

on the radiographs, which were seen at some stage in six of our cases. Sometimes bronchography will show the communication; this occurred in three of the patients, and in two of these fluid levels were not seen on the radiographs.

Despite careful dissection a communication was demonstrated in only two of the specimens. The poor correlation between the radiological and the pathological findings suggests that spontaneous closure of the communication occurs. This may be one reason for the considerable changes in the appearance of serial radiographs.

Tomography accurately demonstrates the situation and extent of the lung lesion but in our experience fails to outline the aberrant artery. This vessel may not be demonstrated even with the aid of angiocardiology (Pinney and Salyer, 1957). Anticipation of the presence of the vessel is essential in the event of surgical treatment, which might otherwise lead to catastrophic haemorrhage (Bruwer, 1955); but neither angiocardiology nor aortography appears warranted, since the likely presence of the artery should be inferred from the clinical and radiological characteristics of the condition.

Tuberculosis in association with bronchopulmonary sequestration has been reported on several occasions. The infection may involve another lobe of the lung (Tosatti and Gravel, 1951), the lung tissue adjacent to the defect (Edge *et al.*, 1957), or the sequestered segment itself (Boyd, 1953; Smith, 1955; Johnston, 1956).

In one of our patients (Case 4) thoracotomy was undertaken with a provisional diagnosis of bronchopulmonary sequestration and associated tuberculosis, since acid-fast bacilli had been present in the sputum. Sputum cultures subsequently proved negative for *M. tuberculosis*, and no histological or bacteriological evidence of tuberculosis was found on examination of the resected specimen.

The natural history of bronchopulmonary sequestration is incompletely known. Most of the patients reported have been surgically treated and have had histories of repeated or chronic chest illness; there have been no follow-up reports of patients who have been treated conservatively. Since some patients have no symptoms until later life, intervals of many years between respiratory illnesses (10 years in Case 6) are not uncommon, and some patients become symptom-free after treatment with antibiotics, it is possible that the outlook without surgery is not always one of chronic respiratory ill-health. Resection offers a complete and permanent cure and is bound to commend itself when no general contraindication to surgery exists; nevertheless, there is some justification for regarding the recurrence of infection, rather than its occurrence, as the indication for surgery.

#### Summary

The clinical, radiological, and gross anatomical features of intralobar sequestration of the lung are described. Case reports of 10 patients are presented, nine of whom were operated upon. It is suggested that in patients with this condition a strong presumptive diagnosis may be made clinically.

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## THE PREVALENCE OF ANAEMIA IN THE COMMUNITY

### A SURVEY OF A RANDOM SAMPLE OF THE POPULATION

BY

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It is suspected that anaemia is common in Great Britain to-day, but, apart from some surveys of special groups of the community, no attempt has been made to determine its prevalence in the general population since the war.

In an attempt to obtain up-to-date information about the distribution of haemoglobin values, packed cell volumes, serum-iron and vitamin-B<sub>12</sub> levels, and mean cell diameters, we have carried out surveys in population samples of two defined communities—one industrial and the other agricultural. We report in this paper the results of our first survey, which was done as a pilot study in a South Wales mining valley—the Rhondda Fach—in association with the Epidemiological Research Unit of the Medical Research Council Pneumoconiosis Research Unit (see Cochrane *et al.*, 1955), who had planned a survey of chronic bronchitis, ischaemic heart disease, and rheumatoid arthritis there during May and June, 1958.

#### Sample and Procedure

Details of the sample are shown in Table I. During the weeks between the census and the actual start of the survey 21 names had to be withdrawn (8 persons had died, 11 had left the area, and 2 had given erroneous date of birth), leaving an available sample of 779 subjects, of whom 193 were women and 586 men. These 779 subjects were visited and invited to come to a centre in Ferndale, the largest town of the Rhondda Fach. A total of 723 (543 men and 180 women), or 92.8% of this available sample, were examined. Between 30 and 40 people were seen each day and each person was in the centre for about 45 minutes, during which time many tests were made. In view of this fairly full

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programme it was impracticable to elicit symptoms which might have been attributable to anaemia, nor were we able to inquire into dietary habits. No attempt was made to diagnose anaemia on clinical grounds because of the known limited usefulness of inspection

TABLE I.—Random Sample

Occupation Group	Age-group	Living in Valley at Census	Sampled	Proportion of Population	Died, Left Area, etc.	Refused	Examined
Miners and ex-miners	35-44	1,127	100	1/11	2	8	90
	45-54	1,283	100	1/13	—	5	95
	55-64	1,114	100	1/11	3	4	93
Non-miners	35-44	495	100	1/5	6	9	85
	45-54	338	100	1/3	3	8	89
	55-64	146	100	1/1.5	—	9	91
Women	55-64	1,535	200	1/8	7	13	180
Total		6,038	800		21	56	723

of the conjunctivae and hands (McAlpine *et al.*, 1957). We did not ask about the taking of iron tablets, but each person was directly questioned about injections which might have been given for Addisonian anaemia.

Methods

Venepuncture was done with iron-free 20-ml. all-glass syringes, using new needles (18 s.w.g.), and 2.5 ml. of blood was added to 25 mg. of dry E.D.T.A. (dipotassium salt) for determination of haemoglobin, packed cell volume, and preparation of blood films. The remainder of the specimen was placed in a sterile unused iron-free universal container for determination of serum-iron and serum-vitamin-B<sub>12</sub> levels.

It was not possible to have a field laboratory in Ferndale, and the specimens taken during each day, most of them in the evening, were stored at 4° C. overnight in Cardiff. A pilot study in a small series of

normal blood samples showed that storage in this way produced no significant change in haemoglobin level or P.C.V. During the next morning, haemoglobin and P.C.V. determinations were carried out, and two blood films made from each E.D.T.A. sample. The serum was separated from the clotted blood samples, using iron-free apparatus, and frozen at -20° C. until required for serum-iron and vitamin-B<sub>12</sub> determinations.

Haemoglobin levels were determined in duplicate as oxyhaemoglobin in an E.E.L. photoelectric colorimeter, using a yellow-green filter (Ilford No. 625). P.C.V. were measured in duplicate after centrifuging in a Hawksley microhaematocrit for five minutes. Mean cell diameters (M.C.D.) were measured on thin unstained blood films by the diffraction method, using a Waterfield halometer. Leishman-stained blood films from each subject were examined. Serum-iron levels were measured by the method of Ramsay (1953) as modified by Jordan (1956). Serum-vitamin-B<sub>12</sub> levels were determined by microbiological assay, using *Euglena gracilis* as described by Ross (1952). Both serum iron and serum vitamin B<sub>12</sub> were estimated in duplicate whenever sufficient serum was available. Results of the M.C.D. and serum-vitamin-B<sub>12</sub> estimations, together with their relationship to the other indices measured, will be published separately.

Before the survey began, arbitrary levels of haemoglobin, below which "anaemia" would be designated, were agreed upon—12.5 g./100 ml. (85%) or less in men and 12 g./100 ml. (81%) or less in women. If a subject was so designated, a red-cell count was done and the mean cell volume determined: a total and differential white-cell count and a reticulocyte count were also done. Each anaemic subject's general practitioner was immediately notified, and the patient was seen again, an offer of further investigation being made both to the patient and to the doctor.

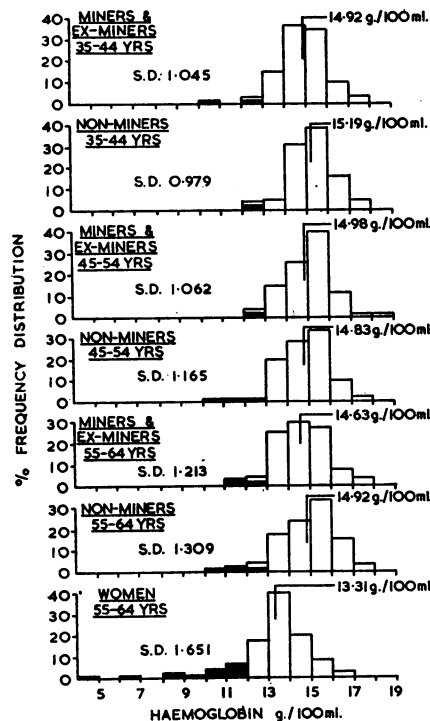


FIG. 1

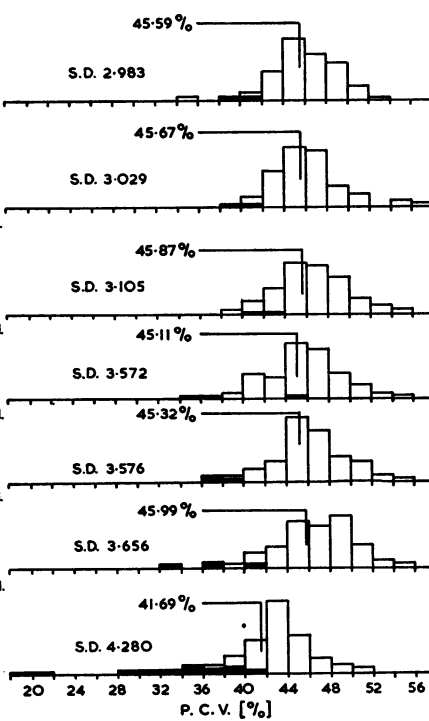


FIG. 2

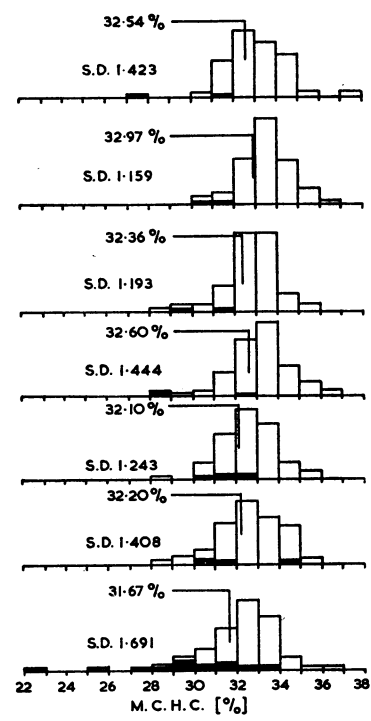


FIG. 3

FIG. 1.—Frequency distributions of haemoglobin values in a random sample of the Rhondda Fach. Black area=anaemia. FIG. 2.—Frequency distributions of P.C.V. values in a random sample of the Rhondda Fach. Black area=anaemia. FIG. 3.—Frequency distributions of M.C.H.C. values in a random sample of the Rhondda Fach. Black area=anaemia.

## Results

**Frequency Distribution of Haemoglobin Values.**—The frequency distribution of haemoglobin values and the mean haemoglobin values for each group and their standard deviations are shown in Fig. 1. It can be seen that in respect of the mean values the group of women differ, as would be expected, from the rest. It can also be seen, however, that they have a larger spread of values and the distribution is skew, with a longer tail of lower values; the index of this is significant ( $g. = -1.767 \pm 0.181$ ). On analysis of the six groups of males the standard deviations are quite similar but the means differ significantly ( $0.05 > P > 0.01$ ), and this appears to be a matter of overall spread for the six means, since no single simple comparison—for example, miners and non-miners—reaches the 5% level of significance.

**Frequency Distribution of P.C.V. Estimations.**—The women again differ from the men in means and standard deviation, as shown in Fig. 2, but the groups of men do not differ among themselves.

**M.C.H.C. Estimations.**—When the M.C.H.C. values were studied (Fig. 3) it was again seen that the women differed from the men, but there is also a significant difference in the mean M.C.H.C. between the six groups of men ( $P < 0.001$ ). This appeared to be due to significant differences between miners and ex-miners on the one hand and non-miners on the other, and to a significant regression of M.C.H.C. on age. Thus it can be shown that miners' and ex-miners' M.C.H.C. =  $33.46 - 0.023 \times \text{age}$ , while non-miners' M.C.H.C. =  $34.55 - 0.039 \times \text{age}$ . The two slopes  $-0.023$  and  $-0.039$  do not differ significantly ( $t = 1.262$ ;  $0.30 > P > 0.20$ ) and Fig. 4 shows these slopes fitted to the data. The difference in level of M.C.H.C. at all ages is significant ( $t = 2.128$ ;  $0.05 > P > 0.02$ ). Thus it may be concluded from our findings that at all ages miners and ex-miners have a lower M.C.H.C. than non-miners, and that the M.C.H.C. declines with age at an average rate of 0.031% per year. It appears that in non-miners M.C.H.C. falls faster and in miners and ex-miners more slowly than the average, but this difference may be a chance one.

**Serum Iron.**—Of the 723 subjects examined, sufficient serum was available in all but six of the men and three

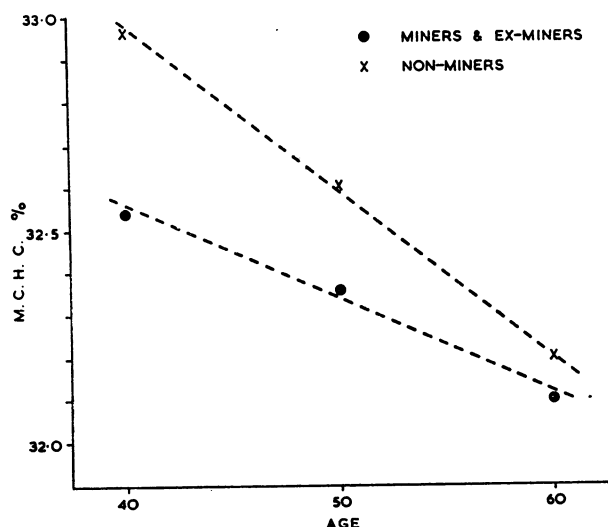


FIG. 4.—Comparison of M.C.H.C. of non-miners with miners and ex-miners in a random sample of Rhondda Fach men.

of the women, giving a total of 714 specimens. The mean serum-iron concentration of the miners and ex-miners, taking all age-groups together, was  $118.4 \mu\text{g./100 ml.}$ , and of the non-miners  $123.3 \mu\text{g./100 ml.}$  Thus there is a statistically significant difference between these two occupational groups of  $4.9 \pm 1.08 \mu\text{g./100 ml.}$ , though it seems unlikely that this difference is of any clinical significance. It can be shown that there is a positive correlation, though of low degree, between serum iron and M.C.H.C. ( $+0.19$ ), but that there is little or no correlation between serum iron and age over the groups studied. Of the women studied the mean value for serum iron was found to be much lower than that of the men—namely,  $103.8 \mu\text{g./100 ml.}$  These mean figures agree with those usually accepted for normal men and women.

## Cases of Anaemia

The prevalence of anaemia in the various age-groups is given in summary in Table II. The histograms (Figs. 1, 2, and 3) show the way in which the cases of anaemia are distributed throughout a considerable range of P.C.V. and M.C.H.C. values. An attempt was made to find the cause of the anaemias, but there was a disappointing response to our offer of further investigation in hospital. We decided, therefore, to discover what we could by questioning the anaemic people in their homes.

**Anaemia in Men.**—Table III shows details of the 18 cases of anaemia and gives the known or probable aetiological factors. Because of the small numbers in each group no breakdown for age or occupation has been made. Three men included in the sample were receiving vitamin-B<sub>12</sub> treatment for Addisonian anaemia; none of these was anaemic.

TABLE II.—Prevalence of Anaemia in the Various Groups of Subjects Examined. Anaemia Designated if Haemoglobin 12.5 g./100 ml. (85%) or Below in Men, 12 g./100 ml. (81%) or Below in Women

Subjects	Age	Cases of Anaemia	
		No.	Percentage
Miners and ex-miners ..	35-44	2	2.2
Non-miners ..	35-44	2	2.4
Miners and ex-miners ..	45-54	2	2.1
Non-miners ..	45-54	3	3.4
Miners and ex-miners ..	55-64	5	5.4
Non-miners ..	55-64	4	4.4
Total ..		18	3.3
Women ..	55-64	25	13.9

TABLE III.—Details of 18 Cases of Anaemia in Men

Type of Anaemia	Hb (g./100 ml.)	Age	Probable Aetiological Factors
Hypochromic M.C.H.C. < 31% (8 cases)	10.5	43	Deficient diet (mentally defective)
	10.6	47	Peptic ulcer
	11.1	58	Partial gastrectomy
	11.6	55	No obvious cause
	12.2	44	Peptic ulcer
	12.4	51	Partial gastrectomy
	12.4	46	Chronic lymphatic leukaemia
	12.5	64	Recent prostatectomy with blood loss
Borderline hypochromic M.C.H.C. 31% (6 cases)	11.4	64	Deficient diet (living alone)
	11.5	59	Carcinoma of stomach
	11.6	59	" " larynx
	12.1	42	Peptic ulcer
	12.4	38	No obvious cause
	12.5	46	Partial gastrectomy
Orthochromic M.C.H.C. > 31% (4 cases)	10.8	59	Chronic renal disease
	11.1	52	? malabsorption syndrome
	12.0	61	Haemorrhoids
	12.2	56	No obvious cause

**Anaemia in Women.**—Table IV summarizes the cause of anaemia adjudged to be the most important in each case, and iron-deficiency hypochromic anaemia is clearly shown to be the most common type found.

TABLE IV.—*Details of 25 Cases of Anaemia in Women*

Type of Anaemia	Hb (g./100 ml.)	Age	Probable Aetiological Factors
Hypochromic M.C.H.C. < 31% (17 cases)	4.1	62	Deficient diet; no other obvious cause
	8.2	61	No obvious cause
	8.2	58	Deficient diet
	8.9	58	" "
	9.7	64	" "
	9.8	63	Deficient diet and haemorrhoids
	10.0	60	Deficient diet
	10.2	56	Previous heavy menstruation
	10.7	59	" and deficient diet "
	10.8	58	No obvious cause
	11.2	64	Deficient diet
	11.2	61	" "
	11.4	56	Previous heavy menstruation
	11.5	57	Deficient diet and haemorrhoids
11.5	63	Previous heavy menstruation and deficient diet	
11.6	60	Previous heavy menstruation	
11.8	60	No obvious cause	
Borderline hypochromic M.C.H.C. 31% (5 cases)	10.3	56	Haemorrhoids
	10.4	56	Previous heavy menstruation
	10.7	58	Haemorrhoids
	11.1	61	Previous heavy menstruation
	11.4	63	Haemorrhoids
Orthochromic M.C.H.C. > 31% (2 cases)	11.7	57	Fibroids
	11.9	61	Previous heavy menstruation
Macrocytic (1 case)	6.8	62	Addisonian anaemia (serum vitamin B <sub>12</sub> , 27 µg./ml.)

#### Follow-up Study on the Anaemic Subjects

While the main purpose of any epidemiological study is to inaugurate preventive measures, actual cases of disease discovered during a survey require further investigation and treatment. As most of the cases of anaemia discovered were of the hypochromic type we decided for reasons of practicability to offer iron to all the anaemic subjects. The patients' general practitioners were asked to prescribe oral ferrous sulphate 3 gr. (0.2 g.) t.d.s. for six months. At the end of this time the 43 subjects originally found to be anaemic were visited at home to get a further specimen of blood. Two of the 43 had left the area and two had died from disease known to have been present at the time of the initial survey—one from carcinoma of the stomach and one from advanced renal disease. Of the remaining 39, 24 were women and 15 men.

**Men.**—In the follow-up examination of the 15 men the haemoglobin had risen in 13 and fallen in 2, but 4 were still anaemic. Table V shows that, whereas there

TABLE V.—*Follow-up Results in 15 Anaemic Men*

	Initial Survey	Follow-up
Mean haemoglobin (g./100 ml.)	11.8	13.2
" M.C.H.C. (%)	30.1	30.8
" serum iron (µg./100 ml.)	75.6	69.6

was an increase in the mean haemoglobin values, the mean M.C.H.C. had barely increased and the mean serum-iron level had fallen slightly.

**Women.**—Of the 24 women examined, the haemoglobin had risen in 20, remained the same in 1, and fallen in 3, but 8 were still anaemic. Of the 16 subjects with iron deficiency studied, only 12 showed a rise in haemoglobin, but it may well be that the iron prescribed was not taken regularly. Table VI shows the increase in

TABLE VI.—*Follow-up Results of 24 Anaemic Women*

	Initial Survey	Follow-up
Mean haemoglobin (g./100 ml.)	10.2	12.7
" M.C.H.C. (%)	29.3	31.0
" serum iron (µg./100 ml.)	59.4	81.8

mean haemoglobin, M.C.H.C., and serum-iron values after the iron therapy. The one subject with Addisonian anaemia showed an excellent response to vitamin-B<sub>12</sub> therapy.

#### Discussion

Because of inevitable differences in techniques employed in previous haematological surveys it is difficult and probably unwise to compare our data too closely with other results. Furthermore, in some previous surveys the detailed age structure of the population studied has not been given, while in others only selected groups of the population have been examined—Service personnel (Shorthouse and King, 1951), certain groups of adults and children (Berry *et al.*, 1952), and the elderly (Hobson and Blackburn, 1953).

It may be said, however, that on the whole the mean haemoglobin levels of 14.9 g./100 ml. for the men (aged 35–64) and 13.3 g./100 ml. for the women (aged 55–64) in the Rhondda are lower than those found by Berry *et al.* (1952) and slightly lower than that of the M.R.C. survey (1945). Thus Berry *et al.* (1952) found a mean haemoglobin value of 15.9 g./100 ml. for male clerical workers and 15.6 g./100 ml. for male factory workers. They also found a mean haemoglobin value of approximately 14.1 g./100 ml. in employed women, and of 13.5 g./100 ml. in housewives. In the M.R.C. survey (1945) the results were 102.2% (Haldane) for men and 93.7% for women—all age-groups being included. That the men in our survey do not show higher mean values for haemoglobin is perhaps surprising because of the possibility of polycythaemia occurring in association with the chronic respiratory disease prevalent in the miners and ex-miners.

The P.C.V. values are much what one would expect, but the M.C.H.C.s are rather more interesting. On the whole the mean figures for M.C.H.C. in all groups studied were low—none was as high as 33%. The fall of M.C.H.C. with increasing age is an interesting finding, as is the fact that at all ages the values for miners and ex-miners are lower than for non-miners. The values for serum iron are also lower in the miners and ex-miners than in the non-miners, but there is no evidence that they fall with increasing age, at least over the age-groups studied in this survey. Thus it may be inferred that, whatever is responsible for the fall in M.C.H.C. with age, it is independent of the correlation of M.C.H.C. and serum-iron level. The most likely explanation of these findings is that increasing age results in a slight diminution of iron utilization for haemoglobin synthesis without affecting the total iron economy of the body. The occupational difference may possibly be explained by some genetic factor, but more probably by some difference in working conditions, financial status, or dietary habits, details of which have not been investigated.

The serum-iron concentrations in all our subjects were estimated in an attempt to obtain some measure, other than the M.C.H.C., of iron deficiency in the general population. A community survey of serum-iron levels has not been done before, and we therefore have no figures with which to compare them. Whether the serum-iron level is in fact a satisfactory index of iron deficiency is open to some doubt because it is subject to fluctuations at different times of the day, from one day to the next, and in association with infections (Ramsay, 1957). It may therefore be that the measurement of serum iron is not a very rewarding investigation

in epidemiological studies, as it is tedious and time-consuming, and requires much special preparation of glassware. It is hoped that more detailed information will be available later, when a comparison with our rural community is made. It is possible that measurement of the total iron-binding capacity of the serum might have been of more value than the serum iron, but shortage of serum and time precluded this.

As we did not know the frequency distribution of haemoglobin values in this part of the country before our survey started, we decided on arbitrary figures below which anaemia was to be designated—12.5 g./100 ml. (85%) or less in men and 12 g./100 ml. (81%) or less in women. These figures are similar to those used by Davidson *et al.* (1943), who designated "clinical anaemia" as being present in men when the haemoglobin was less than 85% (Haldane) and less than 80% in women. From a review of our frequency distributions of haemoglobin values it would appear that the arbitrary level chosen for women is a reasonable one but that the figure for men may be too low. It is difficult to be dogmatic about this, for while we have now examined a random sample of the general population we cannot claim that our subjects were necessarily normal. For this reason no simple statistical concept of normality can be evoked such as, for example, designating as normal those values which do not differ from the mean by more than twice the standard deviation of the mean value. It is of interest to note that in a W.H.O. (1959) publication dealing with the detection and evaluation of the anaemia problem of a community it is recommended that anaemia be considered to exist when the haemoglobin value is less than 14 g./100 ml. in men and less than 12 g./100 ml. in women.

We would have liked to know more about the cause of the anaemia discovered, but this proved difficult in practice. As a general therapeutic measure, however, it was decided to offer iron to all our anaemic subjects and to keep them under observation for six months. As workers in this and other fields have found, however, not all subjects so enjoined take prescribed medication regularly: some of our subjects failed to return to their doctors for a further supply of iron; some doctors failed to prescribe further iron; some subjects attributed dyspepsia, some constipation, and a few diarrhoea to iron therapy.

Iron-deficiency anaemia was the commonest type found, and it is suggested that the rather high prevalence of post-menopausal iron-deficiency anaemia in women is due to a chronic anaemia starting during the child-bearing years, followed by a diet inadequate in iron-containing food, protein, and ascorbic acid. In the men in this series the anaemia discovered has been of more sinister import than in the women. In both sexes a number of subjects who had been designated as having borderline hypochromic or normochromic anaemia responded satisfactorily to the administration of iron, thus supporting Beutler's (1959) contention that a degree of iron deficiency may exist in some people without hypochromia.

It is usually held that present or past blood loss is the most important factor in the pathogenesis of iron-deficiency anaemia, and this has been stressed again in this country by Bedford and Wollner (1958) in their study of elderly hospital patients, although "idiopathic" hypochromic anaemia has been described in Service personnel (Shorthouse and King, 1951; Leonard, 1954;

Forshaw, 1954). We do not know how much intestinal blood loss has contributed to the anaemia discovered in either the men or the women in this series. In order to discover this it would have been necessary to test faeces for occult blood or to look for haemorrhoids, but it is very doubtful if either a stool collection or a rectal examination of a random sample of the community would have been viewed with favour or equanimity by the people on whose co-operation the success of such studies as this depends.

### Summary

A survey to determine the prevalence of anaemia has been carried out in over 90% of a random sample of 600 men (300 miners and ex-miners, 300 non-miners) between the ages of 35 and 64, and of 200 post-menopausal women aged 55 to 64 living in an industrial community in South Wales.

The mean haemoglobin level for men was 14.9 g./100 ml. and for women 13.3 g./100 ml. In the men, the miners and ex-miners have been shown to have both a lower M.C.H.C. and a lower serum-iron concentration than the non-miners. There is a progressive fall of M.C.H.C. in both groups with increasing age.

Three per cent. of men had haemoglobin levels to 12.5 g./100 ml. or less, and 14% of women had haemoglobin levels of 12 g./100 ml. or less. The majority of these cases designated as anaemic were of the hypochromic type. Further investigation and therapy were offered to those discovered to be anaemic, and it was found that the women responded to iron therapy better than the men.

This survey could not have been carried out without the assistance and advice of many people. It is a pleasure to acknowledge our indebtedness in particular to Professor A. L. Cochrane and to the members of his epidemiological research team of the Medical Research Council Pneumoconiosis Research Unit; to the Board of Governors of the United Cardiff Hospitals for their help and ready provision of facilities to one of us (G.S.K.), who held a Cardiff Royal Infirmary Research Fellowship in Medicine during the time of this survey; to Mr. P. D. Oldham, of the Medical Research Council, for detailed statistical analysis and advice; to the staffs of the medical unit and institute of pathology of the Welsh National School of Medicine for very considerable secretarial and technical assistance; to Miss Sweet and Mr. R. J. Marshall, of the department of medical photography, who prepared the diagrams; to all the people of the Rhondda Fach who so willingly co-operated in this survey; and, finally, to Professor Harold Scarborough for his constant advice, interest, and encouragement.

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