

# Iron deficiency anaemia – how far to investigate?

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## Abstract

Since 1980 investigations, by this group, of patients with iron deficiency anaemia and no obvious cause, have been limited to upper gastrointestinal endoscopy, with small bowel biopsy, and barium enema. This study attempted to follow up 93 consecutive patients whose anaemia remained obscure after these investigations to determine the outcome and assess the safety of this limited approach. In 1991/92 questionnaires were sent to the general practitioners. Eighty three completed questionnaires were received. Ten patients had died all unrelated to the iron deficiency anaemia. The mean follow up of the 73 living patients was six years (range 4–12). Sixty five (89%) had a normal haemoglobin concentration and only 15 were still taking oral iron. Possible causes for the anaemia were found in 17 – non-steroidal anti-inflammatory drug use in 10, menstruation in two, gastrectomy in three, poor nutrition in two. No other cause emerged. It is concluded that this limited investigative approach is safe.

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Iron deficiency anaemia is a very common condition in general medical practice. There are many possible causes and often the likely cause is suggested from the routine history and examination of the patient (for example, menorrhagia, poor diet, malabsorption, inflammatory bowel disease, rectal bleeding). There is a substantial group of patients, however, in which the cause is not obvious and it is difficult to know how far to investigate. Even after extensive investigation the cause may remain elusive. It has been our policy for the past 12 years to limit investigation of such patients to upper gastrointestinal endoscopy, with endoscopic small bowel biopsy, and barium enema. Sigmoidoscopy was not considered a necessary part of the investigation in the absence of a recent change in bowel habit, observed rectal bleeding, or an abnormality on digital rectal examination. Faecal occult blood testing was not done. We know the yield of routine investigations in iron deficiency anaemia<sup>1,2</sup> but do not know the outcome in those with no detected cause. To determine the outcome and to assess how safe this approach is we have followed up 93 consecutive patients presenting between 1980 and 1988 with iron deficiency anaemia in whom the above investigations were negative.

## Method

### PATIENTS

Records were kept from 1980 of all patients, referred to one physician, with iron deficiency

anaemia, in whom a cause was not established after upper gastrointestinal endoscopy, small bowel biopsy, and barium enema. Mild diverticular disease seen on barium enema was not considered a cause of anaemia nor was a hiatus hernia, minimal oesophagitis or Barrett's oesophagus without oesophagitis. Iron deficiency anaemia was defined as a haemoglobin concentration below 11.5 g/dl for women and 13.8 g/dl for men, a mean corpuscular volume below 80 fl and, where available, a ferritin less than 13 ng/l. Ninety three consecutive patients presenting between 1980 and 1988 whose notes were still available were followed up. Details of the haemoglobin concentration, red cell counts, and ferritin were recorded at presentation, together with details of non-steroidal anti-inflammatory drug (NSAID) use and other medical problems. Questionnaires were sent to the general practitioners of all these patients in 1991/1992. Enquiry was made about the patient's current health, whether a cause for the anaemia had emerged, the most recent haemoglobin concentration, and the continued need for iron treatment. This information was supplemented by examination of the hospital case notes. In cases of death the cause was established either from the case notes or from the Registrar of Births and Deaths.

## Results

There were 31 men and 62 women. The mean age was 61 years (range 21 to 85). The mean haemoglobin concentration was 7.0 g/dl (range 2.5 to 12.0 g/dl). From the 93 questionnaires, answers were received from 89 (96%). In six cases the patients had moved away and no recent information was available. Of the 83 on whom follow up information was available, 10 had died. The Table shows the causes of death. In none was the cause thought to be related to iron deficiency. The mean follow up interval of the remaining 73 (25 men; 48 women) was 6.1 years (range 4 to 12). One had minor lower oesophagitis, one had a Barrett's oesophagus without oesophagitis. Several had minor diverticular

### Details of patients who died during follow up

Sex	Age*	Cause of death	Initial Hb (g/dl)	Latest Hb (g/dl)
M	70	Myocardial infarction	9.2	13.1
F	79	Myocardial infarction	9.0	11.5
F	73	Myocardial infarction	11.3	14.7
F	91	Myocardial infarction	7.3	12.2
M	65	Bronchopneumonia	4.7	10.0
F	90	Bronchopneumonia	5.0	–
F	84	Postoperative (obstructed hernia)	5.5	13.6
F	71	Postoperative (hip replacement)	6.2	13.5
M	69	Chronic renal failure	9.6	–
F	73	Drug overdose	6.4	13.1

\*At presentation, Hb=haemoglobin concentration.

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disease of the colon. A possible cause for the anaemia was found in 17 patients. Ten patients (nine women) had been taking NSAIDs – in two this consisted of just occasional aspirin and five took an NSAID regularly for rheumatoid arthritis. In two patients the cause of anaemia may have been menstrual loss because they both settled after menstruation had stopped. In three men gastrectomy may have been the cause and in two poor nutrition may have been responsible. In no other patient did a cause emerge.

Of 73 patients still alive 15 (all women) were still taking oral iron. They all had a normal haemoglobin concentration. Of the remaining 58 who were not receiving iron all except eight (one woman; seven men) had a normal haemoglobin concentration. These low haemoglobin concentrations ranged from 11.2 to 13.4 g/dl.

### Discussion

This study suggests that extensive investigation to establish a precise cause for obscure iron deficiency anaemia is not necessary if upper gastrointestinal endoscopy, small bowel biopsy, and barium enema are normal. It is known that such patients may have one of a variety of conditions such as arteriovenous malformations in the small intestine or colon (including angiodysplasia and telangiectasia), Meckel's diverticulum, Crohn's disease, and small bowel smooth muscle tumours.<sup>3</sup> It is doubtful, however, whether these conditions require treatment in the absence of symptoms and complications as long as the haemoglobin can be maintained with oral iron treatment. Moreover, complete investigation may require invasive angiography and laparotomy, which are not without risk. The most important condition to exclude is colonic carcinoma. A barium enema detects most carcinomas and colonoscopy would be even more reliable and might be preferred to barium enema if the resources were available. In this series we feel that no carcinoma was missed by barium enema in view of the follow up exceeding four years.

The need for sigmoidoscopy in patients with obscure iron deficiency anaemia is contentious. We have yet to see a patient whose iron deficiency arose from a problem in the rectum or lower sigmoid in the absence of observed rectal bleeding, a change of bowel habit, or abnormality on digital examination. For that reason we have not considered sigmoidoscopy an essential part of the investigation, but would do it if the patient was an unreliable historian. This study helps justify that confidence. Many departments of radiology require a sigmoidoscopy before a barium enema, but this seems to be an unnecessary constraint when the indication for the barium enema is simply iron deficiency and when there are no symptoms of rectal disease. Of course, if colonoscopy is used instead of barium

enema there would be no need for a separate sigmoidoscopy.

The need for routine small bowel biopsy might be questioned but during this study two to three cases of coeliac disease were diagnosed each year among the patients investigated for iron deficiency anaemia.

One surprising finding emerging from this study is the existence of a common but unrecognised entity – transient cryptogenic iron deficiency anaemia. Of those patients still alive at follow up between four and 12 years later, 89% had a normal haemoglobin concentration, and only 23% of these were still receiving iron treatment. Only one patient who had been receiving NSAIDs was still anaemic and that was a man with rheumatoid arthritis whose haemoglobin concentration was 12.7 g/dl. Women are more likely to achieve a normal haemoglobin concentration – in fact only one of 48 women was anaemic at follow up compared with seven of 25 men. Appreciation of this should be very helpful in the management, including reassurance, of such patients.

Another surprise is the apparent reluctance of men (or their general practitioners) to continue iron treatment. The supervision of iron treatment was usually left to the general practitioners and was variable. Despite seven men still being anaemic not one man was still taking iron; whereas 15 women were still taking iron although none was anaemic. It is difficult to give precise guidelines but it is now our practice to recommend that oral iron be given until the haemoglobin concentrations and red cell counts are normal, and that these are remeasured at about three monthly intervals for a year and further iron given as necessary. If the haemoglobin remains normal after a year it should then be checked after a further year or sooner if the patient becomes symptomatic. Anaemia developing after that should probably be reinvestigated. Unnecessarily long courses of oral iron should be avoided because of the risks of iron overload.

If anaemia cannot be controlled with oral iron more detailed investigation should be considered including colonoscopy, small bowel radiology, small bowel enteroscopy,<sup>4</sup> and gut arteriography.<sup>3</sup> If these are negative and frequent blood transfusions are required, laparotomy with synchronous whole gut endoscopy and external inspection of the transilluminated gut should be considered.

1 McIntyre AS, Long RG. A prospective audit of investigations in out-patients with iron deficiency anaemia. *Gut* 1991; 32: A1245.

2 Till SH, Grundman MJ. A prospective audit of patients presenting with iron deficiency anaemia and faecal occult blood loss. *Gut* 1992; 33 (suppl): S31.

3 Thompson JN, Salem RR, Hemingway AP, Rees HC, Hodgson HJF, Wood CB, *et al.* Specialist investigation of obscure gastrointestinal bleeding. *Gut* 1987; 28: 47-51.

4 Morris AJ, Wasson LA, MacKenzie JF. Small bowel enteroscopy in undiagnosed gastrointestinal blood loss. *Gut* 1992; 33: 887-9.