

TABLE IV.—Tolerance to Iron

Group	Intractable Diarrhoea and Vomiting (Removed from Experiment)	Gastro-intestinal Symptoms (Persevered with Treatment)
A	6	6
C	3	3
D (mol-iron)	1	1

ferris ammonii citras was even better tolerated and proved equally efficient. The mol-iron tablets are easier to prescribe and to take than this latter preparation, but the increased expense involved and the world shortage of molybdenum may delay the routine use of these tablets (which are now made in England). The important point to realize is that many pregnant women cannot tolerate ferrous sulphate pills and therefore do not take them.

This investigation suggests that a high percentage of pregnant women in Bradford suffer from iron deficiency, and that the administration of iron together with calcium and vitamin D prevents both the microcytic and the "physiological" anaemia of pregnancy. An idea to be considered further is whether iron deficiency may in some way be associated with the occurrence of miscarriage and hypertension (see Table V). The only disadvantage of maintaining the haemoglobin level at its normal value throughout pregnancy would

TABLE V.—Additional Observations

Group	Miscarriage	Hypertension (Blood Pressure Exceeding 140/90 mm. Hg on at Least 2 Occasions)	Post-partum Haemorrhage—More than 20 fl. oz. (570 ml.)
A	—	—	3 (one required blood transfusion)
Control (B)	2 $\left\{ \begin{array}{l} 18 \text{ weeks} \\ 28 \text{ "} \end{array} \right.$	5 (1 eclampsia)	1
C	—	1	1 (required blood transfusion)
D	—	1	1

appear to be a slightly increased risk of post-partum haemorrhage. We therefore conclude that the so-called "physiological" anaemia of pregnancy is in reality the expression of iron deficiency, and that the diet in Bradford, and probably in many other centres, is and is likely to remain deficient in this mineral. It would clearly be important to see whether the controlled administration of iron to a much larger group of women would decrease the high incidence of hypertension in pregnant women in Bradford, and whether the maintenance of the normal haemoglobin level throughout pregnancy is associated with the accepted figure for the increase in blood volume.

### Summary and Conclusions

A review of haemoglobin readings obtained from 2,000 consecutive cases at or below the 16th week of pregnancy showed that about 60% were subnormal, and that 6.5% of the women were severely anaemic.

The changes in haemoglobin and packed cell volume readings which occurred during pregnancy in matched groups of young healthy women lead us to conclude that: (a) the "physiological" anaemia of pregnancy is associated with a low or subnormal mean corpuscular haemoglobin concentration; (b) normal (non-pregnant) blood values are maintained if therapeutic doses of ferrous sulphate are administered throughout pregnancy; and (c) the administration of ferrous sulphate, or of molybdenized iron, from the 24th to the 32nd week of pregnancy, results in recovery from the commencing "physiological" anaemia, followed by maintenance of normal (non-pregnant) blood values.

The mol-iron tablets were not found to be more efficacious than ferrous sulphate tablets either in preventing or treating the "physiological" anaemia of pregnancy, but they were better tolerated. We would suggest

that ferrous sulphate is not a suitable preparation for the routine administration of iron in antenatal clinics.

We think that the controlled administration of iron to a large group of women should be undertaken in order to see whether the incidence of hypertension would thereby be lessened. It would also be of interest to determine whether the maintenance of the normal haemoglobin level throughout pregnancy is associated with the accepted value for the increase in blood volume.

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## HAEMOGLOBIN LEVELS IN ADULTS AND CHILDREN

BY

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This paper reports the results of haemoglobin studies on 245 males and 266 females of adult age employed in clerical and industrial work, on 214 housewives under 60 years, all living in and around London, and on 1,628 boys aged 6, 10, and 14 years living in two Lancashire towns (I and K), one Surrey town (J), and one Gloucestershire town (L) (see Table I). The method was the same as that employed in earlier studies (Magee and Milligan, 1951), except that oxyhaemoglobin was the pigment determined instead of alkaline haematin. As before, many precautions were taken to ensure accuracy—the two photometers were re-checked by the National Physical Laboratory, pipettes were re-calibrated, and blood was drawn by finger-prick after a period of rest, depending on the previous state of activity of the individuals. The findings are expressed as grammes of haemoglobin per 100 ml. of blood, and, for comparison with previous findings, especially those of the M.R.C. 1943 Survey (M.R.C., 1945), as Hb% on the Haldane scale.

TABLE I.—Haemoglobin Levels g./100 ml. and Percentages (Haldane), compared with 1943 Haemoglobin Survey

Category	No.	Present Survey Mean and Standard Deviation (g. Hb/100 ml. Blood)	% Haldane and Standard Deviation	Mean 1943 Survey. % Haldane Scale
<b>Adult Males</b>				
A. Clerical workers	94	15.9±1.1	107.1±7.1	Mean of all married men 102.4, all single men 102.1
B. Factory "	100	15.6±1.0	105.5±6.9	
C. " "	51	15.5±1.1	104.9±7.3	
Total ..	245			
<b>Employed Females</b>				
D. Clerical workers	100	14.1±1.1	95.4±7.4	Mean for all manual working women 92.5, all unmarried 94.4
E. Factory "	101	14.1±1.3	95.0±8.7	
F. " "	65	13.6±1.4	91.8±9.2	
Total ..	266			
<b>Housewives</b>				
G. London borough	115	13.5±1.5	91.3±10.2	91.5
H. " "	99	13.6±1.2	91.9±8.3	
Total ..	214			
<b>Schoolboys aged 6:</b>				
Town I ..	147	13.1±0.8	88.8±5.6	Two samples, 87.1 and 94.0
" J ..	150	13.8±1.0	93.0±6.8	
<b>Schoolboys aged 10:</b>				
Town I ..	196	13.5±1.0	91.2±6.6	91.0
" J ..	133	14.0±0.8	94.2±5.7	
<b>Schoolboys aged 14:</b>				
Town I ..	176	14.3±0.9	96.8±6.0	Two samples, 97.6 and 97.9
" J ..	190	14.7±1.0	99.5±6.5	
" K ..	184	14.6±1.1	98.8±7.4	
<b>Town L:</b>				
1. Modern schools	211	14.6±0.9	98.7±6.5	" "
2. Grammar "	165	15.0±0.9	101.5±6.1	" "
3. Public "	76	14.9±0.7	100.5±5.1	" "
Total ..	1,628			

**Methods of Sampling**

Adult males and females were selected at random; a letter was sent to every *n*th person on the roll of employees asking if he or she would co-operate; the refusal rate was low. No person of income above £1,000 per annum was included.

For housewives, streets were chosen at random and two constant house numbers in the street were nominated. If for some reason the housewife could not participate the house number adjoining was taken. The refusal rate was low. The tests were carried out in their own homes, and pregnant or lactating women and women over 60 were excluded, but no woman was excluded on the grounds of apparent ill-health. However, some housewives excused themselves from participating on health grounds. They numbered one-seventh of all refusals. Since, so far as we could judge, ill-health of a comparable degree existed among those housewives whose haemoglobin levels are reported here, we think that there is no bias from this cause.

For boys, the whole school population of the age groups 6, 10, and 14 years in certain schools, chosen for convenience, were examined.

**Results**

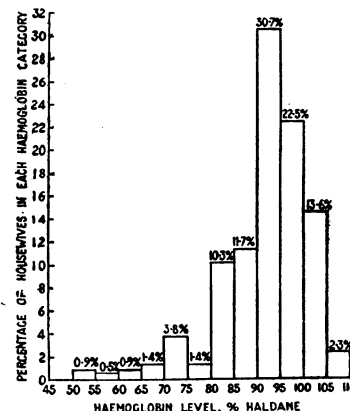
**Adult Males.**—The mean haemoglobin level in clerical workers was slightly higher than that in manual workers (Table I). But the difference is not statistically significant, since it is less than twice its standard error. All three means are higher than those obtained in similar people in the 1943 Survey—102%. The higher value for the clerical workers in the present survey is in harmony with the findings of Adcock *et al.* (1948), who obtained higher values in sedentary men than in those of similar age receiving similar diets but engaged in more strenuous occupations—for example, the mean level for the Foot Guards was 99.9% and for R.A.M.C. hospital workers 103%. Adcock *et al.* did not make similar comparisons for women engaged in different occupations.

**Adult Women.**—The values obtained in the present survey for women show no consistent differences between the clerical

and the manual workers, but it should be remembered that the occupation of the manual workers was far from strenuous. Taking the three groups of women (D, E, and F) as a whole, they compare favourably with the 1943 means for women manual workers and for unmarried women—92.5 and 94.4%, respectively.

**Blood Donors.**—There were 15 men and 28 women in the above groups (A–F) who had been blood donors for the National Blood Transfusion Service. Their mean haemoglobin levels were 104% for men and 94% for women. Among these were two men with haemoglobin levels of 104 and 111% and six women with levels of 86, 92, 92, 97, 100, and 86% who, for no disclosed reason, had been rejected on the last occasion they presented themselves for bleeding.

**Housewives.**—The means for the two groups of housewives (Table I) show no differences either between themselves or from the 1943 mean—91.5%. The distribution curve is negatively skewed (see Chart). The S.D. of the two groups is 9.65, which means that on a normal distribution 2.3% of the values would fall below 72.3% and 2.3%, above 110.9%. There are no values above 110.9, but 5.6% of the total are below 72.3%. In practically all these women



Percentage distribution of haemoglobin levels in 214 housewives.

medical reasons for the low haemoglobin levels were elicited by questioning, and all of them were reported to their family doctors.

**Boys.**—The haemoglobin determinations on boys were only part of a much more comprehensive survey which involved physical measurements, physical efficiency tests, medical examinations, inquiries into living conditions, and other socio-economic matters. A detailed analysis of the data, which will be published later, shows that where higher mean haemoglobin levels were observed they were merely one facet of a general physical superiority, which was reflected in larger stature, greater weight and strength, and an earlier onset of puberty. Among the socio-economic factors with which these differences were associated, non-dietary as well as dietary factors appear to be responsible. The various haemoglobin values compare favourably with those obtained in 1943 on boys of the same age.

**Discussion**

It has been suggested that the higher average haemoglobin level in male clerical workers (Group A) than in male manual workers (Groups B and C, Table I) is attributable to the, presumably, more active life of the latter. It might, however, be suggested that the difference is due to higher incomes and presumably better diets of the clerical workers. We were unable to obtain the incomes of Group A, but we found it for most men in Groups B and C. In Group B there was no relationship between income and haemoglobin levels. In Group C the mean haemoglobin of 16 men with incomes at or above £350 per annum was 106.4%, and of 22 men in the same group with incomes at or below £300 per annum, 103.7%. A similar relationship was found for employed women in Group F; 13 of these with incomes of £250 per annum or more had a mean of 94.9%, and 46 with incomes of £200 per annum or less a mean of 91.0%. These numbers are small, and an element of chance cannot, therefore, be entirely excluded. There would seem, however, to be some sort of relationship

between income and haemoglobin level, but this might be explained by the higher-paid workers being older and leading a more sedentary life than the lower-paid ones.

There was no evidence of a difference between the haemoglobin of married and that of unmarried men. Employed married women, on the other hand, had a higher mean level than spinsters in all three groups, D, E, and F, the differences being 0.65, 2.5 and 3.0%, respectively. These differences were found to be independent of income.

In 187 of the housewives the effect of parity could be investigated. Over the range 0-3 children no change in level was found, but the level for mothers of four or more children was well below that of the rest (Table II).

TABLE II.—Haemoglobin Levels of Housewives According to Parity

No. of Pregnancies	No. in Sample	Mean Hb % Haldane
0	14	90.2
1	62	91.4
2	64	90.8
3	31	91.7
4 and over	16	86.2

In the study of Magee and Milligan (1951) the haemoglobin of women who had borne three or more children and who were either pregnant or within 65 weeks after labour was lower than in comparable women who had had a smaller number of children. In the present survey all pregnant and nursing women were excluded, and it may be that this effect of repeated pregnancies disappears gradually.

#### Summary

Haemoglobin levels were determined in 245 adult men and 266 adult women employed in clerical and industrial work, on 214 non-pregnant and non-nursing housewives under 60 years living in and around London, and on 1,628 boys aged 6, 10, and 14 years living in two Lancashire towns (I and K), one Surrey town (J), and one Gloucestershire town (L). The mean findings are set out in Table I.

So far as they are comparable with the M.R.C. survey of 1943 the present findings are about the same or on a slightly higher level. Of the 214 housewives 5.6% had values less than 72.3% (Haldane). Medical reasons for the low levels were elicited by questioning.

Male clerical workers had higher values than male manual workers, a difference attributable to the more active lives of the latter. In some of the groups of men and women a direct relationship between income and haemoglobin level was observed; this difference may have been due to a more leisurely life in the higher income groups.

The haemoglobin level of boys of town I was lower than that of the boys of any of the other towns, and that of grammar and public school boys in town L was slightly higher than for modern school boys in the same city. The reasons for these differences in boys living in different parts of England and in different surroundings are being further investigated.

ADDENDUM.—Since writing the above, the doctors of women with Hb below 80% have tried the effects of iron therapy, in almost every case with satisfactory results. The proportion (8.9%) of women with Hb below 80% in this unselected sample and their ready response to iron medication suggests that the work of the general practitioner would be facilitated by routine Hb determinations in women patients. The colour of the mucous membranes, as reported elsewhere (Adcock *et al.*, 1949) may fail as an index of Hb level, but the Tallqvist method provides a

simple and inexpensive means of ascertaining the Hb level with sufficient accuracy for practical purposes. This method was found by Macfarlane *et al.* (1948) to compare surprisingly well with other more complicated procedures.

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## EFFECT OF VITAMIN-K PREPARATIONS ON HYPOPROTHROMBINAEMIA INDUCED BY DICOUMAROL AND TROMEXAN

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The administration of dicoumarol (3,3'-methylene-bis-(4-hydroxycoumarin)) or "tromexan" (bis-3,3'-(4-oxycoumarinyl)-ethyl acetate) in the treatment of thromboembolic states may lead to severe or even fatal haemorrhage. Although careful control of treatment by repeated estimation of the blood prothrombin levels reduces this risk, a reliable and convenient antidote against such potent therapeutic substances would be of great value. Both dicoumarol and tromexan are anticoagulants by virtue of their causing hypoprothrombinaemia, and the two measures recommended to reverse this effect are the administration of preparations possessing vitamin-K activity and the transfusion of blood. There is no doubt that the latter treatment gives immediate and significant results, but for it to be most effective the blood must be in sufficient quantity. It is not always easy to meet this requirement, and reliance may be placed on the use of vitamin-K preparations such as are commercially available.

There is a measure of belief, based on experimental observations carried out during the past ten years, that these vitamin-K preparations are capable of reversing dicoumarol-induced hypoprothrombinaemia. From the available evidence at hand there can be no doubt that substances with vitamin-K activity do possess such powers, but there is still much confusion regarding the practical value of the various preparations which are available for this purpose.

It is hoped that the experiments described below will provide more conclusive evidence concerning the action and therapeutic value of these preparations.