Unsuspected anaemia: The case for population screening

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A NUMBER of surveys have been carried out to determine the incidence of anaemia in certain samples of the general population. Kilpatrick and Hardisty (1961) examined 600 men between the ages of 35 and 64, and 200 postmenopausal women aged 55 to 64 living in an industrial community in South Wales. Kilpatrick (1961) compared these findings with those obtained in a rural area (Wensleydale). Fry (1961) reviewed the cases of anaemia met with in his practice (urban Kent) during a period of ten years (1950–1960), and there was an extension of this work (Fry 1966) with retrospective studies. Elwood (1964) presented data on the distribution of haemoglobin levels, packed cell volumes, and mean cell haemoglobin concentrations in a random sample of healthy women living in Belfast. All these workers found a variable but disquietingly high incidence of unsuspected anaemia.

Following an observation of the apparently high incidence of anaemia in local general practice, we set out to determine as accurately as possible the incidence of anaemia in the general population of Shrewsbury and the rural areas immediately surrounding the town (a total of approximately 60,000 inhabitants). An attempt was also made at an aetiological classification.

The Borough of Shrewsbury is the centre of an agricultural community, supporting much light and some heavy industry. Coloured immigrants form a very small percentage of the population. This study differs from those previously reported in that the random sample was drawn from all age groups in a combined urban and rural population.

As a guide to similar procedures on a larger scale, we have tried to assess the cost of the survey and to decide whether universal or selective population screening would be the more justifiable economically.

Method

We found that the practice of one of us (R.M.A.M.) gave a sample that is random as far as age is concerned. The practice list is analysed in an age-sex register, as recommended by the Royal College of General Practitioners, and this enabled us to prepare an age 'profile' of the practice. Figure 1 is an analysis of the practice population by age, from 95 years to less than one year, reading from left to right. This is shown annually by the interrupted line and on a five-year basis by the solid line. Figure 2 compares this quinquennial age profile, shown again as a solid line, with comparable analyses (scaled down for comparison) of the population of England and Wales (shown by an interrupted line) and the population of the Birmingham Regional Hospital Board area (shown by a dotted line). There is a remarkable similarity in the three curves.

A one-in-four random sample of the practice list (approximately 3,100) was taken (figure 3). The hatched narrow segment indicates random substitutes for patients

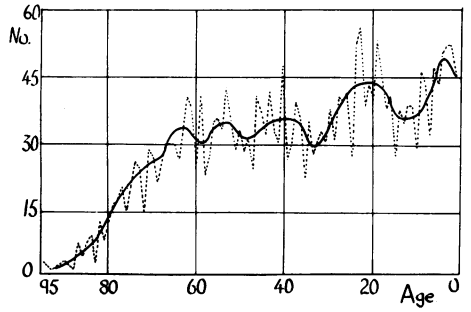

Figure 1.

Analysis of practice population by age.
– – – – – – on an annual basis.
———— on a quinquennial basis.
The ordinates indicate the number of patients

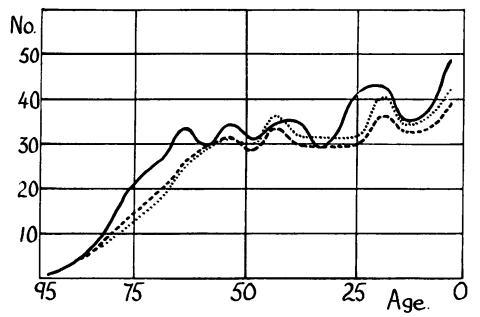

Figure 2.
Populations analysed by age.
———— Practice population.
– – – – – – Population of England and Wales } Scaled down to be comparative
. . . . . Population of Birmingham Regional Hospital Board Area } Scaled down to be comparative

who could not be located, e.g. because of unreported change of address or temporary absence (less than three per cent).

This sample of almost 800 people was subdivided into three groups: Group 1 are those aged 70 and over, who form 12 per cent of the population; Group 2, those aged from 15 to 69 (66 per cent) and Group 3, those under 15 years of age (22 per cent). Letters were written to all, asking them to submit to a thumb prick; those over 70 years of age were visited at their homes and the remainder were asked to come to the laboratory. Figure 4 compares the practice population, shown as a solid line, the sample, shown as an interrupted line, and the response we obtained, shown as a dotted line (again scaled for comparison). The sample appears to be representative, and the response, totalling 584 or 73 per cent, was surprisingly good, particularly as we were unable to advertise this scheme.

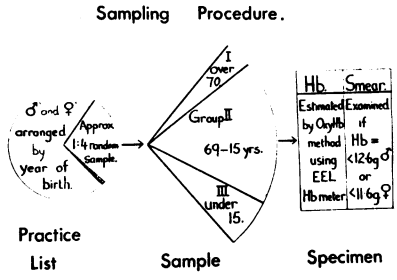

Figure 3.
Sampling procedure.
Diagrammatic representation of: (i) how the random sample was obtained; (ii) how the sample patients were grouped by age for the purpose of specimen collection, and (iii) the screening tests performed.

Results

The cases were analysed in the manner shown diagrammatically in figure 5. The dotted line represents the total sample requests (800); the inner segment bounded by solid lines represents the response (584). We subdivided these into three groups whose numbers are shown approximately by the areas on this divided segment, viz.:

Into Group A we placed the 419 who were not anaemic, i.e. all males whose haemoglobin was over 12.6 g. and all females whose haemoglobin was over 11.6 g. No further investigations were carried out on these patients. Patients were classed in Group B if the haemoglobin was between 12 and 12.6 g. in males and 11 and 11.6 g. in females. If there was nothing particularly obvious on the stained film, no further investigations were carried out on this group of people, who totalled 89. The last group, Group C, who numbered 76, was made up of males with haemoglobins of less than 12 g. and females whose haemoglobin was less than 11 g. The lower limit of normal for haemoglobin in boys aged 1–3 years was taken as 11 g.

The social class distribution of these patients in Group C, estimated according to the

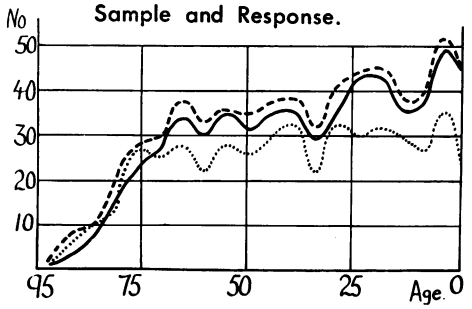

Figure 4.

Comparison of practice population, sample and response.

Good correlation is shown between the practice population (————), and the sample (- - - - -)
Sample response is indicated thus: .....
(Scaled for comparison)

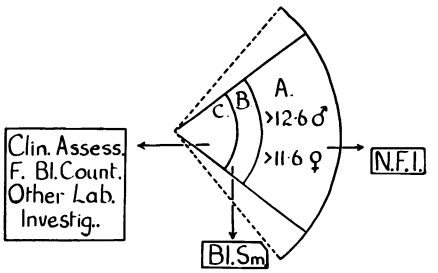

Figure 5.

Investigation of sample response, which is indicated thus: ————. The total sample is shown in this way:- - - - - -.

A — Patients not anaemic.
B — Patients with trivial anaemia
C — Patients with significant anaemia.

N.F.I. No further investigations.

Bl. Sm. Examination of blood smear only

Registrar General's classification, was as follows: II, 22; III, 32; IV, 22; which follows closely the distribution in the practice population.

An analysis of the incidence of anaemia according to 5-year age groups was made for both sexes, as shown in figures 6 and 7. The number of patients tested in each group is indicated in the upper abscissa, and the ordinate indicates the percentage of this number who were found to be anaemic. In both figures the hatched areas indicate the

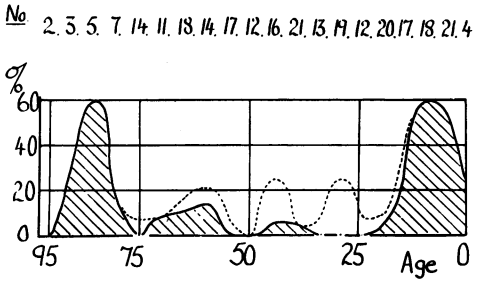

Figure 6.
Incidence of anaemia—males.

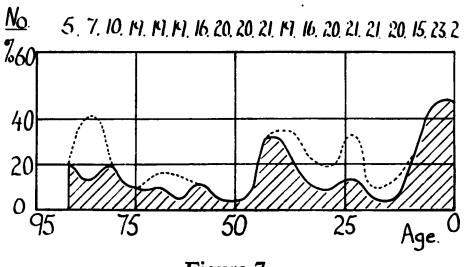

Figure 7.
Incidence of anaemia—females.

patients from Group C and the areas between the solid and broken lines indicate the patients from Group B. It can be seen that in both sexes the greatest incidence of anaemia occurs in the young and in the very old, and that in females it is also significant in the child-bearing period of life. What is so remarkable about these last two figures is that the majority of the patients did not have symptoms sufficient to make them consult their doctor, or if they did, anaemia was not an apparent diagnosis on clinical grounds.

All the patients in Group C had at least two haemoglobin estimations, both of which yielded low results. It now remained to discover why they were anaemic. A clinical assessment was carried out on all these patients. Their past medical records were reviewed, with particular reference to haemoglobin levels, and the response to the treatment of those who had suffered from anaemia previously. We then carried out such laboratory investigations as seemed relevant to determine the cause of the anaemia. A few of those included in the random sample were known to be anaemic at the time of the survey. They included five females, four with blood-loss anaemia (two menorrhagia,

one ulcerative colitis and one haematemesis) and one girl with a past history of urinary infection, who had iron and folate deficiency. In addition, there were two males, one boy with iron deficiency and one man with blood-loss anaemia from haemorrhoids.

TABLE I
CLASSIFICATION OF THE ANAEMIAS

	70+		69–50		49–15		14–10		9–0		Totals
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	
Fe. defic.		1		1		2			5	10	19
B_{12} defic.			1								1
Folate defic.	1	1				1	1			2	6
Diet. defic.	1						2		3	2	8
Blood loss		3	2	2	1	6	1		2		17
Secondary..	2		1	1	1	1	1		8	1	16
Pregnancy..						5					5
Unclassified	1	1	1				1	1	1	2	8
Totals	5	6	5	4	2	15	6	1	19	17	80

This indicates the different types of anaemia found in both sexes and in the various age groups. The total (80) exceeds the number of patients in Group C (76) because in four cases there was more than one cause of the anaemia.

Table 1 is an analysis of the types of anaemia found, according to age and sex. Iron deficiency occurs mainly in girls under nine years of age and the diagnosis was made mainly from the film, occasionally from the serum iron level, and by noting the response to iron therapy. The single new case of pernicious anaemia had a haemoglobin of 10 g. but a serum B_{12} level of only 25$\mu\mu$g/ml., and on questioning clearly had early subacute combined degeneration of the cord, which unfortunately shows only minimal improvement after five months' treatment with vitamin B_{12}. Of the folate deficiencies, two occurred in the very old, a feature which is now being increasingly recognized (Read *et al.* 1965); one was in a woman of 37, and three in children, where the cause was probably dietary.

The dietary deficiencies occurred mainly in children under nine years of age. Some of these were regarded as 'relative' deficiencies, as most of these children were either tall or very large for their age groups.

Eleven of the blood-loss anaemias occurred in women, six of whom had menorrhagia and two of these patients bled from other sources as well (haemorrhoids, varicose vein ulcers). Two had chronic blood loss from ulceration in hiatus hernia and one died from this. In three there was either clinical or biochemical evidence of gastro-intestinal blood loss, but no lesion could be demonstrated, although we suspect gastric erosions due to aspirin in two of them. Of the remaining six patients with this type of anaemia, three were boys, all of whom had persistently positive occult blood in the faeces. Of the three men in this group, one was receiving butazolidine, another had haemorrhoids and consumed much aspirin, and in the third, a young man of 18 who declined follow-up, there was biochemical evidence of gastro-intestinal blood loss.

The secondary anaemias, occurring in young boys, were usually due to chronic upper respiratory tract infection. In the older age groups there were such various causes as hypertensive renal failure and chronic wound infection.

None of the five pregnancy anaemias detected in this survey was severe (range 10.8 g. to 9.7 g.). However, all the five women found to be anaemic were unmarried. None of the six pregnant married women included in the survey was anaemic. The

unmarried women presented at antenatal clinic later in pregnancy than those who were married and were, therefore, late in beginning iron and folate supplements.

In the unclassified group, the cause of the anaemia is still not certain.

Discussion

The justification for any scheme, such as this survey, for the early detection of anaemia lies in the incipient nature of the majority of anaemias and of the underlying diseases if present. Furthermore, it helps to level out the uneven demands made by the population, i.e. by investigating large numbers of potential patients who do not consult their doctor spontaneously (Black 1966) in contrast to those who may be considered to seek medical assistance too often.

It is generally agreed that there is little correlation between symptoms, physical signs and the haemoglobin level (Wood and Elwood 1966). Thus, selection by symptoms would result in an incomplete or biased group receiving medical care. Clinical examination of patients is clearly not enough to exclude the diagnosis of anaemia, and the diagnosis, therefore, depends on the objective demonstration of its presence by the examination of a blood sample. This task requires considerable attention to detail as, for example, excessive venous compression (with syringe samples) or finger or ear squeezing (with capillary samples) can cause considerable errors. It must also be remembered that the results also depend on technical competence and that the tests themselves are liable to error.

Having established that there is anaemia, it is not possible to decide the correct therapy without further investigation. Indeed, it may be detrimental to the patient to attempt treatment without reference to the laboratory and it will almost certainly make the work of the laboratory more difficult.

We found that 13 per cent of those tested were anaemic and almost half of these were children of nine years or under, a fifth were women of child-bearing age, and the remainder were fairly equally distributed between the sexes and different age groups. The findings suggest a high incidence of iron deficiency in young children, and also highlight chronic upper respiratory tract infection as a potent cause of secondary anaemia in this age group.

No less significant is the finding of combined deficiencies, which we have assumed to be dietary, in seven children aged 14 years or under. These children were all growing fast and were above 75 percentile of weight or height, or both (Stuart and Meredith 1946). It is postulated that relatively limited quantities of essential materials, especially iron and folic acid, in the typical diet, are insufficient for the high demands of very rapid growth. These cases were not confined to those of poor social circumstances. The majority of patients in Group C have shown symptomatic improvement in response to specific therapy, although there was not always a concomitant rise in the haemoglobin level.

The organization of this survey was time-consuming, but the greater part of the work was done out of ordinary laboratory hours. Contacting people included in the survey was a laborious procedure, but was necessary so that we could obtain a random sample. This problem does not arise with the 'health weeks' run by local authorities, who are not seeking a random sample, and can use the local press to advertise the scheme. Administrative costs in this survey amounted to nearly £60. The cost of the haemoglobin estimations is difficult to assess; if estimated on the basis of unit cost (Ministry of Health publication 1965) it would amount (with follow-up tests) to £577, but for obvious reasons this must be regarded as an exaggerated figure. The test itself is cheap, simple and specific, but the cost does not end there. Follow-up procedures in those found to be anaemic are liable to cost far more than those incurred in the initial screening. This means that the cost to the National Health Service is unlikely

to be reduced, but in the long term one would hope that benefits would accrue from decreased morbidity.

Some people believe that we should wait for anaemic patients to develop symptoms before treating them, and that anyway early diagnosis does little if anything to shorten or alter the so-called 'natural' course of disease. While we agree that this may be true for certain disorders, such as carcinoma of the bronchus, or of the stomach, the same cannot be said of the majority of conditions giving rise to anaemia. Indeed, anaemia may be the first detectable sign of some conditions which can only be treated successfully if diagnosed early. Furthermore, as we have shown, many children are anaemic, and they are unlikely to complain spontaneously.

Another criticism of screening procedures is that "the finding of inexplicable abnormalities in a well population produced psychiatric difficulties which outweighed the value of the screening programme" (*Brit. med. J.* 1967b). So far there is no evidence of an increased tendency to hypochondriasis in the patients we investigated, although a few parents were anxious about the findings in their children. However, this was outweighed by the gratitude of those whose health was improved as a result of treatment. Surveys of a biochemical nature have produced a large number of unexplained abnormal results, but in our study only eight out of 76 patients had low haemoglobin levels the causes of which have so far remained unexplained. One interpretation could be that these patients are not truly anaemic, and that there should be a broadening of the spectrum of physiological normal. It may give support to the view, held by some, that consecutive analyses on individuals are more significant than isolated single tests (*Brit. med. J.* 1967b).

Even if it is conceded that screening the whole population, or screening those who present themselves voluntarily at clinics, is a wasteful procedure, then we still think it reasonable to screen certain sections of the population who appear from this survey to be particularly prone to anaemia. Indeed, the very people who most need to be tested are those least likely to attend screening clinics voluntarily. These populations 'at risk' would appear to be:

(1) Children under ten years of age (and siblings of anaemic children). Hutchison (1965) recommends screening the young, particularly—

   (*a*) those in whom the mother was anaemic during pregnancy
   (*b*) premature or dysmature babies
   (*c*) those with inadequate diet
   (*d*) those with repeated intercurrent infections.

   An alternative to this is to give iron much more readily to young children just as we do to pregnant women.

(2) Females aged 15 to 50 years: it has been shown that iron deficiency is common in women of all ages (Kilpatrick and Hardisty 1961, Kilpatrick 1961, Parsons *et al.* 1965) and it is well recognized that the majority of women are unable to meet the additional nutritional demands of pregnancy. This makes it advisable to give supplemental iron and folic acid to all pregnant women (*Brit. med. J.* 1964, 1966 and 1967 (a), Willoughby and Jewell 1966). It is only fair to say, however, that this is not a universal view, and that some authors doubt that the haemoglobin concentration is a satisfactory indicator of anaemia in pregnancy, or that the diets of most pregnant women in Britain are verging on iron deficiency (Thomson *et al.* 1967).

(3) People over 65 years of age: these views are in accordance with those expressed by Parsons *et al.* (1965) that haemoglobin estimations should be made more frequently in the elderly.

We would also recommend, although no such patients were included in this survey, the routine screening of:

(4) Patients who have undergone gastrectomy: it has been known for a long time that iron deficiency may develop after gastrectomy, but only in recent years have megaloblastic anaemias due to Vitamin B_{12} and folic acid deficiency been recognized as a complication of this surgical procedure (Mollin and Hines 1964, Gough *et al.* 1965).

(5) People with certain 'hazardous' occupations, e.g. workers with lead, radio-isotopes and aromatic hydrocarbons—although provision is already made for the supervision of the majority of these people.

Our findings suggest that screening for anaemia in these selected groups of the population would be a rewarding procedure yielding a relatively high incidence of anaemia.

Summary

Eight hundred people in a random sample of the population were approached and 584 agreed to submit to haemoglobin estimations. Seventy-six were found to have significant anaemia, and an aetiological classification was made.

As it has been shown that the incidence of anaemia in the population as a whole is much higher than is generally suspected, it is suggested that larger scale screening procedures should be adopted, and the feasibility of this is considered.

Acknowledgements

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EUGENICS, A.D. 1742

There is no one who will deny, that there are hereditary Diseases, proceeding either from one or other of the Parents; or question but that the Gout, Epilepsy, Stone, Consumption, etc. sometimes flow from the Parents to the Children. Whole Families proceeding from the same Stock, often end their Lives by the same Kind of Disease. For the prolific Seed often so rivets the morbid Disposition into the Foetus, that it can never afterwards be removed by any Art or Industry whatsoever. But let those who prefer a strong, vigorous, and healthy Offspring before Money, take care to avoid epileptic, scrophulous, and leprous Mothers.

Walter Harris: *De morbis acutis infantum.*
A treatise of the acute diseases of infants, 1742.