SYMPTOMS OF IRON DEFICIENCY ANAEMIA

A COMMUNITY SURVEY

BY

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Anaemia is usually defined in terms of a reduction in the concentration of haemoglobin or the number of red cells in the peripheral blood. In the community at large, iron deficiency is by far the most common cause of anaemia. The symptoms of iron deficiency anaemia are said to depend on three factors: the causative disorder, the reduced oxygen-carrying capacity of the blood, and the disturbances of cell function consequent upon anoxia (Wintrobe, 1961). In chronic anaemia, certain physiological compensations occur in the circulatory system; cardiac output is usually increased and the circulation time may be diminished. Subjects may become aware of this as palpitations. Shortness of breath, if it occurs, is usually related to exercise. Anginal pain may also be precipitated by exercise during which the oxygen demands of the myocardium cannot be fully met. Deficient cerebral oxygenation may result in symptoms such as fatigue, faintness, and lack of concentration. It has been suggested recently, that some symptoms, such as fatigue, may be due to a deficiency of iron at the cellular level rather than to anaemia or anoxia as such (Beutler, Larsh, and Gurney, 1960).

The symptoms mentioned above, according to medical textbooks (Garland and Phillips 1953; Tidy, 1949; Davidson, 1958), are reported by anaemic patients. However, although there is a plausible physiological explanation for these symptoms, the same symptoms commonly occur in people who are not anaemic, and in some may be ascribed to other diseases, including the psychoneuroses. Some doubt has been cast on the validity of considering symptoms as useful indicators of haemoglobin concentration (Berry and Nash, 1954). Iron deficiency anaemia is extremely common in many populations (Jacobs, Kilpatrick and Withey, 1965) and any association with these symptoms could be coincidental.

If there is a causal link between anaemia and its supposed symptoms, then there will be a negative association between haemoglobin level and the severity of these symptoms in the general population,

that is, the lower the haemoglobin level the more severe the symptoms. The present study was designed to find out whether or not such an association exists in the general population.

SUBJECTS

All persons between the ages of 15 and 74 years, living within a quarter of a mile of a Local Health Authority clinic in certain prescribed streets, were interviewed at home and asked to take part in a haematological investigation and a dental survey. The results of the latter are not relevant for the purposes of the present paper. Mention was made at the initial interview that a sample of blood would be taken when they attended the clinic. Of those people who were approached, 70 per cent. agreed to take part.

METHODS OF ASSESSMENT

(i) Questionnaires

It is impossible to have complete confidence in any one method of symptom assessment, and because of this the three following procedures were adopted.

Two of the methods of symptom assessment (A and B), examples of which are shown in the appendix, were in self-administered form, and were attached together to constitute the questionnaire. The symptoms assessed are listed in Table I. The third

TABLE I
SYMPTOMS ASSESSED

<i>Method A</i>	<i>Method B and C</i>
Fatigue	Fatigue
Faintness	Dizziness
Palpitations	Palpitations
Pain in Chest	Irritability
Swelling of Ankles	Headache
Breathlessness	Breathlessness
Pallor	
Lack of concentration	

method of assessment (C) contained exactly the same material as one of the self-administered forms (B), but was administered to a subsample (all females between the ages of 35 and 55) at a home interview. This subsample of females was assessed in both ways, but there was no evidence that one method of assessment influenced the other. A comparison of the methods will be reported elsewhere.

Eight symptoms were investigated in the self-administered form (A). For each symptom, four questions had been constructed, graded for severity, and each answered by "Yes" or "No". As each of the four statements has two possible answers, there are therefore sixteen possible patterns of responses. Each symptom was scored on an arbitrary sixteen-point scale.

Methods B and C were devised to solve some of the problems associated with existing forms of symptom assessment (Ingham, 1965). Examples of some of these difficulties are:—the construction of a scale of increasing severity for a particular symptom and the elimination of some response sets found with simple 'Yes'/'No' questionnaires. As an example of the latter: people vary in their willingness to agree or disagree with statements, to some degree independently of the statements. However, although Method C has been shown to be successful in previous surveys, it requires an individual interview. Because of the numbers involved in many surveys, a self-administered form (B) was devised.

For Methods B and C, seven statements were constructed of increasing severity for each symptom. Pairs of statements, selected according to a procedure described by Ingham (1965), are presented to the subject who is instructed to indicate which statement from the pair is nearer to what he feels is true for him. Using seven statements, twelve scale positions can be defined.

In addition to the home visits made to the subsample of females to administer the individual form of symptom assessment (C), home visits were made for two other reasons. Some people did not return their questionnaires to the clinic within 14 days of receiving them. They were visited by one of the investigators (M.M.W.) and asked to co-operate. If they had had difficulty in understanding the questionnaire, they were given assistance. Others, who returned questionnaires only partially completed, were visited, and if necessary were helped to complete the questionnaire correctly.

(ii) Haematology

A sample of venous blood was taken from each subject.

Haemoglobin concentration (cyanmethaemoglo-

bin) and packed cell volume (microhaematocrit) were estimated for each person by a single observer.

RESULTS

The distributions, by age, for males and females are shown in Table II. Home visits were made to 40 per cent. of all individuals who attended the clinic, either to retrieve questionnaires or to complete them, and 5 per cent. of these refused to co-operate further after they had attended the clinic.

TABLE II
DISTRIBUTION OF GROUP BY AGE AND SEX

Age Group (yrs)	Sex		Total
	Male	Female	
15-	15	35	50
25-	12	23	35
35-	42	28	70
45-	41	36	77
55-	16	34	50
65-	4	9	13
Total	130	165	295

Table III shows the distributions for males and females of haemoglobin concentration. There is an

TABLE III
DISTRIBUTION OF HAEMOGLOBIN CONCENTRATIONS (g./100 ml.) BY SEX

Hb (g./100 ml.)	Sex		Packed Cell Volume (per cent.)	Sex	
	Male	Female		Male	Female
	No.	No.		No.	No.
7.5	-	3	28	-	1
8.0	-	-	29	-	1
8.5	-	-	30	-	-
9.0	-	3	31	-	2
9.5	-	2	32	-	-
10.0	-	1	33	-	2
10.5	-	6	34	1	1
11.0	3	2	35	-	3
11.5	-	8	36	-	12
12.0	1	24	37	1	12
12.5	-	19	38	-	16
13.0	5	21	39	3	22
13.5	22	35	40	8	21
14.0	13	15	41	9	21
14.5	31	19	42	13	11
15.0	23	6	43	20	10
15.5	10	1	44	19	17
16.0	19	-	45	18	7
16.5	1	-	46	12	3
17.0	1	-	47	8	2
17.5	1	-	48	5	1
			49	6	-
			50	-	-
			51	2	-
			52	-	-
			53	-	-
			54	1	-
Mean Hb S.D.	14.78 1.13	13.02 1.47	Mean PCV S.D.	44.24 3.12	40.01 3.39

indication of negative skewness in the females (see Elwood, 1964), but there does not appear to be any in the males.

The distributions for males and females of three of the eight symptoms assessed in the more conventional part of the questionnaire (A), are shown in Table IV. None of these distributions appeared to be normal, nor indeed were the distributions of the remaining five symptoms. Ideally, these distributions should be normal, and this is particularly true if change is being assessed, for example during treatment with iron. Scatter diagrams were constructed to examine the nature of the relationship, if any, between the symptoms and haemoglobin concentration; no obvious association was apparent and there was no suggestion of a curvilinear relationship.

Correlation coefficients between the symptom grades and haemoglobin concentration, and also those between symptoms and packed cell volume are shown in Table V. Only the correlations for 'pallor' in females are significant and in the predicted direction. If the hypothesis had been, that there is a positive association between symptoms and haemoglobin level, then it would have been supported by the correlation coefficients for several symptoms in the males.

TABLE V

CORRELATIONS BETWEEN EIGHT SYMPTOMS AND HAEMOGLOBIN AND PACKED CELL VOLUME

METHOD A

Symptom	165 Females		130 Males	
	Hb (g./100 ml.)	Packed Cell Volume (per cent.)	Hb (g./100 ml.)	Packed Cell Volume (per cent.)
Fatigue	+0.07	+0.11	+0.02	+0.08
Faintness	-0.01	-0.09	+0.09	+0.21
Palpitations	-0.06	-0.06	-0.05	+0.03
Pains in Chest	-0.04	+0.01	+0.21	+0.26
Swelling of Ankles	-0.11	-0.09	+0.13	+0.19
Breathlessness	+0.07	+0.11	+0.09	+0.17
Pallor	-0.27	-0.30	+0.05	+0.09
Concentration	+0.06	+0.07	-0.01	+0.06
Haemoglobin		+0.86		+0.84

For $r > 0.20$, $P < 0.05$

The results obtained using the less conventional form of symptom assessment (B) (see Table VI) support the results noted above, in that the correlations between symptoms and haemoglobin concentration or packed cell volume are not significant and in the expected direction. Also, several of the correlation coefficients for males are positive and large. The distributions of the six symptoms obtained by using this method of symptom assessment (B) approximated more closely to normality than those from Method A. Again, scatter diagrams were constructed to investigate any possible curvilinear relationship which might exist between the symptoms and haemoglobin level, but there was no indication of any.

TABLE VI

CORRELATIONS BETWEEN SIX SYMPTOMS AND HAEMOGLOBIN AND PACKED CELL VOLUME

METHOD B

Symptom	165 Females		130 Males	
	Hb (g./100 ml.)	Packed Cell Volume (per cent.)	Hb (g./100 ml.)	Packed Cell Volume (per cent.)
Fatigue	-0.00	+0.06	+0.10	+0.10
Dizziness	-0.01	-0.07	-0.06	-0.06
Palpitations	-0.01	+0.00	+0.11	+0.14
Irritability	-0.02	-0.06	+0.11	+0.02
Headache	-0.06	-0.09	-0.09	-0.09
Breathlessness	+0.06	+0.13	+0.21	+0.29

For $r > 0.20$, $P < 0.05$

DISCUSSION

In general, the results of this study give little support to the view that symptoms, currently believed to be associated with anaemia, are related to haemoglobin concentration. The only evidence for such an association applies to "pallor" in the female sample but not in the males, and "pallor" can be considered as a subject's assessment of her own haemoglobin level.

The symptoms we studied have long been accepted as common features of anaemia, and are considered

TABLE IV

DISTRIBUTION OF THREE SYMPTOMS FROM METHOD A, BY SEX

Symptom	Sex	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Mean	S.D.
Breathlessness	Male	59	52	—	10	—	—	—	—	—	—	—	3	—	—	—	6	1.59	3.43
	Female	52	89	—	11	—	—	—	—	2	—	—	3	—	—	—	8	1.10	3.72
Fatigue	Male	21	27	—	7	6	11	1	1	3	21	—	2	1	5	—	24	6.25	5.55
	Female	13	36	2	9	3	16	1	—	9	15	1	5	1	8	—	43	7.42	5.76
Palpitations	Male	35	61	1	3	—	2	1	—	16	1	—	2	—	—	—	8	2.82	4.20
	Female	32	82	1	2	—	1	4	—	23	3	1	—	1	6	—	9	3.42	4.50

to have a reasonable physiological basis in many cases. It is, therefore, surprising that the present study reveals very little evidence of an association between these symptoms and haemoglobin level. This is true for all three methods of symptom assessment.

Five possible explanations are described below:

(1) There may be no association at all between symptoms and haemoglobin level. The belief that such an association exists may have arisen from the facts that mild iron deficiency anaemia is very common in the general population (Elwood 1964; Kilpatrick and Hardisty, 1961) and that patients attending a general practitioner or clinic for any reason whatever often report these symptoms—an association with a low haemoglobin level being entirely coincidental.

(2) Anaemia may in fact produce symptoms, but so may many other conditions. In the general population, the relationship between haemoglobin level and symptoms may be masked by these other causes, and so may not be detected in a study such as ours. Our results lend some support to both this and the previous explanation (1). However, it is not possible to discriminate between them from the data obtained for mild anaemia in this survey.

(3) It is possible that a relationship between haemoglobin level and symptoms does exist for severely anaemic subjects. This hypothesis has not yet been investigated fully. However, in this present survey, eight women had haemoglobin concentrations below 10 g./100 ml., and the results of an analysis confined to these women are shown in Table VII. Although none of the correlations is

significant, they are all in the predicted direction with the exception of 'breathlessness' and 'faintness' assessed by Method A.

(4) Although there is no association between symptoms and haemoglobin concentration for the general population, there may be for patients who have solicited medical aid. A survey is being made of patients who attend their general practitioners, with the aim of investigating this hypothesis.

(5) The apparent lack of association between symptom grade and haemoglobin level could be due in part to the use of haemoglobin level as an index of anaemia. There is variation between individuals in the normal haemoglobin levels for any group of subjects. Thus a subject may have a lower haemoglobin level than his optimum, and yet by the use of a defined haemoglobin level as a criterion of 'anaemia' he may be judged normal. It would be of interest, therefore, to relate change in symptoms to change in haemoglobin concentration, after the administration of iron. This was in fact done on a group of females selected from the present survey, and the evidence from this treatment trial did not support this explanation (Elwood and Wood, 1966).

CONCLUSION

This investigation does not in general support the view that there is a relationship between the symptoms studied and haemoglobin level for people who are not severely anaemic. If there is an association between symptoms and anaemia, then it may apply only to those subjects with haemoglobin concentrations less than 10 g./100 ml. Our evidence for this is based on only eight persons. More evidence is required from a larger sample of severely iron-deficient subjects.

Finally, if little or no association exists between symptoms and mild anaemia, then any programme of preventive medicine must take this into account. Selection by symptoms may result in an incomplete or biased group receiving medical care.

SUMMARY

A survey was carried out to investigate the association, commonly believed to exist, between symptoms and anaemia. No convincing evidence was found to support the view that symptoms are related to haemoglobin level. Despite the use of three different methods of symptom assessment, only women's assessment of their own degree of pallor was found to have a significant correlation with haemoglobin level. Limited evidence was found to suggest that in severe anaemia, symptoms and haemoglobin level may be associated. However, for mild anaemia there is either no association or

TABLE VII

CORRELATIONS BETWEEN SYMPTOMS AND HAEMOGLOBIN AND PACKED CELL VOLUME FOR EIGHT FEMALES WITH Hb BELOW 10 g./100 ml.

Method	Symptoms	Hb (g./100 ml.)	Packed Cell Volume (per cent.)
A	Fatigue	-0.55	-0.34
	Faintness	+0.47	-0.19
	Palpitations	-0.62	-0.68
	Pain in Chest	-0.52	-0.52
	Swelling of Ankles	-0.11	-0.08
	Breathlessness	+0.13	+0.38
	Pallor	-0.21	+0.12
	Concentration	-0.22	-0.50
	Haemoglobin		+0.70
B	Fatigue	-0.53	-0.34
	Dizziness	-0.21	-0.39
	Palpitations	-0.31	-0.70
	Irritability	-0.22	-0.41
	Headache	-0.60	-0.62
	Breathlessness	-0.02	+0.19

For $r > 0.71$, $P < 0.05$

other common ailments effectively mask any relationship which might exist.

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APPENDIX

METHOD A (Sample)

In this section please answer EVERY question.

Put a ring round your answer like this

Do you feel your heart thumping after running, or after climbing stairs? ...	...	...	YES	NO
Do you ever feel your heart thumping when walking at a normal speed? ...	...	...	YES	NO
Do you ever feel your heart thumping when moving about the house? ...	...	...	YES	NO
Do you ever feel your heart thumping when resting in bed? ...	...	...	YES	NO
Do you get pain in your chest when doing unusually heavy work? ...	...	...	YES	NO
Do you ever get pain in your chest when you walk up a slight hill? ...	...	...	YES	NO
Do you ever get pain in your chest when walking at a normal speed? ...	...	...	YES	NO
Do you ever get pain in your chest when moving about the house? ...	...	...	YES	NO

METHOD B (Sample)

For each pair, choose the statement which is nearer for you, then put a cross in the hole alongside it.

-
- ☐ I never feel dizzy.
- ☐ Sometimes I feel quite dizzy.
-
- ☐ All the time I can feel my heart pounding very heavily.
- ☐ I often feel my heart pounding quite heavily.
-
- ☐ I usually feel dizzy.
- ☐ Sometimes I feel quite dizzy.
-