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The role of chronic blood loss in the pathogenesis of postgastrectomy iron-deficiency anaemia

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SUMMARY The role of chronic blood loss in the pathogenesis of postgastrectomy iron-deficiency anaemia was assessed by measurements of blood loss over periods of up to three months, using a whole-body counter and ^{59}Fe. Eleven patients were investigated and eight of these were selected because of a history of iron-deficiency anaemia. Six were shown to be losing blood abnormally, five at a rate of over 150 ml per month. None of the three patients without a history of anaemia lost more than 60 ml per month. At gastroscopy contact bleeding from the mucosa of the gastric remnant was observed in four of the six patients losing blood. The results indicate that in some patients chronic blood loss plays an important role in the pathogenesis of postgastrectomy iron-deficiency anaemia.

There has been controversy over the part played by chronic gastrointestinal blood loss in the pathogenesis of postgastrectomy iron-deficiency anaemia. Witts (1966) suggested that intermittent bleeding associated with gastritis of the gastric remnant might be an important factor, and Kimber, Patterson, and Weintraub (1967), who measured the faecal loss of infused ^{51}Cr-labelled red cells in a group of eight patients, demonstrated losses of up to 6·5 ml/day. However, in a more recent paper Baird, St. John, and Nasser (1970), who studied a larger group by the same method, failed to confirm this work and concluded that occult gastrointestinal blood loss is not important in the pathogenesis of postgastrectomy anaemia. This paper describes a study designed to examine this possibility further using ^{59}Fe and the Oxford whole-body counter (Warner and Oliver, 1966).

Patients and Methods

Eleven patients, nine males and two postmenopausal females, who had undergone partial gastrectomy five to 24 years previously for peptic ulcer were investigated. Eight were selected because of a history of iron-deficiency anaemia; three of these had received treatment. At the beginning of the study four of the patients had haemoglobin levels of less than 10g/100 ml (Table). No abnormality other than partial gastrectomy could be found on radiological investigation of the gastrointestinal tract.

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Chronic blood loss during intervals of up to three months was calculated from measurements of the rate of loss in whole-body activity following the intravenous injection of 4 μCi ^{59}Fe using a whole-body counter, and the blood volume. Details of the method have been described before (Callender, Witts, Warner, and Oliver, 1966; Holt, Mayet, Warner, and Callender, 1967). The blood volume was estimated from knowledge of the patients' heights and weights (Nadler, Hidalgo, and Bloch, 1962). In addition, the rate of loss of activity was measured in nine control subjects. These comprised six normal male volunteers, two posthysterectomy and one postmenopausal women who were otherwise normal. Their ages ranged between 26 and 64 years.

As a preliminary investigation, two tests of iron absorption were carried out. In one test ferrous iron absorption was measured from 5 mg ferrous sulphate and 50 mg ascorbic acid

labelled with 2-3 μCi ^{59}Fe. In the second test absorption of ferric iron was measured using 5 mg ^{59}Fe ferric chloride. The doses were given in solution after a two-hour fast. A proportion of food iron occurs as ferric iron and it was thought that the use of ferric chloride might give some assessment of the patients' ability to absorb food iron.

In seven patients the gastric remnant and stoma were examined gastroscopically using an Olympus gastroscope with facilities for photography, exfoliative cytology, and biopsy under direct vision (Williams, Truelove, Gear, Massarella, and Fitzgerald, 1968). In some patients biopsies from two sites were taken. The friability of the gastric mucosa and its tendency to bleed on contact was assessed by stroking the mucosa firmly with the cytology brush under direct vision.

In addition the results from studies of two further patients are presented. One of these (case 12) had undergone vagotomy and pyloroplasty and the second (case 13) had been treated by gastroenterostomy and vagotomy (Table).

Results

The clinical details of the patients and measurement of blood loss and iron absorption are summarized in the Table.

BLOOD LOSS

The rate of loss of whole-body activity following the intravenous injection of ^{59}Fe is shown in the Figure where graphs of the activity in eight patients with a history of anaemia (cases 1-8), are compared with graphs of activity in three patients with no history of anaemia (cases 9, 10, and 11). The range of loss in the nine controls is shown for comparison. Six of the patients with a history of anaemia lost activity at a rate greater than normal. The calculated rate of blood loss in the six patients ranged between 90 and 230 ml per month and three patients (cases 1, 3, and 5) lost at a rate of 200 ml or more per month (Table).

The patient who had previously undergone gastroenterostomy with vagotomy (case 13) also lost blood abnormally, but no significant loss was detected in the patient treated by vagotomy and pyloroplasty (case 12).

IRON ABSORPTION

Seven of the 10 patients in whom tests of iron absorption were carried out were iron deficient (serum iron less than 70 μg per 100 ml) at the time of study. In only one patient (case 5)

Case No.	*Age (yr)*	*Sex*	*Type of Operation*	*Interval since Operation (yr)*	*Previous Symptoms*	*Haemoglobin (g/100ml)*	*MCHC (%)*	*Serum Iron (μ/100ml)*	*Gastroscopic Findings*
1	62	M	Polya for duodenal ulcer	15	—	7·7	28	34	Marked hyperaemia with contact bleeding
2	56	M	Billroth I for gastric ulcer	9	Severe iron-deficiency anaemia (Hb 4g/100ml) 6 years previously	6·4	25	14	Marked gastritis throughout remnant
3	49	M	Polya for acute gastric ulcer	18	—	6·9	26	20	Marked superficial gastritis with contact bleeding
4	67	M	Polya for duodenal ulcer	23	Mild iron-deficiency anaemia (Hb 10g/100ml) 5 years previously	12·9	30	66	Marked gastritis with contact bleeding
5	52	F	Polya for duodenal ulcer	5	—	8·7	30	22	Peristomal gastritis with contact bleeding
6	34	M	Polya for duodenal ulcer	11	Mild iron-deficiency anaemia (Hb 10g/100ml) 12 months previously	13·2	33	24	Not done
7	68	M	Polya for duodenal ulcer	24	Mild iron-deficiency anaemia (Hb 10g/100ml) 15 years previously	13·2	36	116	Not done
8	69	F	Billroth I for gastric ulcer	13	Gastrointestinal haemorrhage (Hb 8g/100ml) 6 months previously	14·7	33	103	Marked gastritis throughout
9	60	M	Polya for duodenal ulcer	8	—	13·5	34	54	Mild-moderate gastritis
10	61	M	Billroth I for gastric ulcer	20	—	17·2	37	130	Not done
11	56	M	Polya for duodenal ulcer	13	—	13·7	33	45	Not done
12	61	M	Vagotomy and pyloroplasty for duodenal ulcer	6	Mild iron-deficiency anaemia (Hb 11g/100ml) 4 months previously	16·0	36	74	Marked superficial gastritis with contact bleeding in prepyloric area
13	56	M	Gastroenterostomy and vagotomy for duodenal ulcer	20	—	6·7	29	11	Peristomal gastritis

Table *Clinical details and results of measurements of blood loss and iron absorption in 11 postgastrectomy patients*[1]

[1]Two further patients who underwent different operations are also included.

was a compensatory increase in absorption of ferric chloride demonstrated, suggesting that in six patients the absorption of food iron would be poor and fail to increase in response to iron deficiency. Absorption of ferrous iron was not impaired and all the iron-deficient subjects absorbed more than 20% of the administered dose.

GASTRITIS

The gastroscopic findings in seven patients and the histological appearances at biopsy in six are described in the Table. On direct examination the mucosa appeared abnormal in all the patients examined, and in four the mucosa bled freely after it had been stroked firmly with the cytology brush. Superficial gastritis or atrophic gastritis was found on gastric biopsy in five patients examined histologically; the histological appearance in one patient was normal. In no case was a stomal ulcer found.

Discussion

These results indicate that chronic blood loss does occur in some patients following partial gastrectomy and support the findings of Kimber *et al* (1967) who suggested that blood loss plays an important role in the development of postgastrectomy iron-deficiency anaemia. Although the magnitude of loss described here, in the order of 150-200 ml per month, is not great compared with monthly losses of over 500 ml found in some patients with hiatus hernia (Holt, Mayet, Warner, Callender, and Gunning, 1968) or 400 ml in some patients with inactive ulcerative colitis (Stack, Smith, Jones, and Fletcher, 1969), its significance is greater because of defective absorption of food iron. In normal subjects absorption of food iron increases in response to iron deficiency but such an adjustment does not occur in the postgastrectomy state (Baird and Wilson, 1959; Turnberg, 1966). The poor absorption of ferric iron in six of the seven iron-deficient patients described here supports this view.

Baird *et al* (1970), who measured the faecal loss of infused ^{51}Cr-labelled red cells, found no important blood loss in a group of 19 patients in whom no cause for anaemia other than the postgastrectomy state could be found. Nor, apart from one case, was there any greater tendency to gastrointestinal bleeding during the administration of aspirin by mouth compared with a group of control patients treated in the same way. They therefore concluded that occult gastrointestinal blood loss is not an important cause of postgastrectomy iron-deficiency anaemia. The

Site of Gastric Biopsy	*Histology*	*Iron Absorption (%)*		*Calculated Blood Loss (ml)*		*Interval of Study (wk)*	*Percentage Retention ^{59}Fe at End of Study*
		Ferrous Iron	*Ferric Iron*	*Per Month*	*Total*		
Fundus Peristomal area	Atrophic gastritis Atrophic gastritis	22	2	230	800	14	83
Peristomal area	Focal atrophic and superficial gastritis	20	0	150	450	12	90
Fundus Peristomal area	Normal Gastric atrophy	30	5	220	720	13	87
Fundus Peristomal area	Normal Superficial gastritis	23	0	190	700	15	82
Fundus Peristomal area	Normal Normal	53	17	200	650	13	85
		23	0	20	40	10	99
		6	2	60	150	10	97
Fundus Peristomal area	Chronic superficial gastritis Chronic superficial gastritis	2	1	90	300	13	90
		Not done		20	60	13	99
		15	0	30	100	14	98
		21	3	0	0	14	96
Fundus Gastric antrum	Severe atrophic gastritis Severe atrophic gastritis	12	9	0	0	11	100
Fundus Peristomal area	Chronic superficial gastritis Chronic superficial gastritis	Not done		300	750	10	83

Table *Continued*

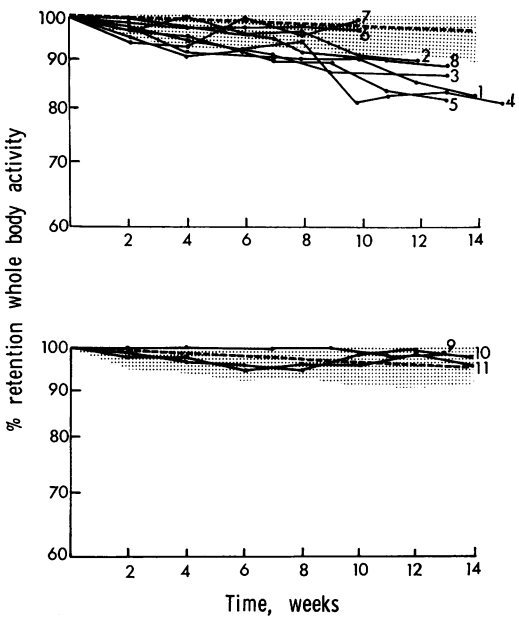

Figure *Percentage retention of the administered dose plotted against time in weeks. The graphs from eight patients with a history of iron-deficiency anaemia (cases 1 to 8: upper diagram) are contrasted with graphs from three patients (cases 9, 10, and 11: lower diagram) with no history of anaemia. The mean loss in nine controls is indicated by the broken line and the range of losses is enclosed in the shaded area.*

present study and that reported by Baird *et al* (1970) differ in a number of ways. First, our patients were investigated whilst attending as outpatients and it is possible that the dietary habits of patients living at home differ from those of patients in hospital, being more likely to lead to mucosal damage and consequent haemorrhage. Secondly, our studies were carried out over periods of time of up to 15 weeks so that there was a greater chance of detecting intermittent loss. The intermittent nature of the blood loss in some patients is illustrated in the Figure. For example, in case 5 most of the fall in whole-body activity occurred between weeks 8 and 10. One of the patients reported by Kimber *et al* (1967) lost blood only episodically.

Most of our patients, like those reported by Kimber *et al*, were studied while still iron deficient. In contrast, Baird *et al* (1970) corrected the iron deficiency of their patients before measurements of blood loss were made. It is therefore possible that the iron-deficient state might predispose to mucosal haemorrhage.

From our observations at gastroscopy, it seems likely that blood loss is associated with increased friability of the mucosa in the peristomal area of the gastric remnant and a greater tendency to bleed from it following trauma. However, the degree of gastritis at biopsy varied widely, and in one patient (case 5) shown to be losing blood biopsies both from the fundus and stomal areas were normal, yet the mucosa near the stoma bled readily on contact.

A number of factors may collectively contribute to the development of iron-deficiency anaemia following partial gastrectomy. First, the patient may have been iron deficient at the time of operation because of previous gastrointestinal haemorrhage. Second, appetite may be poor following partial gastrectomy and lead to a diet deficient in iron (Baird, Blackburn, and Wilson, 1959). Third, food iron may be poorly absorbed, and fourth the patient may bleed occultly from the gastric remnant even 15 or 20 years after operation.

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