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# The Early Diagnosis of Anaemia

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In July, 1965, the Office of Health Economics held a colloquium on Surveillance and Early Diagnosis in General Practice at Magdalen College, Oxford. It was apparent from the discussion at this meeting that General Practitioners believed that if they were to act effectively in this field, they had to have clear cut information on current screening methods and the impact of early diagnosis of disease on the long term health of the patient. As a result of this view the Advisory Committee set up by the Office of Health Economics came to the conclusion that the best method of furthering this issue was to ask experts in a number of relevant clinical fields to write short papers specifically for General Practitioners. The Early Diagnosis of Anaemia is the seventh of these papers in the ensuing series. Other papers in the series are:

- 1. The Early Diagnosis of Raised Arterial Blood Pressure
- 2. The Early Diagnosis of Visual Defects
- 3. The Early Diagnosis of Cancer of the Cervix
- 4. The Early Diagnosis of Depression
- 5. The Early Diagnosis of Ischaemic Heart Disease
- 6. The Early Diagnosis of Some Diseases of the Lung



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IRON deficiency anaemia is a very common condition in the United Kingdom. Prevalence is greatest amongst women of child-bearing age and elderly men and women. Detection is easy, accurate and fairly cheap by means of a simple battery operated haemoglobin meter. Anaemia is not a disease entity in itself, but a result of various causes. Thus, its morbidity rate and mortality rate are the collective ones for all the many underlying causes.

The three main causes of iron deficiency anaemia are blood loss, which is by far the

most important, inadequate dietary intake and malabsorption of iron.

For many years conventional and arbitrary levels of haemoglobin have been used to define anaemia. While such measurements have obvious convenience, arbitrary definitions based on them have limitations. The significant feature is not haemoglobin concentration per se, but the clinical symptoms, if any, that result from that concentration in an individual together with the fact that further investigations may be indicated.

Unless or until the underlying disease condition can be discovered, it is reasonable to give treatment with iron. Ferrous salts are better absorbed than ferric salts. Iron and folic acid should also be administered to all pregnant women especially in the last trimester.

IT IS fairly generally believed that the morbidity and mortality from any medical condition would be reduced if that condition could be diagnosed early. While this may be true in many human diseases it is suggested that some long-held tenets in relation to anaemia might be critically re-examined.

Anaemia is said to be present when the number of red cells, or their content of haemoglobin, or both are reduced. Because neither the severity nor the type of anaemia can be accurately defined clinically some laboratory tests are necessary. Anaemia may be due to a deficiency of one or more factors essential for normal blood formation such as iron, vitamin  $B_{12}$  folic acid; or due to excessive blood destruction; or due to aplasia or hypoplasia of the bone marrow; or due to causes as yet undetermined. This paper is primarily concerned with iron deficiency anaemia because it is the commonest variety found in the United Kingdom.

#### Criteria of Anaemia

Consideration must be given to the problem of what is meant by anaemia and by which criteria it may be defined. For many years conventional and arbitrary levels of haemoglobin concentration have been used to define anaemia. Thus it has been considered to be present by most workers if the haemoglobin concentration is 12.5g/100ml (85 per cent) or less in men and 12.0g/100ml (80 per cent) or less in women. These are convenient levels but their use has been criticised by Pryce<sup>1</sup> and Elwood<sup>2</sup>. One anomaly is that men have to be proportionately more anaemic than women before they are defined as having the condition. The figures suggested by the World Health Organisation<sup>3</sup> are more nearly related to the differences in haemoglobin concentration found in the two sexes namely 14.0g/100ml or less for men and 12.0g/100ml or less for women.

If a random sample of the adult population of the United Kingdom is studied, it can be shown that the haemoglobin concentration in men is normally distributed but that it is slightly skewed to the left in women. In a study done in South Wales<sup>4</sup> it was shown that the mean value for men was 14·9g/100ml and for women 13·3g/100ml. From many points of view the concept of anaemia as a clear-cut entity is a misleading one as any value chosen, below which anaemia is said to exist, is merely one point in a continuous distribution. While it is important to bear this in mind when thinking about the general problem of anaemia, it is nevertheless administratively desirable, particularly if screening procedures are being considered, to have some level below which action is taken. This will be further considered later.

#### Prevalence of Anaemia

Iron deficiency anaemia has been extensively studied in the United Kingdom during the last few years. It was known to be common before and during the 1939/45 War<sup>5</sup>.

It has since been shown that while iron deficiency anaemia is still a very common condition 4.6, it is not as prevalent as it was before the War<sup>7</sup> and there are signs that the prevalence is falling 8.9.

It is of interest that a number of surveys by different workers using different methods have shown that the amount of anaemia among women is remarkably similar though these surveys have been done in areas which might be expected to have differing dietary habits and social composition. Thus Morgan<sup>10</sup> has drawn attention to the similarity of his findings in a practice in urban Birmingham with those in industrial South Wales<sup>4</sup>, rural Wensleydale<sup>6</sup> and suburban Beckenham<sup>11</sup> which have nearly all shown the prevalence of anaemia among women of childbearing age to be close to 25 per cent. It has also been shown that the prevalence of anaemia falls somewhat at or about the menopause but rises again in the later age groups and that a considerable proportion of both elderly men and women are anaemic 12.13,14,15,16. It has also been shown that anaemia in men is very uncommon until the later years and the difference between the two sexes in the early years is due to the precarious balance between iron intake and iron loss in women of childbearing years. Anaemia before the menarche is rare as shown in a study of Cardiff school children where no non-menstruating 14 year old girls could be designated as being anaemic whereas 4 per cent of menstruating girls of the same age were so<sup>17</sup>. The findings of some of the epidemiological surveys are summarised in figures 1-4.

It is known that iron is absorbed largely from the upper part of the small intestine and that the amount ingested varies quite considerably as does the amount absorbed. But, for adults in the United Kingdom, the iron content of the diet averages about 15mg per person per day of which approximately 10 per cent i.e. 1.5mg is absorbed. Men lose approximately 1mg of iron/day from the skin and gastrointestinal tract, but women, who also lose that 1mg/day, lose, in addition a variable amount of iron in menstrual blood which may amount to as much as the equivalent of a further 1.0mg a day. Thus while a negative iron balance is extremely unlikely in men, imbalance is almost inevitable in women. In women too, there may be increased needs for iron in pregnancy and lactation. That it is the iron loss from the body rather than dietary iron intake which is the major determinant of iron status in normal individuals has recently been clearly shown by Davis, Jacobs and Rivlin in a dietary survey in apparently healthy subjects.

#### The Detection of Anaemia

Pallor is not a reliable sign of anaemia as the observer variation is high<sup>20</sup>. Neither is questioning of people a reliable method of its identification as so many of the symptoms of anaemia are of a non-specific variety<sup>21</sup>.

In the past, estimation of haemoglobin concentration has meant either the posses-

Figure 1

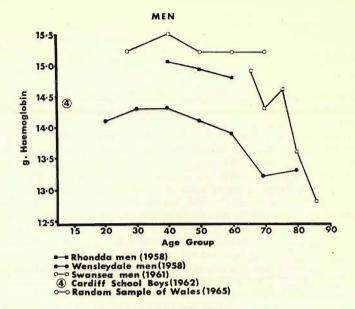


Figure 2

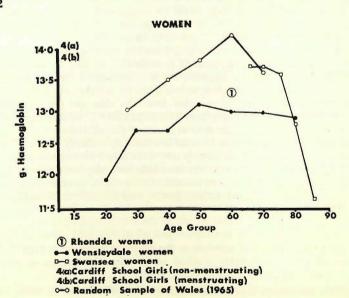


Figure 3

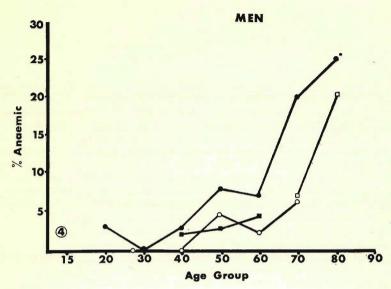
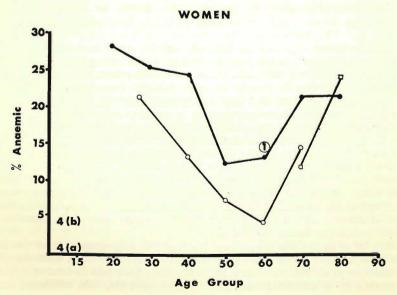


Figure 4



sion of expensive equipment requiring calibration and constant checking or the use of cheaper but inaccurate devices for haemoglobinometry. The present availability of a simple battery operated apparatus such as the A.O. Spencer Haemoglobin meter for haemoglobin estimations using a drop of whole blood means that accurate results can be obtained in any surroundings and without a laboratory<sup>22</sup>. The use of Tallqvist papers is now recognised as being so inaccurate as to be useless and the earlier haemoglobinometers to be little better. The estimation of haemoglobin can only be in the nature of a preliminary investigation but with readily available disposable syringes and needles, venous blood can and should be used for further tests. Most laboratories will now measure the haemoglobin concentration (Hb. in g/100ml) by the cyanmethaemoglobin method, measure the packed cell volume (PCV per cent) and from these figures, drive the mean cell haemoglobin concentration (MCHC per cent). An appraisal of the changes in a stained blood film will also be given so that in the majority of instances a firm diagnosis may be made but in a minority further tests will have to be carried out before a final diagnosis can be made.

Thus, the detection of anaemia by modern methods is easy, accurate and fairly cheap. If early diagnosis of anaemia—or for that matter of any other condition—is important then presumably the general public should be allowed and indeed encouraged to attend clinics which could either be held continuously or during 'health weeks'. This has been tried in centres such as Rotherham<sup>23</sup> and some degree of success is claimed. It is possible however, that any such scheme as this might be wasteful in relation to the detection of anaemia as the very people who should be assessed such as the busy housewife in her childbearing years, the elderly and those who fear that they may be ill, may not come forward. There is also a risk that the public will be satisfied that after one such examination with its obvious limitations that this need not be repeated and that any symptoms which they have are not due to serious disease. It would not be easy to invite only people with symptoms thought to be due to anaemia as these are of a non-specific variety and do not have the direct relevance of, say, cough in relation to mass miniature radiography for tuberculosis or cancer of the lung.

If any screening procedure is considered necessary or desirable it should be done by the family doctor who in the course of a year will see something of the order of 70 per cent of the patients on his list. Many practitioners are already doing haemoglobin estimations and this approach is almost certainly better than health surveys with the limitations already mentioned.

It may be of course that it is not the haemoglobin concentration itself that is important but iron deficiency. Thus practically all surveys have taken the haemoglobin concentration as an indicator but it is known that minor falls in haemoglobin need not necessarily be associated with iron deficiency and that iron deficiency may be

present without anaemia. This last group has been designated sideropoenia or latent iron deficiency. More complicated and more expensive tests are necessary for its identification than have been described up to now and include the measurement of the serum iron concentration, the iron binding capacity of the serum and examination of the bone marrow. Sideropoenia is a controversial subject and much more work on this subject is required.

Further Investigation of Anaemia

As there are many different types of anaemia, it is clear that accurate diagnosis and the determination of aetiology must precede treatment. There are three main causes of iron deficiency anaemia, which may of course co-exist, namely, blood loss, inadequate dietary intake and malabsorption of iron. Of these, blood loss is by far the most important cause of anaemia and next to uterine blood loss, loss from the gastro-intestinal tract should be considered. This is especially important in older people as Bedford and Wollner<sup>14</sup> found a positive faecal occult blood test in 55 per cent of a random selection of 156 admissions to hospital of patients aged 65 years or more. The importance of blood loss in the production of iron deficiency anaemia is readily apparent when it is remembered that the loss of 10ml of blood means the loss of 5mg of iron—equivalent to about three times as much as is normally available from the average daily diet.

The possibility of excessive aspirin taking should be borne in mind. Salicylates have for many years been recognised as occasionally causing acute gastric haemorrhage, but it is only recently that their importance in chronic blood loss has been realised. A number of studies have shown that about 70 per cent of patients taking aspirin by mouth show evidence of alimentary blood loss and where this has been measured with 51 chromium labelled red cells, a mean daily loss of about 4ml was found<sup>24</sup>. The publication 'MIMS' lists 40 different preparations among the analgesics which contain aspirin or sodium salicylate and this list does not include many of the popular

preparations sold over the pharmacists' counter.

The extent of further investigation of a patient with iron deficiency anaemia depends largely on the age and sex of the patient. Thus in women from the onset of menstruation to the menopause, iron deficiency anaemia is so common that unless anything in the history or physical examination suggests underlying disease, it is reasonable to give treatment with iron. If there is no response, or an inadequate response after an effective course of therapy, further assessment is indicated. It should of course be remembered that probably the commonest cause of non-response is non-taking of the prescribed medication. That this is true was well shown in a study<sup>25</sup> where a simple screening test to check ingestion of prescribed iron demonstrated that 28 per cent were failing to carry out the treatment prescribed.

Men of all ages, and women in their later years, should be more carefully considered and while it is true that many women through pregnancy, menstruation and lactation probably never completely replenish their iron stores after menstruation has ceased, this is an assumption which should not be too readily made. It is impossible to be dogmatic about the extent of further investigation as this will depend on the condition of the patient and local facilities, but it will often be necessary to have at least a faecal occult blood test done—though this test has its limitations—and probably barium studies of both the upper and lower intestinal tracts<sup>26</sup>. The presence of bleeding haemorrhoids must not be overlooked but laparotomy as a diagnostic measure should only have to be resorted to on rare occasions.

Inadequate dietary intake may be either relative of absolute. This is particularly so in women in the reproductive epoch especially if there is a rapid succession of pregnancies or heavy menstruation. Babies particularly if they are premature or if they are weaned late may suffer from iron deficiency anaemia and the elderly, particularly if housebound may do so too. Malabsorption of iron though a less important cause of iron deficiency anaemia, nevertheless should be entertained as a possibility and coeliac disease, idiopathic steatorrhoea and the post-gastrectomy state considered. The time-lag of several years between partial gastrectomy and appearance of deficiency states must not be forgotten. Thus 265 patients were investigated by Deller and Witts<sup>27</sup> 1-12 years after partial gastrectomy. It was shown that iron deficiency was common and B<sub>12</sub> deficiency not rare. A progressive fall in the level of the serum vitamin B<sub>12</sub> was found after operation, the steepest fall occurring during the first 6 years. Altogether anaemia was detected in 54 (20 per cent) of the 265 patients. This was B<sub>12</sub> deficiency alone in 4 cases, B<sub>12</sub> and iron in 12, and deficiency of iron alone in the remaining 38.

### Treatment of Anaemia

Apart from the removal if possible of any underlying cause of iron deficiency anaemia, the low haemoglobin concentration itself demands further consideration. It may be questioned whether the average haemoglobin for women is the optimum haemoglobin for that sex and Elwood and Wood<sup>28</sup> state that there is no clear relationship between symptoms and anaemia nor any demonstrable beneficial effect from iron therapy in women with haemoglobin levels above 10g/100ml. Nevertheless most clinicians would give iron to those people in whom iron deficiency anaemia had been demonstrated and this is probably especially desirable in children who may be anaemic due to low birth weight, prolonged milk feeding, late weaning, or anaemia of the mother<sup>29</sup>.

As far as iron therapy is concerned, ferrous salts are better absorbed than ferric salts and they are better absorbed by a patient with iron deficiency anaemia than in a normal person. Ferrous sulphate (N.F.) 200mg three times a day after meals is still

probably the best form of treatment if only because it is the cheapest. With effective treatment, haemoglobin should rise by approximately 0·15g (1 per cent) per day but iron therapy should be continued after the haemoglobin has reached 'normal' so that the body iron stores may be replenished. This necessitates approximately a further three months therapy. As far as expense is concerned, for the same dose of iron each day (as elemental iron) the cost of a month's preparation may vary from 2s. 11d. in the case of ferrous sulphate (N.F.) to 14s. 5d. for the most expensive controlled release preparation.

Many patients on iron medication complain of various symptoms such as dyspepsia, diarrhoea, constipation and other symptoms, but a careful study by Kerr and Davidson, 30 has shown that many of these complaints are of psychological origin. Having said that however, it is of little use in trying to persevere with a preparation of iron that the patient claims produces an upset as she will in all probability stop taking it in any event. Alternative preparations therefore on occasions are indicated. Parenteral iron in general should be reserved for those people who either do not respond to standard oral treatment or require fairly urgent therapy. Saccharated oxide of iron for intravenous use, iron dextran or iron sorbitol citric acid complex may be employed for intramuscular use. There is however some animal experimental work which suggests that iron dextran produces sarcomata and while there is no suggestion that this is so in man, one would, on general principles prefer to limit the use of such a substance.

#### Anaemia in Pregnancy

Anaemia in pregnancy poses some special problems. Iron deficiency anaemia is common and may be due to one or more causes, such as anaemia having been present before pregnancy and exaggerated by the relative increase in plasma volume which occurs in pregnancy and/or a deficient intake of iron in relation to the increased demand of the growing foetus. Chanarin, Rothman and Berry<sup>31</sup> have shown that iron deficiency of greater or less degree is the rule in pregnant women and is most marked in patients not receiving oral iron supplements. In the majority of such patients, no more than one 200mg tablet of ferrous sulphate (containing 105mg elemental iron) is required each day.

Not only is iron therapy in pregnancy important in its own right but it also reduces the likelihood of megaloblastic anaemia of pregnancy. It has been clearly demonstrated that a severe iron deficiency state can induce a secondary defect in folate utilisation<sup>32</sup>. In this respect the pathogenesis of megaloblastic anaemia in pregnancy has much in common with megaloblastic anaemia in post gastrectomy patients. In both there is an association of iron deficiency and megaloblastic anaemia. It is also likely that in both iron deficiency, by producing an additional stress on folate or B<sub>12</sub> metabolism, plays

an important part in converting a sub-clinical folic acid or Vitamin B<sub>12</sub> deficiency into an overt megaloblastic anaemia. Increased metabolic demands and limited body reserves coupled with poor dietary intake readily lead to the development of folate deficiency during pregnancy often with serious results to both mother and foetus. Thus while prophylactic iron therapy in pregnancy will prevent iron deficiency anaemia and reduce the prevalence of megaloblastic anaemia, the latter can only be eliminated entirely by folic acid supplementation<sup>33</sup>. The desirability or otherwise of this has led to much discussion.

Ideally women should be persuaded to improve their dietary and cooking habits and if possible to space childbearing. The principal dietary sources of folate are, fish, green vegetables, liver, kidney and some fruit. Local circumstances may influence the extent to which prophylactic supplements are required and in relatively affluent and educated communities among which the dietary intake is generally adequate and the incidence of folate depletion is low, the routine administration of folic acid supplements are thought by some to be unnecessary. But it is felt by many now that all pregnant women should have additional folic acid and that this is especially important in those pregnant for the fifth or subsequent time, those carrying multiple pregnancies, those giving a history of folate deficiency or severe anaemia in a previous pregnancy, those who have suffered recurrent abortion and those receiving anti-convulsive therapy during pregnancy<sup>32</sup>.

The question of dosage of folic acid has been carefully studied. The minimum daily oral requirement in a non-pregnant adult is probably of the order of  $50\mu g/day$  and there is little doubt that these requirements are increased in pregnancy<sup>31,32</sup> but the magnitude of the increase is not definitely known. Work by Willoughby and Jewell<sup>34</sup> in an ante-natal clinic in Glasgow has helped to clarify the problem. In this study, oral supplements of 100, 300 and  $450\mu g/day$  folic acid were given to groups of pregnant women and it was concluded that the minimum oral requirement of folic acid in late pregnancy is close to  $300\mu g/day$ . Tablets containing this dose are commercially available. It is admitted that by giving folic acid without full investigation first that there is a theoretical risk of treating an unrecognised case of Addisonian (Vitamin  $B_{12}$  deficiency) anaemia. Against this is the relative rarity of this condition occurring in the childbearing years together with the suggestion that women with Addisonian anaemia before the menopause are infertile.

It is recommended that iron and folic acid be administered to all pregnant women especially in the last trimester.

### The Significance of Anaemia

If anaemia—or for that matter any other medical condition—is important, then its recognition and treatment should fulfil several conditions. Its recognition should be

made by methods which are reproducible, acceptable, sensitive and cheap. Its morbidity and mortality should be influenced by early recognition; thus the symptoms and signs attributable to anaemia should be improved by treatment, whether of the underlying cause or simply by an improvement in the haemoglobin level irrespective of the underlying cause. By the same token, if anaemia is an important cause of morbidity and mortality in the country, then these should be improved by its recognition and treatment. If its importance lies as an early marker of underlying disease, then recognition of this underlying disease should result in an improved prognosis of that condition either in relation to its morbidity or to its mortality. The treatment of anaemia should if possible be cheap and should not be harmful in itself. These points must be considered in more detail.

As far as the methods available for the diagnosis of the different types of anaemia by laboratory examination are concerned, it is now generally accepted that such methods are on the whole valid, reasonably accurate and relatively inexpensive. Even so there is bound to be a certain amount of observer variability in relation to the results and while this may not be very important from an individual point of view, it might assume a very much greater importance in relation to countrywide epidemiological studies.

It has been suggested that if anaemia were an important problem, then it would have a definite morbidity and mortality rate which could be measured, and when measured could be used as a baseline to evaluate possible different therapies. At first sight this is a reasonable suggestion, but on reflection several problems became evident. The main one is that because anaemia is not a disease entity in itself but a result of various causes, its morbidity rate and mortality rate are the collective ones for all the many underlying causes. Thus one would not expect to be able to compare the treatment of anaemia for excessive menstrual bleeding with the treatment of anaemia secondary to gastric carcinoma. It is not denied however that further long term follow-up studies of various groups of people with anaemia would be extremely useful. As far as the symptomatology of anaemia is concerned, it might be reasonable to expect that the symptomatology would be benefited by therapy irrespective of underlying cause. Even this is not of necessity true and again it might be difficult to compare the response of treatment of excessive menstrual blood loss to blood loss from a malignant growth.

The symptoms and signs of anaemia described in most text books of medicine include general fatigue and lassitude, breathlessness on exertion, dizziness, giddiness, dimness of vision, headaches, insomnia, pallor of skin and mucus membranes, palpitations, tachycardia, anorexia and dyspepsia, paraesthesia and evidence of myocardial insufficiency. There are reasonable physiological explanations for most of these symptoms and signs. Because anaemia is usually defined in terms of a reduction in the

concentration of haemoglobin or in the number of red cells in the peripheral blood, symptoms—apart from the symptoms of the causative disorder—result from the reduced oxygen carrying capacity of the blood and the disturbances of cell function consequent upon anoxia. No one is in any doubt that acute anaemia as exemplified by haemorrhage causes faintness, hypotension, tachycardia, etc., but the symptoms of chronic anaemia with the undoubted physiological compensations that occur are less clearly defined and those previously mentioned may also occur in people who are not anaemic and in some may be ascribed to other diseases, including the psychoneuroses.

The symptoms of iron deficiency anaemia have recently been studied in a community survey by Wood and Elwood<sup>21</sup>. Their hypothesis was that if a causal link existed between anaemia and its supposed symptoms, the lower the haemoglobin level the more severe would be the symptoms. Their study was designed to find out whether or not such an association existed in the general population but they could find no evidence that this was so in people not severely anaemic. There was a suggestion however, that with haemoglobin levels of less than 10g/100ml that there was an association, but the numbers were too small for the authors to be sure about this. Most clinicians however believe that symptoms are related to severity of anaemia but the point is taken and must be borne in mind in relation to treatment of less severe degrees of anaemia.

Further work by the same authors 28,35 has been done in relation to the effect of oral iron therapy on the symptoms of anaemia. By means of a controlled trial, women found to have haemoglobin levels above 10g/100ml were given, at random, either iron or a placebo tablet of identical appearance. Symptoms were assessed before and after two months treatment and although the mean haemoglobin level in the group given iron showed a significant rise, there was no convincing evidence of a significant improvement in any symptoms. These findings are in contrast to those of Beutler, Larsh and Gurney36, and this study, while not strictly comparable with the previous one, is however the only other published controlled trial on this subject. Here, non-anaemic women suffering from fatigue were given iron in a double blind controlled manner. Benefit was demonstrated as shown by improvement in symptoms and this was especially so in those women who though not 'anaemic' did have a degree of sideropoenia as evidenced by a low serum iron concentration or a reduction in marrow haemosiderin. Thus these workers considered that the symptoms of fatigue were due to a deficiency of iron at the cellular level. Before dismissing the symptomatology of anaemia as unimportant and irrelevant, it should be borne in mind that all the British studies have been done in women, that the degree of anaemia was not severe and that the iron therapy was given—while sufficient to raise the haemoglobin concentration—might not have been sufficient to replenish the body iron stores.

Even if any symptoms attributed to anaemia could not be helped by its early recognition and treatment, it might be hoped that by using anaemia as a marker of serious underlying disease that the morbidity or the mortality of that condition would be altered. Leaving aside the anaemia discovered in women and thought or found to be due to menstrual blood loss and turning to other groups of people, the evidence is not very complete. This is shown well by a follow-up study of 371 patients with iron deficiency anaemia seen in the Nuffield Department of Medicine in Oxford in the 20 year period 1941-1960<sup>37</sup>. These workers showed that in 149 patients with gastrointestinal blood loss, loss from a known cause was an aetiological factor in the anaemia. In a further 59, positive occult blood tests were obtained, but no cause was recognised either initially or at subsequent follow-up. It was also found that quite a proportion of the people originally discovered to have iron deficiency anaemia would, when followed up, be found to have relapsed despite extensive investigation and treatment. Neither in that study nor in one in South Wales<sup>8</sup> was there any very clear evidence of sinister disease having been missed; but again care in interpretation must be taken because in the Oxford study, patients were referred to a Medical Department and therefore likely to be 'selected' in South Wales and the study (although cross sectional), was a relatively small one.

While anaemia may be associated with conditions such as gastric and duodenal ulceration it is very rarely the presenting feature of these conditions and therefore cannot be used as a marker for the detection of peptic ulcer. It certainly can be the first sign of cancer of the stomach or large bowel but it has been argued by some that the early recognition of these conditions has made little difference to the expectation of life after treatment. Again it should be recognised that this may be true in our present state of knowledge of therapy of cancer but need not necessarily be true in the future and for that reason various methods of early recognition of carcinomata should be kept in mind.

Another reason for trying to prevent and treat iron deficiency anaemia is in relation to gastric acidity. Much work has been done on this over the years and it now seems fairly clear that (a) iron deficiency anaemia causes gastric atrophy rather than it is the result of it; (b) gastric atrophy with its concomitant hypoacidity results in reduced absorption of iron; (c) if this atrophy persists, a vicious circle occurs which may predispose to Addisonian anaemia and gastric carcinoma; (d) if iron deficiency anaemia is treated successfully below the age of 30, this gastric atrophy and low acid output is reversible but if the person is over 30 this is not so and the hypochlorhydria may progress to achlorhydria even with successful treatment of anaemia <sup>38</sup>.

Screening of Anaemia.

There is a widely held and comforting belief that earliness of recognition of a condition

and success of treatment are closely linked. While it is undoubtedly true that the early detection of, for instance, tuberculosis by mass miniature radiography benefits not only the individual, but the community at large, it is no less true that the economic consequences of certain diseases spread beyond the affected individual and this in the world of today may be just as important as the spread of infectious disease was in the world of yesterday.

Though hard data are still scanty, intuition suggests that treatment at a stage before symptoms have appeared offer the best chance of arresting or even reversing the disease process. While intuition may be correct, intuitive beliefs must be validated by statistical evidence. In screening, division into positives and negatives must be made at an arbitrarily selected point; if the point is at a low level, there will be a few false negatives and many false positives; if at a high level, these results will be reversed and there may be no definite method of separating the positives into true and false. Any treatment will have to be given to all the positives and inevitably will be given unnecessarily to some of them. It should also be remembered that early detection is concerned with a changing and not a static process of disease development.

The main challenge of pre-symptomatic medicine is for epidemiological research to demonstrate recognition of a pre-symptomatic illness, to determine whether suspected pre-symptomatic pathology goes on to symptomatic disease and then if it does to test how best to treat it in its very early stages. It should be recognised by all medical people that the present need is for much more research including careful evaluation of all screening techniques.

As far as anaemia is concerned accurate and inexpensive screening procedures are available. However because of the known high prevalence of the condition even they might cost the National Health Service a considerable amount of money especially as they would have to be repeated at frequent intervals. Care must be taken too in thinking about anaemia in different situations in which a clinician may find himself in relation to early diagnosis. In one, a patient may present to his doctor with symptoms—whether due to anaemia or not—and it is clear that the doctor must do what he thinks best for that individual. In another, when because it has been deliberately sought, anaemia is discovered as a result of a survey, the situation is more complex. In the first the doctor is a 'healer' and in the second an 'evangelist' 39.

There is much about anaemia that is not known and yet it would be wrong to take too nihilistic a view about the situation. For, if no investigations were ever done or treatment ever given unless there had been data from controlled trials which gave evidence of benefit, then little medicine would be practised at all. Much still depends on clinical judgement and skill.

References 17

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