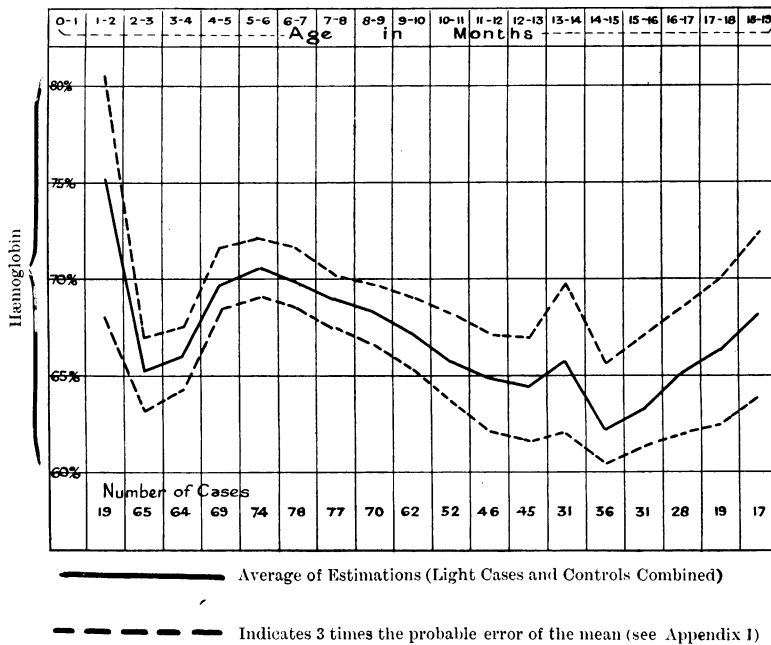
Effect of sex. There appeared to be little, if any, difference between the sexes in the hæmoglobin level, and separate curves are, therefore, not shown.

Effect of season. The season curves (Charts V and IX), suggest a slight drop in the hæmoglobin level from November to May and a slight rise in the summer months. Confirmatory evidence of a seasonal variation is, however, wanting,

TABLE A. EFFECT OF BIRTH WEIGHT ON HÆMOGLOBIN LEVEL.

Birth weight.	No. of cases.	% showing Hb. below 60%.
Under 5 lb.	14	86%
5 lb. odd	16	31%
6 lb. „	43	28%
7 lb. „	56	18%
8 lb. „	44	16%
9 lb. and over	27	15%
	Total 200	Average 25%

CHART VI.
AVERAGE HÆMOGLOBIN PERCENTAGE IN ARTIFICIALLY FED INFANTS AT DIFFERENT AGES.



as the same type of curve does not always repeat itself (see Chart V), and if the curves are corrected for age (see Charts X and XI and Appendix), they fail to prove any seasonal difference that does not fall within the limits of possible chance variation. The difference in Chart XI may perhaps reflect the lesser incidence of infections in summer. It would be interesting to have further data on the point.

THE HÆMOGLOBIN LEVEL IN BREAST-FED INFANTS.

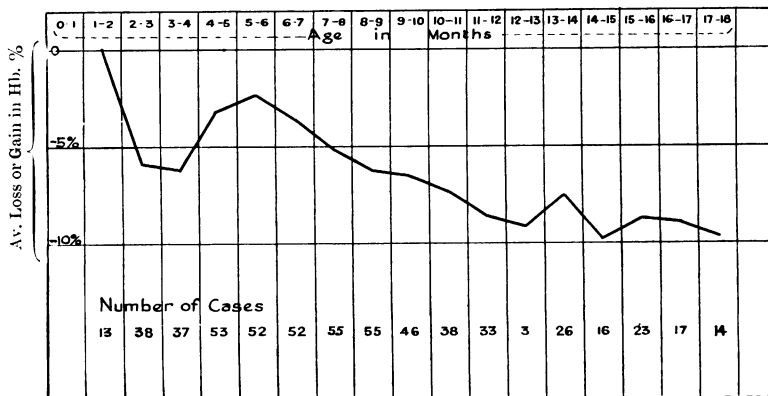
To obtain regular hæmoglobin estimations on a series of apparently healthy breast-fed infants proved more difficult than to obtain similar figures for the artificially fed and the total numbers are consequently small; 74 infants in all.

These when first seen were, for the most part, sub-normal; in fact, they were similar in type to the artificially fed infants. An infant was counted as breast-fed if it received nothing but breast milk until 7 months of age, supplements of fruit juice or cod-liver oil not being taken into consideration. Chart XII shows the average hæmoglobin level for each month of age. The type of curve, (irregular on account of the small numbers), is, on the whole, similar to that of the artificially fed infants, but is higher at every age. At what may be regarded as the critical points of the curve, i.e., at two months, five months and twelve months, it is more than 5 per cent. higher; nevertheless, after the first month of life it reaches 75 per cent. only between five and seven months of age.

COMPARISON OF THE CONTROL GROUPS WITH OTHER GROUPS OF INFANTS.

The infants so far considered were all out-patients either at the Queen's Hospital for Children or at a clinic for ailing children. The criticism may, therefore, be made that in spite of suggestions to the contrary, these do not give

CHART VII.
AVERAGE LOSS OR GAIN IN HÆMOGLOBIN PERCENTAGE AT EACH MONTH OF AGE.
(LIGHT CASES AND CONTROLS COMBINED.)

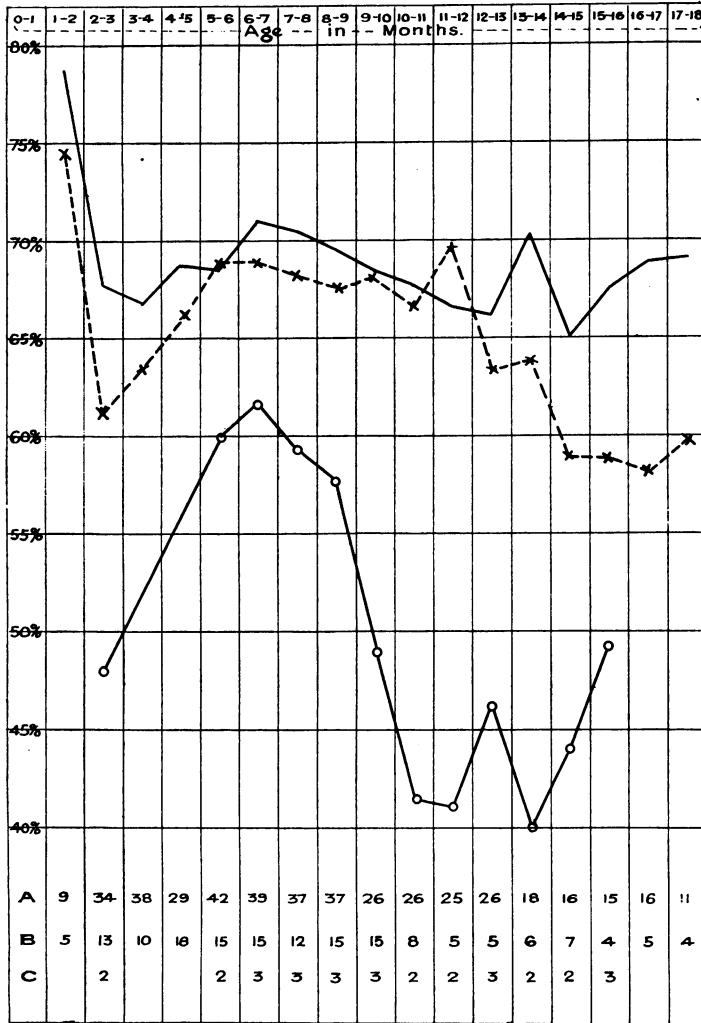


a true picture of the average hæmoglobin level in artificially fed infants. It will probably be admitted, however, that infants attending a good welfare centre are at least up to the average of infants of working-class mothers in the district.

53 children were, therefore, examined in the spring of 1926 at the Infant Welfare Centre of the General Lying-In Hospital, Lambeth. The level of health here was probably above the average for such institutions in London, because the numbers attending the centre are comparatively small, and the help and advice given to individual mothers considerable. Of the 53 infants tested, 32 were entirely breast-fed or had been so fed until 7 months of age, and 21 were partially or entirely artificially fed. A certain number were believed to have received iron for short or irregular periods. Among those over one month only one exceeded 75 per cent., and the average hæmoglobin percentage, excluding infants under one month, was 70 per cent. for 28 breast-fed, and 66 per cent. for 21 bottle-fed babies. These figures for unselected

welfare centre cases are, as it happens, actually slightly lower than the corresponding figures in the control series from the Queen's Hospital and the Bethnal Green clinic: these were approximately 73 per cent. for breast-fed, and 69 for artificially fed infants when first seen.

CHART VIII.
INFLUENCE OF BIRTH WEIGHT ON THE AVERAGE HÆMOGLOBIN PERCENTAGE.



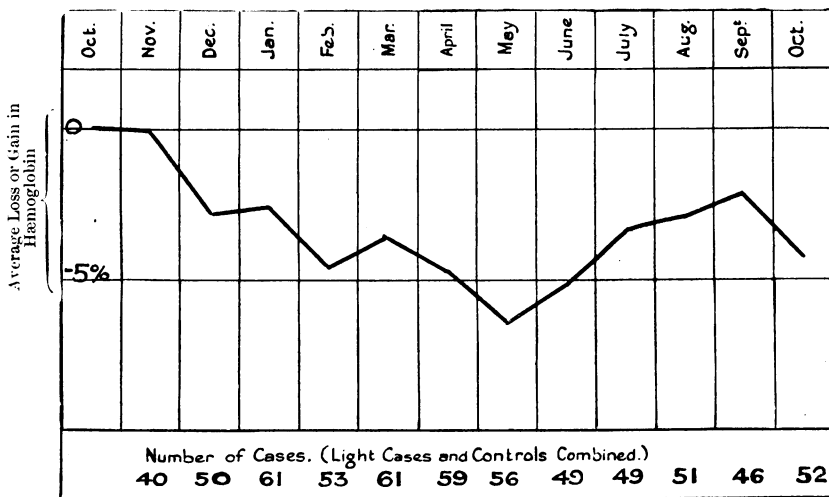
A.—No. with Birth weight over 7 lb. ————— Birth weight over 7 lb.
 B.— " " " " of 5-7 " x---x---x " " of 5-7 "
 C.— " " " " under 5 " o—o—o " " under 5 lb.

The method of feeding might also be held accountable for the haemoglobin level found in the artificially fed group. Infants on other methods were, therefore, also examined. In 1923 the author estimated the haemoglobin percentage in 21 infants, the majority of whom were entirely artificially fed,

at the Infants' Hospital. The type of case was similar to that followed up at the Queen's Hospital, but the methods of feeding differed and included "humanized feeds" and veal broth from early infancy. The children's ages varied from 3 to 18 months, and the average hæmoglobin level was again 69 per cent.

Another set of figures for comparison was taken from 33 infants, artificially fed from an early age, who were kept under observation in an institution in Vienna.¹¹ The average of the last hæmoglobin estimation on each infant before discharge, or before the administration of iron, was 62 per cent. The ages of the infants varied from 5 to 18 months. They were on two contrasted types of feeding: one group received until 9 months only dried milk with added fruit juice and cod-liver oil, and was protected from rickets; the other group received fresh cow's milk with heavy carbohydrate additions and fruit juice, and was not protected from rickets. The latter group was given vegetable

CHART IX.
AVERAGE LOSS OR GAIN IN HÆMOGLOBIN PERCENTAGE AT EACH MONTH OF THE YEAR.



purée daily from six or seven months of age onwards. There was no evidence that one group was superior to the other in hæmoglobin content of the blood. Only four of the infants were over twelve months old, and their hæmoglobin percentages lay between 39 per cent. and 58 per cent.

The estimations here and at the Infants' Hospital were made by the author and are, therefore, not strictly comparable with those in the main groups.

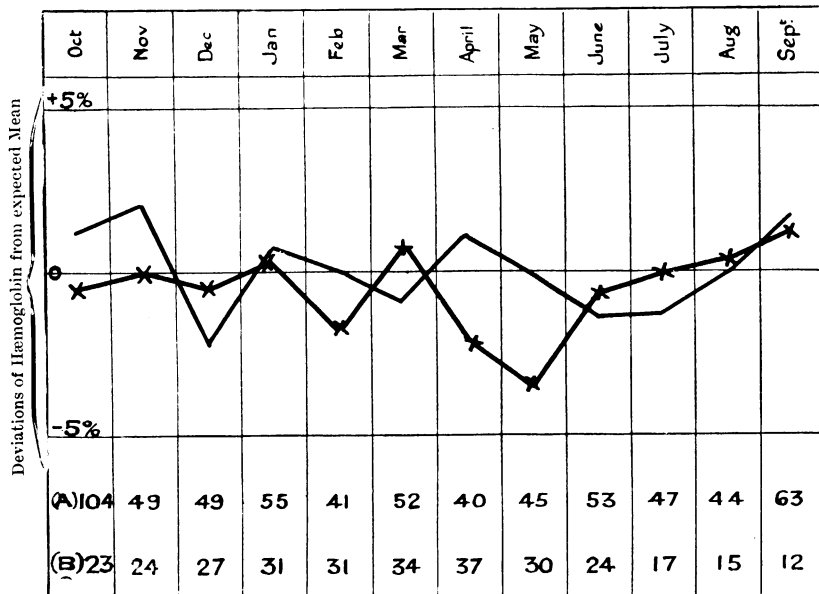
EFFECT OF IRON ON HÆMOGLOBIN LEVEL IN ARTIFICIALLY FED INFANTS.

So far the investigation showed that all the groups of artificially fed infants had during most of the months of infancy a hæmoglobin level averaging between 60 per cent. and 70 per cent. Many individuals, of course, were very much lower than this. The effect of iron medication was next tried. It was argued that if the normal hæmoglobin level ranged between 60 per cent. and 70 per cent., the administration of iron would presumably leave it unchanged; if, also, these

values indicated anæmia, but the anæmia was due to some dietetic defect other than iron deficiency, or to repeated minor attacks by micro-organisms, then again no great effect was to be expected from iron treatment.

Iron salt used. The salt used was iron and ammonium citrate. This was chosen on account of its ready solubility and easy toleration. A sample was kindly examined by Dr. S. S. Zilva, who found it to be a pure salt and to contain 20.8 per cent. of iron. Recent experimental work indicates that the iron preparations in common use differ greatly in therapeutic value, and the choice of a salt is, therefore, of considerable importance. Mitchell^{12, 13} *et al.* have shown, since this work was begun, that iron and ammonium citrate is a particularly effective salt in experimental anæmia in rats.

CHART X.
SEASONAL HÆMOGLOBIN CURVES CORRECTED FOR AGE.



The Curves represent the deviation of the observed Hæmoglobin percentage in each calendar month from the "expected mean" Hæmoglobin calculated for their ages.

A.—Number of Control Cases

B.—Number of Light Cases

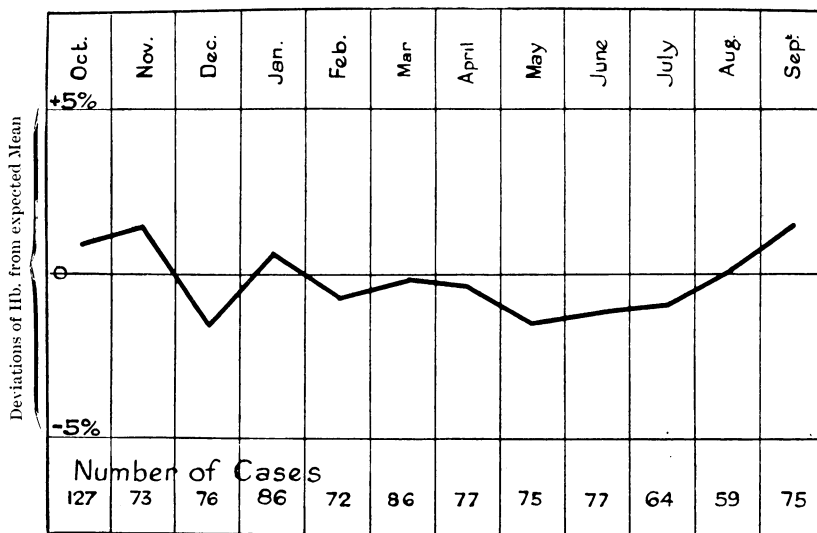
————— Control Cases

×—×—× Light Cases

Dosage and method of administration. Except for very young infants, or those with some digestive trouble, the dose given varied between $4\frac{1}{2}$ and 9 grains daily, though this was occasionally exceeded. The iron was at first ordered as a mixture, sweetened with syrup, given in three doses daily, generally in the milk. So much uncertainty attached to this method of administration among out-patients that another and more satisfactory method was tried. From January to December, 1927, the West Surrey Central Dairy Co. (vendors of "Cow & Gate" milk), kindly arranged through their chemist, Mr. J. Tavroges, B.Sc., to supply the writer with dried milk containing added iron and ammonium citrate, thus greatly facilitating the regular administration of

iron. This salt was added in solution before the milk was dried on the rollers. The amount added was $31\frac{1}{2}$ grains to each pound of dried milk, so that if one pound was consumed in one week, the intake of iron and ammonium citrate per day was $4\frac{1}{2}$ grains. This milk was supplied to mothers from the Queen's Hospital. In many cases, for those infants taking under $1\frac{1}{2}$ -lb. of dried milk per week, an additional $2\frac{1}{4}$ grains of the iron salt daily was ordered in the form of a mixture, but the total dosage per day still varied between $4\frac{1}{2}$ and 9 grains or a little more. At the Bethnal Green clinic the iron mixture alone was used as the medicated dried milk was not available. For very young infants, or those recovering from digestive disturbances, the precaution was taken of beginning the salt gradually. The iron was excellently tolerated. Very occasionally it appeared to cause looseness of the stools if the whole dose was given at the outset.

CHART XI.
SEASONAL HEMOGLOBIN CURVE CORRECTED FOR AGE—COMBINED LIGHT
CASES AND CONTROLS.



It was found wise to warn mothers that the stools would be dark, and there were occasional complaints that it increased the odour of the stools. Older infants occasionally tired of the dried milk.

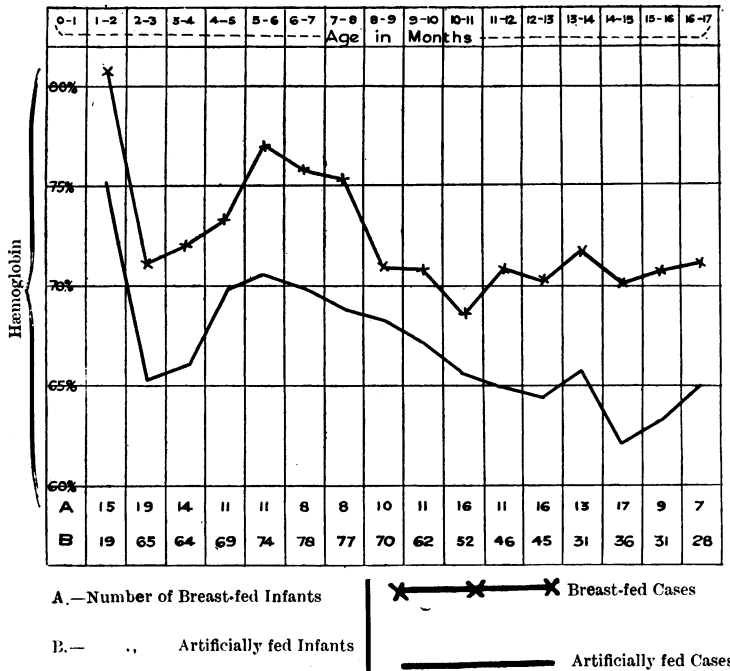
A record was kept of each packet of medicated "Cow & Gate" milk sold or given to a mother, and as there was little likelihood of the food being thrown down the sink, in contradistinction to the possible fate of medicine, it became possible to estimate accurately the amount of iron and ammonium citrate consumed by each infant. Many mothers fetched the child's weekly supply of dried milk with absolute regularity.

A. *Cases treated in 1925-26.* During 1925-26 a large number of the children given iron were selected on account of anæmia, and had been previously included in the control or the light treatment group. The number of cases was 35, and the results of treatment are given in Chart XIII, showing the average hæmoglobin percentage after 1, 2, 3, etc., months of treatment. These

infants started with an average of 57.9 per cent., and rose steadily in the course of six months to nearly 80 per cent., an average increase of over 20 per cent., though in the previous four months they had shown an average drop of 6 per cent. This curve is constructed not from selected iron cases, but from every case having iron during this period and attending for hæmoglobin estimations. Of the 35 cases, only one showed no increase in hæmoglobin percentage, and that case had no iron for four out of the six weeks under observation.

B. Cases treated in 1926-27. These were artificially fed and of the same type as to the control series of 1925-26. They were not selected anæmic infants, and the average initial hæmoglobin percentage was almost identical with that of the controls. They numbered 132, of whom about 60 were infants who had been included in the control series before October, 1926.

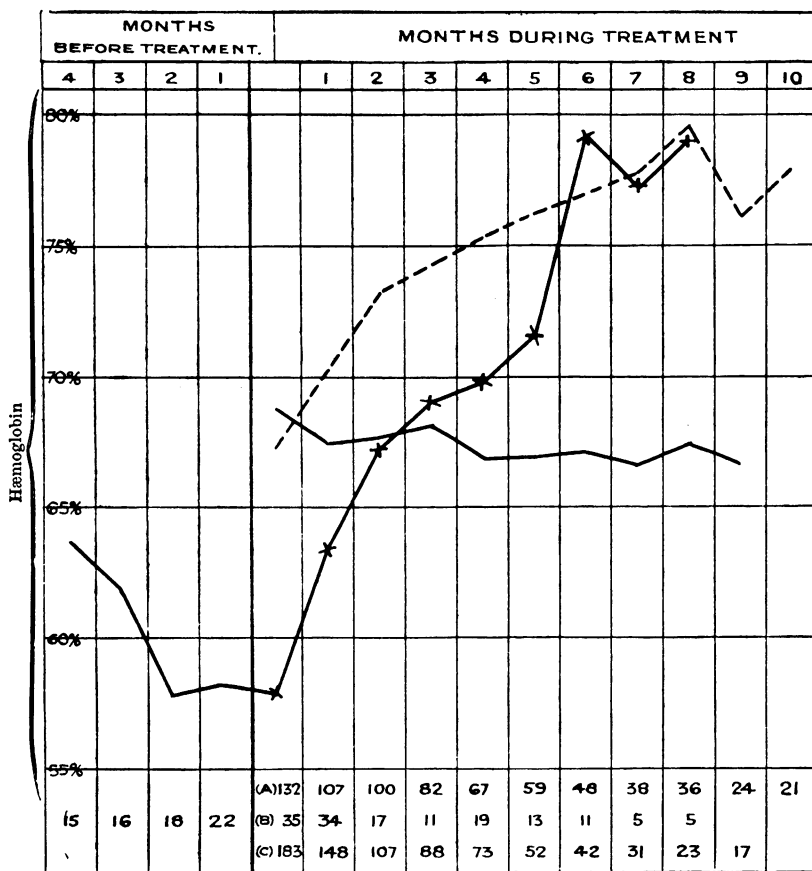
CHART XII.
AVERAGE HÆMOGLOBIN PERCENTAGE OF BREAST AND ARTIFICIALLY FED INFANTS AT DIFFERENT AGES.



Cases classified according to time under treatment. Every child who had iron for any period and attended for hæmoglobin estimations is included (see Chart XIII). There is no doubt that many of them did not take their iron regularly, but on account of the difficulty of drawing any line between those who did and those who did not, all are included. The average hæmoglobin percentage in the blood at the outset is almost identical with that of the controls, the rise in the curve is less steep than in the case of the children starting at a lower level, but it is steady and reaches nearly 80 per cent., an average rise of 12 per cent. In individual cases getting regular treatment the rise might be dramatic; as, for example, over 30 per cent. in three weeks.

CHART XIII.

EFFECT OF IRON TREATMENT. CASES CLASSIFIED BY DURATION OF TREATMENT.



A.—Number of Iron Cases 1926-27
 B.— „ „ 1925-26
 C.— „ Control Cases 1925-26

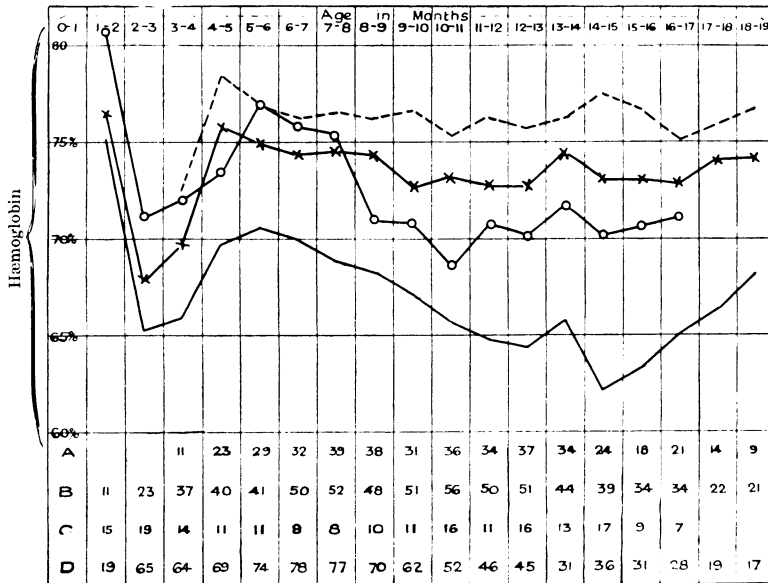
--- Iron Cases 1926-27 (all cases treated)
 x—x—x „ 1925-26 „
 — Control Cases 1925-26 „

Cases classified according to age. Chart XIV shows the 1926-27 children grouped by age. Again, for reasons given above, every case given iron is counted. It must be remembered that at every month of age new cases were included so that this curve does not represent the hæmoglobin level produced by continuous iron treatment from an early age. It will be seen that in the cases examined iron administration did not prevent an initial drop by two months to 67.8 per cent., but the number receiving iron regularly during the whole of the month preceding this observation was very small. From two months onwards the iron cases are consistently higher than the artificially fed controls. At four months old, the iron cases average 6 per cent. higher in hæmoglobin, at twelve months 8 per cent., and at 18 months 6 per cent. If those estimations are excluded in which there was definite evidence of inadequate

dosage during the preceding month, the curve is 2 per cent. to 4 per cent. higher still, and remains above 75 per cent. from four months onwards. From five months old onwards it remains higher than that of the breast-fed controls.

Chart XV shows the effect obtained according to the age when iron was first administered. The numbers are small, but the facts seem clear. The later iron therapy is begun, the lower the hæmoglobin level tends to be throughout infancy. Those given iron before two months old have reached approximately 80 per cent. by four months old, and do not drop below this level. By ten months old the infants started between two and four months have reached 81 per cent.; those started between four and seven months are at about 74 per cent.; those started at seven to ten months are at about 70 per cent., and the controls are at 66 per cent.

CHART XIV.
EFFECT OF IRON TREATMENT. CASES CLASSIFIED BY AGE.



- A.—Number of Iron Cases 1926-27 omitting those known to have had under 4½ grn. daily
 - B.—Number of Iron Cases 1926-27 (all cases)
 - C.— „ „ Breast-Fed Infants
 - D.— „ „ Control Cases—Artificially fed
- Iron Cases 1926-27—omitting cases known to have had under 4½ grn. daily in previous month
 - x—x—x— Iron Cases 1926-27 (all cases)
 - o—o—o— Breast-fed Infants
 - Control Cases—Artificially fed

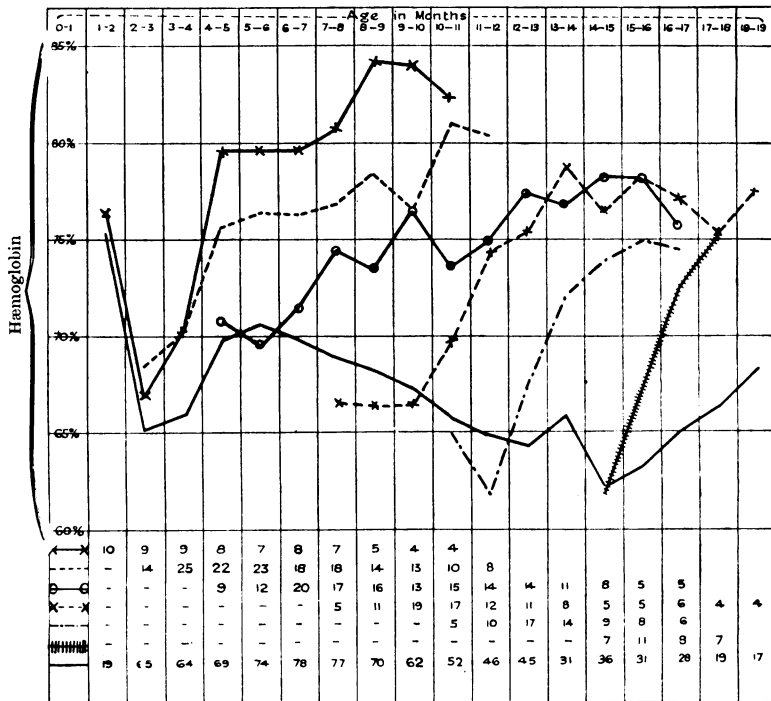
Number of infants whose hæmoglobin reached 80 per cent. The effect of iron administration on the hæmoglobin curve may be examined in another way, namely, by considering the number of infants in the different groups who reached 80 per cent. hæmoglobin after two months of age. Of the total control series only 7 per cent. reached this figure during the whole period of investigation. Of the corresponding iron-treated series 59 per cent. reached 80 per cent., although many were known to have had little iron, whereas of those who received an adequate amount of the medicated "Cow & Gate" milk 81 per cent. did so (Table B).

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TABLE B. THE EFFECT OF ADMINISTRATION OF IRON ON HÆMOGLOBIN LEVEL.

Series.	No. of cases.	Reaching 80% hæmoglobin	
		No.	percentage
Series at Queen's Hosp. and Bethnal Green Clinic (including light treated cases), 1925-1926	273	19	7%
Total iron series (including every case), 1926-1927	132	78	59%
Cases receiving dried milk containing iron for not less than 1 month at the rate of 4½ grn. of iron and ammonium citrate daily	75	61	81%

CHART XV.
EFFECT OF IRON TREATMENT. CASES GROUPED BY AGE OF FIRST TREATMENT (1926-27).



NOTE.—Cases starting treatment from 4 months old onward show in 3 curves a drop preceding the rise. This is due to the fact that new untreated cases are included among these observations. Some infants included in these curves are known to have had no iron medication for a month at a time.

- ✕ — ✕ — ✕ Beginning Treatment under 2 months old
- - - - - " " at 2.4 " "
- — ○ — ○ " " " 4.7 " "
- ✕ - - ✕ - - ✕ " " " 7-10 " "
- . . . - " " " 10-13 " "
- ||||| " " " 13-16 " "
- Controls (Artificially fed Infants)

Percentage of children whose hæmoglobin was raised by iron. Of 132 infants, including every child given iron in 1926-27, the final hæmoglobin estimation was higher than the first in 81 per cent. (107 infants), and the same or lower in 19 per cent. (25 infants). Thirteen of the 25 can be accounted for as follows: four were infants under two months of age whose initial hæmoglobin level was 83 per cent. to 110 per cent.; eight were known to have had very little iron for the preceding month, and one was a case of acute mastoiditis.

THE EFFECT OF IRON ON GENERAL HEALTH.

The infants receiving iron were strikingly better in colour and looks than the control groups: not only that, but they looked healthier than any group of working-class infants the author has yet observed in London. Though the improvement in appearance was unmistakable, it is desirable to ascertain whether this was accompanied by any improvement in growth and in resistance to infection.

Resistance to infection. A comparison of the amount of intercurrent illness in two groups of outpatient infants attending at varying intervals must necessarily be subjective and open to fallacy: still, it is worth attempting. In order to secure sufficient numbers, infants observed in 1925-26 were used to control the iron-treated cases of 1926-27. This has the obvious disadvantage that an epidemic might completely mask the true conclusions as to the incidence of infection in the two groups. The mortality rate is not necessarily a true index of the morbidity rate, but with infants it seems legitimate to assume that any marked change in the morbidity rate for respiratory or gastro-intestinal disorders would be reflected in the mortality rate. A calculation based on the Registrar General's weekly returns shows that the average weekly deaths of infants in London from all causes (including deaths from diseases of the respiratory tract and from gastro-enteritis) did not differ markedly during the two winter periods under consideration, and it is assumed, therefore, that these periods are comparable. The two summer periods, however, differed in that the deaths from gastro-enteritis were twice as many in 1926 (the control period) as in 1927, and no deductions can, therefore, be made from the figures for the incidence of this disease in summer (Table C).

TABLE C. AVERAGE WEEKLY MORTALITY IN LONDON; COMPARISON OF PERIOD OF OBSERVATION OF CONTROL CASES WITH PERIOD OF OBSERVATION OF IRON CASES.
(Figures calculated from the Registrar-General's Reports.)

Period.	Deaths under 1 yr. from all causes.	Deaths under 2 yrs. from dis. of respira- tory tract.	Deaths under 2 yrs. from diarrhœa and enteritis.
Winter—			
Period of observation of control cases	118	46	19
Period of observation of iron cases	111	49	15
Summer—			
Period of observation of control cases	77	14	20
Period of observation of iron cases	64	13	10

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In compiling Tables D and E, the author counted as an illness any disturbance of health which caused a definite flattening of the weight curve or loss of weight, as well as all attacks of otorrhœa and all specific fevers which necessitated a suspension of attendance. No case in the iron series has been included which had previously been included in the control series, since it was known that these had improved in general health while under observation in the control group. The Tables show both winter and summer results, and give separate figures for the diseases of the respiratory tract, of the digestive tract,

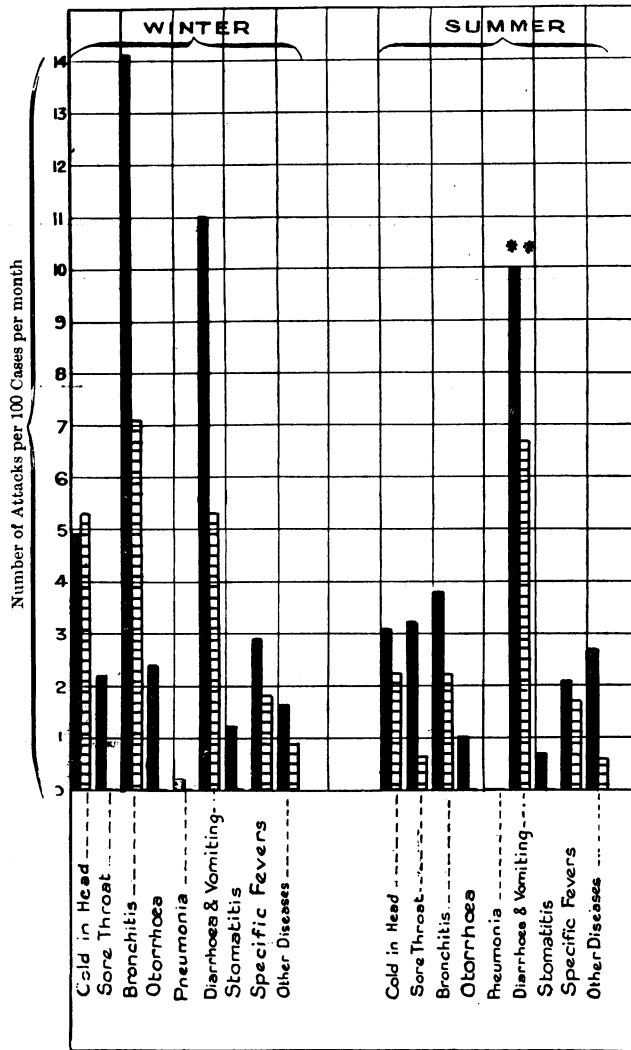
TABLE D. INTERCURRENT ILLNESSES.

	Winter. October–April.				Summer. May–September.			
	Control cases.		Iron cases.		Control cases.		Iron cases.	
	135		35		100		52	
Av. months of observation per infant	3.04		3.22		2.91		3.37	
Disease.	No. of attacks.	No. of attacks per 100 cases per month.	No. of attacks.	No. of attacks per 100 cases per month.	No. of attacks.	No. of attacks per 100 cases per month.	No. of attacks.	No. of attacks per 100 cases per month.
Respiratory tract:—								
Cold in head	20	4.9	6	5.3	9	3.1	4	2.2
Sore throat	9	2.2	0	—	10	3.4	1	0.6
Bronchitis	58	14.1	8	7.1	11	3.8	4	2.2
Otorrhœa	10	2.4	0	—	3	1.0	0	—
Pneumonia	1	0.2	0	—	0	—	0	—
Digestive tract:—								
Diarrhœa or vomiting ..	45	11.0	6	5.3	29	10.0	12	6.7
Stomatitis	5	1.2	0	—	2	0.7	0	—
Specific fevers	12	2.9	2	1.8	6	2.1	3	1.7
Other diseases	7	1.6	1	0.9	8	2.7	1	0.6
Total	167	40.5	23	20.4	78	26.8	25	14.0



and for total attacks of illness. The total morbidity rate of the iron cases both in winter and in summer is about 50 per cent. of that of the control cases (Table E), and a reduced morbidity is present in each group of diseases. For respiratory diseases the comparison proves so strikingly in favour of the cases treated with iron (the incidence being approximately half), that the difference can scarcely be attributed to chance. The figures obtained for gastro-enteritis are less convincing on account of the differing mortality rates during the two periods, but the winter figures suggest that here too iron has diminished the incidence of the disease.

CHART XVI.

EFFECT OF IRON TREATMENT. THE INCIDENCE OF INTERCURRENT ILLNESSES.



NOTE.—The figures for diarrhoea and vomiting in Summer, marked **, are not comparable, see Table C.

 Control Cases
 Iron Cases

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TABLE E. NUMBER OF ATTACKS OF INTERCURRENT ILLNESS PER 100 CASES PER MONTH.

	Total attacks all diseases.		Attacks of diseases of the respiratory tract.		Attacks of diseases of the gastro-intestinal tract.		Attacks of specific fevers.	
	Per 100 cases per month.	Expressed as percentage of attacks in controls.	Per 100 cases per month.	Expressed as percentage of attacks in controls.	Per 100 cases per month.	Expressed as percentage of attacks in controls.	Per 100 cases per month.	Expressed as percentage of attacks in controls.
Winter :—								
Controls	40.5	—	23.8	—	12.2	—	2.9	—
Iron cases	20.4	50%	12.4	52%	5.3	43%	1.8	62%
Summer :—								
Controls	26.8	—	11.3	—	10.7	—	2.1	—
Iron cases	14.0	52%	5.0	44%	6.7	63%	1.7	81%

TABLE F. COMPARISON OF INCREASE IN WEIGHT OF IRON CASES AND CONTROLS.

	No. of cases.	No. of observations.	Average age		Average time under observation.	Average % deviation.		Difference between % deviation at end and beginning of observation
			at beginning of observation.	at end of observation.		at beginning of observation.	at end of observation.	
			Weeks.	Weeks.		A.	B.	
Boys.								
Control Cases	89	103	29.3	43.2	13.9	—18.07	—11.60	6.47
Iron Cases	30	32	28.8	49.5	20.7	—14.54	— 3.10	11.44
Girls.								
Control Cases	87	96	33.2	48.2	15.0	—21.51	—14.09	7.42
Iron Cases	31	34	25.0	47.6	22.6	—21.79	— 8.57	13.22
Boys and Girls.								
Control Cases	176	199	31.2	45.6	14.4	—19.73	—12.80	6.93
Iron Cases	62	66	26.8	48.5	21.7	—18.27	— 5.92	12.35

Control Cases. Babies up to 2 years old attending in 1925–1926.

Iron Cases. Babies up to 2 years old who attended in 1926–1927 and received iron for 4 weeks and upwards. Cases previously included in the control group have been excluded.

Normal Weight. Griffith's standard weight curve for healthy breast-fed infants has been taken as the normal.

Average percentage deviation from normal weight (columns A and B), is the average for each group of cases of
$$\frac{(\text{observed weight} - \text{normal weight}) 100}{\text{normal weight}}$$

Rate of Recovery. It was moreover, noticeable in the course of the work that the rate of recovery was considerably better in the iron group than in the control group, although this cannot be represented in the table.

Rate of Growth. To compare the rate of growth, the same groups of cases were used, i.e., the iron cases who had not previously been included in the control group were compared with the whole control group (see Appendix II). The average period of attendance was longer in the iron group, which makes a fair comparison difficult. Table F shows that both groups started 18 per cent—19 per cent. under normal weight, and that whereas controls improved by 6·9 per cent., iron cases improved by 12·4 per cent., i.e., they caught up on the normal by nearly double as much, though in a longer period.

DISCUSSION.

The normal percentage of hæmoglobin in the blood in infancy.

It is reasonable to assume that giving iron by mouth will not raise the hæmoglobin level above the normal : consequently it may be concluded that the normal after three months of age is not less than 80 per cent. Concerning the earlier months no definite conclusion is possible from this work except that at two months the normal is probably over 70 per cent. since the average of the breast-fed infants was 71·4 per cent. at this age, and these were not a selected healthy lot. The author hopes, however, to be able to pursue the question further in the future.

The prevalence of anæmia.

If these conclusions hold good, and the normal after three months of age be taken as 80 per cent., then nearly all the infants in the samples of population examined showed some degree of anæmia. It is true that in many individual cases this was slight, but in a considerable number the hæmoglobin percentage was reduced to three-quarters or less of the normal. This was so in 14 per cent. of all infants at the General Lying-In Hospital Welfare Centre and in 12 per cent. of the artificially fed infants when first seen at the Queen's Hospital for Children and the Bethnal Green Clinic. Examination of the complete figures for the control cases reveals the fact that 25 per cent. of these artificially fed infants fell below three-quarters of the normal hæmoglobin percentage at some time when examined during the first two years of life (see Table A). If, as the author believes, these samples of artificially fed infants are representative of those attending welfare centres, then the great majority of bottle-fed London infants are anæmic.

As regards breast-fed infants, the evidence is less conclusive, but is sufficient to suggest that a very large proportion of these, particularly after eight months of age, are also anæmic. No evidence concerning other areas of the British Isles is given, but the appearance of London infants compared with those in other parts of Britain would not suggest that London is peculiar in its anæmic babies.

Ætiological factors in this type of anæmia.

The hæmoglobin age curve has been shown to have a double drop, the first lasting till two months old, the second beginning about five or six months old. The first drop, like the second, appears lower in artificially fed than in breast-fed infants, and greater in those of low birth weight than in bigger babies; but the present investigation can offer no evidence as to the cause of the first drop.

The second drop, from five months old onwards, can be eliminated by the administration of iron; in fact, the whole level of the curve from four months old can be raised by this means.

What ætiological factors are at work in bringing about the prevalent anæmia in infants from four months old onwards? We are not here concerned with the child who is acutely ill with some septic or other infection, with one of the primary blood diseases, with nephritis or with sarcoma, but with the anæmia prevalent among infants in fair general health. Holt states that the commonest causes of anæmia in young children are "improper feeding, rickets and unhygienic surroundings."

Hygiene. The facts that the disease was shown not to have a well marked seasonal incidence, and that treatment with the mercury vapour quartz lamp had no prophylactic or curative effect, proved that lack of ultra-violet light was not an important ætiological factor. Moreover, outdoor life with the attendant exposure to fresh air and improvement in general health did not cure anæmia which had already developed.

Diet. It is well known that prolonged and exclusive milk feeding and grave errors in diet, such as lack of anti-scorbutic, cause anæmia. This investigation has shown that anæmia develops with many types of feeding in widespread use, e.g., breast milk, fresh and dried cow's milk, with low, medium or high carbohydrate additions, as well as with "humanized" feeds, so that it cannot be said to be associated with any one type of feeding.

Vitamin insufficiency has been suggested as a cause of widespread anæmia, but in the present cases the anæmia could be prevented or cured without altering the quantity of any vitamin in the diet. It developed in spite of the supply of vitamin-A in cod-liver oil, vitamin-D in cod-liver oil and through ultra-violet light treatment, vitamin-C in fruit juice, and vitamin-B and presumably E in a liberal milk allowance. In view, however, of the great emphasis laid upon rickets as a cause of anæmia, it should be stated once more that the incidence of anæmia in the Vienna investigation was not greater in the group of infants developing rickets than in those protected from rickets. Whether vitamin-D deficiency plays a part in the splenic anæmia of infancy is still unknown.

Czerny¹⁴ and others have emphasised that a toxic effect from cow's milk fat plays an important part in the production of anæmia in infants. The present investigation shows clearly that the anæmia under consideration can be prevented or cured without altering the quantity of milk or of milk fat in the diet.

Iron. So much for negative evidence. The positive evidence concerns iron. Its prophylactic and curative effects support the view that deficiency of iron is the main ætiological factor in the anæmia demonstrated to exist so widely in infancy from four months of age onwards. Its administration brought about an increase in hæmoglobin in 81 per cent. of artificially fed infants, and the author's deduction is that all these children suffered from iron deficiency. It is well known that during the period of milk feeding an infant is largely dependent for its iron needs on the store laid down in the liver before birth. In the premature, this store, being very small, is rapidly exhausted; hence the chief cause for the early and severe anæmia which occurs in all premature infants. Is this store deficient also in other infants? Possibly an investigation now in view may give evidence on this point. The greater amount of anæmia present in artificially fed infants than in those of the same type on the breast is presumably associated with the smaller percentage of iron in cow's milk and a smaller percentage retention. This investigation provides no evidence as to whether there is any associated factor concerned in iron metabolism.

Iron treatment of anæmia is, of course, nothing new, but it is not generally known that without iron medication the great majority of artificially fed babies become anæmic, and that with it an improvement can be brought about in over 80 per cent. of such infants.

Effect of iron deficiency on the general health of the infant population.

The administration of iron brought about a striking improvement in the general health of artificially fed infants as evidenced by improved appearance and increased resistance to infection. The statistical evidence as regards weight is not conclusive, but so far as it goes, is in favour of the iron cases. This shows that iron deficiency is at the present time responsible for a great amount of ill-health, and probably for a considerable number of infant deaths resulting from poor resistance. The administration of iron should considerably diminish the yearly toll of deaths from broncho-pneumonia, which is so often secondary to diseases of the upper respiratory tract and bronchitis.

Prophylaxis of anæmia.

Artificially fed babies should be given iron before two months old (see Chart XV), as otherwise the infant will probably develop anæmia. Moreover, the sooner iron therapy is begun the higher the general level of hæmoglobin is likely to be. Iron and ammonium citrate is an effective salt; possibly the poor results recorded from iron therapy in alimentary anæmia by some writers is due to their use of some other less active salt. Iron treatment should be continued throughout infancy as it has been found that omission of iron even for a few weeks may be associated with a drop in the hæmoglobin.

Many breast-fed babies also require iron treatment.

Iron administration to bottle-fed infants on a large scale throughout the country could be most easily carried out by a small addition of iron to dried milk as this form of milk is already very widely used in infant feeding, and by such a method the chances of regular administration are greatly enhanced. This

would bring about an improvement in the health of the infants not less in the author's opinion than that now being brought about by the measures taken for the prevention of rickets.

SUMMARY.

An investigation embracing 541 infants under 2 years of age upon whom 2,561 hæmoglobin estimations were performed demonstrated the following facts :

1. There is a typical hæmoglobin age curve for the first year of life, showing a double drop with an intermediate rise, the first drop during the first two months of life, the second beginning at five months of age (Charts VII and XII).

2. The normal hæmoglobin percentage in the blood in infancy from four months upwards is at least 80 per cent. as estimated by Haldane's hæmoglobinometer.

3. The great majority of artificially fed infants and many breast-fed infants in London are anæmic.

4. Treatment with the mercury vapour quartz lamp, as here given, had no influence in preventing or curing this anæmia (Charts I and III), and no definite relation was shown between seasonal intensity of ultra-violet light and the incidence of anæmia. Outdoor life did not cure it.

5. Anæmia develops in infants on many types of diet, and no evidence was here obtained to associate it with vitamin-deficiency or with a fat-toxæmia.

6. This prevalent anæmia is due to iron deficiency, possibly with some associated factor, and shows itself from about four months of age. It can be prevented or cured by the administration of a soluble iron salt by mouth (Charts XIII and XIV), which raised the hæmoglobin in over 80 per cent. of unselected artificially fed infants.

7. Iron can be satisfactorily and successfully administered in the form of iron and ammonium citrate contained in a dried milk powder, or added in solution to the daily feeds and is excellently tolerated by infants. The percentage of infants reaching 80 per cent. hæmoglobin was eleven times as great in the group receiving medicated dried milk as in the control series (Table B).

8. Iron should be given to artificially fed infants from the first months of life, as the hæmoglobin can thereby be maintained at a higher level than if it is begun later (Chart XV). Its early administration is particularly important in babies who are small at birth (Table A).

9. Artificially fed infants receiving such iron show a striking improvement in general health and resistance to infection (Table E), as well as probably better growth (Table F), as compared to similar infants without iron treatment. The incidence of diseases of the respiratory tract, as assessed by the author was in the iron group only half that in the control group (Table E).

Conclusion. The evidence produced indicates that a marked improvement in infant health and probably also in infant mortality would result from the wide use of dried milk containing a small iron addition, or from the regular administration of an iron mixture, from the early months of life.

The author's gratitude is due to the British Medical Association who rendered this work possible by the grant of the Ernest Hart Scholarship for 1925-26, followed by another scholarship for a second year.

The author is particularly indebted to Miss Lorel Goodfellow who has co-operated in the work throughout and has carried out all the blood examinations. Generous help has also been received from many persons to whom the author offers her very sincere thanks. Professor Major Greenwood, F.R.S., and Miss E. M. Newbold, M.Sc., have examined statistically the children's weights and many of the data on the hæmoglobin of the blood; Sister F. M. Westbrook has had charge of the light treatment and the infants' charts at the Queen's Hospital for the Children, and she and the nurses working with us at the Hospital and at the Bethnal Green clinic have given us their unstinted help throughout the two years of our work.

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APPENDIX I.

STATISTICAL EXAMINATION OF CERTAIN HÆMOGLOBIN
CURVES.

By

E. M. NEWBOLD, B.A., M.Sc.
The National Institute for Medical Research.*Seasonal Variation in Hæmoglobin.*

Chart V shows the mean hæmoglobin values for each calendar month of the year separately for babies who had, and who had not, light treatment, and also for both groups combined. There is not much evidence of any seasonal variation, except for some suggestion of lower values in the early summer—especially in May among the light cases. Before testing the significance of this it seemed well to see how much the variation might be due to varying ages and varying lengths of treatment in the values for the different months. Charts IV and VI show the hæmoglobin measures according to age for the two groups and for both combined—the later values with few observations are of course of little value, but the broad resemblance between the light and non-light curves in the first year of life suggests that for the earlier months the shape of the curve is reliable (see the following section). Chart I shows the hæmoglobin measures for varying lengths of treatment. Over the range where there are enough observations the curves are very flat, especially that for light and non-light combined, so that correction for length of treatment would hardly be worth while.

From the figures for the combined age curves, the “expected” values of the hæmoglobin measure for each calendar month were calculated on the basis of the ages of the babies in that month. The deviations of the observed hæmoglobin measure from the “expected” thus calculated were found and are plotted on Charts X and XI. When light and non-light cases are combined there is again little evidence of seasonal effect. When they are taken separately, the light group still shows a low value for May. The mean deviation for hæmoglobin for May is -3.5 but its standard deviation is 1.5 , so that it may quite easily be a chance fluctuation from the value -7.3 which is the mean deviation for all the calendar months together. Thus unless the suggestion of a drop in the hæmoglobin value in the early summer in light cases is confirmed on other data, we cannot attach any weight to it, as we might on these numbers easily get a variation of this order by chance.

Reliability of the Variation of the Hæmoglobin Level with Age.

The mean values of the hæmoglobin measure for different months of age are given in Table G, also the standard deviation of the observed individual values about these means,

TABLE G. VARIATION OF THE HÆMOGLOBIN LEVEL WITH AGE.

Ages.	Light cases.			Non-Light cases.			Light and Non-Light cases combined.		
	No. of observations.	Mean.	Standard Deviation.	No. of observations.	Mean	Standard Deviation.	No. of observations.	Mean	Standard Deviation.
0-1	—	—	—	2	99.00	9.00	2	99.00	9.00
1-2	3	65.33	2.05	16	73.13	14.81	19	75.26	14.28
2-3	13	64.08	5.61	52	65.46	7.78	65	65.18	7.42
3-4	18	63.56	6.11	46	66.83	6.54	64	65.91	6.59
4-5	23	69.26	5.22	46	69.98	6.66	69	69.74	6.23
5-6	24	69.67	5.77	50	70.92	6.47	74	70.51	6.28
6-7	26	68.73	6.39	52	70.48	5.96	78	69.90	6.16
7-8	27	68.30	5.32	50	69.28	6.46	77	68.94	6.10
8-9	22	69.00	7.09	48	67.90	5.83	70	68.24	6.28
9-10	20	67.45	6.07	42	67.10	7.78	62	67.21	7.27
10-11	17	67.59	6.56	35	64.89	8.42	52	65.77	7.96
11-12	19	66.74	6.58	27	63.41	8.70	46	64.78	8.06
12-13	16	63.56	8.82	29	64.86	8.45	45	64.40	8.61
13-14	11	65.64	—	20	65.90	—	31	65.81	10.04
14-15	12	58.00	—	24	64.21	—	36	62.14	10.19
15-16	13	59.46	—	18	66.00	—	31	63.26	10.27
16-17	11	61.73	—	17	67.35	—	28	65.14	7.90
17-18	5	64.40	—	14	67.07	—	19	66.37	7.40
18-19	5	66.00	—	12	69.08	—	17	68.18	7.90
19-20	4	62.25	—	10	65.70	—	14	64.71	6.91
20-21	4	63.50	—	8	62.63	—	12	62.92	5.53
21-22	3	66.00	—	9	66.22	—	12	66.17	6.93

If σ is the standard deviation of a set of observed values, the standard deviation of a mean of n of these values is $\frac{\sigma}{\sqrt{n}}$ and the probable error $.67449 \frac{\sigma}{\sqrt{n}}$. It is probable that the true mean value lies within 3 times the probable error of the observed mean on either side of it. Charts IV and VI show the mean values for light and non-light, and both combined observed in this sample, and the dotted lines on either side in Chart VI block out the area within which it is probable that the true mean lies. It may be noted that for the first year of life (except the first month) the band of unreliability is relatively small, this is confirmed by the similar course of both light and non-light cases, which is shown in Chart IV. In the second year of life (see Chart VI) the number of cases is too small for any great confidence in the course.

Effect of Light Treatment on Hæmoglobin Level.

Chart IV shows that the course of the hæmoglobin level is very much the same in both light and non-light groups in the first year of life. The differences are within their probable errors. In the second year the cases are too few for a difference to be detected. There is no evidence on these data that light treatment has altered the hæmoglobin level.

* In most cases here we have used the empirical value $\sqrt{n}-3$ instead of \sqrt{n} , as when n is small, the usual formula gives too small a value for the s.d. of the mean.

APPENDIX II.

STATISTICAL EXAMINATION OF THE WEIGHTS.

Based on the statistical calculations kindly made by

Professor M. GREENWOOD, F.R.S., & Miss E. M. NEWBOLD, M.Sc.

The following method was adopted to compare the increase in weight of the group of infant's getting iron with that of the control cases :—

(a) Taking Griffith's weight curve as the standard of normal, the weight of each infant at the beginning and at the end of the period of observation was expressed as a percentage of the normal.

(b) The percentage of relative weight was averaged, (1) for control cases, and (2) for iron cases, for the beginning and for the end of the periods of observation respectively.

(c) The difference between the average relative weight at the beginning and at the end of treatment for each group gave the average increase in weight for that group.

Some infants after a period in the control group were given iron (see pp. 133-4). It was found that these infants were, when first given iron, for the most part, older and nearer normal weight than the controls at the beginning of their periods of observation, and their improvement in weight while on iron was considerably less than that of the younger infants whose weight at the outset was much further removed from the normal. In the endeavour, therefore, to obtain a fairer comparison of weights, all infants previously in the control series were excluded from the iron series selected for weight comparison. The results are shown in Table F. This shows that both as regards age and weight the two groups were comparable at the beginning of treatment, but the period of observation for the iron cases was longer than that of the controls. At the end of the period of observation, the control cases averaged about 87 per cent. of normal weight and the iron cases about 94 per cent. ; the iron cases having approached the normal weight curve by 12.35 per cent. and the controls by 6.93 per cent.